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ORNL-TM-1162

CONTAINMENT CRITERIA FOR LABORATORIES HANDLING INFECTIOUS AGENTS

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ORNL-TM-1162

Contract No. W-7405-eng-26

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MAY 1965

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ABSTRACT

This document defines and establishes containment criteria to assure safety within laboratories handling infectious agents. Also included is the classification used for establishing the relative hazard of any given virus or biologic agent, the duties of responsible investigators, and the responsibilities of the Biohazards Committee. The containment criteria specified herein have been established to assure safety in laboratories engaged in biological research.

I. INTRODUCTION

In any classification of infectious agents used as a guide in establishing containment criteria, a number of factors must be considered. The pathogenicity of an agent may vary profoundly with its portal of entry into the body; e.g., agents usually causing lethal infections (such as rabies virus and Japanese B virus) cannot penetrate the intact skin, whereas less virulent agents (such as Leptospira icterohemorrhagiae and Treponema pallidum) readily do so. The possibility of infections resulting from inhalation exposure also cannot be ignored. It is evident, therefore, that the mode of exposure to a pathogen and the integrity of the defenses of the exposed individual are crucial in determining whether disease will ensue and what course it may take.

The effects of prophylactic immunization and the existence of effective means of therapy also influence the potential hazard of exposure to any given agent.

The mode of handling and the quantity of the infectious agent being used are of great importance. For this reason, separate containment criteria have been established for the zonal centrifuge program in which large quantities of viral or virus-like agents can be concentrated in a small volume, making any accident or mistake in technique of greater consequence than under the usual laboratory conditions.

The classification is predicated on the premise that the agents in question have access to persons exposed under the usual conditions of infectivity and resistance. Special allowances for increased or de-

creased pathogenicity may be indicated, depending on the circumstances of exposure, effectiveness of safeguards, and other modifying factors. Agents that are non-pathogenic as they occur in nature may conceivably be harmful in the massive concentrations obtainable with modern production and purification techniques (biogen, zonal centrifuge, etc.) This, however, is a new question requiring further exploration before precise evaluation is possible.

It must also be recognized that new viruses are continually being discovered in human beings and animals, the pathogenicity of which remains to be determined (e.g., "Viruses in Search of Disease", Ann. N.Y. Acad. Sci. 67:290-445, 1957), and that "new" pathogenic effects of "old" viruses are, likewise, noted from time to time (e.g., the recent disclosure that certain human adenoviruses and pox viruses exert carcinogenic and cocarcinogenic effects in laboratory animals). It is entirely conceivable, therefore, that periodic revisions may be necessary for certain agents, when these agents are found to have a greater pathogenicity for man than currently recognized.

The basic philosophy of safety which governs the containment criteria is of paramount importance. The recommendations of this Committee, if followed, should assure a safe working environment for the highly trained professional investigator as well as the laboratory technician or maintenance craftsman. In all cases, the risk involved in an experiment will be compared with the potential rewards. Human illness which can be prevented with reasonable care will not be considered an acceptable risk. Care must also be exercised to prevent even easily treatable illnesses or those which cause minor disability.

Unsafe "short cuts" or technique violations to meet deadlines or to save money cannot be justified.

II. CLASSIFICATION

The following classification is formulated as a guide to aid in the assessment of hazards associated with the handling of infectious agents. This classification is considered applicable only to exposure under routine laboratory conditions and to unattentuated or unaltered agents. Any agent in a concentrated form may conceivably gain pathogenicity, but a precise prediction of the risk under these circumstances cannot be made from experience to date. Any agent used in massive concentrations must, therefore, be considered individually in light of the circumstances attending its use.

Group A. Non-pathogenic to man or animals.

Group B. Non-pathogenic to man; infectious to animals but not productive of lethal epidemic disease.

Group C. Non-pathogenic to man; oncogenic (cancer producing) to animals.

Group D. Non-pathogenic to man; highly infectious to animals (likely to cause lethal epidemic disease).

Group E. Mildly pathogenic to man (producing only mild, non-disabling, non-lethal disease).

Group F. Moderately pathogenic to man (producing occasionally severe and disabling disease, rarely lethal).

Group G. Highly pathogenic to man (producing severe, often disabling disease, occasionally lethal).

Group H. Extremely pathogenic to man (producing severe, often lethal disease).

Since the relative hazard associated with handling particular infective agents depends to a great extent on the population exposed, the Committee will investigate and classify each agent accordingly; e.g., classification of a particular virus should be consistent with the manner in which it is being handled as well as the population which is being exposed. The effects of exposure of a general population to a particular virus could mean that this virus should be designated a Class F agent. If, however, it can be demonstrated that all individuals handling this virus have an acquired immunity or if an immunity can be induced in such individuals, the Committee will logically classify this virus in Group E for containment purposes. However, some appropriate precautions (see Basic Requirements, No. 6) will be necessary even then to avoid exposure of unimmunized workers.

