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Box , Vila Real , Portugal, tp. This article was submitted to Biosafety and Biosecurity, a section of the journal *Frontiers in Bioengineering and Biotechnology* Received Nov 21; Accepted Apr The use, distribution or reproduction in other forums is permitted, provided the original author s or licensor are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms. This article has been cited by other articles in PMC. Abstract Advances and research in biotechnology have applications over a wide range of areas, such as microbiology, medicine, the food industry, agriculture, genetically modified organisms, and nanotechnology, among others. However, research with pathogenic agents, such as virus, parasites, fungi, rickettsia, bacterial microorganisms, or genetic modified organisms, has generated concern because of their potential biological risk “ not only for people, but also for the environment due to their unpredictable behavior. In addition, concern for biosafety is associated with the emergence of new diseases or re-emergence of diseases that were already under control. Biotechnology laboratories require biosafety measures designed to protect their staff, the population, and the environment, which may be exposed to hazardous organisms and materials. Laboratory staff training and education is essential, not only to acquire a good understanding about the direct handling of hazardous biological agents but also knowledge of the epidemiology, pathogenicity, and human susceptibility to the biological materials used in research. Biological risk can be reduced and controlled by the correct application of internationally recognized procedures such as proper microbiological techniques, proper containment apparatus, adequate facilities, protective barriers, and special training and education of laboratory workers. To avoid occupational infections, knowledge about standardized microbiological procedures and techniques and the use of containment devices, facilities, and protective barriers is necessary. Training and education about the epidemiology, pathogenicity, and biohazards of the microorganisms involved may prevent or decrease the risk. In this way, the scientific community may benefit from the lessons learned in the past to anticipate future problems. They involve the study and manipulation of modified living organisms, genetically modified organisms GMOs , transgenic plants, animals or microorganisms, and the production of vaccines carried out in special laboratories with different biosafety and biosecurity levels according to the pathogenicity of the organisms under study Mattiasson, Since microorganisms and GMOs may be harmful or pathogenic to animals and humans, the possibility of enhanced virulence through genetic manipulation or increased drug-resistance, among other routes, implies putting specific biosafety and biosecurity procedures in place. To guarantee public health, every possible scenario of an outbreak arising through the release of a bio-hazard into the environment cannot be neglected Nordmann, Biosecurity includes a set of preventive measures that vary according to the organisms which are under study. Biosafety and biosecurity are terms which are frequently referred to with similar meanings in the literature. While the differences between the two concepts have been specified academically, in practice, when one is actually working hands-on in a laboratory it is more difficult to draw such distinctions as referred by Daoust-Maleval Moreover, Bakanidze et al. In the other hand, biosecurity is referred to all the preventive measures to avoid or reduce the risk of transmission of infectious diseases in crops and livestock, quarantined pests, or GMOs Baltz et al. The objective of this review is to highlight the main risks associated with biological investigation in laboratory, the potential laboratory-acquired infections LAIs by laboratory personnel, and suggested recommendations to avoid them. Biotechnology in Health and Biosafety Advances and research in biotechnology have applications over a wide range of areas, such as microbiology, medicine, the food industry, waste management, agriculture, GMOs, and nanotechnology, among others Thompson, ; Baltz et al. Biosafety cuts across different human and veterinary science. The first infectious diseases acquired in a

