SCHLESINGER AND BUCHBINDER, LLP
ATTORNEYS AT LAW
1200 WALNUT STREET
NEWTON, MASSACHUSETTS 02461-1267

STEPHEN J. BUCHBINDER
ALAN J. SCHLESINGER
LEONARD M. DAVIDSON
SHERMAN H. STARR, JR.
HEATHER G. MERRILL
PAUL N. BELL
KATHERINE BRAUCHER ADAMS
JULIA V. WILDE
FRANKLIN J. SCHWARZER
RACHAEL C. CARVER

TELEPHONE (617) 965-3500
FACSIMILE (617) 965-6824

OF COUNSEL
ROBIN GORENBERG

March 30, 2015

Marc C. Laredo, Chairman
Land Use Committee
Board of Aldermen
1000 Commonwealth Ave.
Newton, MA 02459

Re: Docket # 2-15 - The Atrium 300 Boylston Street

Dear Chairman Laredo;

The Bulfinch Companies are looking forward to appearing before the Committee tomorrow night.

On March 5 I sent you a letter summarizing responses as of that date to questions which had been raised at and after the public hearing as to rDNA research. Since that time we have received other questions from members of the Board and the public, and our FAQs have been updated in the form attached.

Also, after the public hearing the Committee submitted written questions to the Newton Biosafety Committee for their review. As you know the Biosafety Committee met on March 12 and subsequently filed its report in response to your questions. In particular, in response to your hypothetical question as to whether the Atrium would "...be an appropriate site for a qualified Level I or Level II laboratory use..." the Committee responded:

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

For your convenience a copy of the Biosafety Committee's report is attached.

The Biosafety Committee report re-affirmed and was specific on some of the general points we made in our presentation:

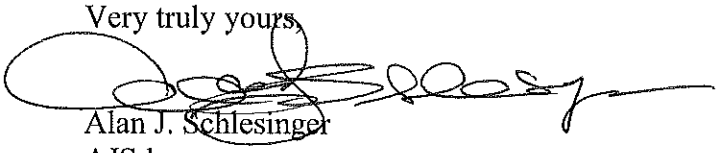
- BSL 1 activities are not separated from other activities, are performed on open bench tops and are the types of activities in high school labs and municipal water testing labs

- BSL 2 activities are separated from other activities with the use of protective equipment and training of personnel. BSL 2 laboratories are typical in hospitals and doctors offices
- rDNA research is a subset of BSL 1 and BSL 2 activities. In Newton all rDNA research is under the supervision and control of the Health Department on recommendations of the Newton Biosafety Committee.

We have noted that in addition to the high schools Newton does now have 2 prior rDNA facilities at Wells Avenue and Nevada Street and a large number of facilities with BSL 1 and BSL 2 activities including Newton Wellesley Hospital and most recently the Beth Israel Deaconess facility at Chestnut Hill Square.

We have also looked at the regulatory provisions for rDNA in surrounding communities, and we find there are a variety of controls in place. Cambridge is the city which most aggressively seeks the life sciences companies, but Lexington has allowed its Biosafety Committee to permit up to BSL 3 faculties in certain districts. Needham, like Newton has a special permit requirement in certain commercial districts and a Board of Health regulation. Waltham allows "research labs.." as of right in various commercial zones subject to the Waltham Biosafety Committee review. It is clear that the emerging pattern is to allow BSL 1 and BSL 2 activities in connection with typical medical uses and schools and to add a level of local implementation of National Institute of Health standards on rDNA research through the local Biosafety committees.

Very truly yours,



Alan J. Schlesinger
AJS:lmp

cc: Land Use Committee
Aldermen Lappin, Baker, Fuller
Alexandra Ananth, Director of Current Planning

Biosafety Questions and Answers for 300 Boylston Street – The Atrium

March 30, 2015

Question #1: ***Where do Biosafety Levels 1 and 2 exist in Newton?***

Received At: City of Newton Land Use Committee, 2/3/2015, by Alderman Albright and Alderman Fuller.

The only facilities we are aware of which have been approved through the Board and the Biosafety Committee are:

(i) Matritech, Inc. at 330 Nevada Street - Board Docket # 247-95 approved in 1995; and

(ii) Karyopharm Therapeutics, Inc. at 75-95 Wells Avenue Board Docket # 365-14 approved in 2014

Matritech is limited by its special permit to Biosafety Level 1. Karyopharm is not limited by the terms of its special permit but the Planning Department report of October 31, 2014 indicates that their work will be performed at Biosafety Level 1 and Level 2.

