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Summary

- Who & what is ELSIE
- Impetus for Formation
- Core Objectives
- Benefits
- Governing Structure
- Current Activities
 - Safety Information Working Group
 - Materials Information Working Group
 - Detail on Protocol Concepts
- Acknowledgements

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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

Safety (Toxicological) Database

- Eliminates repetitive literature searches on the same chemicals
- Encourages shared peer knowledge
- Eliminates unnecessary repetitive animal testing
- Speeds new medicines to market
- Reduces cost while improving the safety of all medicines

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Impetus for Formation:

Improve Risk Assessment & Decision-making

Materials (Controlled Extractables) Database

- Allows for a QbD approach to packaging selection
 - Screening of materials for safety issues
 - Simplifies the regulatory testing
 - Reduces the risk of poor material choices
- Enables rapid start to leachables testing on individual drug products
- Speeds new medicines to market while reducing costs

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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.

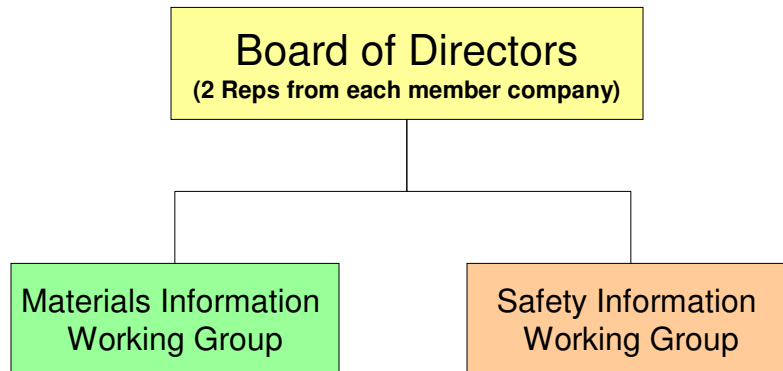
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Benefits of ELSIE Deliverables

- 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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Progress and Current Activities

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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Safety Information Working Group

Progress and Current Activities

- Goal: Develop database of safety information on extractables and leachables
- Progress:
 - Finalized the safety contents and format for the chemicals in the database
 - Shared for feedback with the FDA on 4 May 2009
 - Compiled a list of 210 chemicals to be researched and added to the database.

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Safety Information Working Group:

Current Activities

- Identify priority compounds for input into database during first phase
- Develop new sources and methods for capturing safety information
- Piloting a computer database application with member companies
- Continue to collect and compile leachables and extractables lists

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Materials Information Working Group

Progress and Current Activities

- **Goals : Develop a database of extractables information that covers a variety of product types (e.g., parenterals, inhalation products, ophthalmics)**
- Progress:
 - Finalized a pilot analytical testing protocol for the generation of controlled extractables
 - Identified and conducted molding studies on 2 materials for pilot program
 - Polyethylene and PVC plastic

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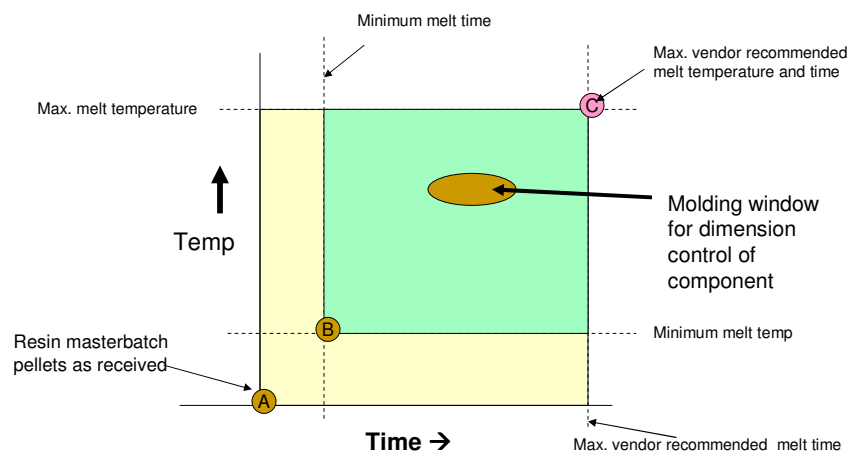
Materials Information Working Group:

Current and Future Activities

- Sourcing parts of the pilot protocol to volunteer CRO analytical labs (ongoing)
- Evaluate the study results
- Finalize the ELSIE material's protocol based on pilot results (1Q/2010)
- Initiate testing of materials with CRO analytical laboratories for database population (2Q/2010)

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Design Space Concept for Molding



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

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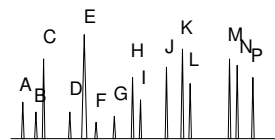
Material Extractables Method Summary

- Standardized Protocol
 - 7 Solvents
 - Water - pH 2.5, neutral, 9.5 ; IPA; IPA:Water(1:1), MeCl₂; 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.



Knowledge Space

Controlled Extractables

Forced Extraction Testing

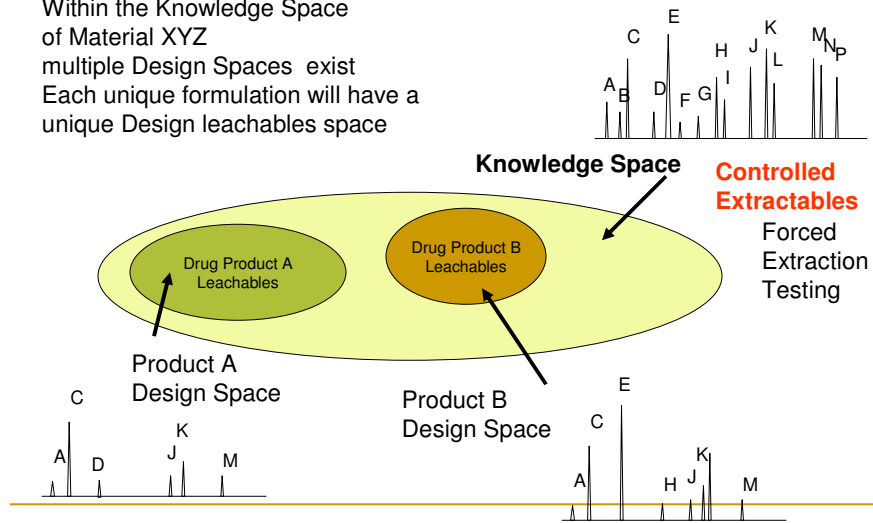
7 solvents plus 4 analytical techniques

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

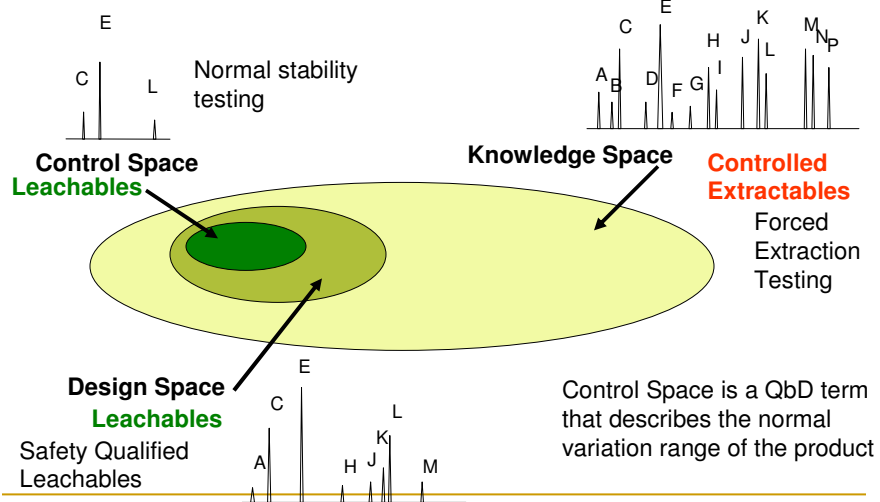
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E&L Design Space Leachables

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



E&L Control Space



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