laboratory were reported at the time of Pasteur and Koch in However, several decades passed before the connection between human diseases and the handling of pathogenic microorganisms was understood Sulkin, ; Traxler et al. The first safety measures in microbiology laboratories that work with pathogenic microorganisms were implemented in North America and the United Kingdom at the beginning of the s. These measures included laboratory training and education about the correct use of personal protective equipment and physical containment measures designed to limit the potential spread of biological agents Frommer et al. After that, safety measures were applied in laboratories that work with GMOs. One of the most important considerations in the development and application of biotechnology is the maintenance of both biosafety and biosecurity measures at high levels. The Cartagena Protocol on Biosafety is an international regulation of the use of GMOs resulting from modern biotechnology. This agreement, which focuses specifically on the transboundary movement of GMOs, promotes biosecurity by establishing rules and procedures for the safe transfer, handling, and use of GMOs McKenzie and Ascencio, Since biotechnology could be a potential threat to the population, the Biological Weapons Convention " a multilateral disarmament treaty focused on the prohibition of biological and toxins weapons Millett, ; Bakanidze et al. Biotechnology investigations have developed a wide range of powerful tools and processes to improve human and animal health. Good laboratory practices regarding biosafety and bioethics are essential measures to avoiding LAIs. Some publications have evaluated the effectiveness of biosafety and biosecurity measures in traditional laboratories Kimman et al. Monitoring laboratory infections is one of the most important methods of evaluating the effectiveness of containment measures McLean et al. Biological Risk Classification Pathogenic microorganisms represent only a small proportion of the biological hazards of concern in laboratory investigations. Their control importance is based on their potential threat to humans, animal populations, and also agriculture. In addition, they can be responsible for large-scale infections with huge economic costs and environmental consequences Bosia, In addition, new viruses are constantly emerging that threaten the lives of humans and animals. All laboratory staff who work with biological samples are exposed to a number of infectious materials and subject to risk from clinical specimens and cultures. Since hazardous agents can be transmitted in the laboratory by inhalation, inoculation, or through the skin, among others, it is necessary to know the characteristics of the agents in study according to their risk to the health of laboratory staff, and to the human and animal population in case of an outbreak Corrao et al. Biological agents of risk group 1 include those unlikely to cause disease in man, biological agents of risk group 2 include those that can cause disease in humans and pose a danger for workers with little chance of spreading among them or to the community. In addition, there is prophylaxis and effective treatment available to the community. Biological agents of risk group 3 include those that can cause serious illness in humans, represent a serious danger to workers with risk of spreading to the community, and there is an effective treatment or prophylaxis. Finally, the biological agents of risk group 4 include those that can cause severe disease in humans and represent a serious danger to workers, with likelihood of being spread to the community and there is usually no effective prophylaxis or treatment World Health Organization WHO , However, there are other biological risk classifications by country, based mainly on national policies. In the United States, biological hazards are also classified into four risk groups, from minimal hazard risk group 1 to those responsible for very serious diseases risk group 4 , as described by the Centers for Disease Control and Prevention CDC Center for Disease Control and Prevention CDC , Taking into account the pathogenic effects to humans and the potential danger to the environment, the classification of pathogenic agents as well as their containment measures should be undertaken with a single goal: Moreover, investigation with infected transgenic animals that carry the genes of an infectious agent must be subjected to a proper risk evaluation and also subject to correct handling with specialized containment facilities and equipment. The specialized containment can address the risks of aerosolized particles, such as in studies of tuberculosis or lymphocytic choriomeningitis, and animals such as poultry infected with influenza World Health Organization WHO , ; OIE, ; Shinnick and Gilpin, Biological Risks to Health in Biotechnology Laboratories There are many biological risks in health biotechnology, such as bacteria, viruses, rickettsiae, fungi, and parasites Liberman et

