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Perspectives from the CAACB on the Current Benefits and Challenges of NGS Adoption for Viral Safety Testing

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The recent ICH Q5A(R2) guidelines and upcoming Eur. Ph. 2.6.41 chapter both support the use of next-generation sequencing (NGS) as a replacement or orthogonal assay for viral safety testing, yet implementation and validation of NGS has been slow at best. To better understand the benefits and challenges of NGS adoption, this presentation will focus on lessons learned from the Consortium on Adventitious Agent Contamination in Biomanufacturing (CAACB). Since 2010, 75% of CAACB member companies that experienced a contamination report NGS as the most useful tool for viral identification. When it comes to viral detection, however, CAACB members report continued use of the in vivo virus test, with 94% of members using it for cell line characterization and 50% of members using it for virus seed testing and/or lot release testing, despite the fact that the in vivo virus test has not been reported to detect a virus contamination that was not also detected in another concurrent assay. For CHO-based products specifically, only two CAACB members have transitioned to using NGS for cell bank testing and no members have reported its use for lot release. CAACB members, however, demonstrate a clear interest in NGS as an alternative method, with 69% of member companies actively evaluating replacement of in vivo assays and 63% evaluating supplementing in vitro assays with NGS. Some members are also including NGS in their IND filings. This is mainly motivated by reducing animal use, but also due to NGS having a greater breadth of detection and the expectation that NGS will have greater sensitivity than the in vivo virus test, ensuring a safer product. Companies still face significant challenges to adoption, including concerns of high false positive rates, buy-in from upper management, and lack of harmonization across regulatory authorities.

