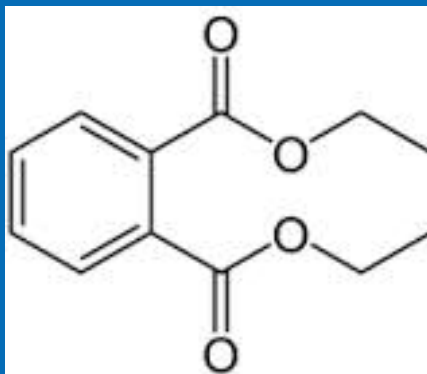


# Preliminary Materials for the IRIS Assessment of Diethyl Phthalate (DEP)

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## General Information

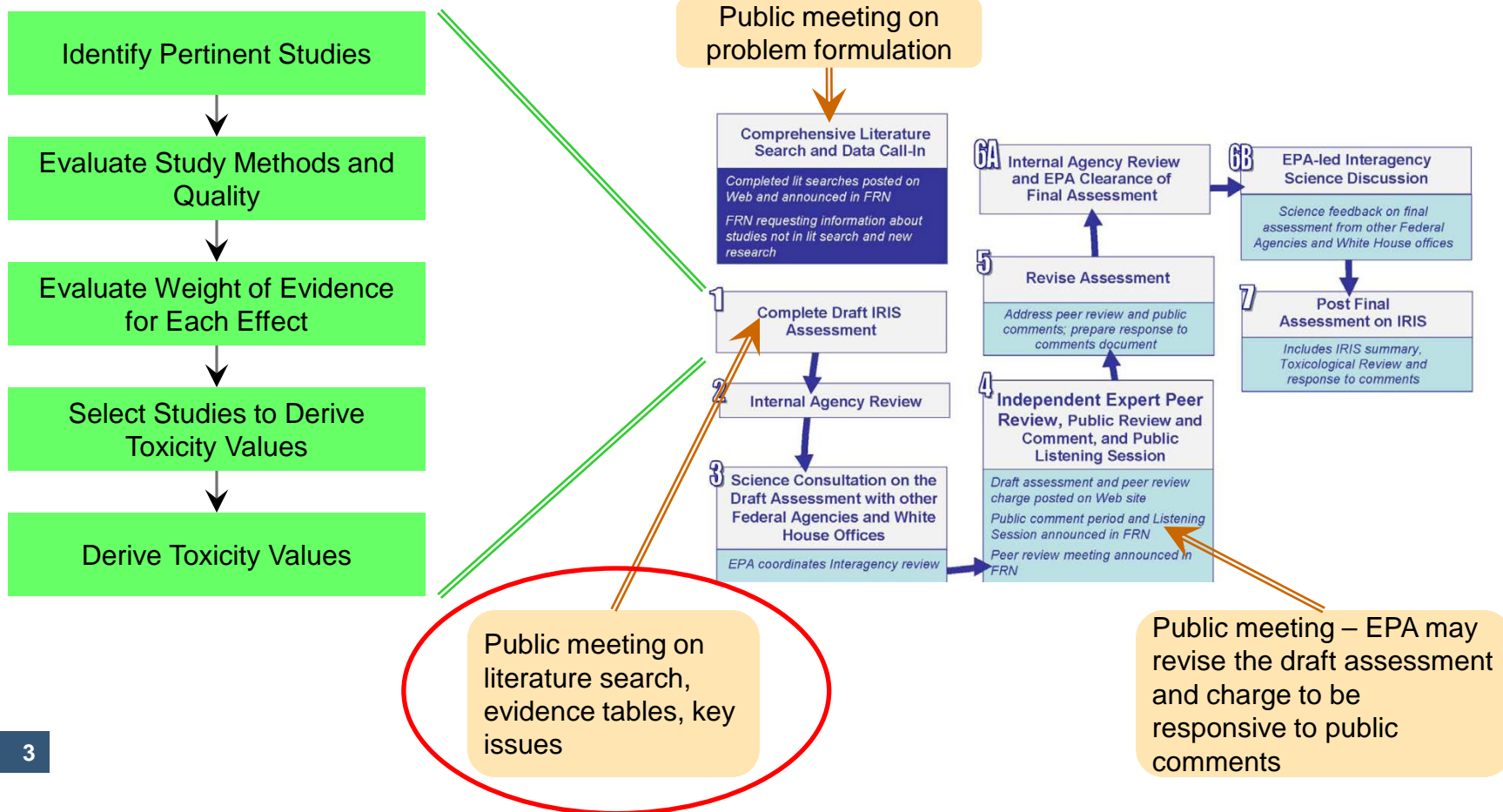
- DEP is a colorless liquid with a slight aromatic odor that is soluble in water and slightly volatile
- DEP is used as a plasticizer to help maintain flexibility in plastic polymers
- Humans may be exposed to DEP through dermal, oral, and inhalation routes.
  - Personal care product use (e.g., cosmetics, shampoo, lotions, etc)
  - Other potential sources of exposure are food and drinking water, airborne dust, and industrial applications
- In 2009-2010, MEP was detected in 100% of NHANES samples tested, indicating ubiquitous exposure to DEP in the general population
  - MEP levels higher in adults compared to children, and higher in women compared to men
  - Some differences by race/ethnicity (higher levels among non-Hispanic Blacks compared to Mexican-Americans and non-Hispanic Whites)



