

Deep Water Horizon Oil Spill: Lessons learned in applying novel assessment methodologies in emergency response

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Deepwater Horizon

Oil Exploration Platform Explodes April 20, 2010

- Estimated 4.9 million barrels of South Louisiana Crude released

1.8 million gallons of dispersant used

- 1072K surface; 771K subsea
- Corexit 9500A (9527 early in spill)

EPA Administrator calls for a less toxic alternative

- Verification of toxicity information on NCP Product Schedule
- ORD involvement in assessments of dispersant toxicity



EPA Oil Dispersant Oversight

- Clean Water Act & Oil Pollution Act (1990)
- EPA Office of Emergency Management
 - National Oil and Hazardous Substances Pollution Contingency Plan
 - NCP Product Schedule Categories
 - Dispersants
 - Surface Washing Agents
 - Bioremedial Agents
 - Misc. (sorbents, solidifiers, etc.)
- Inclusion on schedule does not authorize use
- Product information (toxicity, effectiveness) must be supplied by manufacturer (40 Code of Regulations, Part 300, Subpart J, Appendix C)

Gulf Oil Spill EPA R&D Charge

- Dispersants were going to be used and EPA was in charge of authorizing which one(s) to use
- Ideally, use the most effective formulation with the lowest toxicity
- Toxicity metrics
 - LC50 for mysid shrimp and silverside minnow
 - LC50 for cell culture (human)
 - Endocrine effects (estrogen, androgen, thyroid receptors: ER, AR, TR) – relevant to fish and humans
 - Broad *in vitro* activity screen
- Return results in < 6 weeks

EPA Toxicity Studies

Phase I: Dispersant toxicity

- Acute toxicity: fish and invertebrate
- Comparison to toxicity info from NCP Product Schedule
- Human cell line cytotoxicity
- *in vitro* estrogenicity, androgenicity

Phase II: Oil & oil-dispersant mixture toxicity

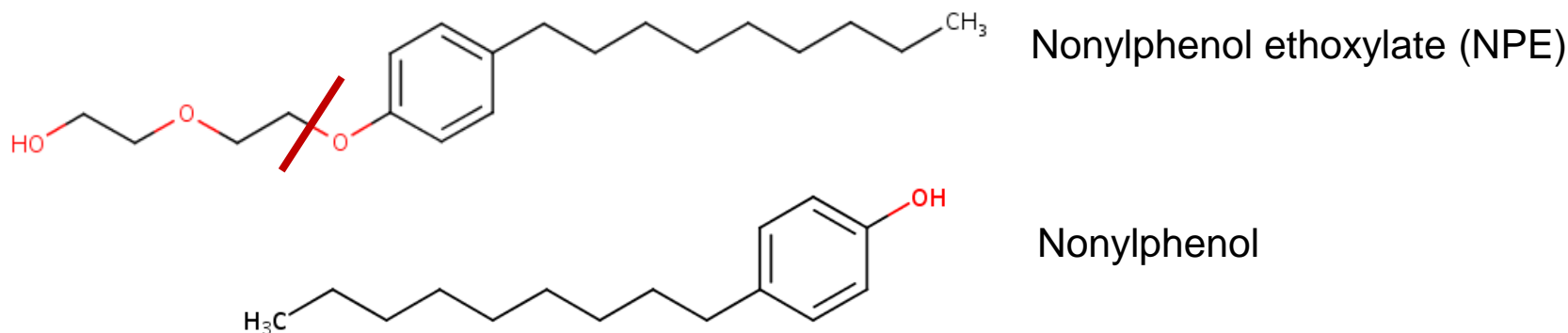
- Acute toxicity: fish and invertebrate
- Oil-only
- Dispersant+oil

What is a dispersant?

- Complex mixture
- Proprietary / Confidential Business Information
- Hydrocarbon component
 - Breaks up clumps of oil
 - Kerosene-like
- Detergent / surfactant component
 - Solubilizes oil components into water
- Water
- Colorants
- Stabilizing agents

Why worry about ER activity?

