Occupational Reproductive and Developmental Hazards

[A Case of a Pregnant Airplane Part Finisher]

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September 10, 2016
DISCLOSURES

NONE
OBJECTIVES

- Understand the issues and challenges associated with identifying, evaluating and managing reproductive and developmental hazards in the workplace.

- Navigate resources available for providing knowledge and management support when caring for patients with reproductive or developmental exposures in the workplace.
R.E: 26 year old female...

- **CHIEF COMPLAINT**
  - Referred by her PCP
  - Concerned about effect of work-related exposures on current pregnancy
  - Mild intermittent headache, easy fatigability and positional lightheadedness
  - Intermittent difficulty breathing, throat irritation, nasal irritation

- **HPI**
  - G1P0. Realized she was pregnant at 12 weeks. Is now 18 weeks pregnant.
  - Works as an airplane part inspector and sander at an aerospace metal finishing company
  - Informed employer of pregnancy at 14 weeks → job duties changed to that of airplane part masking
  - Difficulty breathing, throat irritation, nasal irritation resolved with job duty change
  - Primary symptoms since job duty change are intermittent headache, easy fatigability and positional lightheadedness
OCCUPATIONAL HISTORY

Airplane part inspecting and sanding (9 months)
- Inspects airplane parts that have been painted with E-primer and dried
- Cleans parts using methyl ethyl ketone (MEK)
- Sands parts that had been painted with E-primer and dried
- PPE: Gloves (impermeable to MEK), Dust mask
- Engineering controls: centralized ventilation system in the facility with vents located several feet away from her work table
- Housekeeping: once a day sweeping away of dust generated from the sanding process
- Exposure monitoring: unavailable

Airplane part masking (1 month)
- Uses tape to mask and plug airplane parts prior to painting
- PPE: Gloves
ENVIRONMENTAL EXPOSURE HISTORY

- Residential locale: Rainier Beach
- Building type: Single family home in good condition; working smoke and CO detectors
- Year residence built: 1998
- Local industry: None
- Drinking water source: Municipal
- Heating system: Gas
- Stove type: Electric
- Flooring type: Carpet
- Pets: None
- Pesticide/herbicide use: None
- Ingested non-food items: None
- Childhood residential history: grew up in Cambodia with access to a municipal water source. Denies any known chemical exposures while living in Cambodia.
- Hobbies: walking, watching movies
PAST MEDICAL/SURGICAL HISTORY
- No history of illnesses, hospitalizations, surgeries

OBSTETRIC/GYNECOLOGIC HISTORY
- G1P0
- Age at menarche: 12
- Cycle characteristics: 30-day average cycle length, regular; 4 day menstruation with low - moderate flow

MEDICATIONS
- Prenatal vitamin 1 tab PO daily

ALLERGIES
- No known drug allergies

SOCIAL HISTORY
- No tobacco, alcohol or recreational drug use

FAMILY HISTORY
- Mother - heart disease, hypertension
PHYSICAL EXAMINATION

VS: BP 93/53 mmHg, Pulse 80, Temp 97.2 °F (36.2 °C), Wt 104 lb (47.2kg), SpO2 100% on room air

General: healthy, alert, no distress.
Skin: Skin color, texture, turgor normal. No rashes or concerning lesions.
HEENT: Normocephalic; no masses, lesions, tenderness or abnormalities. Lids/periorbital skin normal, conjunctivae/corneas clear, PERRL, EOM's intact. External ear canals clear. TM's intact. Nasal mucosa without edema, or drainage; intact septum. Lips, mucosa, tongue, teeth and gums normal; posterior oropharynx without erythema or drainage.
Neck: Supple. No cervical adenopathy. Thyroid symmetric, normal size, without nodules
Lungs: Clear to auscultation bilaterally
Heart: Normal rate, regular rhythm and no murmurs, clicks, or gallops
Abdomen: Gravid, bowel sounds present and normally active
Psych: Normal mood and affect
DIAGNOSTICS
- 16 week obstetrical ultrasound → normal
- CBC, 2 hour GTT, UA → normal
- HIV, HCV, HBV, HSV 1&2 → negative
- Genetic Screen (Down Syndrome, Trisomy 18) → negative
- Rubella → immune
DEFINITIONS

- **Reproductive toxicity**: the occurrence of adverse effects on the reproductive system of a male or female that may result from exposure to occupational or environmental agents.

