LIFE SCIENCES

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RESIDUAL HOST CELL DNA QUANTIFICATION

SGS

BIOLOGICS TESTING

Manufacturers of vaccines and other biological products must ensure that final products derived from continuous mammalian cell lines contain low levels of residual host cell DNA (HCD). The presence of HCD in the final product is of significant concern due to:

- Potential transfer of activated cellular and/or viral onco-genes, particularly if the cell substrate is tumourogenic
- Production of infectious viruses from viral DNA
- Aberrant gene expression by insertion of sequences into sensitive control regions of genes

Stringent guidelines stipulate the maximum amount of DNA that should be present in the clinical lot. For example, a vaccine production using a continuous non-tumourogenic cell line such as low passage Vero should be limited to a maximum level of 10ng of cellular DNA per dose. There may be instances where continuous cell line DNA is considered to pose a great risk: for example, if the cell contains retroviral proviral sequences and limits of 100pg per dose can be recommended. Therefore, in many cases the maximum amount of residual DNA per dose should be set on a case-by-case basis dependent on the product and its application.

THE METHOD

SGS uses the Applied Biosystems 7900HT and Quantitative TaqMan PCR (qPCR) technology to quantify residual DNA in the drug substance. Various other methods exist to detect Residual HCD, namely Threshold assay (ELISA-based Anti-DNA antibody) and DNA Hybridization (slot-blot assay). SGS offers qPCR because it is the most robust, reliable, reproducible and sensitive method for this purpose and is approved by worldwide regulatory authorities.

HCD assays at SGS are compliant with Ph.Eur. 2.6.21 'Nucleic Acid Amplification techniques', USP <1140> 'Approaches for detecting trace nucleic acids (residual DNA testing)' and the new chapter on HCD in Ph.Eur. 10.0, 2.6.35 ' Quantification and Characterisation of Residual Host Cell DNA.'

RESIDUAL DNA QPCR ASSAYS	EQUIPMENT & LABORATORIES	CUSTOM CONSULTANCY SERVICES
• CHO • MDCK • *E.coli* • Vero • Human • NS0 and SP2/0 • HEK 293/PER.C6 • Yeast/Insect • HeLa S3	• IQ, OQ, PQ • ABI 7900HT Systems • Labcaire PCR6 & PCR 8 cabinets • Dedicated PCR laboratories	• Design & Development • Assay Validation & Transfer • Custom Protocols • Regulatory Consultancy • Expert Report Writing • Complex Testing Strategies

At SGS reporting of HCD in a sample is from an extract that is assessed for DNA recovery and matrix interference. Negative controls are included at every stage of the process, giving confidence in the result reported.

In addition to quantification of HCD in a sample, SGS can detect the DNA fragment size in a sample. The combination of the Qiagen® extraction system and PCR which detects fragments of 200bp and greater provides an assay capable of determining the presence of fragments greater than or equal to 200 bp in size.

HCD assays at SGS are compliant with ph. Eur. 2.6.21, USP <1140> and the Ph.Eur. 10.0 new chapter 2.6.35 'Quantification and Characterisation of Residual Host Cell DNA'. Reporting of HCD in a sample is from an extract fully assessed for DNA recovery and matrix interference. PCR and extraction controls are included in all HCD assays.

Because SGS has extensive experience in sample preparation and qPCR and is able to analyze samples from various matrix compositions with high quality results and rapid turn-around-time.

ABOUT SGS

SGS provides a comprehensive range of biosafety services such as: virology, cell and molecular biology as well as microbiology and electron microscopy. Health Authorities, including the US FDA and the EMA, require companies to undergo safety testing to demonstrate that all cell banks, viral banks, raw materials of animal origin, bulk harvests, and batches of clinical drug are free of bacteria, fungi, mycoplasma, viruses and other potential contaminants.

SGS's global centre of excellence for cell bank characterization & virus testing is located in the United Kingdom and provides services with ultimate reliability, highest GLP/cGMP quality & scientific expertise.

As trailblazers in the development of the biosafety testing industry, our SGS Vitrology team in Glasgow have developed and validated novel nucleic acid technologies, such as real-time PCR, RAPD, Sequencing, Non-radioactive Southern Blotting, Next Generation Sequencing (NGS).

We offer a comprehensive range of integrated solutions, including biosafety testing & characterization of raw materials, cell bank & virus seeds, unprocessed bulks/viral harvests and drug substance/product.

For any of your biologics, we help you comply with the global regulatory guidelines and testing requirements. Our team of experienced scientists have over 20+ years' experience in GMP, FDA, EP, ICH compliant validated assays.

- Global Network
- Rapid turnaround times
- Data management and Reporting

CONTACT US

+44 (0)141 952 0022

biosafety@sgs.com

www.sgs.com/Lifesciences

www.sgs.com/Linkedin-Life

WHEN YOU NEED TO BE SURE