III. DUTIES OF RESPONSIBLE INVESTIGATORS

For the safety of all personnel handling infectious agents, the following policies have been established:

1. The classification in Section II of this report will be the guide used by the Biohazards Committee in considering applications for work with these agents.

2. Although agents in Groups A, B, or C may be used without specific approval by the Biohazards Committee, the Committee must concur with the investigator on all matters of classification regarding specific agents. In addition, approval by the Animal Health Committee of the Biology Division is required for work in that Division with agents in Groups B, C or D.

3. Approval must be obtained from the Biohazards Committee before any other agents are to be used in any experiment or study. Requests for approval, including the agent or agents to be used and the nature of the experiment, should be made in writing at least two weeks before the date of the proposed experiment.

4. The Division Director, through the group leader, is primarily responsible for the safety of personnel working with hazardous agents. The activities of the Biohazards Committee in no way reduce this responsibility.

5. Unannounced inspection visits of facilities may be made to assure the Committee that its recommendations are being followed and to assist in developing new safety techniques if they are indicated.

6. Visitors to any facility working with hazardous agents shall be limited to those who have a vital interest in the work performed. All safety precautions which apply to the investigator and his staff will also apply to visitors.

7. Any unusual incident, such as a spill, break in containment, or failure in exhaust ventilation, shall be reported immediately to the Health Division, a careful record of what happened shall be recorded by those present at the time of the incident, and a copy shall be sent to Dr. T. A. Lincoln, Health Division, Building 4500, ORNL.

8. At such time as requests are made for studies using agents in Classes D, E, F, G, and H, the containment and safety requirements for the specific agents will be reviewed individually by the Committee which will make recommendations to the Division Director, with a copy to the responsible investigator.

9. New Construction: It is suggested that all new proposed construction where it is anticipated that agents in Groups B thru H may be used, shall be reviewed by the Biohazards Sub-Committee prior to the conceptional design report, and again at the Title 1 and Title 2 Engineering stages.

IV. CONTAINMENT CRITERIA FOR CONVENTIONAL LABORATORIES

Based on the information contained in the three previous sections, the following criteria are considered applicable to conventional laboratories for the handling of infectious agents:

Class Zero - Conventional - No Special Containment: This category involves no special precautions for containment. It includes agents classified in Group A of Section II.

Class 1 - Conventional - Minimal Containment: This class of containment includes agents in Groups B, C, and E of Section II.

The laboratory area shall be under negative pressure with respect to surrounding areas and its exhaust air handled separately. Exhaust stacks shall be separated as far as possible from air intake systems and shall be of sufficient height and location so that reflux will not occur in the event of exhaust system failures nearby.

Transfer hoods or cubicles in such facilities shall be provided with a filtered exhaust system similar to those required of hoods for radioisotopes.

High speed centrifugation in the Spinco Model L and similar centrifuges shall be carried out in leak-proof tubes such as those developed at the Oak Ridge Gaseous Diffusion Plant.

Facilities in this category shall have equipment available for sterilization of all contaminated apparatus.

Personnel shall have adequate training and knowledge in handling the agents under study. Entry to these facilities shall be limited to persons authorized by the responsible investigator.

Class 2 - Conventional - Moderate Containment: This category includes agents classified in Groups D and F of Section II.

In addition to the aforementioned requirements in Class 1 - Conventional, the following criteria apply:

All exhaust systems in this category shall have "absolute type" filters, with provision in the exhaust system for filter sterilization prior to filter change by a steam formaldehyde purge or an equivalent procedure. A standby exhaust system is recommended in case of the failure of the primary system and to operate while filters are being changed. The integrity of this system will be verified by a filter test procedure using DOP (Dioctyl Phthalate) or its equivalent and shall be shown to be 99.95+% efficient for 0.3 to 0.7 micron particles. Maintenance personnel handling filters shall be protected by rubber gloves and masks of a suitable type.

The facilities shall be separated from other adjacent areas by air locks.

Maintenance personnel entering these areas shall be required to take appropriate precautions as directed by the responsible investigator.

Class 3 - Conventional - Maximal Containment: This category includes agents in Groups G and H of Section II.

In addition to all foregoing requirements, facilities in this category shall require a separate building, preferably isolated from other areas.

All work shall be performed in freon-tight glove boxes and all infected animals shall be housed in freon-tight negative pressure isolators. Provision shall be made to sterilize the unit and all waste from these animals

All effluent drains from contaminated laboratories and animal rooms shall be included in drainage system of the two-tank, live steam injection type or similar process whereby all waste is decontaminated prior to entrance into common plant systems.

Entrance to all potentially contaminated areas shall be through a primary pass-through shower and a secondary UV air-lock, with appropriate air pressure differentials to maintain the contaminated area under negative pressure with respect to all other areas.

All material from contaminated areas shall be sterilized prior to

exit.

Maintenance and inspection personnel shall be immunized if possible and equipped with protective clothing, masks, and gloves prior to entering contaminated areas in such a facility.

All rooms containing potentially contaminated material should be vapor tight to allow for Beta propiolactone, or equivalent, decontamination.