al. Regarding biosafety and biosecurity in biomedical laboratories, there is great concern about new vaccines, diagnostic tools, or therapeutic agents, some of which are made by genetic engineering Doblhoff-Dier and Collins, Currently, a main concern of biosafety is due to the emergence of new diseases or the re-emergence of diseases that were already under control Brown, ; Jones et al. In laboratories, there are many tasks that involve numerous risks to the laboratory staff. Thus, any incident associated with a given microbiological hazard is probably most likely to happen in a microbiology laboratory. However, incidents are not associated to a single factor but the interaction of several of them Sewell, ; Kozajda and Szadkowska-Stanczyk, In the near future, advances in microbiology associated with biotechnology will increase the knowledge of viroids, viruses, and bacteria cells that carry novel genetic material, which has been modified or constructed through genetic engineering. Thus, new concerns in biosecurity and environmental health will emerge. Currently, there is an urgent demand for new vaccines against extremely hazardous pathogens such as Ebola Levine et al. The research will involve the manipulation of pathogenic microorganisms that could have harmful effects on public health and the environment. To guarantee the biosafety of laboratory staff and the biosecurity measures of the facilities, the intrinsic and potentially harmful characteristics of all microorganisms under study must be identified. Although research in biotechnology is necessary, nowadays there is a dilemma about the freedom or limitation of these investigations. Thus, gain-of-function GOF research or dual use research DUR have arisen as an important concern, not only among the scientific community but also among the population Casadevall and Imperiale, While GOF is associated with the acquirement of a new activity or the enhancement, a previous function, DUR, is associated with a misuse of science Suk et al. Research with highly pathogenic microorganisms, like H5N1 influenza, anthrax among others, could derive into a serious biological threat to a population or even terrorism Resnik, ; Lipkin, Epidemics of pandemic proportions or improved previous research to develop bio weapons could be an uncontrollable risk for a population. As a result, both GOF research and DUR must be regulated with strong biosafety measures, restricted research, and specific policy as was recently discussed in Germany Karberg, Vectors used in gene therapy Gene therapy, in vivo and ex vivo, use vectors classified as viral or non-viral, which express the gene or genes of therapeutic interest. Non-viral vectors include liposomes, naked DNA, and DNA-protein complexes Doblhoff-Dier and Collins, , while viral vectors derived from viruses that are attenuated in order to prevent destructive infection in target tissues. Non-viral vectors are preferred from the biosafety point-of-view, although they are less efficient than viral. Thus, viral vectors are usually used to avoid this disadvantage. The expression of the information encoded in genes leads to functional modification of infected cells, and the evaluation of these modifications are extremely complex and incomplete when the modified cells belong to the host. The safety of gene therapy vectors has been the focus of regulatory attention by committees. They are required to assess the proportionality between the magnitude of the risks and potential therapeutic benefits, as well as to monitor the occurrence of risks in the experiment once they have been approved Verma and Somia, Biosafety in laboratories with gene therapy manufacture must consider the staff and the patients that may be in contact. In addition, a comprehensive risk assessment of viral vectors must be carried out. Ideally, viral vectors should be designed only to act as transporters of the exogenous genetic material to avoid the development of new replicative viral particles in transduced cells. Thus, it is understood that a viral vector cannot make any escape or reversion in virulent forms. The biohazard of these vectors is determined by their own biological risk to the laboratory staff, by the environment of the exogenous genes they carry and also by the tropism of the recombinant virus Doblhoff-Dier and Collins, Gene therapy, due to its technical and ethical characteristics, is regulated by law. In the United States, the National Institutes of Health and the Food and Drug Administration published several guides to describe the main biosecurity measures with which all laboratories must comply. Utilization of retroviral vectors must be subjected to a previous risk assessment. Since they are highly infectious and may infect and propagate themselves in human cells, they may be considered as an important biohazard to the laboratory staff Thomas et al. The principal biosafety concern when working with retroviruses is the chance of viruses entering the cells and tissues of laboratory personnel through skin lesions

or by accident. The closer the contact the greater the risk, because retroviral particles are extremely labile and short-lived. Even when using defective retroviruses that present a lower risk of infection, laboratory staff must be trained in virology and tissue culture Le Duc et al. Handling of animals infected with retroviruses, especially those that present a potential human cell risk, need high standards of biosecurity measures, particularly for avoiding potential animal escape and the spread of infection. Additionally, when handling infected animals extreme caution must be taken to avoid injuries through bites, clawing, or scratches. Laboratory staff should only be allowed to handle infected animals if they have specific training and always under the supervision of a senior Wolfensohn and Lloyd, Regarding gene therapy, immunomodulation has arisen as a new trend in biotechnology. It can be defined as therapeutic procedures aimed at modifying the immune response Gea-Banacloche, Research in immunomodulation is focused on correcting specific diseases or immuno-deficiencies such as HIV, cancer, allergies, or inflammatory diseases among others. It consists in the hybridization of synthetic genetic sequence in the organisms targeted to express or suppress specific genes in the host. However, the potential biological risk of immunomodulation is associated with the uncertain hybridization and gene expression in the host, which may cause an adverse effect Vo et al. Thus, the main biosafety concern in the laboratory is associated with accidental needlesticks that can cause unpredictable responses in an organism. However, the utilization of oligonucleotides sequences of RNAi or siRNA increases the control of the gene expression Behlke, , and further research is necessary. Vaccines The manufacture of vaccines based on viral or bacterial recombinants are the most common approaches to live GMO vaccines, and are sources of biological risk in biotechnology laboratories.

Chapter 2 : Crime Classification Manual : John Douglas :

The use of biological agents as weapons / Anne M. Berger Wrongful convictions: causes, solutions, and case studies / Peter Shellem Criminal confessions: overcoming the challenges / Michael P. Napier and Susan H. Adams.

