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# ELSIE

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## Summary

- Who & what is ELSIE
- Impetus for Formation
- Core Objective
- Benefits
- Governing Structure
- Current Activities

## ELSIE

- **E**xtractables and
- **L**eachables
- **S**afety
- **I**nformation
- **E**xchange

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## Membership

### Founding Members

- AstraZeneca
- Baxter
- Boehringer Ingelheim
- GlaxoSmithKline
- Pfizer
- sanofi aventis
- Schering-Plough

All pharmaceutical, biotechnology, and medical device companies are invited to join ELSIE. Several additional companies are actively considering membership.

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## History

- Initial discussions in February 2007
- Companies wanted to:
  - Reduce duplicative safety evaluation associated with leachables and extractables
  - Encourage accessibility and use of extractables safety information early in the development process, e.g., during materials selection
- ELSIE formally established in May 2007

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## Impetus for Formation:

### Identify “Best” Knowledge and Increase Knowledge Sharing

- Most extractables and leachables safety data comes from publicly available peer-reviewed scientific journals and government reports and databases. There has not been any industry-wide effort to compile, organize, appraise and summarize these data. Consequently, each company must undertake these efforts separately without benefit of the knowledge and experience gained through collaboration with other experts in industry and government, resulting in significant duplication across companies.

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## Impetus for Formation:

### Improve Efficiency

- Currently, there is no central source of safety data on which to base decisions regarding the need for additional safety studies (e.g., genotoxicity assays and in vivo studies). Therefore, there is a risk that such studies may be replicated unnecessarily.
- With the potential for multiple companies using the same container closure and/or device materials, there is a risk for duplicative animal studies. Sharing these data could support animal welfare objectives.

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## Impetus for Formation:

### Improve Risk Assessment & Decision-making

- The same or similar container closure materials are used in many different pharmaceuticals, biologics, and medical devices. There is no repository of extractables information (e.g., extractables profiles, study protocols) about these materials that could
  - Provide a basis for screening and selecting materials for use in product development; and
  - Expedite further product-specific extraction studies.
- If an extractables/leachables safety issue is not detected until the later stages of development, a company may experience substantial, unanticipated delays in product development, regulatory review, and market introduction, which could deprive patients of timely access to their medications. A database would facilitate early prediction of safety concerns.

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## Core Objective

ELSIE's core objective is to establish a comprehensive database that will provide a jointly-developed and credible source of

- ❑ Safety information on extractables and leachables and
- ❑ Extraction profiles and standardized study protocols for a range of materials commonly used in medical devices and container closure systems.

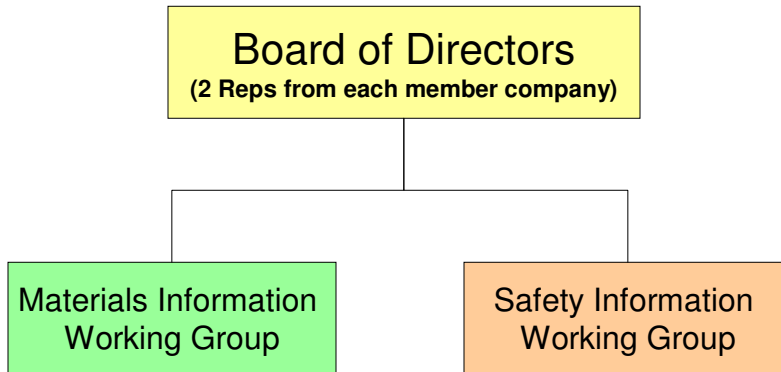
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## Benefits of ELSIE Deliverables

- Improve efficiency of the development process
- Reduce unnecessary animal testing
- Advance regulatory Quality by Design Initiatives
  - ❑ Advance ICH Q8, Q9, Q10 principles
- Strengthen supplier-manufacturer relationships
- Facilitate development of high quality and safe products for patients
- Confirm patient safety and product quality as priority goals of the medical products industry

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## Governing Structure



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## Safety Information Working Group

