Adenoviral Reference Material Working Group
Bid Submission Form
Participation in Assignment of Particle Concentration
RFP 8.0

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 particle concentration to the reference material. The Working Group will select a minimum of six laboratories to perform particle number determinations using the attached standard operating procedure. Laboratories may submit proposals to perform additional methods of determining particle concentration. However they must also commit to performing the standard operating procedure provided by the Working Group. The Working Group encourages submissions from individual laboratories or groups of laboratories proposing to perform alternative particle determination methods. Testing is anticipated to begin in 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, particle concentration 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 particle concentration.

Laboratories may also make proposals to perform other methods to establish particle number. Such proposed methods could include analysis via RP-HPLC, AE-HPLC, electron microscopy, DNA Pico Green, DNA qPCR, etc. The objective of the Working Group in encouraging such submissions is to establish a more accurate extinction coefficient for the OD_{260nm} /SDS assay.

The standard operating procedure provided by the Working Group describes an optical density measurement taken at 260 nm (OD_{260nm}) made after lysing the adenovirus sample using sodium dodecyl sulfate (SDS). The procedure includes sample handling and dilution as well as preparation and use of an excipient blank. A report form is also provided as a separate attachment (Excel spreadsheet).

Each laboratory submitting a proposal should provide a statement describing their experience and capacity to perform the spectrophotometric particle 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,
- how long it will take the laboratory to perform the procedure, and review and report results back 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 particle concentration, 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,
- how long it will take the laboratory to perform the procedure, and review and report results back 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 spectrophotometric 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-$100, but is dependent on the amount of reference material to be 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 Particle Concentration by Spectrophotometric Analysis (included in this file)
- Results Submission Form (Excel spreadsheet) (separate electronic file)

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Please complete the following fields:

Contact Information – RFP 8.0

*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 Infectious Titer

☐ 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 Particle Concentration, RFP 8.0

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.

Spectrophotometric analytical methods have been developed and validated for a range of applications, including viral particle counting, protein and DNA concentration determination, excipient concentration determination and enzyme activity assays. 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 will be a Pharmacia Ultraspec or a Tecan Spectrofluor Plus. Both instruments are included in an equipment qualification schedule and are calibrated against external standard once a month, and against internal standards prior to each use. Full performance and usage records for each instrument are maintained, including annual maintenance records.

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, along with Russell Hodgetts.
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 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 eight weeks.