

# A Call for Establishing an Interagency Epidemiology Peer Review Council (IEPRC) for Chemicals

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## Animal Studies Submitted by the Registrant.

Pure technical grade of test material. Refined strain of test animal. Very restricted diets.

High standards of animal ethics, quality control, GLP and reporting.

Entire study submitted. Can also request additional data and on-site audits.

Transcribed into resource consuming DERs at taxpayer expense.

Subjected to multiple layers of primary secondary and tertiary reviews and peer review.

Data are a quantitative fact (incidence/observations) with dose response.

## Problems with DERs

DERs have to be accurate transcription, cannot misrepresent.

Do not demonstrate that the reviewers actually did anything to verify what they wrote.

Introduces reviewer's biases. Customers of DERs not assured they are seeing both sides of the issues.

Conclusion: Study reports should not be transcribed into DERs.

## First Suggestion: Eliminate DER production

- Standardize formats for submission so methods and materials and obvious responses to treatment do not have to be transcribed into DERS.
- Reviewers will have more quality time to find study inconsistencies/deficiencies and subtle responses to treatment not already reported as well better interpret the study for regulatory purposes.
- Challenges reviewers to make document other Agencies (i.e. WHO, etc) can use.
- Not going to discuss further today.

# Epidemiology Studies from the open literature

- Often Accepted at face value.
- Mixed bag of ethics, QC, GLP and reporting.
- Indefinite level of exposure.
- Very diverse human population.
- Publication only with summary data. Hard to get additional data or on-site audit.
- Often “one person” in charge of project. Selects co-workers and SAP members, introduces program politics.
- No “DER” showing responsibly or qualifications.
- Data usually presented as a probability of an effect not a true quantitative fact.

# Bias: Industry Vs. Academic

- The reason for the extensive review of animal studies is suspicion of registrant biasing study to obscure deficiencies or responses to treatment.
- Academic institutions also have biases! Incentive to publish “positive” result, “hero” image.
- Negative studies may have less chance for additional grants.
- *The squeaking wheel gets the grease!*

## Disparity in Level of Review

Very high bar for acceptability of animal studies.

Very low bar for accepting epi studies from the literature.

This is not serving the public well.

# “Chemical” Epidemiology

- Very important to evaluate chemical for possible unique responses in humans.
- However, very difficult to accurately evaluate exposure and endpoint.
- Pre and post “issue” problems - jump on the bandwagon after “issue” is raised. Further complicating the exposure assessment.

# “Epidemiology” Examples

Vaccinations and autism	Public hysteria - Stopped vaccinating – increase in measles. Not verified by years of costly research. Original report flawed and journal retracted. Primary author largely considered a fraud but still has followers.
Glyphosate-Non-Hodges lymphoma.	\$100Ms in lawsuits awarded. Public ends up” paying”? Still very widely used for residential and commercial applications. Could situation have been avoided?????
Chlorpyrifos and neurodevelopment following <i>in utero</i> exposure (pgm/gm cord blood)	Since early 2000s, much EPA manpower and funding, 2016 SAP indicated unresolved issues and did not recommend study for risk assessment.

# Chlorpyrifos

Feb. 7, 2020 – Washington Post article stating chemical will no longer be manufactured.

“as some scientist said is linked to neurological problems in children”

But does it???

Columbia study - Herculean Task-Authors are entitled to their opinion but study needs to be independently evaluated.

# 2016 SAP and concerns from others on chlorpyrifos

- Many problems identified
- Analytical chemistry
- Incomplete data
- Institution wont provide data (there may be updates)
- Could not do independent analysis before issue became public.

## Mr. Pruitt's "mandate"

- Early 2018, Scott Pruitt, the then EPA Administrator "mandated" that regulatory decisions be transparent and data available for public scrutiny.
- 4000 + responses to Federal Register Notice and were overwhelmingly against "mandate".
- A major reason: Invasion of privacy, people won't participate.
- Current EPA Administrator continues policy.
- Therefore, guidelines for protecting privacy and at the same time making critical data available for independent analysis are clearly needed.

## Second Suggestion: Create Independent *Interagency* Epidemiology Peer Review Council (IEPRC)

- Inspired by my personal experience with chlorpyrifos and EPA's "mandate" for transparency.
- Needs to be *independent* of program politics.
- Goal #1 – Establish Interagency wide guidelines for ethical sharing of critical data.
- Goal #2 – Produce a transparent Council Report based on the analysis of six independent sub-committees that clearly justifies all decisions.