- **Developmental toxicity**: the occurrence of adverse effects on the developing organism that may result from exposures occurring before conception (in either parent), during prenatal development, or post-natal, up until the time of sexual maturation.

- **Exposure Categories**:
  - Chemical agents → e.g. lead, pesticides, solvents
  - Physical agents → e.g. radiation, noise, altitude
  - Physical demands → e.g. prolonged standing, heavy lifting, circadian disruption (shift work)
  - Biological/infectious agents → e.g. measles, mumps, rubella, syphilis, HIV, chlamydia
DEVELOPMENTAL PHYSIOLOGY & TOXICITY
<table>
<thead>
<tr>
<th>OUTCOME</th>
<th>DEFINITION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical spontaneous abortion</td>
<td>Fetal loss by 20 weeks</td>
</tr>
<tr>
<td>Early or subclinical loss</td>
<td>Loss by 6 – 8 weeks</td>
</tr>
<tr>
<td></td>
<td>Short rise and fall in HCG levels</td>
</tr>
<tr>
<td>Congenital anomalies</td>
<td>Structural, physiologic, genetic; major, minor</td>
</tr>
<tr>
<td>Fetal growth</td>
<td>Low birth weight (LBW): &lt; 2500g</td>
</tr>
<tr>
<td></td>
<td>Small for gestational age (SGA): &lt; 10th percentile for age</td>
</tr>
<tr>
<td></td>
<td>Preterm: &lt; 37 weeks</td>
</tr>
<tr>
<td>Fetal, neonatal, or infant death</td>
<td>FD: 21 weeks to term</td>
</tr>
<tr>
<td></td>
<td>ND: 1st month of life</td>
</tr>
<tr>
<td></td>
<td>ID: 1st year of life</td>
</tr>
<tr>
<td>Postnatal</td>
<td>Neurobehavioral development, cerebral palsy, CNS malformations, childhood cancer</td>
</tr>
</tbody>
</table>
FEMALE REPRODUCTIVE PHYSIOLOGY & TOXICITY

PHYSIOLOGY

- Germ cells (oogonia) develop and begin the first meiotic division in utero
- Oocytes remain dormant until follicular activation
- Reproductive cycle: regulated by the autonomic nervous and endocrine systems; mediated by the hypothalamic-pituitary-gonadal axis
- Primary follicle development → proliferation of endometrial tissue → ovulation → endometrial sloughing in absence of fertilization

TOXICITY MECHANISMS

- Genotoxic or cytotoxic harm to oocytes → lack of fertilization, unsuccessful implantation
- Pre-conception mutagenesis → birth defects
- Endocrine disruption of reproductive process → menstrual disorders, infertility
- Oocyte destruction → early menopause
MALE REPRODUCTIVE PHYSIOLOGY & TOXICITY

PHYSIOLOGY

- Spermatogenesis starts at puberty
- Spermatogenesis involves a continuously replicating cell population
- Coordinated hypothalamic, pituitary, and gonadal interactions are critical for proper functioning of male reproductive system

TOXICITY MECHANISMS

- Chemical or physical agents whose toxicity depends on cell division have greater effect on the male germ cell
- CNS/endocrine system → decreased libido, decreased fertility
- Direct testicular toxicity → decreased fertility
- Spermatogenesis or germ cell toxicity → decreased fertility, fetal loss, congenital malformations, childhood developmental disabilities and cancers
## Adverse Reproductive Outcomes

### Female Outcomes

<table>
<thead>
<tr>
<th>Condition</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infertility</td>
<td>No conception in 12 months of intercourse; Specific diagnosis → e.g. tubal disease, endometriosis</td>
</tr>
<tr>
<td>Age at puberty</td>
<td>Age at menarche, breast or pubic hair development</td>
</tr>
<tr>
<td>Menstrual cycle dysfunction</td>
<td>Cycle length, bleed characteristics, pain, anovulation, long follicular phase, short luteal phase</td>
</tr>
<tr>
<td>Age at menopause</td>
<td>Cessation of menstruation</td>
</tr>
</tbody>
</table>

