Lonza

Endotoxin Results and PPC Recovery

Technical Tips

By Lonza Scientific Support, U.S.

The Bacterial Endotoxins Test Monograph (BET) requires that when a final product is being tested for the presence of endotoxin, a Positive Product Control (PPC) is included to confirm that the product being tested, at the validated dilution, is free of interfering factors.

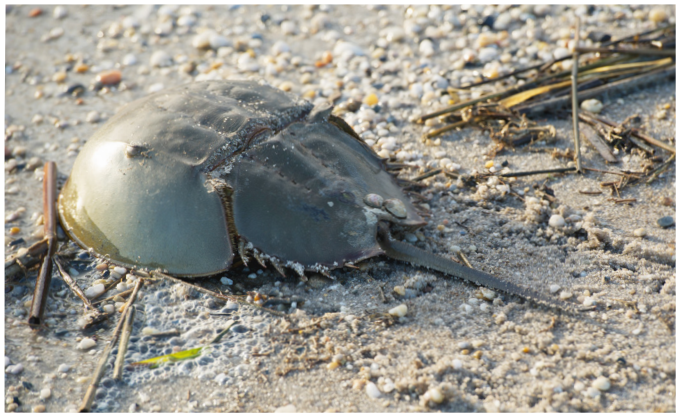
The USP BET Monograph states:
"Calculate the mean recovery of the added endotoxin by subtracting the mean endotoxin concentration in the solution, if any, from that containing the added endotoxin. In order to be considered free of factors that interfere with the assay under the conditions of the test, the measured concentration of the endotoxin added to the sample solution must be within 50% – 200% of the known added endotoxin concentration after subtraction of any endotoxin detected in the solution without added endotoxin."

The Function of the PPC

It should be noted, that the function of the PPC (test sample containing a known concentration of added endotoxin) in the final product test is different from its function in a product characterization study (which should always be part of a validation exercise). During a validation study, the role of the PPC is to indicate the degree of interference present in a series of dilutions up to and including the Maximum Valid Dilution (MVD), to allow the user to select a suitable dilution for the final part of the validation study. Selection of the dilution to be used for the final part of the validation study will depend on several factors:

- The MVD
- The degree of interference that can be overcome by dilution
- The desire to detect/quantify low amounts of endotoxin (increasing dilution raises the detectable limit)

Any dilution that is less than or equal to the MVD can be selected for the final part of the validation study and subsequent release testing, provided that the recovery of the known endotoxin concentration added to the PPC is within 50 – 200%. However, we would normally recommend that users select dilutions that are less than



the MVD, and produced recoveries within the range of 70 – 130%. If the selected dilution produced recoveries outside of this range, then there is always a chance that natural variations in the assay could cause an endotoxin recovery failure for the PPC and thus an invalid result during the final part of the validation or during release testing.

Once a dilution has been selected and validated with a minimum of three different batches of product to show consistency, the product can be tested for final release using this dilution.

Final Product Release Testing

The function of the PPC in the final release test is different from that in the product characterization assay. During release testing, a passing result for endotoxin recovery for the PPC indicates that:

- The product formulation did not change in a way that would impact the validity of the endotoxin testing
- No interfering factors have been introduced e.g. from a sample container

When conducting a final release test, it is mandatory to test the sample in duplicate and also to test the PPC in duplicate. The criteria for a successful product release test are two-fold:

- The calculated endotoxin concentration for the undiluted product is below the specified endotoxin limit for this product
- The recovery of the known added endotoxin concentration in the PPC is within 50% – 200%

Please note that there is no requirement in the BET monograph for the PPC's endotoxin recovery to be any specific value. However, manufacturers would be wise to regard with caution any results where the recovery is right on the limit e.g. 51%.

This means that any sample showing an endotoxin concentration below its established endotoxin limit and for which the PPC's endotoxin recovery is within 50% – 200%, indicates that the product should be regarded as acceptable by any regulatory authority.

Contact Us

North America
Customer Service: +1 800 638 8174 (toll free)
order.us@lonza.com
Scientific Support: +1 800 521 0390 (toll free)
scientific.support@lonza.com

Europe
Customer Service: +32 87 321 611
order.europe@lonza.com
Scientific Support: +32 87 321 611
scientific.support.eu@lonza.com

International
Contact your local Lonza Distributor
Customer Service: +1 301 898 7025
Fax: +1 301 845 8291
scientific.support@lonza.com

Lonza Walkersville, Inc. – Walkersville, MD 21793

Learn more.

RT-DS028 01/24

lonza.com/lal