Transportation of material from the Zonal Centrifuge Facility shall be subject to the recommendations of the Biohazards Committee.

V. CONTAINMENT CRITERIA FOR CONCENTRATION AND SEPARATIONS LABORATORIES

The following containment criteria apply for concentration and separations laboratories and were originally approved by the Biohazards Committee at its meeting on April 3, 1963. They have been slightly changed for this report:

Class 1 - Minimal Containment: No special containment is necessary other than an isolated centrifuge room with UV light, negative pressure, and a filtered exhaust system. As an additional precaution, a change room, shower, and facilities to sterilize work clothes should be present. Special work uniforms should be worn in the facility, and upon completion of work, these should be removed and autoclaved. Personnel should shower and wash thoroughly prior to donning street clothes. This class of containment is applicable to agents non-pathogenic to man and infectious to animals but not productive of lethal epidemics in animals; i.e., agents in Groups B, C, and E of Section II.

Class 2 - Moderate Containment: All work shall be performed in freon-tight glove boxes. Provision shall be made to sterilize all equipment and/or materials removed from these boxes. In addition, all effluent drains from these areas shall be sterilized using a two-tank live-steam injection type or similar process whereby all waste is sterilized prior to entrance into common plant systems. A barrier system is required which will allow all work to be carried out in negative pressure, filtered exhaust, dry boxes through glove ports. A change room, shower,

and facilities to sterilize work clothes shall be used as in Class 1, Minimal Containment of Section V above. A containment system of this type is indicated to prevent contamination of either the operator or the environment. This class of containment is applicable to agents in Groups D and F of Section II.

Class 3 - Maximal Containment: In addition to Class 3, Containment Criteria, provision shall be made to incinerate the exhaust from all "freon-tight" enclosures before discharge to the atmosphere.

Entrance to all potentially contaminated areas shall be through a primary pass-through shower and a secondary UV air-lock, with appropriate air pressure differentials to maintain the contaminated area under negative pressure with respect to all other areas.

All material from contaminated areas shall be sterilized prior to exit.

Maintenance and inspection personnel shall be immunized if possible and equipped with protective clothing, masks, and gloves prior to entering contaminated areas in such a facility.

Under special circumstances, such as the release of infectious materials and unusual decontamination procedures, all personnel should wear a complete suit impervious to acid and vapors, with a self-contained air supply for entry into the centrifuge room. As an

additional precaution, entries should be made only through a decontamination lock where the suit will also be decontaminated before return to the outer room. This class of containment is applicable to agents in Groups G and H of Section II.

VI. RESPONSIBILITIES OF THE BIOHAZARDS COMMITTEE

This Committee is responsible for reviewing the human hazards of work associated with the use of biological agents. Whenever chemical or physical agents are used with biological agents, the Committee shall consider the total hazard and will not be arbitrarily limited. All proposals for experiments on humans, either at ORNL or on the outside, under the direction and responsibility of the ORNL staff, shall be reviewed by this Committee.

Knowledge of existing or proposed use of hazardous biological agents will normally come to the attention of this Committee from the following three sources:

1. From the Division using the agents.
   a. The responsible investigator will submit to the Committee, for review, a proposal for the use of potentially hazardous biological agents in his research.

   b. Human hazards associated with animal work and proposals for their control may be presented by those responsible for the health and care of the animals.

   c. The Division Director may request the Committee to review the hazards associated with certain agents which are, or will be, used by a number of investigators.

2. From the Biohazards Committee

Members of the Committee may become aware of potential hazards because of their own observations and may then request a review by the Committee.

3. From Laboratory Management

Laboratory management may become concerned about the health hazards of a particular experiment or operation and request the Committee to investigate them and make recommendations.

After the Committee has reviewed specific proposals or has completed its investigation of a particular hazard, it will make a written recommendation to the Laboratory Director and Division Director. The latter will accept the recommendation and be responsible for implementing it or will submit his specific dissent in writing to the Laboratory Director, who will decide the proper course of action.

Since all members of the Committee have full time responsibilities, they, therefore, have only a modest amount of time they can devote to investigative or surveillance work. However, since there is no substitute for direct observation and active interest, the Committee, perhaps by assigning specific areas of responsibility, will maintain an active interest in existing or proposed work with the various infectious agents. Whenever they feel that the recommendations of the Committee are not being followed or that new hazards are developing because of

changes in the use of the agents, they should bring this to the attention of the Committee chairman for possible review by the entire Committee.

VII. SUMMARY

The Committee recommends use of the proposed classification and containment criteria to assure the safety and well-being of individuals whose work requires the handling of infectious agents. It considers it to be the responsibility of each investigator to consult with the Committee prior to initiating any experiments involving hazardous infectious agents. The proper classification of an agent will be determined by the Committee. In addition, the Biohazards Committee suggests that it review all new proposed construction of facilities prior to conceptual design reports if it is anticipated that agents in Groups E through H may be used in such facilities.

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