City of Newton
Setti D. Warren
Mayor

HEALTH AND HUMAN SERVICES DEPARTMENT
Linda Walsh, Interim Commissioner
1000 Commonwealth Avenue
Newton, MA 02459

Telephone 617.796.1420 Fax 617.552.7063
TDD/TTY 617.796.1089

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TO: **Marc Laredo, Board of Alderman Land Use Committee, Chair**

FROM: **Linda Walsh, Newton Biosafety Committee, Chair**

RE: **Biosafety Committee Response to Questions from Land Use Committee regarding special permit application for Atrium Center**

DATE: **March 24, 2015**

Question 1

In general, what are Level I and Level II laboratory uses? What is rDNA research or technology and how does it fit in with Level I and Level II laboratory uses? Please provide examples of such uses, explain where such uses are conducted, and whether such uses are considered safe.

BSL (Biosafety Level)-1 and BSL (Biosafety Level)-2 laboratories are facilities that are used to safely conduct life science research under strict federal, state and local guidelines and oversight.

BSL-1: BSL-1 activities pose no or low individual and community risk. BSL-1 Labs are typically not separated from the general traffic patterns of others, work is performed on open bench tops and special containment equipment and devices are not needed. BSL-1 laboratory personnel have specific training in the procedures conducted in the laboratory and are supervised by personnel with general training in microbiology or related field. This is the type of laboratory found in municipal water-testing laboratories, in high schools, and in some community colleges

BSL-2: BSL-2 activities involve agents of moderate potential risk to personnel and the environment. These agents can cause disease in healthy individuals and pose a moderate risk to the environment. Precautions for use of these agents include BSL-1 practices plus limited laboratory access when work with these organisms is being performed and the recommended use of "biological safety cabinets" and/or protective equipment when performing work which may generate aerosols (transferring liquids, rapid mixing, etc.). In BSL-2 labs, personnel have training in the handling pathogenic materials, are familiar with the hazards associated with the specific agents they are using, and are directed by scientists who are competent and familiar with good microbiological laboratory technique. BSL-2 labs may handle clinical materials (biopsies, etc) diagnostic quantities of infectious cultures and human blood.

rDNA: The term recombinant DNA (rDNA) refers to the result of modifying genetic material (DNA), typically in a laboratory setting, to change it in some way. A simple example would be the ability to insert a small piece of new or foreign DNA into the existing DNA of a cell or organism (for example a bacterium) as illustrated in the figure below.

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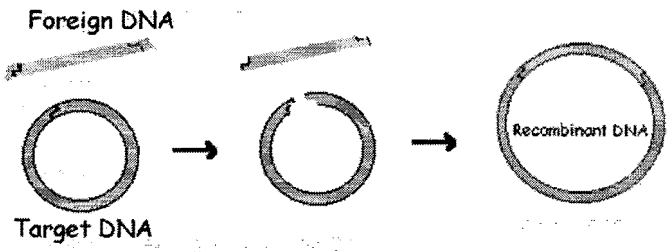

Figure: cartoon illustration of the construction of recombinant DNA (rDNA).

One example of rDNA technology is the insertion of a new or foreign piece of DNA into the DNA of human or bacterial cells being grown in a laboratory. The result is that the modified cells produce medically useful (sometimes lifesaving) materials that they would otherwise not produce. Insulin, for example, can be produced in this way. Recombinant DNA techniques such as that illustrated above are now universally used in life science research and in the manufacture of drugs by the biotechnology and pharmaceutical industries. Other applications of rDNA include but are not limited to basic research into gene structure-function and applied microbiology applications like FROSTBAN which was tested but never marketed (*P. syringae* "ice-minus" genetically altered strain) or for foods based on microbial fermentation.

Safety: Decades of experience has shown that when performed under the appropriate conditions (ie BSL 1, BSL-2, etc) and oversight (see below) the process of modifying the genetic material of cells or organisms in this way is safe and poses little or no risk to workers or to the community in which the work is done.

The potential risks of creating or using rDNA are based on the risks associated with the source of the DNA and its function and are determined according to NIH risk guidelines. People may perform rDNA research in BSL-1 and BSL-2 facilities when they are properly trained and equipped and the facilities have been properly constructed, maintained and all activities are in adherence to official safety guidelines

In the Boston area, there are literally hundreds of BSL-1 and BSL-2 laboratories. Such facilities are found in colleges, universities, medical laboratories, hospitals, and in biotech and pharmaceutical companies.

The safety of such laboratories is such that they are typically found in buildings also containing dining and patient treatment areas, and are in close proximity to schools, daycare centers, and homes.

**Please see appendices for more detailed information and sources about Risk Group definitions, and the practices required of BSL-1 and -2 work.

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Question 2

What are the processes for vetting a laboratory utilizing rDNA technology under federal and/or state regulations as well as under Newton ordinances? Once established, is there any continuing oversight?

The Newton City Ordinance regulating rDNA research requires that laboratories must first obtain a permit from the HHS Commissioner.

The role of the Newton Biosafety Committee (NBC) is to review laboratory applications, ensuring that the applicants plan to adhere the regulations and practices for Biosafety and rDNA research that have been established by the NIH and CDC. If the application is found to be acceptable, a recommendation is given by the NBC to the HHS Commissioner to issue the requested permit.

