

NEXT GENERATION SEQUENCING, THE NEW ALTERNATIVE TO IN VIVO TESTING

Method Comparison: Quality Control Testing of Biologics



TARGET >

Professionals in Pharma and Biotech developing cell therapy, cell banks, virus seeds...

New ICHQ5A(R2) encourages the use of NGS as a replacement for *in vivo* assays

WHAT ARE THE BIOLOGICAL MATERIALS CONCERNED?

A large number of applications and products:

vaccines

recombinant proteins

cell and gene therapies



1 NGS
(RNA sequencing method)



VS

In vivo
(conventional test for the viral safety of cells)



2 Collaboration

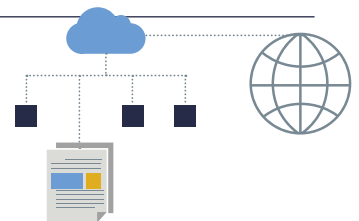


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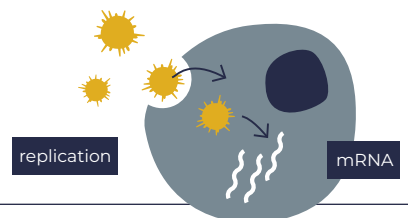
 charles river

3 Goal of study: Generate data to support the replacement of in vivo testing w/NGS approach on cells



4 In vivo = Suckling mice, adult mice, embryonated eggs, guinea pigs* and hamsters*

5 NGS transcriptomic approach



6 Viruses chosen for this study

CATEGORY A

Vesicular Stomatitis Virus, Influenza A

NGS < *In Vivo*

CATEGORY B

Herpes Simplex Virus type 1, Coxsackie viruses A and B, Mumps

NGS < or similar *In Vivo*

CATEGORY C

Echovirus 11, Measles, Bovine Viral Diarrhea Virus

Undetectable in *in vivo* assay

* Guinea pigs and hamsters are used in some tests that are not shown here

As per ICHQ5A(R2): NGS is encouraged as a replacement for in vivo assays

		Animal Testing	NGS	Comments
	Detection range	✗	✓	NGS has a broader range of detection as <i>in vivo</i> testing. Entire families of viruses cannot be detected with animal testing.
	Specificity for virus identification	✗	✓	NGS detection is based on sequencing, which ensures virus detection and identification. Detection using animal models is based on clinical signs which are not specific to viruses and need further investigation for identification.
	Sensitivity	✗	✓	As shown in this study, NGS has greater or equal sensitivity compared to most animal testing.
	Turnaround time	✗	✓	Suckling mice assay takes 28 days for observation period alone. Animal testing failures are common (increased TAT)
	3Rs compliance	✗	✓	Directive 2010/63/EU requires Replacement, Reduction, and Refinement of animal testing whenever possible
	Validation	✗	✓	Animal testing is not validated (due to ethical concerns), NGS is available at a GMP grade. New ICHQ5A(R2) adopted in 2023 and EP 5.2.14 clearly state the use of NGS as an alternative.
	Regulatory acceptance	✓	✓	EP 2.6.16 requires justification for the use of animal testing whereas NGS is considered an acceptable alternative method.

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