AAV Reference Material Working Group
Bid Submission Form
Donation of Repository Services, RFP 5.0

Adeno-associated virus Reference Material (AAVRM) vials are intended to be stored at less than -55 C until shipped under proper conditions to requesters. Bid will also provide for appropriate storage of vials of the titering cell bank and vector plasmid bank vials, and of the vialed reference material and distribution during the characterization phase.

General Requirements for Bidding

Repository should have the capacity to store 5000 to 10,000 X 1mL vials at < -55 C, approximately 100 to 200 x 1 mL titering cell bank vials under liquid nitrogen vapor phase, and 50 X 1ml vector plasmid cell bank vials at <-55 C. All freezers and other equipment used for this project must be validated and have appropriate temperature monitoring, alarm, and recording capability. All deviations must be reported to the AAV Working Group Chairperson.

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 and any other applicable regulations.
- personnel experience with requested processing
- distribution plan
- cost analysis
- proposed cost recovery
- tracking procedures that will be used for receipt of the materials being deposited

The bid should also address prevention of catastrophic loss of stored materials, including information on the possibility of storing material in multiple pieces of equipment, and the availability of emergency back-up power, etc.

The bid should indicate the amount of time required from receipt of the vialed reference material until the ability to distribute vials for the characterization phase. Please include the documentation you will need to support the requirements listed above.

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Bid Submission Form
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Please complete the following fields:

Contact Information:
Individual: Charles Buck (alt: Tom Kollars)
Institution: American Type Culture Collection
Address: 10801 University Blvd, Manassas, VA 20110
Phone Number: 703-365-2724
Email Address: cbuck@atcc.org

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

Please attach:

1. Institution Capability Statement
2. Cost analysis and cost recovery proposal
3. Distribution plan
4. Information/experience in shipping
5. Institution Capability Statement

Submit this completed form and all attached information for receipt **by Friday, February 25, 2005** to the address below.

Williamsburg BioProcessing Foundation
Attn: Adeno-Associated Virus Reference Material Working Group
P.O. Box 1229
Virginia Beach, VA 23451
phone: 757-423-8823 fax: 757-423-2065
e-mail: referencematerial@wilbio.com

Electronic submissions are encouraged.

Please note that all information submitted will be publicly available. Please do not mark any information confidential, as we cannot honor that request.

Please estimate the cost and market value of donated goods and services.

*Final decisions will be communicated by or about **Friday, February 25, 2005***

Donation of Repository Services Bid Submission
In Response to RFP 5.0

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 colder than -55°C, 5,000 to 10,000 AAV Reference Material vials and (2) transferring the vials under proper conditions to requesters. The ATCC will, in addition to maintaining and distributing the vialed reference material, also maintain the project's titering cell bank vials and plasmid cell, and will distribute vials as necessary during the characterization phase of the reference material.

The ATCC has for the past 80 years sought to support biomedical research by fostering the exchange of reagents, the use of standard strains in research laboratories, and the curration of the information associated with the physical holdings. ATCC is the premier global biological resource center for management and distribution of biological agents including their derivatives, reagents and supporting products, and is recognized in the industry and by all U.S. and international regulatory agencies as the model organization for safe and secure preservation and distribution of all categories of biological materials. Additionally, ATCC is a World Health Organization (WHO) designated Microbial Resource Center (MIRCEN), and is a member of the World Federation for Culture Collections (WFCC).

Acquiring, authenticating, preserving and distributing reference cultures and their derivatives to the scientific community is ATCC's mission and principal business. The ATCC can furnish all the necessary services, qualified personnel, material, equipment required for the storage and distribution of the AAV Reference Material.

- ATCC is a venerable, internationally known institution, with a proven reputation for providing well-characterized, authenticated, quality assured living biological materials and reference reagents.
- Our management philosophy emphasizes customer satisfaction, value addition, cost-effective operations and competitive benchmarking for all areas of our enterprise.
- Our reagents are cited as standards by FDA, USDA, AOAC, NCCLS, USP, and WHO as well as organizations and agencies that are involved in public health, diagnostics, and clinical and therapeutic product development.
- We have been a leader in the development of tools (e.g. MAAs and MTAs), and support for the Bayh-Dole Act to facilitate access to and sharing of biological materials leading to technology transfer and commercialization among academia, industry and government.
- We offer a full complement of all required capabilities.
- We offer substantial breadth and depth of staff disciplinary capabilities and facility resources and have the flexibility and experience to respond to anticipated and/or unexpected changes in the user community needs.
- We are a neutral, unbiased, not-for-profit institution with no commercial affiliations that would cause potential conflicts of interest in the acquisition of materials or in the distribution of scarce or non-renewable materials. A testimony to our neutrality is the many competing drug and biotechnology companies who deposit their biological materials in our internationally recognized patent depository and in the safe deposit service.

