PALL Biotech

USD 3355

Accelerator℠ Validation Services

Technical, Regulatory and Scientific Consulting Services to Support Process Qualification and Validation

Filtration. Separation. Solution.℠

Validation Expertise

The evolution of the pharmaceutical industry is arguably faster today than throughout most of its history and is driven by new science, new drug therapies and significant shifts in socioeconomic environments.

This evolution applies macroscopic pressures for change and fuels industry growth but underneath these changes, the validation requirements, driven by cGMP, continue to be a critical contributor to the assurance of quality and patient safety.

Quality Risk Management (QRM) and Quality by Design (QbD) drive a greater awareness of risk, which, in turn, necessitates a deeper understanding of operational performance and how this may impact the critical quality attributes of the drug product. This requires more, and better, data to establish rationales and/or controls that define or mitigate these risks.

Complex formulations including, but not limited to, surfactant solutions, liposomes, lipids, emulsions and lipid-like drug products are increasingly required to meet drug delivery and stability challenges. These introduce new challenges to mature technology such as sterilizing grade filtration.

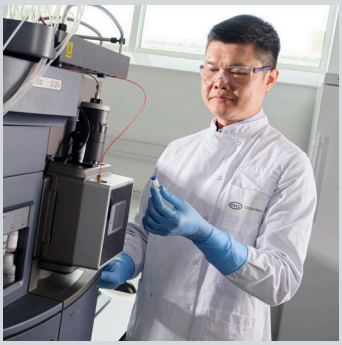
New manufacturing paradigms – While the adoption of single-use equipment, and the controls required to define the safety of these, is commonplace, the first wave of processes that employ elements of continuous processing are now starting to receive regulatory approval. This new design space brings a new validation challenge for many technologies.

Not all processes will be equally impacted by these changes, but developing and maintaining processes, to meet the requirements of regulatory bodies, continues to provide a challenge that must be met.

This often requires specialist knowledge and testing capabilities. It is here that a trusted validation partner provides the knowledge and experience that ensures the delivery of relevant and high quality data needed to support your process.

With over 40 years of validation expertise, Pall has contributed to the development of many of the current standards relating to critical filter validation and the use of single-use systems, and we continue to be at the forefront of the development to support the adoption of continuous processing technology.

Our professional and confidential consultancy services and capabilities include:



Common Tests

- Bacterial retention testing
- Compatibility testing
- Extractables consultancy
- Extractables and leachables testing
- Leachables reduction testing (flush studies)
- Product wet integrity test parameters

Analytical Methods

- Non-volatile residue (NVR)
- FTIR spectroscopy
- LC/UV-MS
- Direct injection GC-MS
- Headspace GC-MS
- ICP-MS

Hundreds of scientists, engineers and technicians providing global coverage and local support

Testing, without appropriate planning, control and project management, rarely delivers what is needed first time. Validation projects are managed by your own dedicated project manager. Once assigned they manage the process from project initiation and scheduling, through protocol development and laboratory testing, to the final report creation and project closure. Throughout this process a clear and transparent dialog keeps you up to date with all progress.

“The first consultation is important to build a good working relationship, understand the process and collect all the relevant information. This allows me to recommend the best validation approach for a right first time study that meets the regulatory requirements.”

Ian Sharkey
Validation Project Manager, UK

Validation of Performance; Critical Filter Validation

Validation of the performance of critical filters, such as sterilizing grade filtration has been required by many regulatory bodies since the 1990s. Pall has supported this need since conception and has always been at the forefront to establishing best practices and industry guidance.

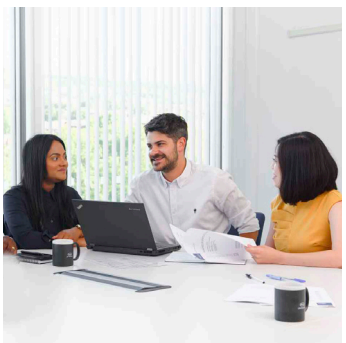
"Regulators recognize that some fluids behave differently and may require greater control of the process parameters to assure sterility of the final drug product. When risks are identified, the nature of these fluids necessitates additional testing to identify those process parameters that will result in a sterile effluent."

