FASTFACTS

GMP compliant residual PEIpro® test: one step closer to commercialization

In the last few years the cell and gene therapy industry has seen an explosion in the number of clinical trials based on the use of viral vectors, and adeno-associated virus and lentivirus-based vectors represent the majority of vectors used. This has caused their manufacturing needs to grow substantially and made the production of safe, high purity viral vectors even more crucial. Leveraging twenty years of expertise, Polyplus-transfection has developed a residual test to guarantee detection of PEIpro® transfection reagent with specificity, sensitivity and accuracy during the viral vector manufacturing process: Residual PEIpro® test.

WHY PERFORM RESIDUAL IMPURITY TESTING?

Transfection is a key step of viral vector production, and therefore transfection reagents are a critical raw material required for the manufacturing of therapeutic vectors. To ensure purity, manufacturers must determine the quantities of raw materials present at various stages of the process, in order to produce a final medicinal product that meets regulatory guidelines and is safe for patient administration.

HOW CAN CRITICAL RAW MATERIALS BE QUANTIFIED AND DETECTED?

The upstream steps of viral vector manufacture generate a complex mixture of both virus and residual amounts of the raw materials used for production. Ideally, manufacturers should determine what quantity, if any, of raw material is still present in the final drug product, as well as the significance of the level detected. To ensure that all traces of transfection reagent are removed during downstream processing, a reliable, validated testing method that tests specifically for residual transfection reagent is required. Polyplus-transfection's Residual PEIpro® test is a unique analytical test designed to detect and qualify the presence of residual PEIpro® during the production of viral vectors at different steps of the manufacturing process (Figure 1).

HOW WAS THE TEST VALIDATED?

The Residual PEIpro® test was validated on six key criteria (Figure 2) on a number of batches of PEIpro® in order to ensure robust results. The test is GMP-complaint, utilizes a HPLC/UV method, and was developed based on regulatory recommendations.

WHY CHOOSE PEIpro®?

The Residual PEIpro® test guarantees specific detection and accurate quantification of PEIpro® transfection reagent at all steps of manufacturing, and in final advanced therapy medicinal products. The test is flexible, and can be adapted to specific manufacturing processes in order to provide the lowest possible limit of detection. With the development of this test, Polyplus-transfection now can offer a fully-integrated package for viral vector manufacturers at each stage of project development. A reliable test for detection of residual transfection agent is key to mitigating risk and manufacturing a final product which is compliant with relevant regulatory guidance, and ultimately, safer for patients.

Figure 1. PEIpro® can be used both in-process and to detect and quantify residual transfection reagent in final product.

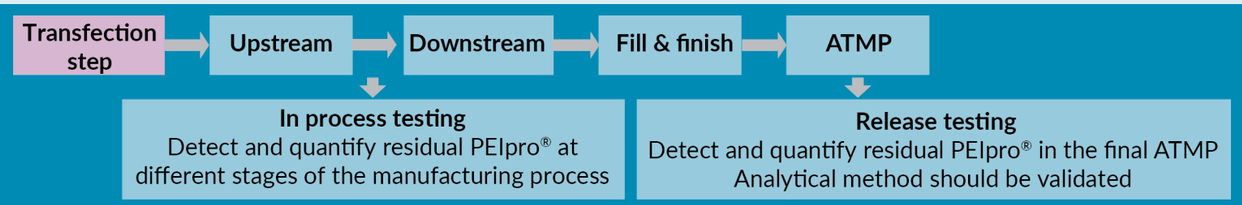
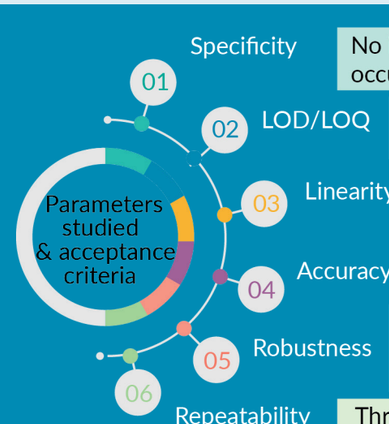


Figure 2. Residual PEIpro® testing acceptance criteria and results.



Specificity	No interference above 5% of the peak area of PEIpro® in PEIpro® reference solution at 20.0 µg/mL should occur at the retention time of PEIpro® in the chromatograms of blank and blank treated as a test solution
LOD/LOQ	LOD & LOQ ≤ reporting thresholds
Linearity	Regression equation of 5 solutions from 4 to 100 ppm Correlation coefficient ≥ 0.99
Accuracy	Inactivated virus spiked with PEIpro® at 4ppm, 10ppm and 100ppm levels, 3 determinations per level. Individual recoveries and mean recovery at each level between 70 and 130%
Robustness	Stability of solutions in vial at autosampler temperature Reference solution recovery between 90 and 110% and spiked test solution of inactivated virus between 80 and 120%
Repeatability	Three series of 6 determinations of inactivated virus spiked with PEIpro® at 10ppm RSDr (series 1, 2 and 3) ≤ 25%; RSDip (series 1, 2 and 3) ≤ 30%

CELL & GENE THERAPY INSIGHTS

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