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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 80 years. The ATCC is experienced in all aspects of the required work scope for acquiring, managing and distributing the AAV Reference Material. ATCC capabilities and experience include:

Experience in Requested (Repository) Services.
The ATCC has been acquiring and accessioning cultures of bacteria, fungi, viruses, cell lines and molecular reagents for distribution to the scientific community since its founding in 1925. In addition to acquiring materials from individuals ATCC has a history of working with institutions and groups, such as the Adenovirus Reference Material Working Group to provide the scientific community with specific resources. ATCC has forged relationships with institutions such as with Johns Hopkins University to make special collections and materials more readily available to the scientific community. The ATCC has utilized Scientific Advisory Committees for more than 35 years to solicit advice from the user community on what resources are needed, and how they can be best managed and distributed. The ATCC currently distributes Adenovirus Type 5 Reference Material (ATCC® VR-1516™) prepared by the Adenovirus Reference Material Working Group.

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 and NIAID's BEI Repository currently housed at ATCC's Manassas, VA facility.

Experience with Export & Import of Virus.
The ATCC receives biological materials on a daily basis from international as well as domestic sources for a variety of purposes including addition to the collections, use in research and development activities, safe deposit, patent deposit, etc. The ATCC routinely requests CDC and USDA permits, when applicable, for the importation of virus stocks. Resources are currently available for handling and storing these materials as needed. Mail room security and safety at ATCC are maintained through segregation and the application of strict protocols.

The ATCC currently ships approximately 230,000 biological reagents and related products to scientists throughout the world and has distributors in Europe, Asia and Australia. 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. As a repository for the Adenovirus Reference Material, the ATCC has distributed vials of VR-1516 to recipients in 18 different countries.

Tracking and Storage Capability:
The ATCC currently maintains inventories for more than 170,000 biological agents, cell lines, derived materials and related products, as well as 7 million DNA clones. Inventories for more than 2 million vials, and approximately 20,000 multi-well plates, as well as other items such as culture media, reagents, kits, packets of kits, etc. are maintained via ATCC's enterprise system. ATCC's enterprise system provides mechanisms for documenting and generating reports on account holders, end-users, and shipments including names of recipients, items shipped, dates shipped, etc.

Distribution and Order Processing:
The ATCC has one of the most sophisticated and comprehensive systems for processing requests for its collection holdings and related products, including establishing customer accounts, processing orders, generating shipping documents, invoicing, and ensuring compliance with all regulations and standards for distribution of biological materials. ATCC's enterprise system provides mechanisms for documenting and generating reports on account holders, end-users, and shipments. At present requests/orders are entered into the ATCC enterprise resource planning (ERP) system (MFG/PRO from QAD) following screening to insure the requestor has a customer account. The ERP and QAD systems monitor inventory, customer orders, inventory control, automated alerts for production and replenish stocks based on past sales history. The ATCC currently ships approximately 230,000 biological reagents and related products to scientists throughout the world and has distributors in Europe, Asia and Australia. Our facility location provides access to an extensive network of air and ground transportation.

Because of the diversity of ATCC activities, processes are in place for collecting fees commensurate with the nature of the distribution. ATCC products include a fee for the item, as well as associated shipping and handling fees.

Database, web page and Product Sheets.
The ATCC maintains large databases in an enterprise system for all of its collection holdings, including more than 7 million DNA clones. The databases have been established to meet the requirements of ATCC's diverse collection holdings, and are monitored to insure quality control through a process of curation and standardization. Information from the database is used to refresh the information on the ATCC web page (www.atcc.org). The ATCC scientific relational database management system has recently migrated to an Oracle database platform. ATCC database structures support the open-ended maintenance of external database identifiers, such as those necessary to construct links for NCBI (Medline UIDs, GenBank accession numbers, PUBMED IDs, PlasmoDB, GeneDB, AnoDB, etc.). Information on the viruses available through the ATCC, including the previously acquired Adenovirus Reference Material, can be searched and viewed under the Animal Virus portion of the "ATCC Cultures" tab on the ATCC web page. Data on each holding is also used to prepare an item-specific Product Sheet that prints out with the shipping papers provided when the holding is distributed.

