September 20, 2000
8th GHTF Conference
Ottawa, Canada

PVC and DEHP

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Dr. Lloyd Tepper, Associate Commissioner for Science at FDA in the early 1970's, once characterized DEHP as "an etiology in search of a disease".

Assessment of DEHP

The Health Question:

- Does exposure to PVC medical devices result in adverse health effects ?

Risk Assessments

- American Council on Science and Health
  (chaired by C. Everett Koop)
- Eastman Chemical
  (chaired by John Doull)
- Health Care Without Harm
- NTP Center for the Evaluation of Risks to Human Reproduction
  (chaired by Robert Kavlock)

Assessment of DEHP

Citizen's Petition:

- June 99 - Health Care Without Harm

  requesting:

  - warning labels on all PVC devices that may leach phthalate plasticizers, and
  - expedite the development and usage of substitute materials

FDA Risk Assessment

Executive Summary
Introduction
Exposure Assessment
Hepatic Effects
Renal Effects
Pulmonary Effects
Reproductive Effects
Developmental Effects
Cardiovascular Effects
Hematological Effects
Cancer
Miscellaneous Effects
Risk Characterization
References

FDA Approach

Risk Assessment Approach Used:

"Margin of Exposure" **MOE**

- Ratio of the lowest dose that produced adverse effects in experimental animals

  (LOAEL)/dose of DEHP received by patients
- Avoids the need to define uncertainty factors

Interpretation of the MOE

- Not “bright line” values, intended to provide a general index of risk
- Large values (> 1000), little likelihood of adverse effects in humans
- Values close to 1, expose humans at the level adverse effects observed in animals
- Values between 10 and 100, risk management activities depends on various factors (nature of adverse effect, size and sensitivity of the affected population, availability of alternatives, etc.)

Risk Assessment Approach

- Identify factors that move the exposure towards 1
  - Size of patient
  - Duration of exposure
  - Characteristic of PVC device
    - Surface Area
    - Coatings
  - Use with substances that increase release of DHEP

Risk Assessment Approach

- Assess Common Clinical Exposures
  - Intravenous fluid administration
  - Intravenous drug administration
  - Total Parenteral Nutrition
  - Enteral feeding
  - Dialysis, Apheresis, ECMO
  - Blood and blood product transfusion

Risk/Benefit Assessment

- Product by product assess:
  - Potential for exposure at levels associated with toxicity in animals
  - Potential impact of toxicity in the clinical setting
  - Benefit associated with use of product causing the exposure
  - Potential alternative products and their risk/benefits

Potential Approaches

- Most products with PVC are not durable goods with long use life-times so changes in products will have rapid market effects;
- Market forces are resulting in the development of alternative materials for many products;
- Precedents exist to require labeling, for example latex containing devices where knowledge of exposure would allow choice of an alternative product

FDA Regulated Products and PVC

Issues

- Drugs: consistent labeling of products that
  - affect release of DEHP, or
  - require dose modification when administered through alternative tubing
- Blood: impact on red cell half-life
- Devices:
  - how will performance be affected by material changes;
  - what is the toxic potential of the new materials

FDA: Next Steps

- Internal review of risk assessment
- Public comment on risk assessment
- Determine which product areas warrant attention
- Develop strategies to improve risk/benefit for specific product areas