- Some dispersants were rumored to contain nonylphenol ethoxylate (NPE)
- Environmental breakdown product is nonylphenol – a weak estrogen mimic
- Large quantities in coastal aquatic breeding grounds could have population-wide effects on reproduction



Constraints

- Dispersant formulations are proprietary
- Manufacturers did not make them public. EPA regulatory offices knew basics of formulations but could not legally let researchers know any of this information
- Manufacturers sent samples to EPA, but EPA was not allowed to send to other parties to test (e.g. universities)
- Google searching uncovered a page suggesting one dispersant contained NPE

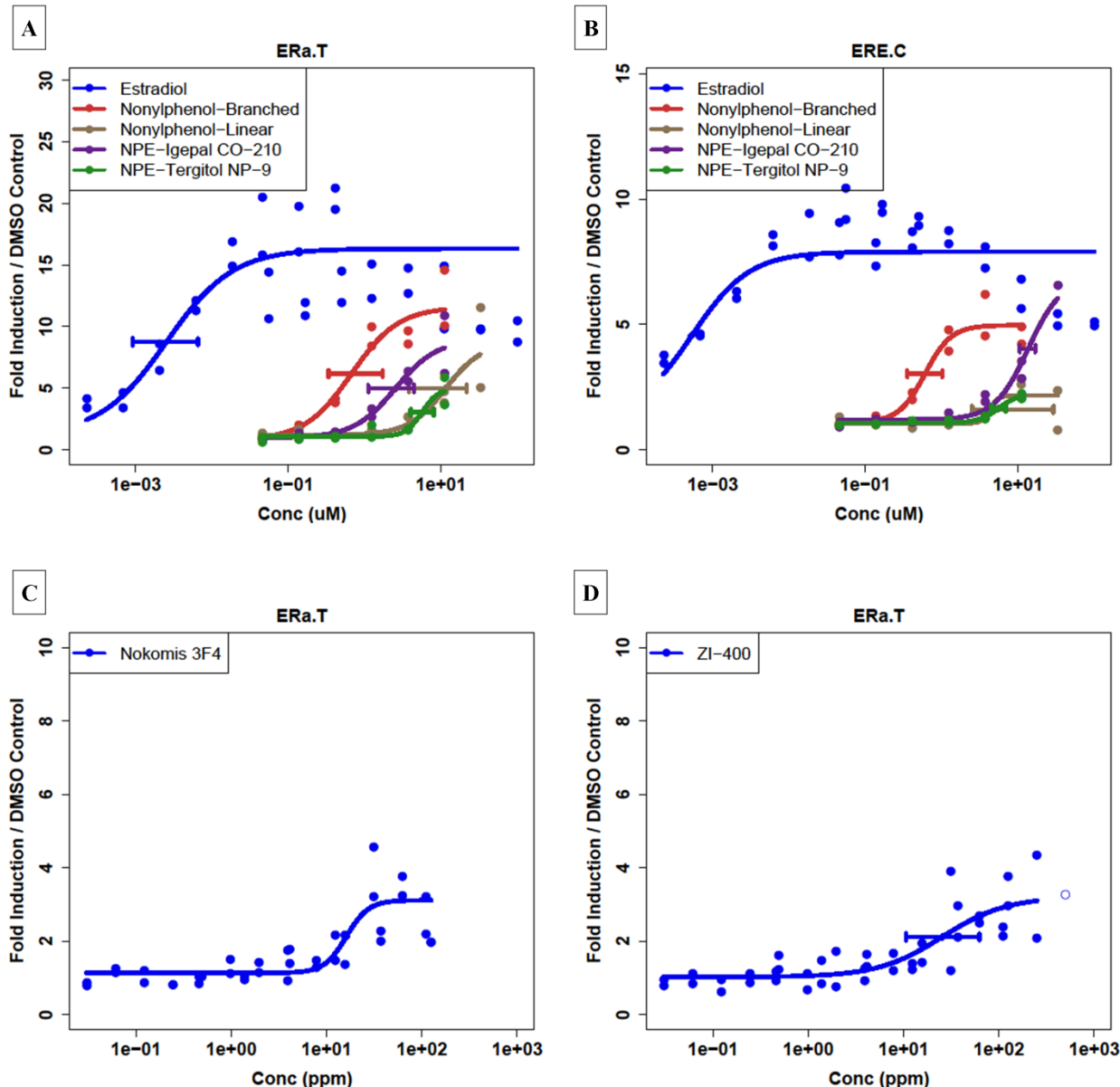
The Dispersants (spill started April 20)