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.

Shipment Capability (Information/Experience):
Shipping and receiving biological materials and reagents is a daily activity at the ATCC. Currently, over 1,000 shipments per week are made to investigators around the world from ATCC's facility in Manassas, VA. ATCC also has distributors in Europe, Asia, and Australia. Sufficient capacity is available to easily accommodate shipment of the AAV Reference material.

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 over 7 million holdings (including clones) and sends out 230,000 specimens a year in over 50,000 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 DHL 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.

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.

Scientific Staff (Experience):
The credibility and long-term sustainability of all ATCC Collections are assured by its accumulated expertise and by the longstanding stability of the organization. ATCC maintains a trained scientific staff to oversee the acquisition and processing new holdings. Currently Charles Buck manages the Animal Virus Collection and

Tom Kollars coordinates the overall ATCC acquisition effort. Biologists and database personnel support the effort of both Drs. Kollars and Buck. The core scientific process of insuring that materials accessioned are properly handled, described in the database, stored and distributed, is supported by full time staff with responsibilities in: regulatory compliance, facility operations, information technology order processing and quality control.

To assure that our compliance procedures are up-to-date, ATCC remains vigilant to changes through daily monitoring of the U.S. Federal Register and other official notifications and communications on changes and new regulations. Internal procedures are in place for assuring communication of these changes to the appropriate ATCC staff so that permitting and licensing compliance requirements are identified for all biological materials distributed by ATCC. Collection Scientists are trained in all regulatory compliance requirements, and the training is updated as changes occur. ATCC Regulatory Compliance staff review the requirements indicated by the scientists and ensure that each item is flagged, if necessary, with the required regulatory permit or license requirements prior to release of the item for distribution.

Shipping Staff (IATA/DOT Experience & Certification):
The ATCC meets or exceeds all regulatory compliance requirements for handling, storage, distribution, and importing and exporting of biological materials. The Regulatory Compliance program monitors the Federal Register as well as other applicable websites on a daily basis to assure compliance with all regulatory requirements and guidelines. All ATCC staff involved in the preparation, packaging, labeling and shipment of infectious agents undergo training in compliance with Department of Transportation regulations (49 CRF Parts 171-180) and International Air Transport Association (IATA) requirements. Inventory and shipping support are provided by ATCC staff with repository experience. The ATCC staff is knowledgeable in the packaging and labeling of biological materials, and the domestic and international regulations for packaging and shipment of infectious agents. The ATCC also has experience in supporting repository distribution from private and from Government repositories.

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. All personnel involved with shipment receive annual training in dangerous goods shipping procedures, in accordance with International Air Transport Administration (IATA) and DOT regulation.

Facilities, Freezers, Alarms and General Bidding Capability.
The ATCC has the required capacity for: (1) frozen storage below -55°C of 5000 to 10,000 1mL vials of virus, (2) approximately 100 to 200 x 1 mL tittering cell bank vials under liquid nitrogen vapor phase, and (3) 50 X 1 mL vector plasmid cell bank vials below -55°C. 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. Bacterial and fungal specimens were originally freeze-dried at ATCC in the 1940's as the only means of effective low temperature preservation of living biological material. However, with the emergence of the use of liquid nitrogen in the early 1960's ATCC quickly developed expertise in cryogenic storage. This allowed the development of ATCC's collections in new areas such as the addition of cell lines and hybridomas. ATCC's leadership as the largest Budapest Treaty IDA for patent deposit purposes is a direct result of this expertise, which has allowed ATCC to store and preserve a larger variety of biological specimens than any patent depository in the world. Currently the ATCC maintains over one hundred freezers, with more than 7 million 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 plan to split the initial stock of 5,000 to 10,000 distribution vials between at least two freezers within its facility as a safeguard against loss.

The Operations wing of the ATCC's Virginia facility provides 7656 net square feet of air-conditioned (66^{o}F to 72^{o}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 extending this capability for the storage of the AAV cell bank, should these conditions be necessary.

The ATCC has a comprehensive biosurety program, which encompasses protection of employees and materials. 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.

