Establishing a surrogate model for inactivation of enveloped viruses to screen viral clearance conditions during biotherapeutics process development

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Abstract

Viral surrogates to screen for virus inactivation (VI) can be a faster, cheaper and safer alternative to third-party testing of pathogenic BSL2 (Biosafety Level 2) model viruses. Although the bacteriophage surrogate, Ø6, has been used to assess low pH BSL2 VI, it has not been used for evaluation of detergent-mediated VI. Furthermore, Ø6 is typically assayed through host cell infectivity which introduces the risk of cross-contaminating other cell lines in the facility. To circumvent contamination, we developed an in-house RT-qPCR (reverse transcriptase quantitative polymerase chain reaction) assay for selective detection of active Ø6 from a population of live and dead phage. The RT-qPCR assay was used to evaluate Ø6 inactivation in cell culture fluid of monoclonal antibody and fusion protein. Complementary Ø6 infectivity was also conducted at a third-party testing facility. The Ø6 RT-qPCR and infectivity data was modeled against VI of three BSL2 viruses, X- MuLV, A- MuLV and HSV-1 in corresponding therapeutics. Both Ø6 methods demonstrate that any VI agent showing Ø6 clearance of [?] 2.5 logs would demonstrate complete BSL2 VI of [?] 4.0 logs. Compared to BSL2 virus testing, this in-house O6 RT-qPCR tool can screen VI agents at 5% the cost and a turnaround time of 2-3 days versus 4-7 months.

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