

Regulatory Implications Panel

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Personal views; not reflective of EPA policy



Consensus on a number of scientific issues relative to risk assessment of mixtures:

- 1. Alterations in omic networks can be reliable indicators of increased hazard or susceptibility to disease, although knowledge is clearly incomplete**
- 2. Chemicals can modify various points in that network to alter the phenotypic outcomes**
- 3. Not necessarily common modes of action but rather common networks underlie common outcomes**
- 4. Chemicals with common networks can occur together in environmental exposures**



Consensus on a number of scientific issues relative to risk assessment of mixtures:

- 4. Great promise shown for biomarkers of exposure and disease (maybe we won't need to test our way out "it")**
- 5. Personalized medicine is going to dramatically change the landscape**
- 6. If we understood mode or mechanism of action that our understanding of cumulative assessment would be better**



Personal Thoughts

I think we should give more consideration to how to facilitate the interpretation of the human data and perhaps less about how to improve or replace the traditional animal bioassay



General Approach for Risk Assessment

1. Looking at chemicals that alter the same disease network and occur together in environmental mixtures
2. Reorienting thinking to be more disease driven vs. chemical driven
3. Focusing on diseases/chemicals that have matching traditional data sets to enable:
 - Proof of concept
 - Value of information
 - Decision rules
4. Useful data is surprisingly limited



Regulatory Implications

- 1. Decision-making will be dependent on the weight of the evidence.**
- 2. Acceptable WOE may differ depending on risk context**
- 3. Decisions will be made case by case.**
- 4. Initially molecular systems informed assessments will be conducted and presented in parallel with traditional assessments**
- 5. We are striving to incorporate other stressor into the equation.**