- Goal: Develop database of safety information on extractables and leachables

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## Safety Information Working Group: Status

- Finalized prototype ELSIE safety information “database”
  - Includes key data fields and illustrates organization, structure and other core aspects of database
- Developed detailed “user requirements” for safety database, including search capability and other tools
- Progressed compilation of leachable and extractable compounds for inclusion in safety database
  - Intended to illustrate vision for database and facilitate priority-setting; current list contains approximately 210 compounds
- Initiated contact with FDA to share information on ELSIE and solicit the Agency’s feedback
  - **Meeting with FDA/CDER/ONDQA and FDA/CDRH on 4 May 2009**

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## Safety Information Working Group: Actions

- Identify priority compounds for input into database during first phase
- Solicit safety information data from member companies
  - ELSIE Secretariat will review, organize and further summarize (as needed) data submitted by companies and then input into database
    - Processes for periodic updating; quality review and assessment will be developed
- Progress development of database application
- Continue to compile leachables and extractables list

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## ELSIE Meeting with FDA (4 May 2009)

- FDA CDER and CDRH have expressed interest in the ELSIE effort
- CDER has indicated interest in a future meeting once further data and progress has been made
- CDRH has indicated interest in continuing dialogue with ELSIE

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## Materials Information Working Group

### Goal:

- Develop database of extractables information (e.g., controlled extractables data and chromatographic profiles, and study protocols) on materials used for container closure systems and devices that could: (i) provide a basis for screening and selecting materials for use in product development and (ii) expedite further product-specific extraction and/or leachable studies
- Currently in pilot stage; feasibility will be assessed during 2009

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## Materials Information Working Group: Status

- Identified and conducted molding studies on 2 materials for pilot program
  - PVC and polyethylene

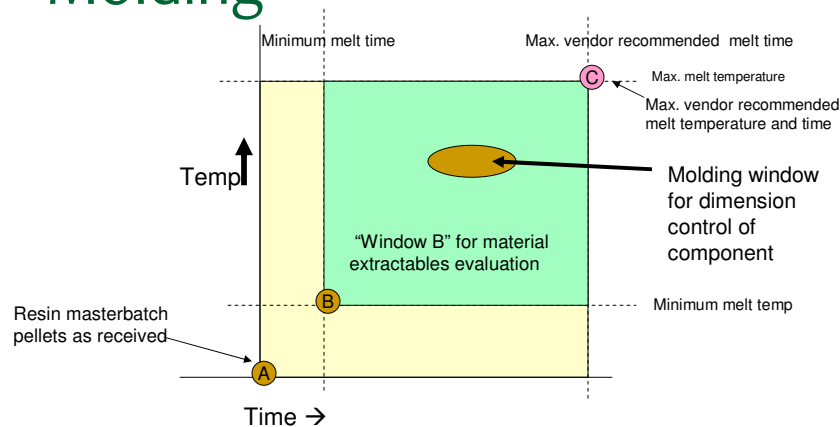
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## Materials Information Working Group: Status

- Developed protocol for Pilot Program: *Controlled Extraction Studies on Materials for ELSIE Database – Qualitative and Semi-Quantitative Studies*
  - Studies to be conducted on the 2 materials (molded and unmolded forms)
  - Covers studies for a variety of product types (e.g., parenterals, inhalation products, ophthalmics), therefore includes wide variety of solvents, and extraction and analytical techniques
  - General principals and findings from the Pilot Program will be used to create more focused protocols

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## Design Space Concept for Molding



Remember - Molding windows change during the life of a drug product

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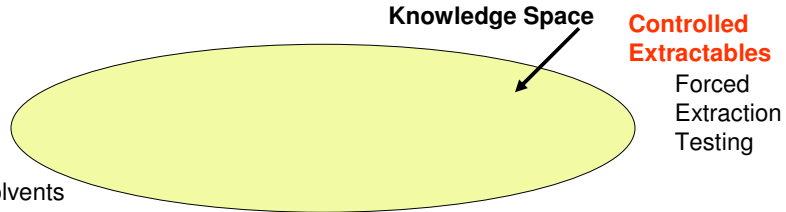
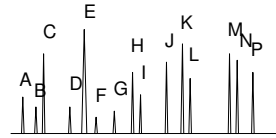
## Material Extractables Method Summary

