

**Adenoviral Reference Material Working Group
Donation of Repository Services Bid Submission
In Response to RFP 7.0**

INTRODUCTION AND SUMMARY

The American Type Culture Collection (ATCC), a not-for-profit corporation, is pleased to offer its services for: (1) maintaining, in nitrogen vapor or mechanical freezers at $\leq -55^{\circ}\text{C}$, approximately 5,000 Adenovirus Reference Material vials and (2) transferring the vials under proper conditions to requesters. The ATCC will, in addition to maintaining and distributing the vialled reference material, also maintain the project's cell bank vials and virus bank vials for production of future batches of the reference material, and will distribute vials as necessary during the characterization phase of the reference material QC.

The ATCC has for the past 75 years sought to support biomedical research by fostering the exchange of reagents, the use of standard strains in research laboratories, and the curation of the information associated with the physical holdings. Since the formation of the Animal Virus Collection in 1950, the ATCC has maintained a close link with the virology community. While the role of the ATCC in maintaining repositories of a wide-range of biologics is well recognized, less known is its role in curating the associated informatics through the development of new tools for capturing, linking and viewing data. For example, the ATCC Bioinformatics group has for a number of years been working with the ICTV and other members of the virology community to develop better descriptors for coding virus information on into databases. This linkage of information with reference reagents increases the value of each, and allows researchers access to the authentic reference strain required to repeat or extend the underlying experimental work. Also those wishing to carry out new studies with a reference strain are able to have confidence that it will be possible to draw appropriate comparisons with previous work based on the same strain or clone.

Importantly the ATCC is experienced not only in long-term preservation of biologics, but also the regulatory, shipping and security issues associated with biohazards. ATCC has strict policies and procedures in place to ensure that cultures are distributed only to qualified organizations and researchers with legitimate and justifiable scientific uses for these materials. It was the ATCC's expertise in all facets of repository management that allowed the ATCC to win the contract to manage the CDC's CASPER repository in Lawrenceville, GA.

ATCC ships cultures direct to all countries in the world except those restricted by U.S. law. For the convenience of our customers, ATCC has appointed LGC Ltd. as distributor in Europe, Summit Pharmaceuticals International Corporation as distributor in Japan, and KORAM Biotech Corporation as distributor in South Korea.

For the collective reasons described above we believe the uniquely valuable reference vials of adenovirus type 5, developed by the Adenoviral Reference Material Working Group and contractors selected to produce this material, should be distributed by the ATCC. ATCC can maximize the availability of the reagents to the community, and insure their long-term curation. Most importantly, the ATCC's current policy is to maintain collections of accessioned materials in perpetuity. This long-term commitment to the preservation of strains and reagents is unique to the ATCC.

BID FORMS AND PROPOSAL DOCUMENTATION

The Bid Submission Form (RFP 7.0) description of Item for Submission, General Requirements for Bidding, and required documents follow. The documentation includes: the Contact Information form; the Donation Information checklist; the Institution Capability Statement; Cost Analysis and Cost Recovery Proposal; Distribution Plan and Shipping Experience.

**Adenoviral Reference Material Working Group
Bid Submission Form
Donation of Repository Services
RFP 7.0**

Item for Submission

Adenovirus Reference Material vials are intended to be stored at $\leq -55^{\circ}\text{C}$ until shipped under proper conditions to requesters. Bid will also provide for appropriate storage of the project's cell bank vials and virus bank vials, and of the vial reference material and distribution during the characterization phase.

General Requirements for Bidding

Repository should have the capacity for frozen ($\leq -55^{\circ}\text{C}$) storage of approximately 5000 vials, capacity to store approximately 15 x 1 mL cell bank vials under liquid nitrogen vapor phase, the capacity to store virus bank vials at $\leq -55^{\circ}\text{C}$ and the ability to monitor temperature during storage and monitoring systems (alarm systems). The bidder should indicate the minimum amount of time the institution can commit to providing repository and distribution services. Proposals should include information regarding shipment capability, experience with export and import of viral materials, experience of personnel or personnel certification in IATA/OT regulations, personnel experience with request processing, distribution plan, cost analysis, and proposed cost recovery. The bid should also address prevention of catastrophic loss of stored materials (possibility of storage in multiple pieces of equipment, availability of emergency back-up power, etc.).