# Composition of the Council: Chief Chairperson and Co-Chairs.

- “Chief” Chairperson and Co-Chairs and standing members.
- The “Chief Chairperson” - responsible for assigning reports to the co-Chairs and assuring overall consistency and transparency.
- To assure *independence* the Co-Chair for a given report cannot be from the department immediately concerned with regulating the chemical.
- Having Co-Chairs provides that more than one issue can be reviewed concurrently.
- Council secretary.

## Six Independent Sub-disciplinary Committees:

1. Ethics\*
2. Endpoint assessment
3. Animal toxicity and SAR
4. Exposure assessment
5. Analytical Chemistry
6. Statistics

\*Provides mechanism for submitting additional data

## Sub-discipline committees

- Will have a standing chairperson and staff that will recruit additional members best qualified to assess the issues for each epi study project.
- Staff will be recruited from the participating agencies as well as qualified scientist from other institutions without a conflict of interest.

# 1. Ethics

- All aspects of ethics.
- Maintain an on-going project to establish standards to assure privacy for inclusion of data in published reports and for submitting requested additional data.
- These standards could eventually be incorporated into grant funding applications.
- Reviews each study and provides special instructions as needed.

## 2. Endpoint Evaluation

- Establish and maintain a compendium of chemicals known to have effects unique to humans.
- -May be hardest to staff. Needs experts with in depth knowledge of the specific endpoint(s) for each study (i.e. assessment of IQ in toddlers, specific types of cancer).
- -Describes what is known about the endpoint, variability of occurrence in sub-populations, difficulties in assessing in humans, what factors including chemicals are known to affect its incidence.
- Declares that endpoints were adequately assessed for or otherwise.
- Size of cohort needed to make a statistical probability credible for the endpoint(s).

### 3. Animal Toxicity and Structure Activity Relationships (SAR)

- Summarizes the animal toxicity studies with emphasis on any indications of the endpoint in the epi study. A representative from the program responsible for the chemical should best do this.
- Addresses any known SAR indications of the endpoint(s) in the epi study.
- Should not need any additional information from the authors.
- Animal and SAR support is helpful but there still may be a very unique response in humans.

## 4. Exposure Assessment and 5. Analytical Chemistry

- Evaluates reliability of all aspects related to how exposure was assessed.
- Was exposure assessed by interview with actual subject or with a co-worker, friend or relative or by telephone.
- Post issue exposure. “jumping on the bandwagon”
- Can work with chemical analysis sub-committee if there are actual chemical data.

## 6. Statistics

- Initially assures that statistical methods used are appropriate as reported.
- Declares and justifies that additional data are needed for an independent analysis.
- Cannot do additional statistics without raw data.
- May be the most frequent requestor of additional data.

# Inter-Subcommittee Communications Prior to the Council Meeting

- Some sub-committees may benefit by communicating
- Must assure that one sub-committee is not trying to influence the other.
- Thus, communications only through the project Co-chair.

# Post Sub-committee Review Council Meeting

- Not open to the public or program responsible for regulating the chemical.
- On completion of sub-committee reports, the Council standing committee, and sub-committee chairs and members meet.
- All sub-committee reports are discussed and each sub-committee can question all others.
- Council secretary will prepare the detailed report
- Chief Chairperson and all members will sign off.

# The Council Report

- Justifies and assures transparency of all decisions.
- All sub-committee reports appended.
- Minority opinions appended.
- Explains why minority opinions were not accepted by the Council.
- States what additional data are needed and justification for it.
- Provides instructions as determined by the ethics sub-committee for obtaining additional data as needed

## The Council's Report –some examples.

- The Council concurs that the study does not demonstrate a correlation between exposure to *chemical* and an adverse outcome.
- The study as published provides a meaningful response in humans and should be included in risk assessment.
- Cannot make a decision and identifies additional data that *needs* to be provided and advises how this should be provided. Assigns time limit for response.
- Declares the study unfit for further consideration and provides details of the deficiencies.

## Response from Concerned Parties

- Any party (i.e. program regulating the chemical, industry, or public interest) will need to specifically address the justifications for the decisions and provide supporting data to challenge the Council's decisions.
- They cannot just say it was bowing to public hysteria or is an industry cover-up.

# Pros and Cons

## **Pros:**

Standardize ethics for obtaining data.

Larger pool of qualified scientists with the right backgrounds.

Sub-committees make independent assessments.

Consistency across agencies in decisions.

Less program politics.

Public should appreciate the resulting transparent Council Report.

## **Cons:**

Challenges the *status quo*.

Motivation-may be hard to get agency participation.

Enforcement- may be perceived as more “red tape”.

## What next?

- The purpose of today's presentation was to get this idea “out there”.
- I would really appreciate any comments/suggestions whether favorable or otherwise.
- My email is [lakinplace@gmail.com](mailto:lakinplace@gmail.com)