Sample Name	Volume Received	Comments	Date Received	Manufacturer/ Source
Corexit 9500	1 L	hazy yellow	11-May-10	Nalco
JD 2000	10 ml	clear yellow	27-May-10	Ethox Chemicals, LLC
DISPERSIT SPC 1000	10 ml	clear amber	27-May-10	Polychem
Sea Brat #4	10 ml	hazy yellow	27-May-10	Alabaster Corp
Nokomis 3-AA	10 ml	clear light color	27-May-10	MAR-LEN Supply inc.
Nokomis 3-F4	10 ml	clear light color	27-May-10	MAR-LEN Supply inc.
ZI-400	25 ml	clear yellow	29-May-10	ZI Chemical
SAF-RON GOLD	500 ml	silver iridescent	4-June-10	Sustainable Environmental Technologies, Inc.

In Vitro Assay Technologies Used

- Competitive binding (Novascreen)
 - Cell-free
 - Dispersants seem to have denatured proteins, given non-specific results
- ER/AR reporter-gene assays (NIH NCATS / NCGC)
 - Agonist and antagonist mode
 - Quantitative cytotoxicity
- Collection of 81 nuclear-receptor-related assays (Attagene)
 - Includes AR, ER, TR
 - Other xenobiotic response pathways
 - Quantitative cytotoxicity
 - HepG2 (liver) cell line
 - CIS and TRANS modes (TRANS is more sensitive)