Question #2: ***Will Biosafety Level 3 and 4 facilities be allowed in the future?***

Received At: City of Newton Land Use Committee, 2/3/2015, by Mr. Feldman.

Biosafety Level 3 and 4 facilities will not be permitted now or in the future at the facility. These laboratories are extremely expensive to build and operate and only a small subset of life sciences research requires these "high containment" laboratories. As a result, they are not common in the Boston area or throughout the world. Revised Ordinances Section 12-28 specifically prohibits containment greater than BL 3, and the lease language will specifically prohibit Biosafety Level 3 and 4 laboratories.

Question #3: ***Where in Newton are life sciences uses adjacent to residential areas?***

Received At: City of Newton Land Use Committee, 2/3/2015, by Alderman Fuller.

The Matritech site is adjacent to a residential area to the north on Nevada Street and is also directly across Nevada Street from a residential area to the West. Residences are also one property and Watertown Street removed to the south.

The Karyopharm site does not abut residences, but we note that it is adjacent to the Solomon Schechter Day School, and 330 housing units are proposed for the next lot beyond the school on Wells Ave.

Question #4: ***Are there other examples of life science companies located adjacent to residential areas?***

Received At: City of Newton Land Use Committee, 2/3/2015, by Alderman Fuller.

The Newton Biosafety Committee report states "In the Boston area, there are literally hundreds of BSL-1 and BSL-2 laboratories." Included in the BSL 1 laboratories are the biology and chemistry labs at our high schools, and included in the BSL 2 laboratories are the hospitals, outpatient clinics and physicians offices throughout the city.

We do note that the medical facilities may not include rDNA research, but in terms of the risk analysis the BSL 1 and 2 ratings are the same.

The City of Cambridge is an excellent example as there are a number of residential areas including apartment complexes that are immediately adjacent to many of the life sciences companies. A map of Kendall Square shows a large number of research companies interspersed with residential, hotel, restaurant, school and daycare uses. Other examples include Shire Human Genetic Therapies adjacent to residences in Lexington, Immunogen in Waltham adjacent to residences in Weston. Other surrounding communities such as the City of Boston and the Town of Watertown have similar examples.

Question #5: ***If the proposed use is safe - why is it so regulated?***

Received At: City of Newton Land Use Committee, 2/3/2015, by Alderman Fuller.

Life sciences research is safe exactly because of being regulated in a consistent and predictable manner. The health, safety and environmental regulations have made the uses safe enough to be accepted by all our surrounding communities.

Question #6: ***What is an example of the type of work that might be undertaken in the laboratory?***

Received At: City of Newton Land Use Committee, 2/3/2015, by Alderman Albright and Alderman Crossley.

There are almost as many different types of work as there are life sciences companies - 450 companies in Massachusetts with nearly 60,000 employees. One company familiar to our consultant (EH&E, Inc.) is established in the Town of Lexington in which they engage in research, development and manufacturing efforts to produce drug therapies for the treatment of genetic diseases caused by protein deficiencies. Other EH&E clients in the greater Boston area are engaged in research to seek treatments for infectious diseases, Cystic Fibrosis, and develop cancer diagnostics. These companies utilize recombinant DNA (rDNA) technology to identify, map and sequence genes, and to determine their function such that therapies can be developed for treating a variety of diseases and health conditions. The research that takes place in these laboratories is undertaken in rooms which are typically on the order of a few hundred square feet. The room is negatively pressurized, that is, air will naturally flow from non-laboratory areas with higher pressure to laboratory areas with lower pressure, thereby preventing air from escaping the laboratory. Laboratories are locked and work may be performed in biosafety cabinets to protect staff and to keep the research materials from being contaminated. Chemical fume hoods exhaust the air. Staff wear lab coats with safety glasses and gloves, and protocols are established for secure disposal of waste, much as in a medical laboratory, a hospital or a physician's office. These companies have biosafety officers that are part of the company's

Environmental Health and Safety Department. Biosafety Officers oversee the compliance and advise the staff on proper procedures to ensure safety and compliance.

Question #7: *Do all life science companies work with Recombinant DNA (rDNA)?*

Received At: City of Newton Land Use Committee, 2/23/2015, by Mr. Feldman, and Imperial Towers Condominium Association, 2/24/2015.

Not all life science companies work with rDNA. While it is a common research tool in life science laboratories, it is not always necessary depending on the goals of the company.