Criteria for the NBC review include ensuring that the planned research can be safely conducted at the proposed biosafety level, according to established CDC and NIH guidelines. The NBC then determines if the facilities, waste disposal plans, employee expertise, etc. are adequate for the proposed biosafety level, and that the training and ongoing oversight of the program meets the requirements of the proposed biosafety level.

Ongoing oversight includes the establishment of an Institutional Biosafety Committee (IBC), which includes representatives from the Health and Human Services Department and community members appointed by the Mayor and Board of Aldermen. The IBC inspects the facility and program annually, and reviews and approves all proposed work requiring biosafety regulation

Question 3

Hypothetically speaking, would the Atrium Wellness Center be an appropriate site for a qualified Level I or Level II laboratory use, including the use of rDNA technology, assuming that such laboratory successfully passed all vetting processes and received a Health Department permit to conduct rDNA technology?

Yes, assuming the tenant successfully passed all the above vetting processes.

Specific applications by potential laboratory tenants will need to be carefully reviewed on a case-by-case basis, and the proposal to perform rDNA work must adhere to established safety guidelines in order for it to be approved by the NBC, as described in the answer to Question 2. Our positive answer to this question does not positively or negatively dispose the NBC to grant approval to conduct work under the rDNA ordinance to any specific applicant.

Email: lwalsh@newtonma.gov

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Appendix 1, 2 and 3

Biosafety Committee Response to Questions from Land Use Committee regarding special permit application for Atrium Center

Appendix 1: NIH/CDC Risk Group Classifications

IN GENERAL, Level I and Level II (or Biosafety Level 1: BSL-1 and Biosafety Level 2: BSL-2) are designations for sets of biology research practices mandated by the National Institutes of Health (NIH) and the Centers for Disease Control (CDC) that aim to manage the risk of working with biological hazards from the RG-1 and RG-2 risk groups.

Table 1: Classification of Infectious Microorganisms by Risk Group

Risk Group Classification	NIH Guidelines for Research involving Recombinant DNA Molecules 2002[2]	World Health Organization Laboratory Biosafety Manual 3rd Edition 2004[1]
Risk Group 1	Agents not associated with disease in healthy adult humans.	(No or low individual and community risk) A microorganism unlikely to cause human or animal disease.
Risk Group 2	Agents associated with human disease that is rarely serious and for which preventive or therapeutic interventions are *often* available.	(Moderate individual risk; low community risk) A pathogen that can cause human or animal disease but is unlikely to be a serious hazard to laboratory workers, the community, livestock or the environment. Laboratory exposures may cause serious infection, but effective treatment and preventive measures are available and the risk of spread of infection is limited.
Risk Group 3	Agents associated with serious or lethal human disease for which preventive or therapeutic interventions may be available (high individual risk but low community risk).	(High individual risk; low community risk) A pathogen that usually causes serious human or animal disease but does not ordinarily spread from one infected individual to another. Effective treatment and preventive measures are available.
Risk Group 4	Agents likely to cause serious or lethal human disease for which preventive or therapeutic interventions are not usually available (high individual risk and high community risk).	(High individual and community risk) A pathogen that usually causes serious human or animal disease and can be readily transmitted from one individual to another, directly or indirectly. Effective treatment and preventive measures are not usually available.[3]

Source of Table:
Biosafety in Microbiological and Biomedical Laboratories, 5th edition.
HHS Publication No. (CDC) 21-1112, Revised December 2009
Please also see:
NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, November 2013. For lists of micro-organisms and their designated Risk Group.

Appendix 2: NIH/CDC Biosafety Level 1 and 2 Practices.

Table 2. Summary of Recommended Biosafety Levels for Infectious Agents

BSL	Agents	Practices	Primary Barriers and Safety Equipment	Facilities (Secondary Barriers)
1	Not known to consistently cause diseases in healthy adults	Standard microbiological practices	▪ No primary barriers required. ▪ PPE: laboratory coats and gloves; eye, face protection, as needed	Laboratory bench and sink required
2	▪ Agents associated with human disease ▪ Routes of transmission include percutaneous injury, ingestion, mucous membrane exposure	BSL-1 practice plus: ▪ Limited access ▪ Biohazard warning signs ▪ "Sharps" precautions ▪ Biosafety manual defining any needed waste decontamination or medical surveillance policies	Primary barriers: ▪ BSCs or other physical containment devices used for all manipulations of agents that cause splashes or aerosols of infectious materials ▪ PPE: Laboratory coats, gloves, face and eye protection, as needed	BSL-1 plus: ▪ Autoclave available

"Standard Microbiological Practices" include:

- Wash hands after completion of work and before leaving laboratory.
- No eating, smoking, drinking, handling contact lenses, applying cosmetics, or food storage.
- No mouth pipetting.
- Careful handling and disposal of sharps.
- Minimize aerosols and splashes.
- Decontaminate surfaces, cultures, and equipment after work is complete.
- Laboratory biohazard signage.
- Ensure appropriate training and supervision of personnel.