Concentration-Response Profiles



Control Data

Igepal and Tergitol are non-ionic surfactants

ERE.T=Attagene ERE TRANS
ERE.C=Attagene ERE CIS

CIS efficacy less than half TRANS efficacy for reference compounds

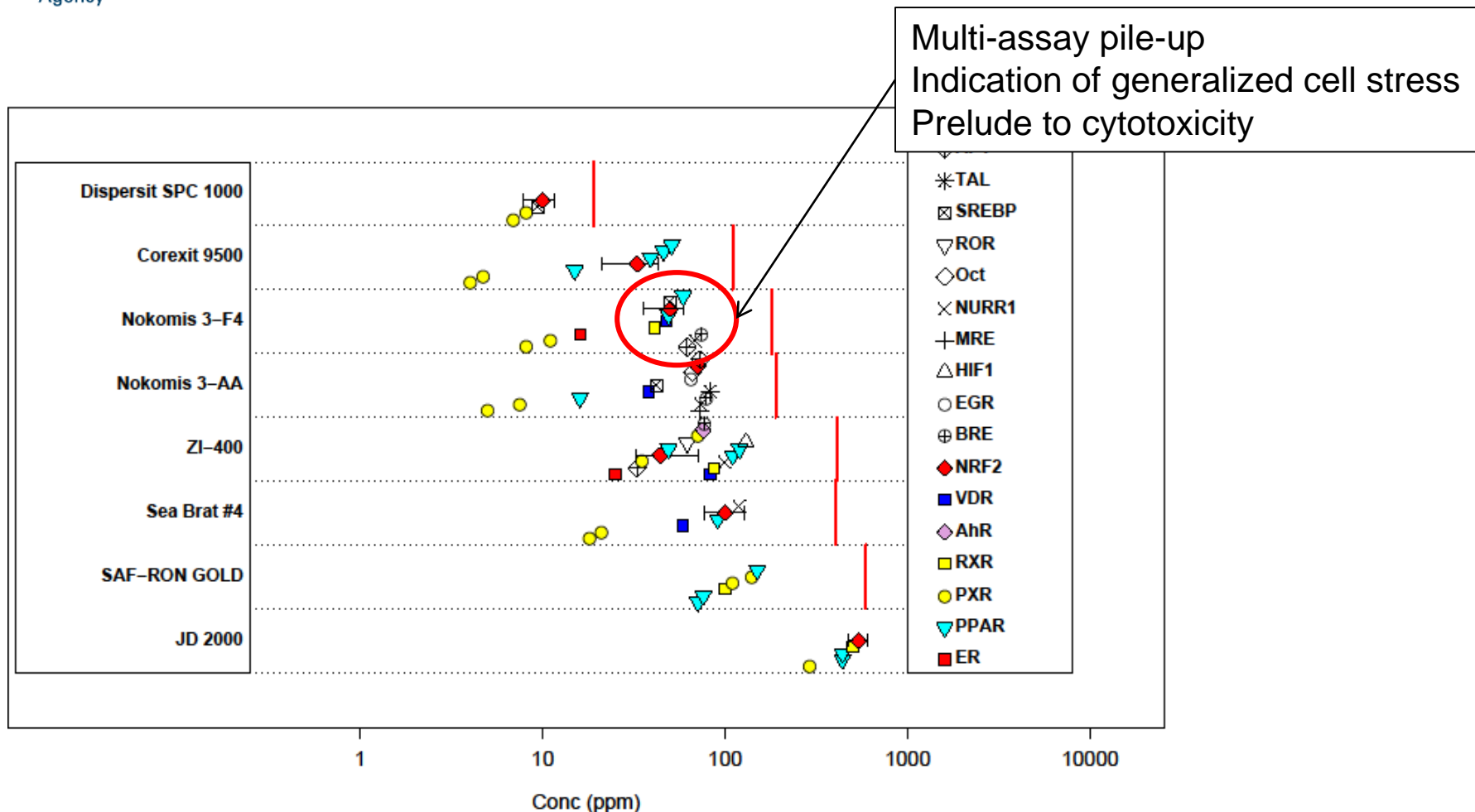
Dispersant Test Data

TRANS assay efficacy near detection threshold for these dispersants, and CIS is below

Further Nuclear Receptor Analysis

- Attagene runs 81 nuclear receptor-related endpoints in 2 multiplexed assays
- Relatively quick and inexpensive
- Many related to xenobiotic response
 - ER/AR/TR
 - PPAR(a,d,g)
 - CAR / PXR / RXR
 - AHR