All the liquid nitrogen storage and freezer monitoring systems at ATCC are connected to both an internal ATCC alarm and an external alarm monitored by a 24-hour monitoring service. The system is designed such that, in addition to temperature and liquid level changes, any power failure resulting from disconnecting the alarm wires, switching off of power to the unit, or an accidental break in the wire, will result in an alarm condition. In such an event, the 24-hour security and surveillance system is capable of initiating an immediate notification and response to all alarm conditions. All freezers are equipped with dual, independent temperature monitoring systems. Both systems can trigger facility alarms independently. Freezer alarms are reported immediately by ATCC personnel to the appropriate scientific staff for advisement and response.

ATCC buildings are serviced by an emergency generator that is activated automatically whenever there is a power failure. These systems supply electricity to freezers (ultra low) as well as liquid nitrogen alarms, incubators and other essential services when the local power is interrupted during storms or for other reasons. These generators are periodically tested. In addition, the ATCC maintains a large supply of dry ice, in excess of the amount used daily (about 1,000 pounds) in shipping biological materials, which can be used for emergency cooling. Spare liquid nitrogen and mechanical freezers are held in reserve in case of mechanical failure.

Cost Analysis and Cost Recovery Proposal

It is proposed that the vials be accessioned, at no charge to the AAV Reference Material Working Group, by ATCC and distributed in accord the current ATCC fee structure to those requesting the AAV Reference Material. Although the ATCC fees are adjusted from time to time, it is envisioned that the initial fee will be $182 per vial unless the Working Group and ATCC come to mutual agreement on some other fee schedule. $182 is the fee currently charged for VR-1450, the replication competent retrovirus reference strain, and VR-1516 (the replication competent adenovirus reference strain). For comparison, if the AAV Reference Material were stored under contract ATCC would collect a fee for the storage of the AAV Reference Material--the “safe deposit” fee ATCC would charge an outside organization for the 5-year storage of 10,000 vials would be approximately $100,000.

As stocks approach a one-year supply, the ATCC anticipates planning for the production of a new batch of material with necessary Williamsburg BioProcessing Foundation and industry input. Depending upon distribution rates and projected revenues, ATCC may in the future 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 Williamsburg BioProcessing Foundation or 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.

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 AAV 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 $86.oo 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.

Distribution Plan

The ATCC proposes to maintain the AAV Reference Strain and the limited cell and virus bank stocks from the Working Group indefinitely, and to make the deposited AAV 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 vialed reference material until the item can ship, due to the need to create database entries and input descriptive and regulatory information, will be approximately four 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. Prior to receipt ATCC will need to have information on the source of the materials and where they will be shipped from and under what conditions they will be shipped. Information will also be required on the actual vial configuration for the material to be deposited so that space can be reserved in the appropriate freezers and ATCC will need clarification with regard to whether there are any restrictions as to what temperature, below -55^{o}C, that the virus can be stored at—i.e. would the vapor phase of a LN freezer or a -70^{o}C mechanical freezer be equally . ATCC will also need, prior to or after receipt of the material, a description of the material (i.e. label description, virus strain, etc), contributor of record (i.e. AAV Reference Material Working Group), recommended storage, recommended host cells, recommended incubation temperature and any characterization data from the preparation of the reference material that should be archived and passed on to the recipients.

The ATCC will maintain in validated nitrogen vapor or mechanical freezers at colder than -55°C, 5,000 to 10,000 AAV Reference Material vials. For the purpose of this proposal it is assumed all material will be in 1ml Nunc-type screw-cap plastic vials, but vials of other configurations (including glass serum vials with crimp-cap closures) can be accepted and managed. The ATCC will, in addition to maintaining and distributing the vialed reference material, also maintain the project's titering cell bank vials and plasmid cell vials. Validated freezers will be used for storage. ATCC also has process in place for GMP receipt, storage and distribution of cell lines and virus, should the Working Group wish to explore that option. Deviations from the agree upon storage conditions

will be reported to the contact provide by the Working Group and/or the Williamsburg PioProcessing Foundation, as appropriate.

During the characterization phase, ATCC proposes to ship vials at no cost to a limited number of test laboratories identified by the Working Group as needing vials to test. For this purpose ATCC will need information with regard to: which labs need how many vials; the contact person at each laboratory; and from the contact at each laboratory their ATCC customer number, which is used to insure that materials are only shipped to sites allowed by US law and in accordance with ATCC policy. distribute to a limited number of , and will distribute vials as necessary during the characterization phase of the reference material. Vials of virus will be shipped in an inner container on dry ice in accordance with IATA requirements for infectious material and in the same packaging configurations that the ATCC has successfully used to ship other cell lines and virus stocks.

