

THE PROPER USE OF EXTRACTABLES DATA - ASPECTS BEYOND EXTRACTABLES-MEASUREMENT

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Appropriate extraction techniques for SUS/SUT and methods for analysis of extractables have been intensively discussed over the last years. Today, several proposals for common methods are available and used to conduct extractables studies in the bio-pharmaceutical industry. Therefore it is expected that the number of available extractables data will significantly rise over the next years and it is worth to (re-)consider their proper use for materials and device qualification and risk assessment. While this exercise is straightforward for container closure systems (CCS), for SUS/SUT the situation is more complex. In CCS applications, a single drug product, in contact with a well-defined container system for long term storage is studied. In contrast to a CCS the number of materials, their dimensions and combinations are highly flexible in SUS/SUT applications. Additionally, SUS/SUT are used under dynamic process-conditions of variable solvents, dwell-times, temperatures, flow-rates etc.

In our contribution we will discuss two major questions that persist and cannot be solved by means of analytics alone:

1. How can we obtain extractables data for SUS/SUT devices of different sizes and for complex device combinations (assemblies)? This aspect is critical for the device industry, because a high number of different devices and combinations are requested by our customers. Further, assembled products from Configured to Order (CTO) or Engineered to Order (ETO) processes utilizing various compounds, even such from various suppliers can increase their amount and combinations nearly infinitely. It is easily conceivable that it is technically impossible to conduct individual extractables studies for each possible combination.
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3. Another aspect which has to be taken into account in the future, is the proper use of extractables data for extrapolations toward potential leachables required for quality risk-assessment. In this context a publication from Jenke & Rabinow (2017) has to be considered, where they showed that the validity of the "intuitive" approach to scale extractables data just by surface area is questionable.

We will show how we can develop methods to overcome these - so far - unsolved problems. The proposed methods will be based on basic physical chemistry principles rather than "intuitive" worst-case assumptions. We will show illustrative examples on how extractables data, obtained by different protocols can be used heuristically in scaling and combination exercises. The limits of the conventional scaling by surface areas are discussed in terms of the influence of equilibrium versus diffusion controlled conditions in long versus short term contact.

Furthermore, an example will be shown for a calculation of potential leachables solely built on physical chemistry considerations and avoiding any generic worst-case assumption.

Jenke & Rabinow: Proper Accounting for Surface Area to Solution Volume Ratios in Exaggerated Extractions
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