

At Siemens Healthineers, our purpose is to enable healthcare providers to increase value by empowering them on their journey toward expanding precision medicine, transforming care delivery, and improving patient experience, all made possible by digitalizing healthcare.

An estimated 5 million patients globally benefit every day from our innovative technologies and services in the areas of diagnostic and therapeutic imaging, laboratory diagnostics, and molecular medicine, as well as digital health and enterprise services.

We are a leading medical technology company with over 120 years of experience and 18,000 patents globally. Through the dedication of more than 50,000 colleagues in 75 countries, we will continue to innovate and shape the future of healthcare. All third party trademarks and brands are the property of their respective owners.

#### References:

1. Design and analysis of shedding studies for virus or bacteria-based gene therapy and oncolytic products: guidance for industry. 2015 Aug. Available from: <http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>
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#### Siemens Healthineers Headquarters

Siemens Healthcare GmbH  
Henkestr. 127  
91052 Erlangen, Germany  
Phone: +49 9131 84-0  
[siemens-healthineers.com](http://siemens-healthineers.com)

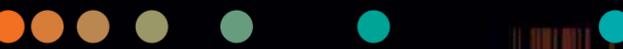
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Molecular Diagnostics  
725 Potter Street  
Berkeley, CA 94710-2722  
USA  
Phone: +1 510-982-4000

# Shaping the future of healthcare

## Gene Therapy Assay Development Services

[siemens-healthineers.com/shl](http://siemens-healthineers.com/shl)



## Cutting-edge gene therapies promise to transform medicine by treating underlying causes of life-threatening diseases.

Siemens Healthcare Laboratory, LLC offers development and testing expertise to enable the success of your gene therapy program.

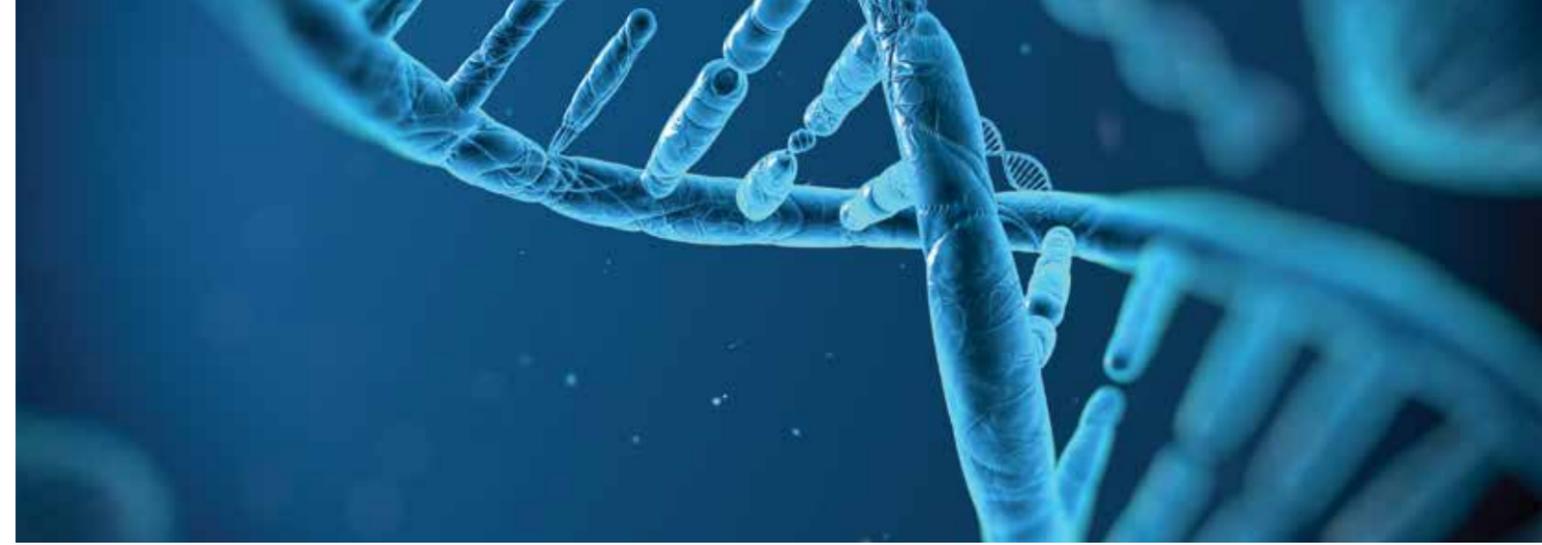


### The right diagnostic solutions in gene therapy development

- Helps your program comply with critical regulatory requirements for gene therapy trials
- May result in better trials outcomes by
  - Helping guide selection of the right subjects for clinical trials
  - Enhancing safety and efficacy