The bid should indicate the amount of time required from receipt of the vial reference material until ability to distribute vials for characterization phase.

Documentation Requirements

To support requirements listed above.

Please complete the following fields:

Contact Information – RFP 7.0

Contact Individual:	Charles Buck
Institution:	ATCC
Address:	10810 University Blvd Manassas, VA 20110
Phone Number:	703-365-2724
Email Address:	Cbuck@atcc.org

Vialing and Freezing Donation Information – RFP 7.0

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

- Donation of Cell Bank
- Donation of Ad5 Wild-type Virus
- Ad5 Wild-type Virus Bank Production
- Ad5 Wild-type Purified, Formulated Bulk Production
- Vialing of Ad5 Wild-type Reference Material
- Donation of Supplies/Other Services

Please attach:

Institution Capability Statement
Cost analysis and cost recovery proposal
Distribution plan
Information/experience in shipping

Institution Capability Statement

The American Type Culture Collection (ATCC) is a not-for-profit corporation, which has distributed reference strains to the scientific community for the past 75 years. Today the ATCC includes six diverse Collections: Bacteriology, Cell Biology, Mycology, Molecular Biology, Protistology and Virology (Plant and Animal) with over 95,000 holdings of biological significance. The credibility and long-term sustainability of all ATCC Collections are assured by its accumulated expertise and by the longstanding stability of the organization. The ATCC is experienced in all aspects of repository management, including: acquisition, long-term preservation, safety and regulatory issues, and shipping requirements for biologicals. This expertise in repository management allowed the ATCC to win the contract to manage the CDC's CASPER repository in Lawrenceville, GA.

The ATCC has the required capacity for: frozen storage at -55°C or lower temperature of approximately 5000 vials of virus, approximately 15 x 1 mL cell bank vials under liquid nitrogen vapor phase, and 50 or more virus bank vials at -55°C or lower temperature. The ATCC currently distributes a replication competent retrovirus as a reference reagent that serves a purpose analogous to that envisioned for the replication competent adenovirus.

The ATCC is also willing to provide a limited number of vials of adenovirus 5 from its existing inventory, as raw material for production, should it be required. However, as there is no particle count data for the existing stocks no formal bid has been submitted. The ATCC is also willing, should its bid to accession the Adenovirus Material be accepted, to dispense the final bulk product. If the material is not dispensed at the ATCC, as part of the repository effort, the ATCC is willing to provide ATCC labels or labeled vials to the entity responsible for dispensing the material in order to have vial labels with an appropriate ATCC number placed in the repository—this will facilitate inventory management.

The ATCC has been maintaining cold rooms and freeze-drying cultures for nearly fifty years, and liquid nitrogen and low-temperature mechanical freezers have been maintained by ATCC for more than thirty years. Currently the ATCC maintains over one hundred freezers, with more than 1,800,000 specimens stored in environments chosen to provide optimum conditions for long term viability. Additionally, ATCC maintains three liquid nitrogen freezers, containing disaster recovery stock at off-site locations. In the present instance the ATCC would also plan to split the initial stock of 5,000 distribution vials between at least two freezer locations within its facility as an additional safeguard against loss.

The Operations wing of the ATCC's Virginia facility provides 7656 net square feet of air-conditioned (66°F to 72°F) and alarmed space for cold rooms, walk in freezers, -20 C freezers, -70 C freezers, and liquid nitrogen freezers. Access to the facility is restricted; stand-by freezers are available and uninterruptible power provided by a backup generator. ATCC engineering staff and outside vendors are used to provide maintenance support for the freezers and coldrooms. The ATCC also has the capability of cGMP storage for clean cell lines and is willing to discuss the possibility of expanding this capability for the storage of the Adenovirus Material, should these conditions be necessary.

The ATCC uses the MFG/PRO's distribution module to monitor inventory balances and to manage purchasing and sales order entry activity. All orders processed by the ATCC are centralized through the order entry team. This construct increases efficiency for order processing while creating a higher level of quality control for the distribution of products.