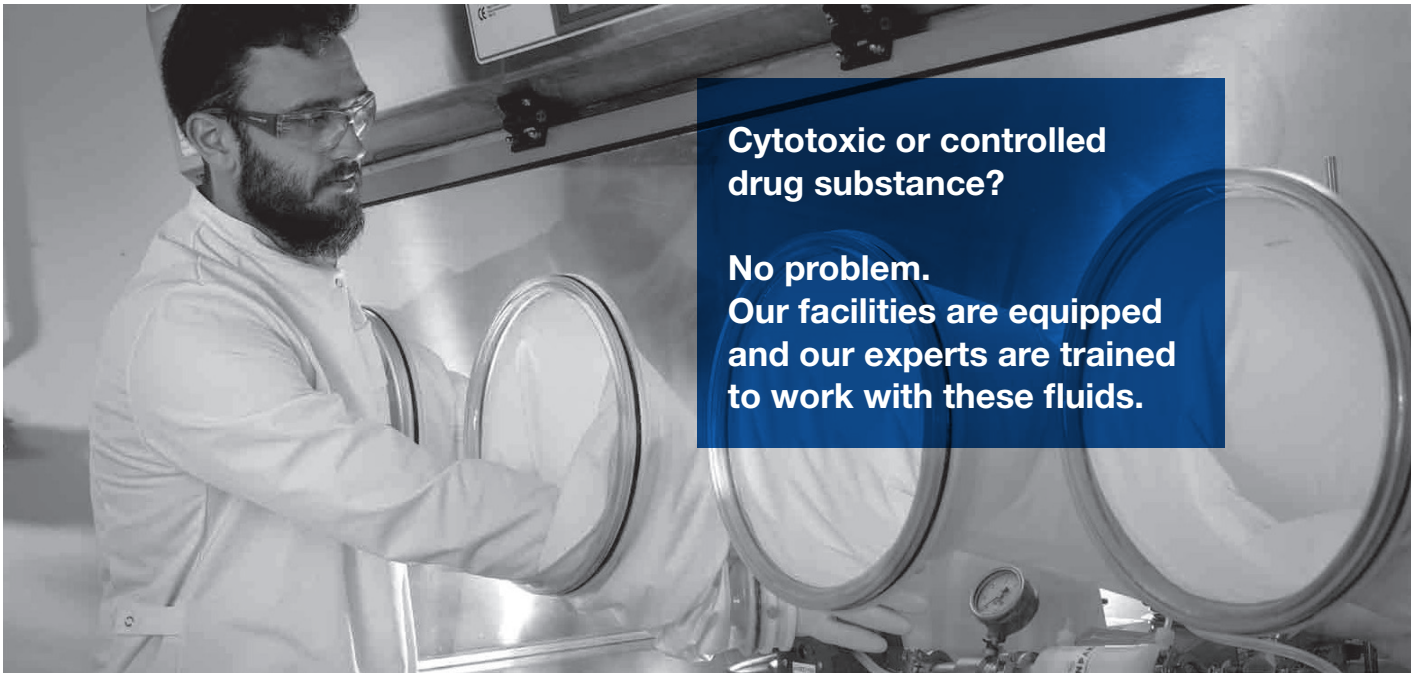
Martha Folmsbee Ph.D, Principle Scientist, USA

Sterility Optimization through the Assessment of Risk (SOAR)

Fluids with known risk factors such as surfactant solutions, liposomes, lipids, emulsions and lipid-like solutions increase the risk of bacterial penetration. This is often only realized when the validation study fails and is a painful and costly discovery that can be avoided. Identifying this risk early is part of Quality Risk Management and this knowledge helps optimize the critical control points within the process and the subsequent testing parameters used during validation. When applied during process development, the SOAR program mitigates these risks and maximizes sterility assurance through Quality by Design.

The SOAR program helps evaluate the risk to sterility of any given set of processing conditions before initiating the formal filter validation study. Where risks are identified, early screening studies can be performed to ensure your filter selection and desired process design space combine to ensure the final filter validation study achieves the desired outcome.





Bacterial Retention

Data to prove the performance of critical sterilizing grade filters under the worst-case process conditions is a regulatory requirement and is needed for license applications and when process changes take the process conditions beyond the approved design space.

These studies include:

Viability Testing – Identifying fluid characteristics to establish appropriate controls and test methods for bacterial retention testing.

Bacterial Retention Testing – Establishing performance data, typically when challenged with *Brevundimonas diminuta* at a concentration of ≥ 10^7 CFU/cm^2. However methods using other challenge organisms such as process isolates can be developed where required.

Qualification Testing

Data that supports the use of a filter in a manufacturing process can be used to define suitability, help to establish optimal process controls and to streamline filtration processes

Typical studies include:

Adsorption Testing & Flush Studies – Whether defining product or excipient adsorption or minimizing leachables with a defined flush volume, good data can influence operational parameters and filter choices to control and minimize the impact on the process.

