US Policy for Disease Control among Imported Nonhuman Primates

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In 1990, in response to the occurrence of Ebola virus (subsequently identified as subtype Reston) infection among cynomolgus monkeys imported from the Philippines, the United States implemented strict disease control measures for handling nonhuman primates during transit and quarantine and initiated importer facility compliance inspections. Disease control measures emphasized protection of workers from exposure, use of containment facilities and procedures, measures to prevent spread of infection among animals, and laboratory testing of animals that die or become ill during quarantine. From 1991–1995, no outbreaks of filovirus infection occurred, and only one other disease outbreak (caused by Mycobacterium species) was recognized. In April 1996, Ebola virus (subtype Reston) infection was identified in another group of cynomolgus monkeys imported from the Philippines. The disease control measures implemented since the first Ebola virus (subtype Reston) outbreak appeared to work well. Currently, the 27 registered importer facilities import ~8500 nonhuman primates annually, and mortality rates are <1.0%. Importer facilities receive regular inspections, and compliance with disease control measures and disease reporting is excellent.

Since the 1940s, when crates of monkeys arriving from yellow fever zones were required to have wire mesh screening to exclude mosquito vectors, the US Public Health Service has regulated the importation of nonhuman primates in order to prevent the introduction and spread of diseases communicable to humans. The current US Foreign Quarantine Regulations regarding nonhuman primates (42 CFR part 71.53) [1] were put in force in 1975 to address historic and emerging infectious disease concerns associated with imported nonhuman primates (notably, African monkeys infected with Marburg virus were imported into Europe in 1967, resulting in human infection, person-to-person transmission, and deaths) [2]. The 1975 regulations prohibit the importation of nonhuman primates for use as pets and require that importers of such animals do the following:

- Register with the Centers for Disease Control and Prevention (CDC).
- Certify that imported nonhuman primates will be used only for scientific, educational, and exhibition purposes.
- Isolate shipments of imported nonhuman primates for 31 days upon arrival.
- Maintain records regarding each shipment of nonhuman primates.
- Report suspected zoonotic illness in animals or workers.

From 1975–1989, registration was primarily an administrative function of the CDC’s Division of Quarantine. Routine quarantine facility inspections and monitoring of the handling of shipments in transit were not performed. Disease control measures during transit and quarantine were variable. In 1989, there were >140 registered facilities importing up to 24,000 nonhuman primates per year (principally macaques). Mortality rates during transit and quarantine were ~20% (unpublished informal telephone survey conducted by CDC, December 1989; Tipple MA). However, no outbreaks of zoonotic disease associated with imported nonhuman primates in quarantine were reported to CDC during this period.

In late 1989, filovirus infection was identified in a group of critically ill and dying cynomolgus monkeys from the Philippines at a registered importer quarantine facility in Reston, Virginia [3]. The virus was subsequently identified as a new Ebola virus strain, subtype Reston (EBO-R). By early 1990, filovirus infection was identified in four shipments of cynomolgus monkeys from the Philippines at three registered quarantine facilities. Nearly 500 animals died or were euthanatized to control the outbreak in Reston. A number of additional disease control measures were implemented in response to that outbreak and the subsequent investigation [4]. Principal among these requirements is laboratory testing for acute filovirus infection (item 8, below) during the mandatory 31-day quarantine to rule out active disease. Following are the requirements and measures that remain in place today.

- Permits are required to import cynomolgus, rhesus, and African green monkeys [5].
- Disease control measures must be followed during transit and quarantine.
- Specialized equipment must be used to minimize exposure of humans to nonhuman primates during transit and quarantine.
- Worker protection measures must be followed to prevent bites and scratches and contact with potentially contaminated material.
- Standard operating procedures must be followed for quarantine activities.

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Workers must be trained regarding the risks and protective measures for exposure to nonhuman primates, and supervision must be provided to ensure compliance with standard operating procedures.

Importers must document arrangements for measures to minimize human exposure to nonhuman primates during all phases of shipment and quarantine.

Cynomolgus, rhesus, and African green monkeys that die during quarantine must be tested for filovirus antigen, using antigen-capture ELISA [6]; those exhibiting signs of illness suggestive of filovirus infection but recovering during quarantine must be tested for IgG antibodies, using ELISA [7].

Importers must screen imported primates for tuberculosis [8], monitor them for signs of other zoonotic diseases of public health significance, and report suspected zoonotic illness in animals or workers to CDC by telephone within 24 h. Shipments must remain in quarantine a minimum of 31 days or, if necessary, longer to rule out or resolve zoonotic illness.

Currently, there are 27 registered importer quarantine facilities importing ~8500 animals per year (again, principally macaques). CDC’s Division of Quarantine inspects facilities prior to registration and periodically thereafter and monitors the handling of shipments upon arrival at ports of entry or at the quarantine facilities. Mortality rates during importation and quarantine are now consistently <1.0%. CDC inspectors have noted improved compliance with the International Air Transport Association Live Animals Regulations. Shipments are now consolidated on pallets, segregated from other cargo, and less often delayed in route, and transit workers are better aware of proper handling procedures.

EBO-R infection was identified in another group of imported cynomolgus monkeys in early 1996 [9]. The single shipment of 100 animals had been imported from the Philippines on 21 March 1996 by a registered importer and divided into 2 cohorts of 50 animals each for quarantine. On 30 March, 1 cynomolgus monkey died following a 3-day illness characterized by anorexia and lethargy. EBO-R infection was promptly identified in this animal. The remaining cohort members were euthanized as an outbreak-control measure, and 3 were found to be infected with EBO-R. The other cohort of 50 animals remained free of signs of infection throughout the quarantine period, which was extended for >30 days beyond the original 31 days. There was no evidence of disease spread to other animals at the facility.

The additional disease control measures implemented since the first EBO-R outbreak appeared to work well during the 1996 outbreak. The registered quarantine facility is operated by a commercial importer of nonhuman primates located in Alice, Texas. They import, quarantine, and condition primates for introduction into breeding colonies at their facility and for distribution to other facilities, all for scientific use. Their last inspection was in January 1995. They have been in substantial compliance with CDC requirements since 1990.

When the first animal in the 21 March 1996 shipment died, the facility submitted specimens to an approved laboratory for filovirus testing, as required by their special permit. The positive results were reported immediately to CDC. Additional sampling, testing, and extension of the quarantine period were done in consultation with CDC, again as required by the permit. Although CDC inspectors did not monitor the handling of this particular shipment upon arrival at the port of entry, CDC was able to verify the itinerary and that cargo workers had complied with disease control measures during multiple previous shipments using the same itinerary.

The current CDC requirements appear to have been effective in minimizing human exposure to the animals during transit and quarantine, in identifying suspect animals during quarantine, in laboratory diagnosis of the infection, in prompting reporting to CDC, and in containing infection within the registered importer quarantine facility. Following the 1996 outbreak, CDC conducted a review and reassessment of the CDC requirements; no changes were made.

References
7. Division of Quarantine, Centers for Disease Control and Prevention. Letter to interested parties concerning the special permit filovirus testing requirements. 5 March 1996.