### Male Outcomes

<table>
<thead>
<tr>
<th>Condition</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infertility</td>
<td>No conception in 12 months of intercourse; Specific diagnosis → e.g. abnormal sperm morphology, azoospermia, oligospermia</td>
</tr>
<tr>
<td>Sexual dysfunction</td>
<td>Decreased libido; erectile or ejaculatory dysfunction</td>
</tr>
</tbody>
</table>
# BURDEN OF DISEASE

<table>
<thead>
<tr>
<th>ENDPOINT</th>
<th>PREVALENCE (%)</th>
<th>UNIT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infertility</td>
<td>6 - 12</td>
<td>Couples</td>
</tr>
<tr>
<td>Recognized spontaneous abortion</td>
<td>8 - 20</td>
<td>Pregnancies</td>
</tr>
<tr>
<td>Birth weight &lt; 2500g (LBW)</td>
<td>~ 8</td>
<td>Livebirths</td>
</tr>
<tr>
<td>Preterm (≤ 37wk)</td>
<td>~ 10</td>
<td>Livebirths</td>
</tr>
<tr>
<td>Fetal death (still birth)</td>
<td>0.7 - 1</td>
<td>Pregnancies</td>
</tr>
<tr>
<td>Infant death (&lt; 1 y)</td>
<td>0.04</td>
<td>Livebirths</td>
</tr>
<tr>
<td>Birth defects (through 1 y of life)</td>
<td>3</td>
<td>Livebirths</td>
</tr>
<tr>
<td>Chromosomal anomalies</td>
<td>0.2</td>
<td>Livebirths</td>
</tr>
</tbody>
</table>

*CDC (2014)*
IMPACT OF ADVERSE REPRODUCTIVE AND DEVELOPMENTAL OUTCOMES

- High medical costs for compromised children (with birth defects, chromosomal anomalies).

- Increasing use of advanced technology to achieve conception and monitor pregnancy.

- Occupational medicine specialists play an important role in helping to assess and manage occupational reproductive and developmental health risks.
CHALLENGES

INFORMATION ABOUT CHEMICAL HAZARDS
- Only ~4000 of the ~84,000 chemicals in the workplace have been evaluated for reproductive toxicity
- Over 2000 new chemicals are introduced annually

SCIENTIFIC AND MEDICAL LITERATURE
- Scarce human data
- Reliance on animal studies for identifying toxicants
- Confounding factors

INDUSTRIAL EXPOSURE LIMITS
- Established without considering protection from adverse reproductive and developmental effects
- Compliance with OSHA exposure limits may therefore not ensure protection of reproductive or developmental health

REPRODUCTIVE (& DEVELOPMENTAL) TOXIC EFFECTS
- Adverse effects in an exposed person may only manifest in the fetus or offspring
- Effects may go unnoticed for long periods (e.g. infertility)
- Normal reproductive function is only expressed intermittently

WORKER EDUCATION
SAFE WORK ENVIRONMENT
FRAMEWORK FOR ASSESSING HEALTH RISKS

- THOROUGH MEDICAL, OCCUPATIONAL, & ENVIRONMENTAL HISTORY
- MULTIDISCIPLINARY TEAM APPROACH
- HAZARD IDENTIFICATION & DOSE-RESPONSE ASSESSMENT
- RISK CHARACTERIZATION
- RISK COMMUNICATION
- RISK MANAGEMENT
FRAMEWORK FOR ASSESSING HEALTH RISKS

- MULTIDISCIPLINARY TEAM APPROACH
  - Occupational medicine specialists
  - Industrial hygienists
  - Pediatric environmental medicine specialists (PEHSU – Pediatric Environmental Health Specialty Unit)
  - Teratology specialists (OTIS – Organization of Teratology Information Specialists)
  - Obstetrician-gynecologists
  - Exposure assessment specialists
  - Toxicologists
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**HAZARD IDENTIFICATION & DOSE-RESPONSE ASSESSMENT**

- **Review SDSs** for occupational and non-occupational agents to which the worker is exposed → identify agents which may have reproductive or developmental risks

- Determine **extent of exposure** to agents identified as reproductive/developmental hazards in the workplace and at home:
  - Frequency of exposure
  - Duration of exposure
  - Routes of exposure
  - Concentration/intensity of exposure
  - Exposure control measures: engineering controls, PPE
  - Data: personal and/or ambient exposure monitoring performed by employer
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RISK CHARACTERIZATION

- GOAL → to determine if the estimated levels of exposure to agents identified as potential reproductive or development hazards pose a risk

Consider all gathered data on toxicity and exposure

Estimated exposure levels VS. levels shown/suspected to cause reproductive or developmental effects

Is exposure to an agent above or near levels associated with adverse effects?

