Last revised 12/17/2010

COMS Policy on Recommended Containment Levels for Adenoviral Vectors in Laboratory Rats, Laboratory Mice and Laboratory Rabbits

I. Purpose

Provide containment requirements for use of adenoviral vectors in laboratory rats, laboratory mice and laboratory rabbits.

II. Applicability

All COMS projects involving the use of adenoviral vectors in laboratory rats, laboratory mice and laboratory rabbits must comply with the requirements of this policy.

III. Definitions

A. BL2-N(72hr)

Animals are housed in BL2-N containment for the first 72 hours following inoculation with viral vector according to the guidelines of the specific institution. Animal care during this time period is handled by either the laboratory personnel (best practice) or animal care workers, depending on the institution. Waste materials such as bedding, feces and urine should be disposed as of biohazardous waste. After a minimum of 72 hours, animals must be placed in a clean cage before animals can be housed at BL1-N for the remainder of experiment. Please consult with your Biosafety Officer, IACUC and/or Animal Facility Manager on approved procedures at your Institutions animal facility.

IV. Implementation procedures

A. Inoculation

1. Inoculations of adenoviral vectors into animals are to be performed within a biological safety cabinet under biosafety level 2 (BL2) conditions. Safer, engineered needles or needle less systems should be used, when possible. Inoculations should be conducted by trained personnel only. The site of inoculation should be thoroughly cleansed to prevent contamination of bedding materials.

B. Housing

1. The level of housing containment for animals inoculated with viral vectors that can infect human cells is dependent on the characteristics of the viral vector, the animal host, inoculation method, and the transgene. For most experiments where common, well described replication incompetent adenoviral vectors are inoculated into rodents, the required housing containment is dependent on the expressed transgene (see table below).
2. A list of common, well described adenoviral vector systems is being developed and will be added to this policy when it becomes available. Vectors not on this list may be approved with at a higher containment level.

Transgene Type	**Housing**
Reporter genes (e.g., green fluorescent protein, LacZ)	BL1-N
Genes with biological activity	BL2-N for first 72 hours post inoculation followed by BL1-N housing (denoted as BL2-N(72hr))
Oncogene or toxin gene (or transgenes with high oncogenic or toxic potential)	BL2-N housing for the life of the animal

C. BL2-N(72hr)

1. Definition: Animals are housed in BL2-N containment for the first 72 hours following inoculation with viral vector. Laboratory personnel are responsible for animal care during this time period. Waste materials such as bedding, feces and urine should be disposed as of biohazardous waste. After 72 hours, lab personnel will place animals in a clean cage and animals can be housed at BL1-N for remainder of experiment. Please consult with your IACUC and/or Animal Facility Manager on approved procedures at your Institution’s animal facility.

2. Rationale: Studies suggest that the potential for shedding of replication competent virus (RCV) is low but not unfeasible.[i,ii] Therefore, a reduction in containment to BL1-N after 72 hours, reduces the risk of exposure to shed virus and allows for a sensible safety factor.

D. Exceptions

1. Animals engrafted or injected with human cells or animal hosts that are permissive for adenovirus replication (e.g., cotton rat, hamster), may be approved at a higher containment level.
2. Depending on the specific project attributes, COMS may require BL2-N housing for the life of the animal regardless of the expressed transgene.
3. This policy is subject to change as new information on viral shedding becomes available.
4. This policy is specific to lab rats, lab mice, not other rodent species. Other animal species may be examined on a case by case basis by COMS.

V. Policy Authority

The Office of Biological Safety (OBS) of the Harvard Medical School is responsible for supporting the Committee on Microbiological Safety. This includes preparation and revising of the COMS Policy Manual for committee review. The Committee on Microbiological Safety (COMS) authorizes this policy.

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[i] Oualikene W, Gonin P, Eloit, M. (1994) Short and long term dissemination of deletion mutants of adenovirus in permissive (cotton rat) and nonpermissive (mouse) species. Journal of General Virology 75 pp 2765-2768.

[ii] Ying B, Toth K, Spencer JF, Meyer J, Tollefson AE, Patra D, Dhar D, Shashkova EV, Kuppuswamy M, Doronin K, et al: INGN 007, an oncolytic adenovirus vector, replicates in Syrian hamsters but not mice: comparison of bio distribution studies. Cancer gene therapy 2009, 16:625-637.