Question #8: *What are examples of how the regulations are applied?*

Received At: City of Newton Land Use Committee, 2/3/2015, by Alderman Crossley, Alderman Lappin, and Alderman Schwartz.

1. Local Regulation: The Newton Ordinance, Revised Ordinances Section 12-21 et seq. provides for creation of the Newton Biosafety Committee comprised of 9 members. In 2014 as part of the City's effort to attract life sciences companies the Biosafety Committee was reconstituted with a very distinguished roster of experts in the field.

Under Section 12-23 each institution conducting rDNA research must establish a separate "Institutional Biosafety Committee (IBC) including the commissioner of Health and Human Services, two community representatives with expertise in rDNA research and technology and/or safety issues and three appointees of the institution, including one designated as the "biosafety officer". The IBC shall meet at least once per year to review projects involving rDNA, inspect the laboratories and review compliance of the facility.

Each institution is required to obtain a permit from the commissioner, and Section 12-24 lists the information required to be filed with the Commissioner and the Biosafety Committee including in part:

(1) A completed application;

(2) A plot plan and floor plan

(3) A listing of all organisms including containment levels and screening processes used;

(4) A plan for systematic monitoring of waste to assure that surviving rDNA organisms will not be released into the environment;

(5) A training program of safeguards and procedures for personnel;

(6) The institution's health monitoring, surveillance and safety manuals including, among other things (a) pre-employment medical examinations, (b) prompt reporting of significant illnesses, (c) retention of medical records, and (d) rodent and insect control programs;

(7) Appointment of a named safety officer;

(8) Orientation programs for the Department of Health and Human Services and Fire and Police Departments.

Section 12-25 provides for a program of inspections to be undertaken at least annually by a contractor retained by the Department of Health and Human Services and paid for by the institution.

2. State Regulation: There are numerous State regulations pertaining to environmental compliance and safety that may apply to life sciences companies in Massachusetts. The one regulation that specifically applies to recombinant DNA as well as non-recombinant microorganisms is "Minimum Requirements for the Management of Medical or Biological Waste (105 CMR 480.000). This is the same regulation that applies to medical waste generated in healthcare facilities such as but not limited to Newton Wellesley Hospital and physician offices. In the laboratory, this regulation requires that medical waste be properly segregated in labeled containers, segregated from regular trash, and disposed by a qualified vendor. Records must be kept to document the disposal. The Massachusetts Department of Public Health (MADPH) oversees compliance with this regulation and may periodically inspect a facility.

3. Federal Regulation: As with State regulations, there are a number of federal regulations related to the environment and worker safety that apply to life sciences companies such as those from the Occupational Safety and Health Administration (OSHA) and the Environmental Protection Agency (EPA). The OSHA Bloodborne Pathogens Standard is an example of a regulation that applies to life sciences companies as well as hospitals, and dentist and physician offices. This regulation is designed to protect workers who may come in contact with human blood and other potentially infectious human materials. It requires worker training, a written safety plan, and measures to reduce the potential for exposure in the work place such as the use of protective measures such as laboratory coats, safety glasses and gloves. OSHA oversees compliance with this regulation and has the purview to inspect a facility.

While not a regulation per se, the National Institutes of Health (NIH) "Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules" (NIH Guidelines) are considered the "gold standard" for work with rDNA and institutions working with rDNA follow these biosafety requirements. If the institution receives federal funding for research involving rDNA, they must comply with the NIH Guidelines as a condition of funding and NIH requires specific documentation to be submitted on a yearly basis to demonstrate compliance. Many communities such as but not limited to the Cities of Cambridge and Newton reference the NIH Guidelines in their respective regulations and require compliance regardless of whether federal funds are received.

Question #9: ***If there is no rDNA, does that mean there is no biosafety and laboratory safety oversight?***

Received At: Imperial Towers Condominium Association, 2/24/2015.

A company that does not work with rDNA may still work with other biological materials such as human blood or bacteria. The laboratory may also work with chemicals, and they will still generate waste. The State regulations (e.g. MADPH) and the federal regulations (e.g. OSHA) listed in the previous section still apply as these regulations are not specific to rDNA only. The company will have a safety program to address the materials in use and the corresponding regulations.

Question #10: ***How will medical waste be removed from the facility?***

Received At: Imperial Towers Condominium Association, 2/24/2015.