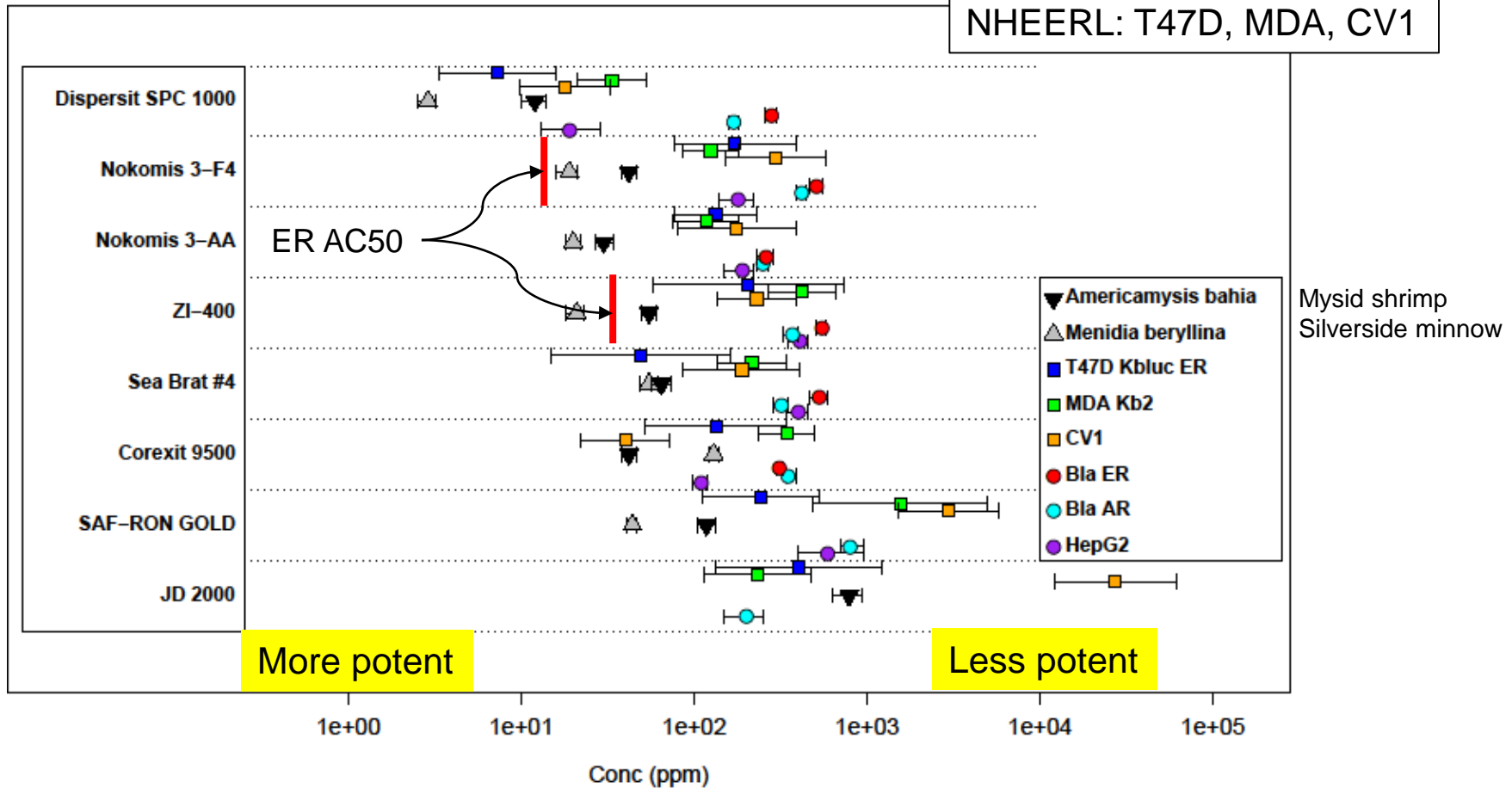
Nuclear Receptor Results



Little specific activity seen except for PXR/ PPAR
Consistent with Xeno-sensing

Dispersant Cytotoxicity Results

Attagene: HepG2
NCGC: Bla ER/AR
NHEERL: T47D, MDA, CV1



Dispersant Conclusions

- Weak evidence of ER activity in 2 dispersants
 - Seen in single, perhaps over-sensitive assay (1 of 6)
 - Not of biological significance
 - Consistent with presence of NPE
 - Activity only at concentrations >> seen in Gulf after dilution
- No AR activity
- No ER activity seen in Corexit 9500
- Corexit is in the middle of the pack for cytotoxicity
- No worrisome activity seen in other NR assays
- Minnow and fish studies largely agreed with earlier results
- Dispersant-oil mixture was no more toxic than oil alone

Oil Spill Was a First Application of the EPA RapidTox Approach

- There are 50K-100K unique chemicals in commerce to which we are exposed
 - ~5000 (<10%) have repeat-dose animal toxicity studies
 - ~1500 have risk assessments – e.g. “safe levels” defined
 - IRIS level risk assessment takes 3-10 years
- This drives the need for rapid “screening-level” risk assessments using “New Approach Methods” (NAM)
 - Available *in vivo* data
 - *In vitro* assay data
 - Models
 - Analogy models (QSAR, Read-across) – does my chemical look like some other chemicals with data?
 - *Ab initio* – *in vitro* to *in vivo* extrapolation