The ATCC utilizes a variety of alarm and access control systems for its operations. Facility and major equipment status are monitored through an engineering alarm system. The system

monitors major fans, air handlers, condensate pumps, and steam generators status. Ultra-low temperature freezers, liquid nitrogen freezers, and some critical incubators are also monitored. Alarms are monitored by ATCC Operations staff 24 hours per day, seven days a week at a central station. Any alarm condition requires the immediate attention of appropriate ATCC Personnel; a call list is maintained for staff response to freezer problems and key staff members are accessible via remote pagers or cell phones. Access to the building is restricted to authorized ATCC personnel through the use of entry card readers. Access to the culture storage areas is further restricted and freezers containing restricted materials are individually locked. Due to the presence of numerous large nitrogen freezers, the oxygen content of the freezer room is monitored and an alarm sounds when the level drops below 19.5%. The ATCC facilities are staffed 24 hours a day by ATCC engineering staff or security service staff.

Cost Analysis and Cost Recovery Proposal

The ATCC is a not-for-profit corporation with a 75-year history of distributing microorganisms and related materials to the scientific community. While many of the ATCC's holdings are expanded in-house, others have been deposited as completed distribution stocks, as will be the case with the Adenovirus Reference Material. Fees are charged for these materials to offset the cost of acquisition, data entry, long-term storage, regulatory review as well as other overhead and curatorial costs. Additional shipping fees—currently \$81.50 for domestic shipments—are also imposed. In this instance, the fees will also support recovery of the cost of shipping a limited number of vials to designated laboratories at no cost to the recipient for testing of the final product. It is further proposed that once all QC has been completed and the materials released to distribution, that each of several institutions designated as participating contributors by the Working Group (but not more than eight such institutions) be eligible to receive two vials of repository stock at no charge.

It is proposed that the vials be distributed in accord the current ATCC fee structure. Although the ATCC fees are adjusted from time to time, it is envisioned that the initial fee will be \$162 per vial unless the Working Group and ATCC come to mutual agreement on some other fee schedule. \$162 is the fee currently charged for VR-1450, the replication competent retrovirus reference strain.

As stocks approach a one-year supply, the ATCC anticipates planning for the production of a new batch of material with necessary FDA and industry input. Depending upon distribution rates and projected revenues, ATCC hopes to be in a position to contract out the production of a new batch of virus under conditions equivalent to that specified for the current batch and then request the assistance of the FDA in locating groups able to assist with the QC of the material. The details of how all this might work will of course depend to some degree upon the time line for the depletion of the initial stocks and the needs of the community at the time replenishment is required.

Distribution Plan

The ATCC intends to maintain the Adenovirus Reference Strain and the limited cell and virus bank stocks indefinitely, and make the deposited reference material available for distribution so long as there is need for the material in the scientific community. It is estimated that the amount of time required from receipt of the vialled reference material until the item can ship, due to the need to create an item number for tracking and input descriptive and regulatory information, will be approximately two weeks. If necessary this lead-time can be reduced through careful coordination with the other participants prior to the actual arrival of the material at the ATCC.

ATCC can accept orders via phone, email and FAX. The ATCC catalog of strains, in which we propose to include the Adenovirus Type 5 Reference Strain, is available on-line at www.atcc.org.

For the convenience of our overseas customers, ATCC has appointed LGC Ltd. as distributor in Europe, Summit Pharmaceuticals International Corporation as distributor in Japan, and KORAM Biotech Corporation as distributor in South Korea.

In order to promote the availability of the new material, ATCC can offer a note in ATCC Connections—ATCC's quarterly newsletter—to increase public awareness of the Adenovirus Reference Material and the role of the various contractors in contributing effort and materials for the common good. The ATCC also has the ability to highlight selected holdings or new accessions at the displays it takes to national meetings such as the Annual American Society for Microbiology meeting.

Parties interested in receiving cultures from ATCC must be able to verify that they have adequate facilities and expertise in working with biological materials. Those that are not already established ATCC customers will have to complete an application to establish their qualifications. For agents which are classified as hazardous, or which could have serious adverse consequences for human health and safety, ATCC relies on domestic regulations promulgated by the Secretary of Health and Human Services. These regulations establish a variety of safeguards related to the transportation and tracking of infectious agents, certain registration and reporting requirements, and procedures for the disposal and destruction of such agents when they are no longer needed for scientific purposes. Facility inspections requirements also exist for certain regulated materials. The Bureau of Export Administration of the U.S. Department of Commerce regulates exports of controlled commodities to countries outside the United States, or their agents. The Department also prohibits persons in certain countries from receiving controlled commodities from ATCC.

