

Treatment

- ✓ AAV
- ✓ Lentiviral
- ✓ Plasmid
- ✓ RNA
- ✓ Oligonucleotide
- ✓ Other

Biodistribution and Shedding

“The biodistribution data, coupled with other preclinical safety endpoints such as clinical pathology and histopathology, help determine whether vector presence or gene expression correlates with any tissue-specific detrimental effects in animals.”*

*FDA Guidance for Industry: Preclinical Assessment of Investigational Cellular and Gene Therapy Products, November 2013

Transcription

DNA

Vector Presence DDPCR, qPCR

“Tissue/biological fluid analysis should be conducted at the molecular level, using a quantitative PCR (Q-PCR) assay to determine the number of vector copies per microgram of genomic DNA at specified time points post-vector administration.”*

RNA

Gene Expression ddPCR, RT-qPCR

“Quantitation of transgene expression using methods such as a quantitative Reverse Transcriptase PCR (RT-PCR) assay can help determine... correlation of the kinetics of transgene expression with desired activity or undesired toxicity profile.”*

Translation

Protein

Protein Expression ELISA, Western Blot

“When determining the safety of an expressed transgene and/or translated protein, sponsors should consider the following: a) local versus systemic expression; b) level and duration of expression, and c) acute versus chronic effects.”*



Guidelines

FDA, EMA, ICH, MIQE

The MIQE guidelines encourage better experimental practice, allowing more reliable and unequivocal interpretation of qPCR results
-Bustin et. al. 2009

Experience

Overcoming Challenges

Off-target amplification
High sample volume
Cross-contamination
Low yield tissue
Multiplexing

Species

- ✓ Dog
- ✓ Minipig
- ✓ Rabbit
- ✓ Rat
- ✓ Sheep
- ✓ Guinea Pig

Excretions

- ✓ Saliva
- ✓ Feces
- ✓ Nasal
- ✓ Tears
- ✓ Urine

Organs

- ✓ Kidney
- ✓ Brain
- ✓ Heart
- ✓ Spleen
- ✓ Blood
- ✓ Gonads
- ✓ Liver
- ✓ Injection
- ✓ Site(s)
- ✓ Other

Definitions

Biodistribution: Shedding:

How a product is spread throughout the body from site of injection

How the product is released or excreted from the body

Our Approach

In-life Phase

- ✓ Perform *in vivo* treatment on a variety of animal models
- ✓ Collect blood and other body fluids
- ✓ Harvest selection of tissues at necropsy
- ✓ Samples collected using sterile technique and in an order to minimize the risk of contamination

Bioanalysis

- ✓ Homogenize tissue on high-throughput platform
- ✓ Isolate DNA/RNA from samples on high-throughput platform and confirm quantity, quality and integrity
- ✓ Work with low yield tissue including blood, muscle, skin and CSF
- ✓ Develop a qPCR or ddPCR method from scratch or transfer an existing method from Sponsor
- ✓ Validate the method according to relevant guidelines
- ✓ Perform sample analysis for DNA, RNA and/or protein
- ✓ Review and analyze data and generate applicable reports

Accreditations

- ✓ FDA Inspected
- ✓ EMA Certified
- ✓ ISO Certified
- ✓ AAALAC Accredited
- ✓ DEA Licensed
- ✓ OLAW Assured
- ✓ USDA Registered



- Genome Copy Titer
- Transduction Efficiency
- Infectivity
- Potency Assay Development
- Pharmacodynamics
- Safety/ Toxicology
- **Biodistribution and Shedding**
- Immunogenicity
- Clinical GLP Bioanalysis
- Potency Release Assay
- Clinical GLP Bioanalysis (LTFU)
- Potency Release Assay

ACF provides *in vitro*, *in vivo* and analytical support to attain an IND or BLA faster

In Vitro Services

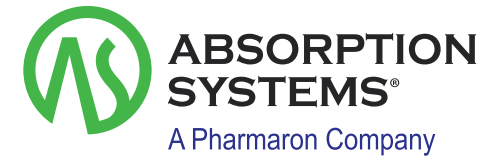
- ✓ Potency Release Assays
- ✓ Enzyme Activity Assays
- ✓ Cell Based Assays
- ✓ Neutralizing Antibody Assays
- ✓ Stability Assays
- ✓ GMP Lot Release Testing
- ✓ Cytokine Release and Migration Assays
- ✓ Vector Infectivity/Transduction Efficiency
- ✓ Proliferation Bioassays using Various
- ✓ Cell Types Cell Viability and TCID50 Titer
- ✓ Sample Management
- ✓ Preclinical and Clinical Bioanalysis

In Vivo Services

- ✓ Biodistribution and Shedding
- ✓ Toxicology
- ✓ Immunogenicity
- ✓ Small and Large Animal Models
- ✓ Regenerative/Stem Cell Testing
- ✓ Full Spectrum Ocular Services
- ✓ Custom Animal Models
- ✓ Immunocompetent and Immunocompromised Models

Analytical Tools and Techniques

- ✓ LC-MS/MS
- ✓ ddPCR, qPCR, RT-PCR
- ✓ ELISA Assays
- ✓ Fluorescent Assays
- ✓ Luminescent Assays
- ✓ Quantitative Western Blot
- ✓ Electrophoresis
- ✓ Chromatography
- ✓ Flow Cytometry



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Biodistribution & Shedding

For Cell & Gene Therapies

Contact us
Analytical CRO dedicated to cell and gene therapies



2021CGTT1

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