Siemens Healthcare Laboratory (SHL)\* is a provider for all stages of gene therapy testing

 <b>1</b> Patient Selection <ul style="list-style-type: none"> <li>• Disease stage</li> <li>• Immune status</li> <li>• Genetic factors</li> </ul>	 <b>2</b> Patient Response <ul style="list-style-type: none"> <li>• Immune response</li> <li>• Protein expression</li> <li>• Improvement</li> <li>• Target tissue</li> </ul>	 <b>3</b> Therapy Efficacy <ul style="list-style-type: none"> <li>• Infectivity</li> <li>• Viral replication</li> <li>• DNA integration</li> <li>• Stability</li> </ul>	 <b>4</b> Monitoring <ul style="list-style-type: none"> <li>• Infectivity</li> <li>• Viral replication</li> <li>• Viral shedding</li> </ul>
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### Critical diagnostic tests for your gene therapy testing needs

- Shedding tests to monitor viral genomic material in a wide variety of sample types
- Proviral DNA tests to detect incorporation of retroviral DNA in tissues or cells
- Cell-based neutralization antibody tests to help identify presence of patient antibodies that may interfere with the therapy (e.g., antibodies to wild-type viruses)
- Cell-based infectivity tests to assess the presence of intact virions in shedding compartments
- Additional molecular characterization or confirmatory testing of therapeutic vectors, coinfections, and/or host factors with qPCR, ddPCR, or NGS platforms

### SHL Recombinant Adeno-associated Virus (rAAV) Assay development process

					
Project Initiation	Shedding Assay Development	Infectivity Assay Development	Performance Studies of Assays	Quality Documentation	Implementation of Clinical Workflow

### Importance of shedding detection during development of gene therapy

- Virus-based gene therapy products and oncolytic viruses may be shed from the patient through biological fluids or skin.
  - May be transmitted from treated to untreated individuals.
- Use of viral vectors in human gene therapy is highly regulated.
  - Regulatory guidance varies from country to country.
    - In the United States, regulations require that shedding studies be carried out during preclinical and clinical development.<sup>1</sup>
  - SHL helps to minimize submission risks by providing comprehensive planning to meet regulatory needs.

### What is Siemens Healthcare Laboratory, LLC (SHL)?

- Owned entity of Siemens Healthcare Diagnostics Inc.
- Offers end-to-end diagnostic solutions for all stages of design, development, validation, clinical trial testing, and manufacturing of IVD kits

### Why SHL?

- CAP-accredited and CLIA-licensed lab
  - Meets United States federal regulatory standards
- Quality and regulatory expertise
- Expertise in IVD manufacturing, LDT development and validation, clinical trial services, research studies, and biomarker discovery
- Scientists with extensive experience supporting gene therapy clinical trials since 2012
- Consultative services
  - Gene therapy test customization and development
  - Regulatory and clinical insights from perspective of diagnostics manufacturer
- Global commercialization of diagnostic tests for patient access
  - Leveraging Siemens Healthineers internal partners

Take the next step and make Siemens Healthcare Laboratory a partner in your journey. Contact us to learn more.

### Our Testing Services support all stages of therapy development and beyond

	How we help you
<b>Biomarker Discovery Research</b>	We help you find the right biomarkers to support your therapy development programs and establish clinical validity for patient stratification
<b>Laboratory Assay Development</b>	We develop laboratory assays <sup>2,3</sup> based on your clinical needs for drug development programs, including RUO, clinical trials, and CLIA analytically qualified type assays
<b>CDx IVD Development</b>	We may develop CE-IVD / FDA PMA assays for global deployment as companion diagnostics for your drug on a broad base of IVD platforms
<b>Reference Laboratory Training</b>	We may run required clinical trial tests for your development programs as a fully certified CLIA laboratory partner from small to large scale testing

\*Siemens Healthcare Laboratory, LLC is an affiliate of Siemens Healthcare Diagnostics Inc.