21st Century Toxicology Workgroup
Project Proposal to PPDC

PPDC Biomonitoring Subgroup A, EPA charge: Data & Information: Identify how existing data relevant to diagnosing overexposure to pesticides can be made more accessible and explore opportunities for additional information.

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Project Name: CARB – Clinician Access to Regulatory Data on Biomonitoring

Goal: Leverage existing information and methods for clinician use to better identify worker and children overexposure to pesticides.

Objectives: Identify existing and review relevant data and methods, and potential biomarkers for both commonly used and toxic-to-very toxic pesticides. Clarify clinician's needs for information and tools. Identify what additional information, tools and diagnostic tests could be developed.

Key Activities:

1. **Exploration of existing Information**: a) Review EPA HED current process for Worker Exposure studies and the information gained; b) Identify information the EU and EPA already hold (pilot) c) review of existing pesticide biomarkers for utility in clinical setting d) Review process for identification and development of biomarkers and/or diagnostic tools.
2. **Determine Existing Needs**: develop and conduct survey a) for clinicians, toxicologists and researchers to determine specifics regarding biomonitoring information and tests and b) for other Subject Matter Experts (SME) as identified by team and c) have EPA to review their needs relative to existing information
3. **Review difference in needs and existing information** Team to Develop Proposal Plan to Close the Gap between existing situation and needs; EPA to make final recommendations. What process must be developed to move from these potential makers found in animal models to useable markers for human diagnosis and study? Test and use the proposed solutions with Team B priority list for biomarkers and make recommendations for the future.

Level of Resources:

HED or OPP scientists, PPDC time, registrant member time, IT support; ~timeframe 1 to 2 years

Key Expertise and partners needed:

Clinicians, Subject Matter Experts = SMEs (CDC, EPA, industry), American Academy of Clinical Toxicology, emergency department physician/toxicologist, biochemists, diagnostic experts.

Next Steps - EPA review of this proposal and report back to PPDC on best way to achieve and utilize subgroup for input

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Considerations and issues: Project scope needs good management; biomonitoring as a whole is a broad research area; for a project to make progress it needs to be focused on set of manageable steps.

Background and Team Progress:

Clinicians seek improved methods to diagnose human poisoning—whether it is for a worker with a known exposure to a pesticide, or identifying a poisoning in the emergency department setting based on an index of suspicion by the clinician.

Registrants produce a large amount of data and information; the salient results are publically accessible via posted reviews from global regulatory bodies. Team members have 1) all been supplied the current relevant guidelines to specific studies relevant to animal metabolism and 2) together reviewed web posting of regulatory assessments for an example pesticide.

Some biofluid (blood and urine) analytical methods are being developed for EU Annex 1 renewal for products "classified as toxic or very toxic (T, T+) or are classified according to Global Harmonized System as: Acute toxicity (cat. 1 - 3), CMR (cat. 1) or STOT (cat. 1)"; CMR is carcinogenic, mutagenic or toxic for reproduction and STOT stands for Specific target organ toxicity.

Team should consider what measureable, metabolomic, proteomic or excretion products are or will be measured in animal models in the process of registration that might be explored as biomarkers or diagnostic tests in humans.

A suggested element for the project is to identify the process for when and how the EPA collects worker exposure information: when data are needed, what data are generated, Information on PHED, the new Ag handlers task force (AGHTF) data, and the HSRB process should be included. EPA HED should be able to supply this information. Fewer worker exposure studies are currently conducted relative to the past for 2 reasons: 1) the Human Studies Review Board (HSRB) has blocked recent typical worker exposure studies by actions such as interpreting what in the past would be *observational* instead as *intentional dosing* of humans (eg if protocol specified a day of week for the application, that's intentional) and 2) registrants may accept existing default exposure estimates used by EPA in worker risk assessments without a need to gather compound specific refinements in order to achieve a registration.

Two additional suggested elements for this project are 1) describing the data EPA are permitted to request as part of the pesticide registration process and 2) clarifying EPA HSRB guidelines and protocols for human exposure studies.