Broader Rapid Risk Assessment Applications

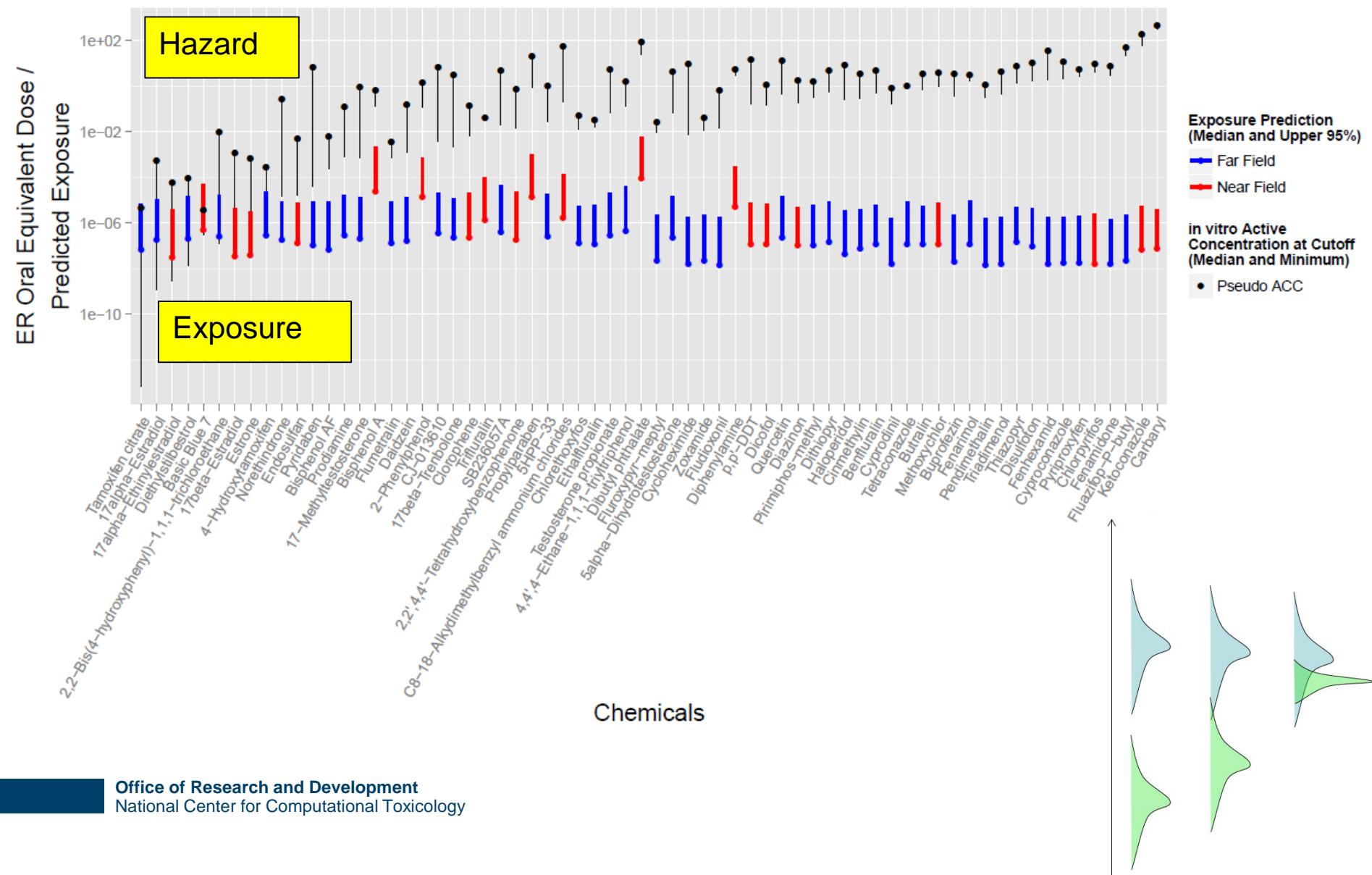
- Prioritization

- Endocrine Disruptor Screening Program – 10,000 chemicals to be screened for endocrine activity
- TSCA inventory – 25,000 chemicals to be prioritized for detailed risk assessment

- Rapid Risk Assessment Potential Opportunities

- 2014 Elk River spill 4-methylcyclohexanemethanol: What effects might this have, and what is the safe level for drinking water?
- Superfund sites – EPA finds 10s-100s of chemicals without risk assessment values – what chemical(s) should drive the cleanup?
- Developing concerns over perfluorinated compounds in the environment

Example of using predicted hazard and exposure to prioritize further testing: ER activity



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