Extractables and Leachables Safety Information Exchange: Creating an Extractables/Leachables Database

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Introduction

The Extractables and Leachables Safety Information Exchange (ELSIE) is a consortium of pharmaceutical, medical device delivery, and biotechnology companies.

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

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

ELSIE was formed in 2007. Current members include: AstraZeneca, Baxter International, Boehringer Ingelheim, GlaxoSmithKline, Pfizer, sanofi-aventis, and Schering Plough.

Why Create A Database?

1. **Identify "Best" Knowledge and Increase Knowledge Sharing**
   - There has not been any industry-wide effort to compile, organize, appraise and summarize extractables/leachables data from public sources

     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.
2. **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 conducted unnecessarily.
3. **Improve Risk Assessment and 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

Why Create A Database?

- 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 detection of safety concerns.

Elsie Governing Structure

ELSIE is managed by a Board of Directors, comprised of two representatives from each member company. The Board convened two working groups: the Safety Information Working Group and a Materials Information Working Group. Information is shared among all these bodies as shown in **Figure 1**.

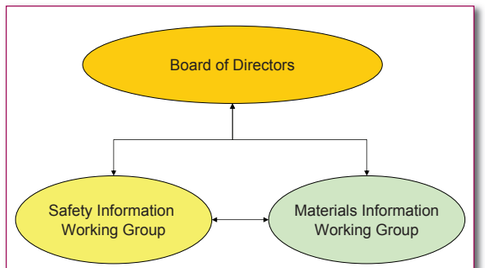

Figure 1. Organization of ELSIE

What Is Elsie Doing To Create A Database?

To date ELSIE has:

- Developed a prototype database for safety information using di-ethylhexylphthalate as a model
- Compiled an initial list of chemical entities for inclusion in the database
- Begun a pilot program to create controlled extraction studies protocols and to generate data, which will be evaluated to define the scope and elements of a materials information database

The safety information database would include publicly available information that is relevant for inclusion in regulatory submissions, and which would be derived from the literature research and prior experience of ELSIE members. The Consortium will, in future, consider the inclusion of proprietary safety data.

Figure 2 shows the general process for creating the safety database.

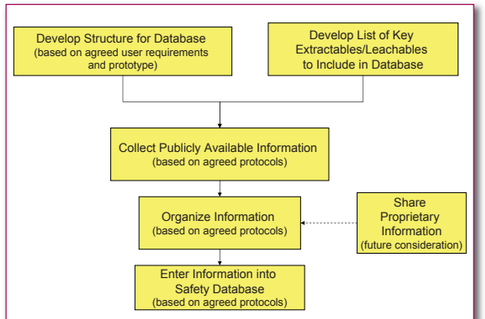

Figure 2. General process for creating the safety information database

Figure 3 shows the general process for conducting the pilot program to assess the feasibility of a materials information database. The pilot program will focus on polymers as a first step. It is envisioned that a materials information database would be linked to the safety information database.

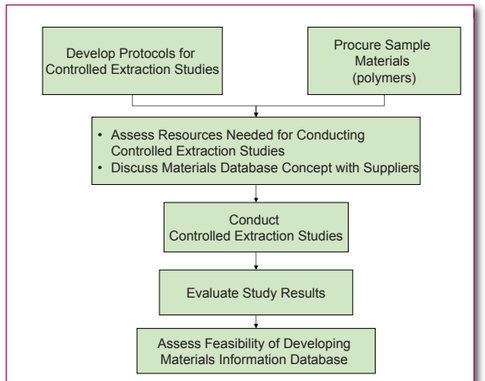

Figure 3. General process for conducting the pilot program to assess feasibility of developing a materials information database

The pilot is envisioned to include extractables assessment for the entire "molding design window" of the polymer materials. The window is bounded by the maximum temperature and residence time the polymer can be subjected to as specified by the polymer's manufacturer.

Figure 4 illustrates how extractables information (e.g., profiles) gathered from un-molded polymer and polymer molded at maximum vendor recommended conditions plus knowledge of potential degradation pathways can be used to build an extractables "knowledge space."

A materials database would include this extractables information and the protocols used to obtain this information.

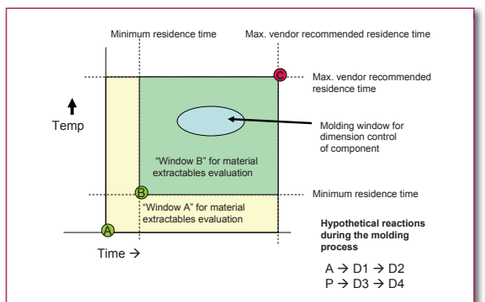

Figure 4. Extractables information on plastic at point A and point C plus knowledge of potential degradation pathways is used to build the molding "knowledge space".

Benefits Of Elsie Deliverables

- Advance ICH Q8, Q9, Q10 and Quality by Design concepts by enhancing the prospects for identifying potential safety issues at the initial stages of the development process, when container-closure materials are being screened and selected
- Reduce duplication of effort and minimize testing
- Facilitate development of high quality and safe products for patients
- Confirm patient safety and product quality as priority goals of the medical products industry
- Strengthen supplier-manufacturer relationships
- Serve as a forum for exchanging experience and perspectives among experts
- Decrease the risk of substantial, unanticipated delays and associated costs

Next Steps

- Development and implementation of user requirements for the safety database
- Prioritization of chemical entities on the list of key extractables/leachables to include in safety database
- Development of protocols for data collection, organization and entry
- Development of protocols for database access
- Complete controlled extraction study protocols
- Assess resources needed to conduct controlled extraction studies
- Discuss materials information database concept with materials suppliers

To Join Elsie

All pharmaceutical, biotechnology, and medical device companies are invited to join ELSIE.

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