Upon completion of the characterization, and approval by the Working Group contact for transfer of the material from quality hold to distribution status, the ATCC will list the AAV Reference Material on the ATCC web-site and begin to accept orders from customers. The ATCC catalog of strains, in which we propose to include the AAV Reference Strain, is available on-line at www.atcc.org. In order to better service international customers, ATCC has developed an extensive network of distributors. LGC Promochem (with offices located throughout Europe) serves as our distributor in Europe, Summit Pharmaceuticals International Corporation as distributor in Japan, KORAM Biotech Corporation as distributor in South Korea, Union Biomed is the distributor in Taiwan, Cryosite is the distributor in Australia and New Zealand, BioGen Pte is the distributor in Singapore and Tin Hang Technology Lim ited is the distributor serving Hong Kong, China and Macau. ATCC can accept orders via phone, email web and FAX.

In order to promote the availability of the new material, ATCC will offer information in ATCC Connections—ATCC's quarterly newsletter—to increase public awareness of the AAV 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 and the Annual American Society for Virology meeting. International distributors will be trained in refererence material offerings and will be prepared to promote the availability at scientific meetings and tradeshows, as well as through their websites and customer visits.

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 customers be limited to 12 vials (or some other agreed upon number) per year to avoid unreasonable depletion of distribution stock. Twelve vials is the annual limit placed in the Adenovirus Reference Material and has served to prevent a single entity from consuming all the available stock with the result that others would not have access to the material. It is additionally proposed that only a portion of the vials provided to the ATCC be initially made available for distribution. Should a pattern of use be detected that would rapidly and unreasonably deplete this resource, steps will be taken to remedy the situation. Finally, should no pattern of abuse be observed additional blocks of vials can be transferred to distribution as necessary. Input from the AAV Reference Material Working Group and/or the Williamsburg BioProcessing Foundation will be needed to optimize the application of any required restrictions.

For the collective reasons described above we believe the uniquely valuable reference vials of AAV, developed by the AAV Reference Material Working Group in cooperation with the Williamsburg BioProcessing Foundation should be distributed by the ATCC. ATCC can maximize the availability of the reagent to the community and insure long-term curration of the AAV Reference Material. 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.

Information/Experience in Shipping

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 US NIH/NIAID BEI Repository.

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, KORAM Biotech Corporation as distributor in South Korea, Singapore and Taiwan, and Cryosite as distributor in Australia.

ATCC distributes over 230,000 biological specimens and related products each year in more than 50,000 shipments. About 25% of ATCC's shipments contain hazardous material at the risk group 2 or 3 level. Shipments of available, in stock reagent materials will be made within seven (7) working days of receipt of requests. Shipment of available

non-hazardous, non-permitted materials to domestic recipients can be made within 24 hours of receipt of request. Available reagents requiring permits or licenses or those subject to other legal controls will be shipped within 48 hours of clearance. The ATCC typically ships orders within 48 hours of receipt of all necessary forms, permits and licensing agreements. Domestic recipients will be notified by phone, FAX, or e-mail, and foreign recipients will be notified by FAX or e-mail of shipments of reagents.

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 every shipped item. ATCC shipping containers have been tested to comply with all DOT and International Air Transport Association (IATA) regulations. Shipping containers have been designed and tested to insure safe delivery anywhere in the world. All materials are shipped by air for prompt delivery, including next day delivery domestically. ATCC packaging is available for frozen shipments that will maintain temperature up to seven (7) days, which is acceptable for expedited delivery anywhere in the world. Long-term vendor relationships afford constant availability of dry ice and other essential packaging materials, even during emergency situations.

All cultures and reagent materials that are transported to and/or accessioned at ATCC are reviewed prior to transport and release for any licenses or permits for importation or interstate transport for received materials, and for domestic or international distribution from ATCC. ATCC SOP no. RA001, entitled “Identification of Licenses and Permits Required for New Cultures and Other Biological Materials Received at ATCC” outlines procedures to determine permit and license requirements for all biological materials transported to and from ATCC, including all accessioned materials. The determination of the regulatory compliance requirements for distribution is made by the appropriate collection prior to release of the material.