Saul Hormats, 90, expert on chemical weapons. During the next 20 years, he often warned of the dangers of chemical warfare, especially to civilian populations. In testimony before the Senate, Mr. Hormats criticized the proposed resumption of nerve-gas production in the s. He predicted in a Wall Street Journal letter published in that "millions of civilians and soldiers would die" in a chemical warfare attack. In his 37 years at Edgewood Arsenal, Mr. He was also an expert in defending against toxic chemical and biological agents. During World War II, he studied how certain chemicals would affect gas masks. He held 12 patents for chemical warfare protective devices. After Berlin fell to the Allies in the spring of , he visited the city and discussed chemical warfare with the German army staff. At that time, he studied sarin, a deadly gas that was found in a German shell. When he opened the metal casing, he suffered night blindness for a week despite having taken safety precautions. He also studied the effects of radiation on military and civilian populations during a nuclear attack. In , he led a delegation of scientists to a NATO meeting. In , he was widely quoted in the news media as an expert on the gas that a fringe group released into a crowded Tokyo subway. Although most of his research at Edgewood was focused on military issues, Mr. Hormats also studied air pollution and its control. Born in Troy, N. He also studied at the University of Maryland. Funeral services were held Friday. Stahl of Islamorada, Fla. The former Anna G. Berger, a lifelong Highlandtown resident, attended city public schools until leaving to help support her family. Her marriage to William Schanze ended in divorce. She loved being around politicians, gamblers and businessmen," said her daughter, Sharon M. Services were held Friday. In addition to her daughter, she is survived by a son, Marion C. Emily Wheelock Reed, 89, librarian at Pratt Emily Wheelock Reed, a former Pratt librarian who fought for intellectual freedom, died Friday of heart failure at Broadmead, the Cockeysville retirement community where she had resided since The former head of adult services at the Enoch Pratt Free Library, she was a career librarian who clashed with segregationist Alabama legislators in and The next year, she found another job.

Chapter 3 : Crime classification manual :

Anne M Berger. Read 11 publications, and contact Anne M Berger on ResearchGate, the professional network for scientists. The Use of Biological Agents as Weapons. In J.E. Douglas, A.W. Burgess.

Criminal Or Forensic Psychology Back cover copy This is the second edition of the landmark book that standardized the language and terminology used throughout the criminal justice system. It classifies the critical characteristics of the perpetrators and victims of major crimes--murder, arson, sexual assault, and nonlethal acts--based on the motivation of the offender. The second edition contains new classifications on computer crimes, religion-extremist murder, and elder female sexual homicide. This edition also contains new information on stalking and child abduction, the use of biological agents as weapons, cybercrimes, Internet child sex offenders, burglary and rape, and homicidal poisoning. In addition, many of the case studies and crime statistics have been updated. Based on the primary intent of the criminal, the Crime Classification Manual leads to an increased understanding of the nature of crime and the individuals who commit such crimes. This is an indispensable reference for law enforcement personnel, mental health professionals, forensic scientists, or anyone whose work brings them into contact with either the offender or the victim of violent crime. Praise for the First Edition "A very useful guide for any professional involved in the investigation or litigation of major felonies. Classification of the elements of crime will facilitate the conduct of criminal investigations and resolution of cases. The skills, techniques, and proactive approaches offered are creatively concrete and worthy of replication across the country. He received investigative experience in violent crime in Detroit and Milwaukee field offices and also served as a hostage negotiator. The University of Virginia awarded Douglas the prestigious Jefferson Award for academic excellence for his work on that study. In Douglas coauthored the first edition of the Crime Classification Manual CCM , the first study of violent crime to define and standardize techniques and terminology to be used by the criminal justice system and academia. Douglas has consulted on thousands of cases worldwide providing case analysis, interview and interrogation techniques, investigative strategies, prosecutorial strategies, and expert testimony. Simpson civil case, and the JonBenet Ramsey homicide. Since his retirement in from the FBI, Douglas has been providing pro bono assistance whenever possible to police and victims of violent crime. Douglas has coauthored both fiction and nonfiction books, including two New York Times best sellers, Mindhunter and Journey into Darkness. His personal Web site, johndouglasmindhunter. She, with Lynda Lytle Holmstrom, cofounded one of the first hospital-based crisis intervention programs for rape victims at Boston City Hospital in the mids. Her work expanded into the offender area when she teamed with special agents at the FBI Academy to study serial offenders of sexual homicide, rape, and child sexual offenses. This work advanced an understanding of the importance of the behavioral footprints in crime scenes and the profiling process. Burgess served as chair of the first advisory council to the National Center for the Prevention and Control of Rape of the National Institute of Mental Health She was a member of the U. Office of Technology Assessment. Wecht Institute of Forensic Science and the Law. Burgess has been principal investigator of many research projects and has written textbooks in the fields of psychiatric nursing and crisis intervention and texts from her research in the crime victim area. She has coauthored over articles, chapters, and monographs in the field of victimology. She also has testified in criminal and civil cases in over thirty states. He served in the U. Air Force and was assigned to the National Security Agency. His career spans thirty years beginning with computer design at Honeywell Information Systems, where he designed four computer systems and rose to the rank of chief engineer. He left Honeywell to join Raytheon, where he served as computer and displays laboratory manager and supervised the design of military computers. He left Raytheon to start Sequoia Systems, a manufacturer of fault-tolerant computers. In he started Data Integrity, where he holds a patent for a solution to the Y2K problem. In addition to his industrial experience, Burgess has taught at Northeastern University, where he was an associate professor, and at Babson College, Boston College, Bentley College, and Boston University as a