HIGH
MODERATE
LOW
NONE
RESOURCES

■ OSHA
- Safety and Health Topics: Reproductive Hazards
- Chemical Sampling Information

■ NIOSH
- Effects of Workplace Hazards on Female Reproductive Health
- Effects of Workplace Hazards on Male Reproductive Health

■ OTHER
- National Birth Defects Prevention Network (NBDPN)
- Organization of Teratology Information Specialists (OTIS)/MotherToBaby
- US National Library of Medicine.TOXNET. Developmental and Reproductive Toxicology Database (DART)
- Pediatric Environmental Health Specialty Units (PEHSU)
EXPOSURE HAZARD & DOSE EVALUATION

FIRST TRIMESTER

- **Methyl Ethyl Ketone (MEK)**
  - Uses (MEK) to clean parts about once a week.
  - Stores used rags in a container without a lid.
  - Small MEK spills 2-3 times a week → odor lasts ~ 20 minutes even after clean up.

- **E-Primer (Cr(VI) compounds, TiO₂, BPA, sec-butyl alcohol)**
  - Sands parts 2-3 times a week for 2 hours each time by hand using sand paper.
  - Is located ~2 meters away from door to painting room which is opened up to 4-6 times an hour during the day for brief periods.

SECOND TRIMESTER

- As in first trimester, up until 14 weeks
- None/minimal after job duty transfer at 14 weeks
## EXPOSURE RISK ASSESSMENT: MEK

<table>
<thead>
<tr>
<th>Methyl Ethyl Ketone (2-Butanone)</th>
<th>Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Colorless liquid with acetone-like odor</strong></td>
<td><strong>MATERNAL RISK</strong></td>
</tr>
<tr>
<td><strong>Exposure Routes:</strong> inhalation, ingestion, skin contact, eye contact</td>
<td>• Asymptomatic → likely &lt; 200 ppm</td>
</tr>
<tr>
<td><strong>Developmental Effects/Toxicity:</strong></td>
<td>• Effectiveness of engineering controls unknown</td>
</tr>
<tr>
<td>• EPA RfC (inhalation): 5mg/m³ (1.7 ppm)</td>
<td>• Air sampling data not available</td>
</tr>
<tr>
<td>• EPA RfD (oral): 0.6mg/kg/day</td>
<td>• <strong>Risk level:</strong> Low</td>
</tr>
<tr>
<td><strong>Symptoms:</strong></td>
<td><strong>FETAL RISK</strong></td>
</tr>
<tr>
<td>• 200 ppm: no significant effects</td>
<td>• Possibly &gt; 1.7 ppm exposure</td>
</tr>
<tr>
<td>• 300 – 600 ppm: eye, nose, &amp; throat irritation</td>
<td>• Some evidence that MEK is a teratogen in mammals</td>
</tr>
<tr>
<td><strong>Prolonged Exposure:</strong> neurotoxic effects – CNS depression, multifocal myoclonus, ataxia, tremor, peripheral neuropathy</td>
<td>• No evidence of teratogenicity in humans</td>
</tr>
<tr>
<td><strong>OSHA PEL, ACGIH TLV, NIOSH REL:</strong> 200ppm (590mg/m³)</td>
<td>• 16 week fetal ultrasound reassuring</td>
</tr>
<tr>
<td>8h TWA</td>
<td>• <strong>Risk level:</strong> Low-moderate</td>
</tr>
<tr>
<td>IDLH: 3000ppm</td>
<td></td>
</tr>
</tbody>
</table>
## EXPOSURE RISK ASSESSMENT: E-PRIMER

