Adenoviral Reference Material Working Group
Bid Submission Form
Participation in Assignment of Infectious Titer
RFP 9.0

Item for Submission

An Ad5 Wild-type Virus is being produced as a reference material for use in defining particle number and infectious units of adenovirus gene therapy vectors. This RFP invites laboratories to participate in the characterization phase, specifically to perform analyses so that the Working Group may assign the infectious titer to the reference material. The Working Group will select a minimum of six laboratories to perform infectious titer determinations using the attached standard operating procedure. Laboratories may submit proposals to perform additional methods of determining infectious titer. However they must also commit to performing the standard operating procedure provided by the Working Group. Testing is anticipated to begin in mid to late September 2001. **All proposals are due to the Williamsburg BioProcessing Foundation by Monday, July 30.** Electronic submissions are preferred.

General Requirements for Bidding

An Adenovirus 5 WT reference material is being produced under the guidance of a Working Group. The producing institution will provide a provisional particle concentration as part of a Certificate of Analysis along with confirmation of identity, functionality, purity, and freedom from adventitious agents. However, infectious titer will be assigned to the reference material through measurements made by different laboratories, all performing a method provided by the Working Group. The Working Group may also incorporate data gleaned from the performance of other methods into the assignment of infectious titer.

Laboratories may also make proposals to perform other methods to establish infectious titer. Such proposed methods must be provided in detail as part of the submission in order to enable the Working Group to determine their utility.

The standard operating procedure provided by the Working Group describes a 96-well plate method using 293 cells to be provided by the Working Group. The read-out for the procedure is cytopathic effect (CPE), which should enable most laboratories to perform the method with minimal training. The procedure includes sample handling and dilution as well as preparation and culture of the 293 cells. A CPE scoring form (Word document) and a report worksheet (Excel spreadsheet) are provided as separate electronic attachments.

Each laboratory submitting a proposal should provide a statement describing their experience and capacity to perform the 96-well-based infectious titer assay described in the standard operating procedure. The statement should specifically address:

- the qualifications of the personnel involved in performing the procedure and reviewing the data,
- the equipment that will be used and its calibration status (for example, pipettors),
- how long it will take the laboratory to perform the procedure, and review and report results back to the Working Group once the sample is received, and
- the laboratory's readiness to begin testing in mid to late September 2001.

For laboratories wishing to also submit a proposal to perform additional methods of determining the infectious titer, the proposal should include:

- the amount of Ad5 WT Reference Material that will be required to perform the proposed analysis,
- a complete description of the method, preferably in the form of an operating procedure,
- the laboratory's experience in performing the proposed procedure,
- the qualifications of the personnel involved in performing the procedure and reviewing the data,
- the equipment that will be used and its calibration status (for example, pipettors),
- how long it will take the laboratory to perform the procedure, and review and report results back to the Working Group once the sample is received, and
- the laboratory's readiness to begin testing in mid to late September 2001.

Documentation Requirements

Capability statement with regard to performing the 96-well infectious titer procedure addressing the points listed above.

For laboratories submitting a proposal to perform additional methods:

Capability statement with regard to performing the proposed procedure addressing the points listed above

A detailed description of the method proposed

Amount of reference material required for the proposed analysis

Submission and Deadline

Submit the completed form and all requested information for receipt **by Monday, July 30, 2001** to the address below. **Electronic submissions are encouraged**. Final decisions will be communicated by or about August 31, 2001 at the latest. Testing is anticipated to begin in mid to late September. Please note that all information submitted will be publicly available. Please do not mark any information confidential, as we cannot honor that request. Please include an estimated cost and market value of all goods and services donated. Participants will be responsible for the cost of shipping the Reference Material to their location (express courier, dry ice). The estimated cost for US domestic locations is US$65 but cost is dependent on the amount of material shipped.

Williamsburg BioProcessing Foundation
Attn: Adenovirus Reference Material Working Group
P.O. Box 1229
Virginia Beach, VA 23451
PH: 757-423-8823
FAX: 757-423-2065

EMAIL: advector@wilbio.com

Additional attachments:

- Standard Operating Procedure for Determination of Infectious Titer Using 293 Cells in a 96-Well Format (included in this electronic document)
- CPE Scoring Form (you will need to make copies of this form to use during the assay; separate electronic attachment)
- Results Submission Form (Excel spreadsheet, separate electronic attachment)

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Please complete the following fields:

Contact Information – RFP 9.0

*Contact Individual:	Dr David Venables Associate Director, Biotechnology Services
Institution:	Covance Laboratories Ltd
Address:	Otley Road, Harrogate North Yorkshire HG3 1PY
Phone Number:	+44 (0)1423 848017
Fax Number:	+44 (0)1423 569595
Email Address:	david.venables@covance.com

***If laboratories are submitting a proposal as a group, a main contact should be provided along with contact information for each participating laboratory (attach additional copies of this form).**

Please indicate if your institution is also submitting proposals for the other activities:

X Determination of Particle Concentration

☐ Short-term/Field Stability Studies

☐ Long-term Stability Study

☐ Other Characterization

☐ Donation of Supplies/Other Services for Characterization Phase

Covance Laboratories Bid to Participate in Assignment of Infectious Titer
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The Covance Biotechnology Department has been established for over 10 years and provides a one-site, fully GLP/GMP compliant facility dedicated to the safety testing of biotechnology, recombinant, gene therapy and blood products to comply with the current internationally recognised guidelines. The facilities are routinely inspected by FDA, UK MCA and our client companies for compliance and validation. Fully trained technical, graduate and post-graduate staff conduct the studies. Reports in support of regulatory submissions for all classes of products have been successfully submitted to regulatory authorities in USA and Europe. Covance has a world-wide network of over 30 offices and this global network of regulatory expertise is accessible to our clients. Covance is also an ISO9000 compliant company.

Covance has been developing and validating methods for the determination of infectious titer of an extensive range of viruses over the last 10 years. These methods have been developed to support Replication competent virus detection in gene therapy products, virus titration in support of the validation of virus removal process steps, as well as validation of methods for adventitious virus detection in a range a raw materials. These assays have been developed and validated (according to the principles outlined in ICH topic Q2B "Validation of Analytical Procedures: Methodology") for both GLP and GMP applications. The equipment used in the execution of these methods is included in an equipment qualification schedule and is calibrated on a regular basis according to a defined schedule. In addition to regular calibration, full performance and usage records for each instrument are maintained, including annual maintenance records, as would be expected for a laboratory operating according to ISO9000, GLP and GMP.

The personnel directly involved in performing the analytical methods are as follows:
David Birch, BSc, Section Head
David has over 20 years experience in virology, immunology and parasitology. Over the past 10 years he has been responsible for all aspects of biosafety testing and virus validation studies performed at Covance, and has been directly involved in developing and validating new viral assays.
Alex Stevenson, PhD, Study Director
Alex has over eight years experience in molecular biology and gene therapy, and has been responsible for the development and validation of Covances' RCA and RCR assays.
Claire Shorrock, PhD, Study Director
Claire has 6 years experience in the field of virology. She completed her PhD within the Virology Department of the National Institute for Biological Standards and Control (NIBSC). Claire has responsibility for virology and QPCR studies conducted at Covance.
Russell Hodgetts, BSc, Experimental Officer
Russell is a graduate scientist who has been conducting virology studies at Covance for the past 4 years. He has been involved in the development and validation of Covances' RCA and RCR assays and is currently completing an MSc by research investigating the development of RCA detector cell lines expressing GFP.

It is anticipated that, assuming material is made available beginning September 2001, the total length of time from receipt of material to sign off of a final report will be twelve weeks.