visiting professor. He is an expert in the area of violent criminal offenders, particularly serial and sexual homicide. He is a specialist in the area of criminology, criminal personality profiling, crime scene analysis, homicide, sexual assaults, threat assessment, workplace violence, and hostage negotiation. He is a twentyyear veteran of the FBI, serving sixteen years in the Behavioral Science Unit as a supervisory special agent and criminologist, retiring in *Patterns and Motives* and the *Crime Classification Manual*. He has testified as an expert witness in civil and criminal cases. He has lectured at and consulted to law enforcement agencies, universities, writers, television networks, and corporations in the United States and abroad. He has appeared on many major television and radio networks and has been featured in numerous printed media articles in major newspapers and magazines worldwide. Ressler has served with the U. Army, ten years of it active duty during the Vietnam era. He retired at the rank of colonel with thirty-five years of service. *Crime Analysis and Investigation*. Douglas and Lauren K. *Classifying Crimes by Severity: From Aggravators to Depravity*. Michael Welner. *Rape and Sexual Assault*. Computer Crimes Allen G. Burgess, and Timothy Baker. *Homicidal Poisoning* Arthur E. Jarvis, and Carl J. *Overcoming the Challenges* Michael P. Napier and Susan H.

Chapter 4 : The Crime Classification Manual : John Douglas :

Crime Classification Manual The Use of Biological Agents as Weapons Anne M. Berger. and the use of biological agents as weapons.

Page ix Share Cite Suggested Citation: The National Academies Press. It violates the fundamental values of the life sciences that I and my colleagues hold dear: My own work has focused on cholera, a disease responsible for the death of thousands of people around the world every year. During the past 40 years, research carried out through international collaboration of scientists has saved many thousands of lives. At the same time, we are firm in the belief that this research should be conducted safely and responsibly. The incidence of either laboratory workers or members of the public being infected is vanishingly small, whether from laboratory accidents or intentional action. Through the years, safety and security practices and procedures have been developed that have successfully prevented accidental or intentional misuse of biological materials. While research with select agents and toxins introduces another level of potential risk, the same sense of responsibility applies. Scientists have not only demonstrated concern about these issues, but also recognize that they have the most at stake should an incident occur. They are best able to identify potential risk, whether from a laboratory door left unsecured or the unusual behavior of a laboratory worker. It is for these reasons that this report focuses on promoting a culture of responsibility, enabling and empowering scientists to be vigilant stewards of their science. Research with select agents and toxins is both necessary and important. Nevertheless, there is the possibility that we can be overzealous, implementing procedures only thought to enhance security. While many current policies and practices are effective, some actions suggested to enhance security are not likely to make select agent research more secure, just more difficult to conduct; this may yield the opposite result: The authoring committee for this report represents a broad cross-section of stakeholders, including select agent researchers, experts in psychology, professionals in biosafety and facility design, and individuals with extensive experience in the issues of science and security. The report represents a consensus of the committee and our best judgment on the most effective ways to both promote security and foster scientific knowledge and a rapid biological response in the event of an emergency. As such, the committee had to make choices about which issues to address, concentrating on those it felt to be most important, most critical, and most effective for enhancing security and enabling research. Thanks to the dedication of both the committee and staff, analysis of the issues included in the report can be considered no less thorough and documented than if we had been given the luxury of time. On behalf of the entire committee, I wish to extend our sincere gratitude to the excellent staff at the National Academies. It is because of the dedication and extraordinary efforts of study director Adam Fagen, Jo Husbands, Rita Guenther, and Carl-Gustav Anderson that we were able to complete this ambitious task in so short a time. The committee was able to identify the most important issues and reach consensus with relative ease because of the superb work of the staff. The tasks were facilitated by a knowledgeable, dedicated, and insightful committee, and I thank my fellow committee members for their commitment that made the study process an enjoyable and rewarding opportunity. Today, researchers in the biological sciences again need to take responsibility for helping to prevent the potential misuses of their work, while being careful to preserve the vitality of Page xi Share Cite Suggested Citation:

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