Similar to a doctor's office or hospital, the waste is segregated into specially marked containers. The containers will be present in the laboratory and the workers will fill them with waste. Full containers will be moved to a locked storage room in the facility. Typically once or twice per week, a waste vendor will pull a truck up to the loading dock to collect the waste for offsite destruction. The containers will be removed from the locked storage room and brought directly to the truck. Paperwork will be completed on site to document the pick-up including the number of containers put into the truck. Once the vendor finishes picking up waste from other clients in the Chestnut Hill area, it will go to a permitted facility where the waste will be destroyed.

Question #11: ***Will clinical trials be conducted at the Atrium?***

Received At: Imperial Towers Condominium Association, 2/24/2015.

It is highly unlikely that a company performing laboratory research would also conduct clinical trials at the facility. Clinical trials are regulated by the Food and Drug Administration (FDA) and must be conducted in facilities that ensure patient privacy and safety, such as a healthcare facility. Companies typically outsource clinical trials to Contract Research Organizations (CROs) or they are conducted in a hospital setting, and clinical trial operations are never permitted to be conducted in a research laboratory.

Question #12: ***Why is a Laboratory Permit being sought, when a tenant has not yet been identified? Shouldn't the Laboratory Permit process be put on hold until a tenant signs a lease?***

Received At: Imperial Towers Condominium Association, 2/24/2015.

A potential life sciences company will want to know before they sign a lease whether they can have laboratory operations at the facility. The life sciences real estate market in the greater Boston area is competitive such that a company is going to select a location where they know they can establish a laboratory before they enter into a lease agreement.

Question #13: ***How do we know what a tenant's safety record is, when we don't know the tenant?***

Received At: City of Newton Land Use Committee, 2/3/2015, by Ms. Phillips, and Imperial Towers Condominium Association, 2/24/2015.

A new start-up company will not have a safety record, but they will be required to quickly establish a safety program in order to comply with the local, state and federal regulations. They cannot start work in the laboratory until they have the safety program established. For example, they cannot generate medical waste until they have met the requirements of the MADPH regulation and hired a vendor to pick up and transport the waste off site for destruction. An established company moving to The Atrium will transfer their existing safety program and adapt it to meet applicable local and state regulations, including filing for new or amended permits. In

addition, the landlord can require as part of the lease that the tenant provide the landlord with specific safety information, such as copies of permits and safety manuals, and inventories of chemicals and biologicals.

Question #14: ***What happens when a company doesn't follow the safety regulations?***

Received At: City of Newton Land Use Committee, 2/3/2015, by Mr. Karp and Ms. Creed.

There are a number of consequences. If a company is inspected by a local, state or federal regulatory agency, and deficiencies are found, there are a variety of sanctions that can occur up to and including loss of a permit, significant monetary fines, negative publicity and closure of the laboratory. The same consequences can occur if there is a serious incident at the facility. Therefore, it is in the best interest of a company to abide by the regulations and do everything possible to be in compliance.

Question #15: ***I'd like to know more about what rDNA is all about. What are some good references in layman's terms?***

The following are provided as resources to give further information related to questions and answers that pertain to rDNA.

http://americanhistory.si.edu/collections/object-groups/birth-of-biotech?ogmt_page=birth-of-biotech-introduction

http://www.cliffsnotes.com/sciences/biology/microbiology/dna-and-gene-expression/recombinant-dna-and-biotechnology

http://www.iptv.org/exploremore/ge/what/insulin.cfm

http://www.chemheritage.org/discover/online-resources/chemistry-in-history/themes/pharmaceuticals/preserving-health-with-biotechnology/berg-boyer-cohen.aspx

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

Public Health
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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.

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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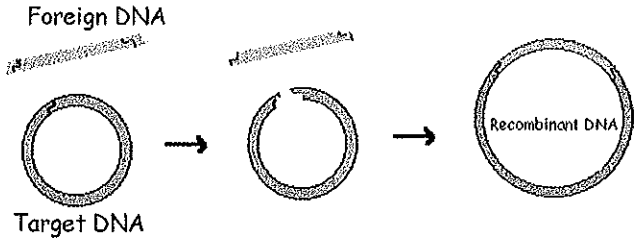

Figure: Cartoon illustration of the construction of recombinant DNA (rDNA).

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.

Email: lwalsh@newtonma.gov

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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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

Appendix 1, 2 and 3

Biosafety Committee Response to Questions from Land Use Committee regarding special permit application for Atrium Center
March 24, 2015

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.