<table>
<thead>
<tr>
<th>Hexavalent Chromium (Strontium Chromate, Barium Chromate)</th>
<th>Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exposure Routes:</strong> inhalation, skin contact</td>
<td><strong>MATERNAL RISK</strong></td>
</tr>
<tr>
<td><strong>Symptoms:</strong> irritation/damage to nasal mucosa, throat, respiratory tract; eye irritation; allergic contact dermatitis; non allergic skin irritation; liver and kidney damage; blood changes</td>
<td>• Dyspnea, throat and nose irritation occurred while sanding parts coated with dried E-Primer → likely &gt; 5 ug/m$^3$</td>
</tr>
<tr>
<td>Well established occupational carcinogen (IARC Group 1) → lung cancer; nasal and sinus cancer</td>
<td>• Effectiveness of engineering controls unknown</td>
</tr>
<tr>
<td></td>
<td>• Air sampling data unavailable</td>
</tr>
<tr>
<td></td>
<td>• Risk level: Moderate – high</td>
</tr>
<tr>
<td><strong>OSHA 8h TWA PEL:</strong> 5ug/m$^3$</td>
<td><strong>FETAL RISK</strong></td>
</tr>
<tr>
<td><strong>NIOSH 8h TWA REL:</strong> 0.2ug/m$^3$</td>
<td>• Animal studies demonstrate possible embryotoxicity and fetotoxicity</td>
</tr>
<tr>
<td><strong>ACGIH 8h TLV:</strong> 50ug/m$^3$ (H$_2$O soluble) and 10ug/m$^3$ (H$_2$O insoluble)</td>
<td>• No human studies showing association between Cr(VI) exposure and congenital abnormalities, still births, or neonatal deaths</td>
</tr>
<tr>
<td><strong>PPE:</strong> Respirator use required to maintain exposure level to below OSHA PEL</td>
<td>• Risk level: Low-moderate</td>
</tr>
</tbody>
</table>
# EXPOSURE RISK ASSESSMENT: E-PRIMER

**Sec-Butyl Alcohol**

**Exposure Routes:** inhalation, ingestion, skin contact

**Symptoms**
- Central nervous system: headache, muscle weakness, giddiness, ataxia, confusion, delirium, coma.
- Gastrointestinal: nausea, vomiting, diarrhea, GI hemorrhage
- Cardiac: cardiac arrhythmias. Cardiac failure
- Other: Renal damage with glycosuria. Liver damage

**OSHA 8h TWA PEL:** 150 ppm  
**NIOSH 8h TWA REL:** 100ppm  
**ACGIH 8h TWA TLV:** 100ppm  
**IDLH:** 2000ppm.

**Risks**

**MATERNAL RISK**
- May have contributed to dyspnea, throat irritation while working with E-Primer
- Effectiveness of engineering controls unknown
- Air sampling data unavailable
- **Risk level:** Moderate – high

**FETAL RISK**
- Not known to harm the unborn child
- **Risk level:** Low-moderate
Titanium Dioxide

**Exposure Routes:** inhalation

**Symptoms:** nose and throat irritation

**IARC group 2B** – possibly carcinogenic to humans → lung cancer

**OSHA 8h TWA PEL:** 15 mg/m³  
**ACGIH 8h TWA TLV:** 10 mg/m³  
**IDLH:** 5000 mg/m³

**PPE:** Respirator use required for exposures above OSHA PEL

**Risks**

**MATERNAL RISK**
- May have contributed to nose/throat irritation. Also possible carcinogen.
- Effectiveness of engineering controls unknown
- Air sampling data unavailable
- **Risk level:** Moderate – high

**FETAL RISK**
- Not known to harm the unborn child
- **Risk level:** Low-moderate
**EXPOSURE RISK ASSESSMENT: E-PRIMER**