## Agency Interest in DEP

- IRIS assessment was posted in 1993
- Much research has been conducted since then including epidemiological studies
- DEP present at more than 80 Superfund sites
- DEP is listed as a hazardous constituent under RCRA, found in industrial ponds and in air around hazardous waste incinerators
- DEP was nominated by the public for inclusion in the EPA's Office of Water Contaminant Candidate List (CCL) for drinking water
- Unique exposure scenarios and potential sensitivities in children

# IRIS Assessments Invite Public Engagement



## Preliminary Materials for the IRIS Assessment of DEP:

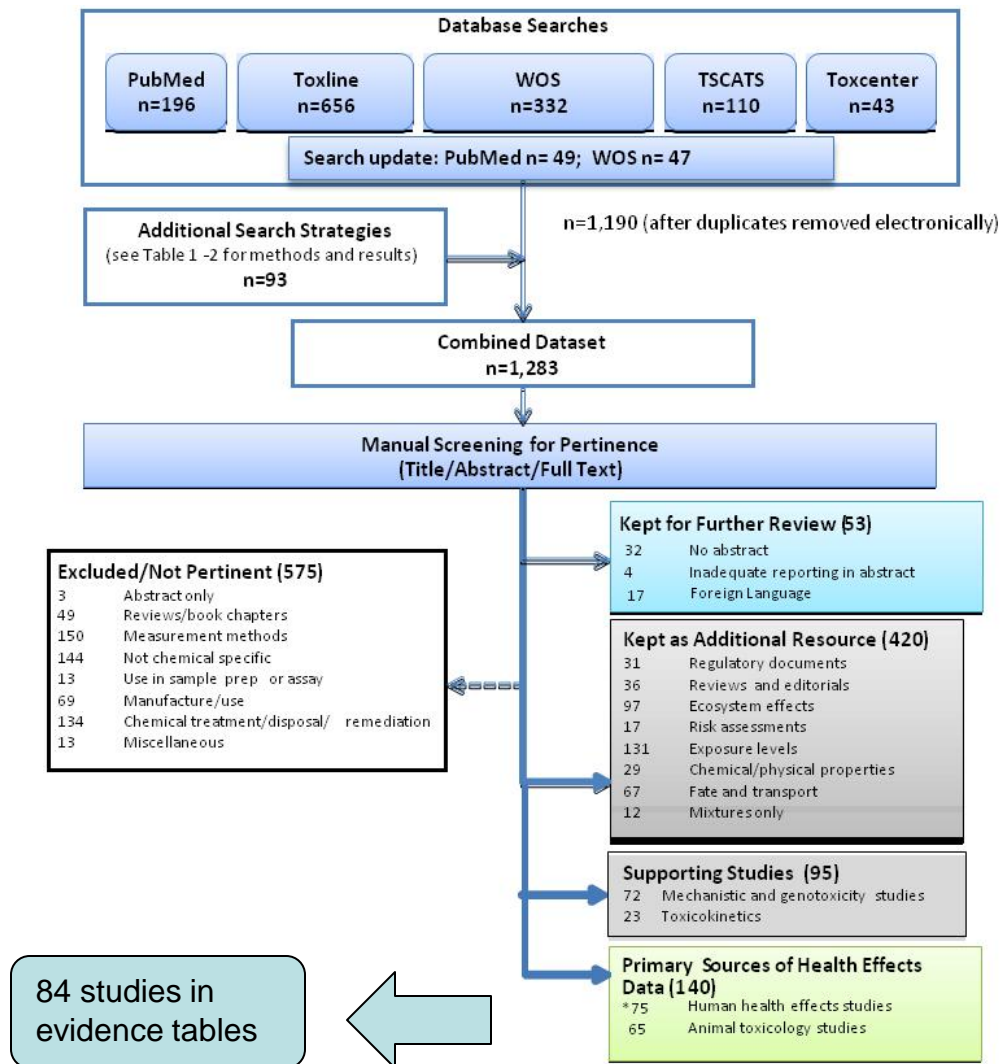
- Planning and scoping summary
- Draft literature search and screening strategy
- Evidence for hazard identification
  - Preliminary evidence tables
  - Preliminary exposure-response arrays