Product Wet Integrity Test Parameter Derivation – Generating process specific integrity test data as an alternative to water or alcohol solutions to reduce process complexity and / or to avoid dilution or potential incompatibility with residual wetting fluids.

Compatibility Testing – Confirming physicochemical suitability under worst-case process conditions.

Extractables and Leachables

The need to define and evaluate the impact of product contact components that may migrate into the drug product to influence the safety, quality or potency of the drug product has grown with the rise of single-use systems.

The approach to performing a suitable risk assessment, and the ongoing evolution of the data to support this, has developed through a number of industry bodies with the help of industry contributors, including Pall. These bodies include the Parenteral Drug Association (PDA), BioPhorum Operations Group (BPOG) and United States Pharmacopeia (USP). While the guidance does vary all approaches support the principles of Quality Risk Management.

Consultancy

Many Pall products are supported by comprehensive analyses of extractables using a growing matrix of solvents such as those recommended in BPOG reports. Data are available upon request, however, interpreting the data to establish the relevance to the proposed process conditions may not be simple. Through our extensive history in the evolution of the understanding of extractables and leachables we can assist with this interpretation and help prepare suitable justification, including toxicological review, in preparation for any license application.

Extractables

Where generic data are not sufficient, we can offer process specific extractables testing that establishes a reasonable worst-case model solvent, worst-case process conditions, the most appropriate test system and optimal analytical methods, typically GC/MS, LC/UV/MS and ICP/MS. These combine to deliver a set of data that can then be used for a subsequent risk assessment.

