Tiered approach to integrating evidence streams assessing \textit{in utero} trichloroethylene exposure and development of congenital heart defects (TCE-CHD)

**Methods**

- **Critical Appraisal of Mechanistic Datasets**
- **Risk Assessment**
- **Study Quality/Functional/Physiological Cell Response**: 1. Excessive cells undergo... 2. Reduced mesenchymal... 3. Apoptosis... 4. Cytostructure, % beating cells, beat rates... 5. Cardiomyocyte function...

**Results**

- **Mechanistic Evidence Integration**
- **Mechanistic Studies**
- **TSCA Study Quality Evaluation**
- **Quality Rankings**

**Conclusions**

- **Consideration of the type of evidence presented**
- **Organization of the data presented**
- **Integration of mechanistic evidence**
- **Risk assessment**

**Objective**

- To identify an approach, and then the mechanistic evidence base to assess the tiered TCE-CHD database

**Introduction**

- **The need for tiered approaches**
- **Evidence assessment**
- **Critical evidence deficiencies**
- **Mechanistic studies were categorized based on the assay type(s) to...”

**Figure 1**: Schematic diagram of the mechanistic evidence base for TCE-CHD

**Figure 2**: “Putative AOP” Posited for Valvulo-Septal Cardiac Defects

**Figure 3**: Summary of TCE-CHD data

**Figure 4**: Pathway AOPs as per TCE-CHD Mechanistic Evidence

**Table 1**: Summary of TCE-CHD data

**Table 2**: TSCA Mechanistic Evidence

**Table 3**: Summary of mechanistic evidence base

**Table 4**: TCE-CHD Study Quality Evaluation

**Table 5**: Summary of TCE-CHD data that not study quality metrics

**Table 6**: Study Quality Evaluation: ABO of key markers

**Table 7**: Study Quality Evaluation: Key markers for TCE-CHD

**Table 8**: Study Quality Evaluation: Key markers for TCE-CHD

**Table 9**: Study Quality Evaluation: Key markers for TCE-CHD

**Table 10**: Study Quality Evaluation: Key markers for TCE-CHD

**Table 11**: Study Quality Evaluation: Key markers for TCE-CHD

**Table 12**: Study Quality Evaluation: Key markers for TCE-CHD

**Table 13**: Study Quality Evaluation: Key markers for TCE-CHD

**Table 14**: Study Quality Evaluation: Key markers for TCE-CHD

**Table 15**: Study Quality Evaluation: Key markers for TCE-CHD