Container Closure Integrity Test as a Substitute for Sterility Testing USP 1207.1 using a Quantitative Leak Test Dye Ingress Method.

For pharmaceutical sterile product packages USP 1207.1 states with well-designed test protocols, taking into consideration the multiple factors and variables that can influence results, liquid leakage risk assessment studies may substitute for microbial ingress risk studies assuming the risk of liquid leakage is equivalent to or greater than that of microbial ingress, with appropriate justification.

To justify validated physiochemical leak test methods, a study comparing the risk of microbial ingress or liquid leakage to leak type/size, and in turn to the likelihood of detection by the physicochemical leak test method would be required. This should include negative and positive controls which are designed and assembled for use in method development and validation with consideration given to container–closure design, materials of construction, characteristics of anticipated package leaks, and impact of product contents on test results. *"Negative controls"* are packages with no known leak, and *"positive controls"* are packages with intentional or known leaks.

Microbial challenge tests provide information on the degree of protection afforded by the product–package against microbial ingress that occurs via active growth or motility through leak pathways and/or by liquid carrier passive transport through leak pathways. Microbiological challenge tests help to clarify the risks to product sterility posed by specific package materials, package designs, or potential package barrier breaches. Sterility risks linked to particular environmental exposure or product use conditions may also demand a microbiological challenge methodology.

For the above to work the maximum allowable leakage limit of the product package need to be known. Where the physicochemical leak test method has a proven detection limit at or below the product-package maximum allowable leakage limit a comparison study of the microbial ingress or liquid leakage risk to physicochemical leak test method capability relationship is likely not needed.

Where physiochemical leak test methods can be justified to substitute for sterility testing it gives pharmaceutical companies a more economical cost saving methodology for testing such as stability trials or in process controls for batch manufacture. To discuss your requirements for validation of a quantitative leak test dye ingress method or performing leak test methodology contact Tepnel Pharma Services.

We have over 40 years of experience with a proven track record of working in partnership with pharmaceutical companies providing pharmaceutical testing services that are not core to their business, releasing people and management time to add value to the pharmaceutical drug development process. Our cGMP pharmaceutical testing facility is located in Livingston, Scotland where we work together with our customers and partners building mutual trust through a sharing of knowledge, expertise and teamwork.

Our services include:

- **Lot and batch release testing**
- **ICH stability testing and storage**
- **Raw materials testing**
- **Pharmacopeial testing**
- **ICH method development and validation**

To find out how partnering with Tepnel can reduce cost and accelerate your drug development programme please contact:

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