\*These materials are available online at:

[http://www.epa.gov/iris/publicmeeting/iris\\_bimonthly-apr2014/mtg\\_docs.htm](http://www.epa.gov/iris/publicmeeting/iris_bimonthly-apr2014/mtg_docs.htm)

## Initial Literature Search and Screening Strategy

- More than 1000 studies identified; 694 were considered pertinent
- 140 identified as primary sources of health effects data
  - 65 animal toxicology
  - 75 human health effects
    - Most not limited to evaluation of a single phthalate
    - Names of all phthalates examined may not appear in the abstract or indexing terms
    - Targeted search was conducted
- 84 studies (61 human, 23 animal) extracted into evidence tables
  - Acute, ocular and dermal irritation, and i.p. studies not included



\*This set of 75 studies was not screened in detail. A targeted literature search for epidemiology studies was conducted using modified search terms to identify human data pertaining to DEP and additional phthalates; from this targeted search, 145 primary studies of human health effects were identified, of which 61 examined DEP or its major metabolite, MEP (See Table 2-2 and Figure 2-2). This targeted search was conducted because most human health effects studies for phthalates are not limited to examination of a single phthalate and the names of all of the phthalates examined in a particular study may not appear in the abstract or indexing terms

# Features of the DEP Database

- Animal data

	<b>Chronic</b>	<b>Subchronic</b>	<b>Reproductive and Developmental</b>	<b>MOA Information</b>	<b>Toxicokinetics</b>
Oral	✓	✓	✓	✓	✓
Inhalation					
Dermal	✓				

- Human data

- cohort studies (including several birth cohort studies)
- nested case-control studies within cohorts
- case-control studies
- population-based surveys

# Study Characteristics to be Considered during Evaluation and Synthesis

## Some examples include:

- Distribution of exposure levels (span or range of exposure contrast; comparison to other studies)
- Correlations between MEP in urine, serum, or seminal fluid are strong ( $r \geq 0.75$ ); measurement in breast milk is more challenging due to limits of detection
  - EPA has greater uncertainty in MEP measures in breast milk
- Consideration of optimal approaches to adjusting (or not) for urinary volume or dilution
  - Creatinine-adjusted approaches may produce biased effect estimate in studies of outcomes related to creatinine excretion (e.g., obesity)
- Potential confounding by exposure to other phthalates
  - Given the relatively low correlation seen between MEP and metabolites of other phthalates ( $r < 0.3$ ), EPA does not consider lack of adjustment for other phthalates to limit interpretation of associations seen with MEP



The evidence tables present data for the following potential hazards:

- *Reproductive and Developmental Effects*
  - Reproductive organ weights, sperm effects, and hormone changes observed in adult males
  - Reproductive organ weights, increased resorptions and early pregnancy loss, and decreased gestational length in females
  
- *Cancer*
  - Evidence for tumors in the livers of female, but not male mice dermally exposed to DEP
  
- *Other Liver Effects*
  
- *Other Systemic Effects*