It is also proposed that 4,500 of the initial 5,000 vials will be placed on a hold status, while distribution of the initial 500 vials of distribution stock is monitored. Should a pattern of use be detected that would rapidly and unreasonably deplete this resource, steps will be taken to remedy the situation. Those remedial steps would depend upon the circumstances, but in the case of a few entities purchasing very large stocks of virus, flags could be established in the ATCC regulatory module to limit orders to 10 vials per order. Alternately, if the depletion were due to more moderate usage by large numbers of users, a price increase might serve to discourage indiscriminate use of this valuable reagent and justify the expenditure required to plan an early replenishment. Finally, should no pattern of abuse be observed additional blocks of 500 vials can be transferred to distribution as necessary.

Information/Experience in Shipping

The ATCC packs and ships cultures and related materials according to Department of Transportation regulations as described in 49 CFR 173.134 and international regulations accepted by the DOT. International transport rules are regulated by the IATA. The ATCC Operations Program maintains the shipping facility and ensures the staff is knowledgeable in the packaging and labeling of biological materials, in compliance with domestic and international regulations for packaging and shipment of infectious agents. ATCC has in storage approximately 1,800,000 vials of biological materials, and sends out 145,000 specimens a year in 44,000 shipments. About 20% of the ATCC's shipments contain hazardous material at the biohazard 2 or 3 level. Written procedures are in place to assure that the proper permits and licenses are obtained for each shipment. ATCC routinely secures permits and licenses from such agencies as the Department of Commerce, Food and Drug Administration (FDA), Fish and Wildlife, and Department of Agriculture. Current contracts and operations are subject to regulation by FDA, Occupational Health and Safety Administration (OSHA), Environmental Protection Agency (EPA), Nuclear Regulatory Commission (NRC), Department of Transportation (DOT), Centers for Disease Control and Prevention (CDC), and United States Department of Agriculture (USDA). The staff picks all agents, packages them for shipment and ensures that all specimens and documents are in

order, and ship via an appropriate carrier. Domestic shipments are typically sent next day delivery via Airborne Express. Foreign shipments are sent by carrier most able to access the ultimate destination (*i.e.*, Federal Express, Nippon, and Expeditors).

In compliance with United Nations (UN) specifications, infectious materials are packaged in double containers, manufactured in accordance with UN Class 6.2/01, for shipment. Shipments are packaged to protect the infectious agent from environmental degradation as well as to prevent unintentional release of hazardous materials. ATCC stocks and provides all shipping cartons, cushioning materials, labels, containers, insulating materials, dry ice and other supplies required to ensure the safe intact arrival of each specimen shipped. Packaging configurations used by the ATCC conform to Dangerous Goods Regulations (DGR, 1997) of IATA Packing Instructions 602 (for Infectious Substances), 650 (for Biological Products and Diagnostic Specimens), and 904 (for Dry Ice). Packaging is marked and labeled in accordance with instructions of DGR Section 7, and associated documentation for shipments is prepared per DGR Section 8. Packaging used for Infectious Substances shipments complies with performance-oriented requirements of DGR Section 6.5.

All personnel involved with shipment receive annual training in dangerous goods shipping procedures, in accordance with International Air Transport Administration (IATA) and DOT regulation. There is also a standard operating procedure in place to assure compliance with regulations governing embargoes, denied persons, and other specially designated entities and individuals as determined in 15 CFR chapter VII, subchapter C, Part 764. This process may be found in Standard Operating Procedure QA:RA2P003, Establishing New Customer Accounts.

The ATCC fully complies with federal regulations that apply to the importation, exportation, trade and sale of those products that are covered by the Federal Fish and Wildlife Laws as described in 50 CFR Parts, 10, 13, 17 and 23. The ATCC does not harvest cells from endangered species or other wildlife. A few cell lines that were deposited prior to the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES) are in the collection. Those products that are covered by federal wildlife laws are distributed in accordance with applicable regulations and valid licenses and permits.