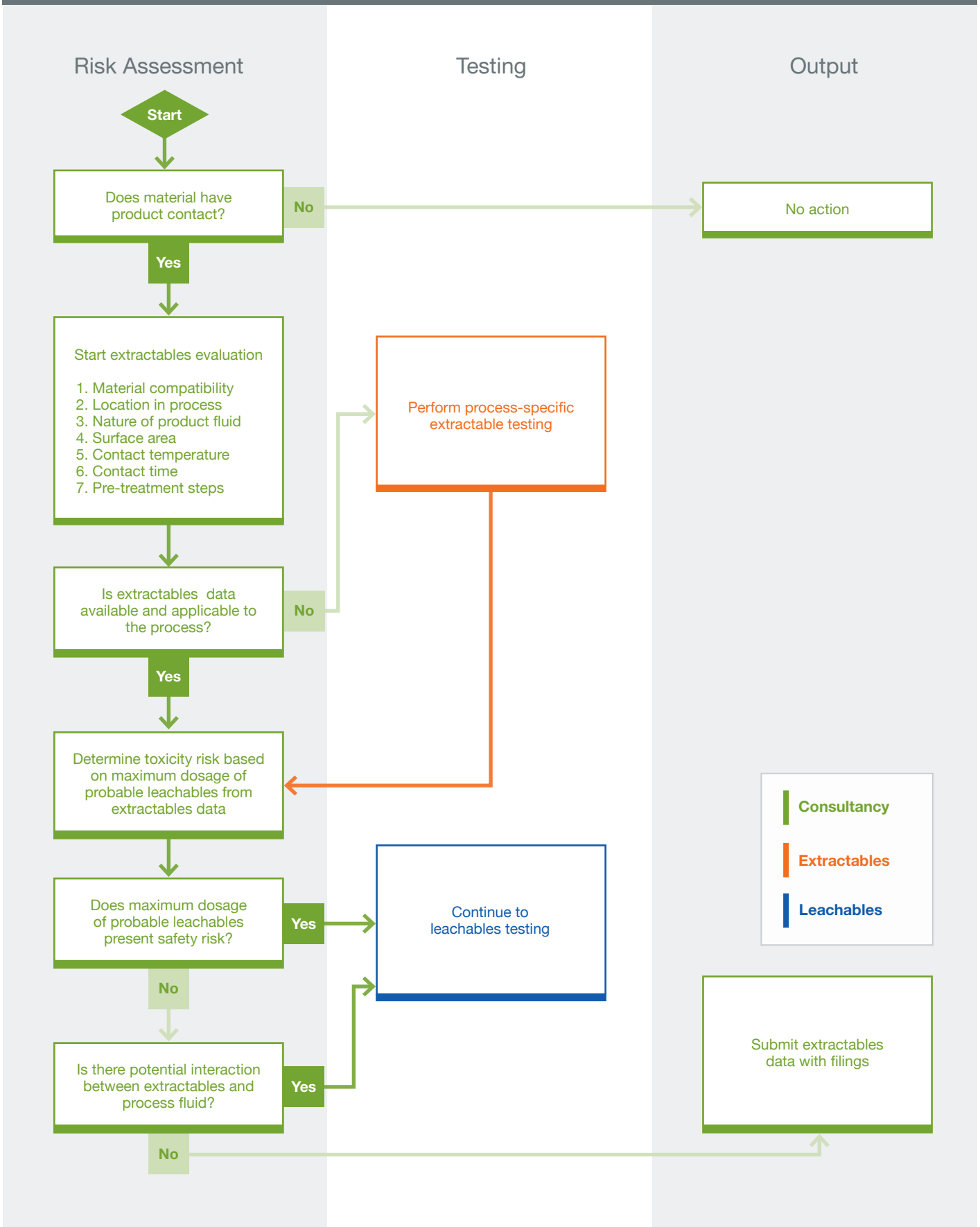
Leachables

When the review of the available extractables reports highlights a need for data that more closely represents the actual process conditions, leachable studies deliver the most relevant set of data. These studies include the selection of extracting fluid which may require a suitable placebo or simulant where one or more product components interfere with the required analytical methods. These data then form the basis of the risk assessment.

"Whether it originates from an existing extractables study or from a product-specific leachable study, data helps to assess potential risks associated with the final product dosage. Our experience enables us to create a robust justification that is clearly reported and matches the current regulatory requirements to help the customer progress quickly, while ensuring patient safety."

Clovin Adarsh, Scientist, Bangalore, India

Extractables and Leachables Evaluation



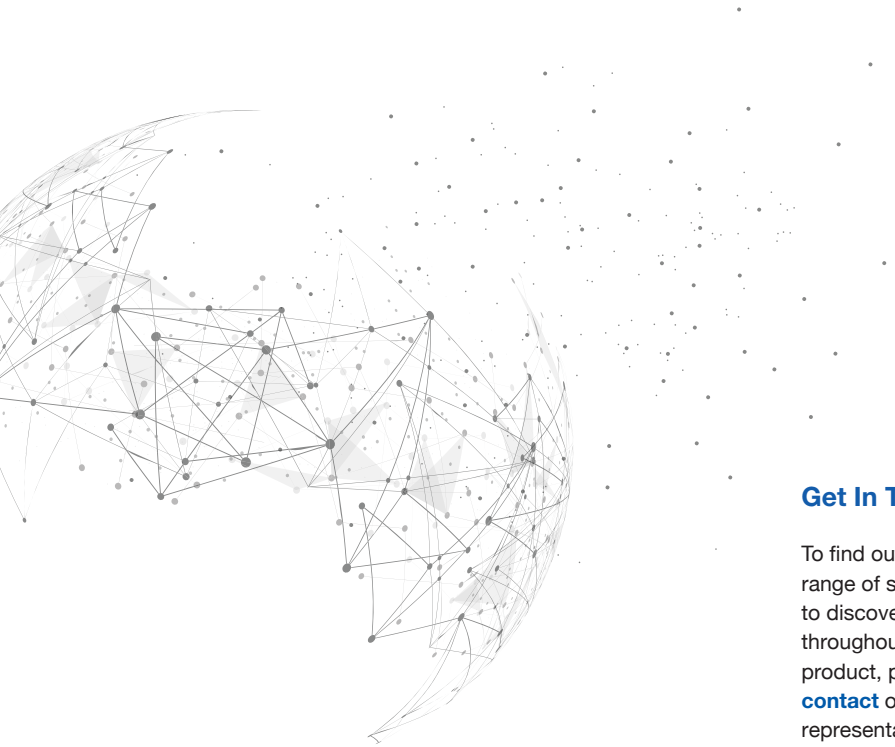
About Pall Biotech

With a global team supporting Pall Biotech, we provide the cutting edge products and services to meet your needs as you discover, develop and produce life saving pharmaceuticals.

Our technology is backed by industry-leading, lifetime support solutions to assist you from upstream to downstream, and final fill throughout all phases of drug development and production.

Our multiple validation hubs sited in key locations mean you can think globally but work with our regional teams, to ensure projects run smoothly and efficiently.

And with over 70 years experience, you can be assured that we have the knowledge, expertise, and global infrastructure needed to deliver the solutions and service you require, to meet the challenges you face in this demanding, exciting, ever-changing market!



Get In Touch!

To find out more about Pall Biotech's range of services and technologies, and to discover how we can support you throughout the lifecycle of your product, please go to **www.pall.com/contact** or contact your local Pall representative.

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