- Standardized Protocol
  - 7 Solvents
    - Water - pH 2.5, neutral, 9.5 ; IPA; IPA:Water(1:1), MeCl<sub>2</sub>; Hexane
  - Analytical Methods
    - GC/MS, FID – neat, direct injection
    - LC/DAD/MS
    - ICP/MS
  - Screening Extraction Methods
    - Sonication; Reflux; Soxhlet; Sealed container; Microwave; ASE; Headspace

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## E&L Knowledge Space Extractables

Knowledge Space for Material XYZ is Determined and Stored by ELSIE in a Database.



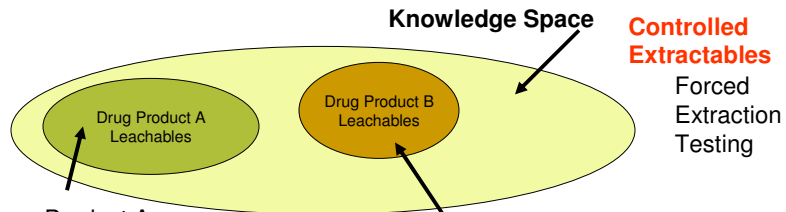
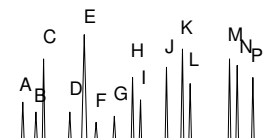
7 solvents plus 4 analytical techniques

Multiple solvents over a wide span of polarity followed by analysis using multiple techniques to "cover" most drug product types

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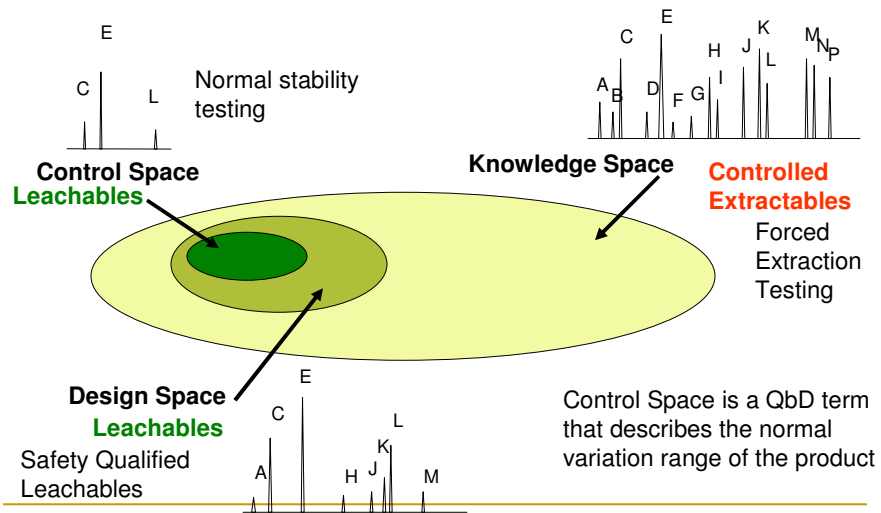
## E&L Design Space Leachables

Within the Knowledge Space of Material XYZ multiple Design Spaces exist. Each unique formulation will have a unique Design leachables space.



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## E&L Control Space



## Materials Information Working Group: Status

- Initiated contacts with CROs for conducting pilot study testing/analysis for ELSIE, on a volunteer basis

## Materials Information Working Group:

### Actions

- Protocol for controlled extraction studies in pilot project to be discussed with CROs
- Coordinated with Safety Information Working Group on planning for 4 May meeting with FDA
- Coordinate with Safety Information Working Group to prioritize compounds for safety database
- Undertake controlled extraction studies
- Assess feasibility of materials database concept based on data and outcomes of controlled extraction studies

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## Acknowledgements

- Special thanks
- Art Shaw, Pfizer
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