Source: Biosafety in Microbiological and Biomedical Laboratories, 5th edition. HHS Publication No. (CDC) 21-1112, Revised December 2009

Appendix 3: More detailed information regarding definitions of biosafety and rDNA work

- A general definition of "biosafety" encompasses the practices, procedures, and use of equipment needed to ensure adequate safety conditions in all facilities that work with potentially infectious microorganisms and other biological hazards. These include health care settings, clinical and diagnostic laboratories that handle human clinical samples, veterinary facilities that work with animal tissue samples, biological research laboratories, and teaching laboratories. All of these facilities must seek to reduce the risks associated with handling potential biological hazards by employing a continuous process of hazard recognition, risk assessment, and hazard mitigation.
- "Biosafety levels" (BSLs) are designations of laboratories in ascending order based on the degree of risk associated with the work being conducted. A biosafety level is a level of the biocontainment precautions required to isolate dangerous biological agents in an enclosed laboratory facility. The levels of containment range from the lowest biosafety level 1 (BSL-1) to the highest at level 4 (BSL-4). In the United States, the Centers for Disease Control and Prevention (CDC) have specified these levels. In the European Union, the same biosafety levels are defined in a directive.
- BSL1 is suitable for work involving well-characterized agents not known to consistently cause disease in healthy adult humans, and of minimal potential hazard to laboratory personnel and the environment. (no or low individual and community risk). A microorganism that is unlikely to cause human disease or animal disease This is the type of laboratory found in municipal water-testing laboratories, in high schools, and in some community colleges teaching introductory microbiology classes, where the agents are not considered hazardous. At BSL-1 there is no specific recommendation that the laboratory be isolated from other parts of the building. The use of gloves and hand washing is one of the most important procedures that can be used by laboratory workers to prevent removal of unwanted microbiological agents, radioactive materials, or chemicals from the laboratory environment.
- BSL2 is similar to Biosafety Level 1 and is suitable for work involving agents of moderate potential hazard to personnel and the environment. (moderate individual risk, low community risk). A pathogen that can cause human or animal disease but is unlikely to be a serious hazard to laboratory workers, the community, livestock or the environment. Laboratory exposures may cause serious infection, but effective treatment and preventative measures are available and the risk of spread of infection is limited. It includes various bacteria and viruses that cause only mild disease to humans, or are difficult to contract via aerosol in a lab setting. BSL-2 differs from BSL-1 in that: laboratory personnel have specific training in handling pathogenic agents and are directed by scientists with advanced training;
- access to the laboratory is limited when work is being conducted;
- extreme precautions are taken with contaminated sharp items; and
- certain procedures in which infectious aerosols or splashes may be created are conducted in biological safety cabinets or other physical containment equipment.

In general, Level I and Level II (BSL-1 and BSL-2) laboratory uses comprise the overwhelming majority of academic, biotech, and pharmaceutical research activities in biology.

In life science research, Recombinant DNA is the general name for taking a piece of one DNA, combining it with another strand of DNA. Recombinant DNA (rDNA) molecules are DNA molecules formed by laboratory methods of genetic recombination (such as molecular cloning) to bring together genetic material from multiple sources, creating sequences that would not otherwise be found in biological organisms. Recombinant DNA is possible because DNA molecules from all organisms share the same chemical structure. They differ only in the nucleotide sequence within that identical overall structure. Using recombinant DNA technology and synthetic DNA, any DNA sequence may be created and introduced into any of a very wide range of living organisms. Following transplantation into the host organism, the foreign DNA contained within the recombinant DNA construct may or may not be designed to make a protein, or other biochemical product. Recombinant DNA is widely used in biotechnology, medicine and research. The most common application of recombinant DNA is in basic research, in which the technology is important to most current work in the biological and biomedical sciences. However, recombinant proteins and other products that result from the use of rDNA technology are found in essentially every western pharmacy, doctor's or veterinarian's office (e.g. recombinant insulin, growth hormone, blood clotting factors, etc), medical testing laboratory (e.g. diagnostic probes and primers to detect HIV, etc.), and in biological research laboratory searching for new cures to disease. In addition, organisms that have been manipulated using recombinant DNA technology, as well as products derived from those organisms, have found their way into many farms, supermarkets, home medicine cabinets, and even pet shops, such as those that sell GloFish and other genetically modified animals.

- Scientists and regulatory bodies such as the CDC and NIH have recognized that the potential existed for organisms containing recombinant DNA to have undesirable or dangerous properties. In the US, agencies like the CDC and NIH have developed rigorous guidelines which mitigate or eliminate risks posed by rDNA research. Research involving rDNA must now comply with the National Institute of Health's "Guidelines for Research Involving Recombinant DNA Molecules" as published in the Federal Register. The recombinant DNA guidelines are applicable to all recombinant DNA research within the United States or its territories, which is conducted at or sponsored by an institution that receives any support for recombinant DNA research from NIH but serve as the basis for all regulations.
- Recombinant DNA (rDNA) research is an example of a situation where the appropriate biosafety level for the work must be considered.
    - Usually, the biosafety level of an rDNA research project is at the same level as the host organism, but this is determined after careful scientific review.