<table>
<thead>
<tr>
<th>Bisphenol A (BPA) Epoxy Resin</th>
<th>Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exposure Routes:</strong> Inhalation, ingestion</td>
<td><strong>MATERNAL RISK</strong></td>
</tr>
<tr>
<td><strong>Occupational exposure symptoms:</strong> eye irritation, skin sensitization</td>
<td>• May have contributed to eye irritation</td>
</tr>
<tr>
<td><strong>IARC group 3:</strong> not classifiable as a human carcinogen</td>
<td>• Air sampling data unavailable</td>
</tr>
<tr>
<td>No specific work place standards exist for BPA.</td>
<td>• <strong>Risk:</strong> Low</td>
</tr>
<tr>
<td><strong>OSHA standard for particulates</strong> (including BPA dust): 15mg/cm³ for total dust; 5mg/cm³ for respirable fraction</td>
<td><strong>FETAL RISK</strong></td>
</tr>
<tr>
<td></td>
<td>• Some laboratory animal studies report subtle developmental effects in fetuses and newborns exposed to low doses of BPA.</td>
</tr>
<tr>
<td></td>
<td>• National Toxicology Program (NTP) → some concern for BPA’s effect on the brain, behavior and prostate gland in fetuses, infants, and children.</td>
</tr>
<tr>
<td></td>
<td>• NTP → minimal concern that exposure of pregnant women to BPA will result in fetal or neonatal mortality, birth defects, or reduced birth weight and growth of offspring.</td>
</tr>
<tr>
<td></td>
<td>• <strong>Risk:</strong> Low-moderate</td>
</tr>
</tbody>
</table>
FRAMEWORK FOR ASSESSING HEALTH RISKS

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■ RISK MANAGEMENT
**RISK COMMUNICATION**

- **Goal:** provide information to allow patients to make informed decisions about their reproductive health risks and health risks to their unborn child
  - Answer all questions fully
  - Provide best available information
  - Include discussion of limitations of that information

**RISK MANAGEMENT**

- **Goal:** Physician, patient, and employer work together to decrease/eliminate potential workplace reproductive & developmental risks identified
  - Exposure reduction/elimination
  - Temporary job transfer
  - Temporary disability leave
  - Permanent job removal
LEGAL CONSIDERATIONS

- **1978 Pregnancy Discrimination (PDA) Act Amendment to Title VII of the Civil Rights Act of 1964**
  - Main source of antidiscrimination protection afforded the pregnant worker

- **Other Laws Protecting the Pregnant Worker**
  - Equal Employment Opportunity Act
  - Americans with Disability Act, and the related ADA Amendments Act (ADAAA) of 2008
  - Family Medical Leave Act

- **US Supreme Court Rulings**
  - Young vs UPS, 2015
  - Johnson Controls Decision, 1991
ASSESSMENT & RECOMMENDATIONS

- **MATERNAL**
  - Reproductive risks: Low
  - Other risks: moderate – high, primarily associated with Cr (VI) exposure
  - **Recommended:** filing a claim; contacting employer for site evaluations, air quality reports, exposure monitoring reports; continuing job transfer duties.

- **FETAL**
  - Developmental risks: first trimester → low–moderate (MEK, Cr(VI), BPA); second trimester → low; third trimester → low
  - **Recommended:** continuing job transfer duties; continuing antenatal care, daily prenatal vitamin, balanced diet, aerobic activity e.g. walking
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- RISK COMMUNICATION
- RISK MANAGEMENT
OBJECTIVES

■ Understand the issues and challenges associated with identifying, evaluating and managing reproductive and developmental hazards in the work place.
  - Information available for a limited number of chemical hazards
  - Scarce human data in scientific and medical literature
  - Industrial exposure limits often established without considering protection from adverse reproductive and developmental effects
  - Reproductive and development toxicity effects may go unnoticed for long periods of time

■ Navigate resources available for providing knowledge and management support when caring for patients with reproductive or developmental exposures in the work place.
  - Framework for assessing reproductive and developmental health risks
  - Numerous online resources
QUESTIONS?

THANK YOU
REFERENCES

- CDC - NIOSH Publications and Products - The Effects of Workplace Hazards on Female Reproductive Health (99-104) [Internet]. [cited 2016 Aug 10];Available from: https://www.cdc.gov/niosh/docs/99-104/
- TOXNET Developmental and Reproductive Toxicology Database (DART) [Internet]. [cited 2016 Aug 10];Available from: https://toxnet.nlm.nih.gov/newtoxnet/dart.htm
- Toxicology Data Network. Methyl Ethyl Ketone [Internet]. [cited 2015 Nov 17];Available from: http://toxnet.nlm.nih.gov/cgi-bin/sis/search/a?dbs+hsdb@term+@DOCNO+99