

## Biological Risk Assessment in the Laboratory: Report of the Second Biorisk Management Workshop

Stefan Wagener<sup>1</sup>, Allan Bennett<sup>2</sup>, Maureen Ellis<sup>3</sup>, Marianne Heisz<sup>4</sup>, Kerry Holmes<sup>5</sup>, Joe Kanabrocki<sup>6</sup>, Joe Kozlovac<sup>7</sup>, Patty Olinger<sup>8</sup>, Nicoletta Previsani<sup>9</sup>, Reynolds Salerno<sup>10</sup>, and Terence Taylor<sup>11</sup>

<sup>1</sup>Public Health Agency of Canada, Winnipeg, Canada; <sup>2</sup>Health Protection Agency, Porton Down, United Kingdom; <sup>3</sup>Department of Foreign Affairs and International Trade, Ottawa, Ontario, Canada; <sup>4</sup>Public Health Agency of Canada, Ottawa, Ontario, Canada; <sup>5</sup>Canadian Food Inspection Agency, Ottawa, Ontario, Canada; <sup>6</sup>University of Chicago, Chicago, Illinois; <sup>7</sup>USDA Agricultural Research Service, Beltsville, Maryland; <sup>8</sup>Emory University, Atlanta, Georgia; <sup>9</sup>World Health Organization, Geneva, Switzerland; <sup>10</sup>Sandia National Laboratories, Albuquerque, New Mexico; and <sup>11</sup>International Council for the Life Sciences, Washington, DC

### Introduction

The Biorisk Management Workshop is held annually at the Canadian Science Centre for Human and Animal Health and organized by the National Microbiology Laboratory's Office of Biorisk Management (OBM), which is part of the Public Health Agency of Canada. Each year experts are invited to discuss important aspects of biosafety and biosecurity and to provide ideas and concepts for advancing biorisk management. The outcomes of the workshop are generally made available to the biosafety community at large. During the 2007 five-day meeting, the group was charged with discussing and, if possible, developing a common approach to biological risk assessment for the laboratory. Three of the five days were used to discuss individual parts of the risk assessment process, while the remaining time was spent developing a draft conceptual model of a unified risk assessment process.

The risk assessment process is a critical step in determining the appropriate biosafety and biosecurity measures for the safe and secure handling of biological agents in the laboratory setting. The risk assessment is also an integral part of a biosafety management system, serving as the basis for both implementing and reviewing a performance-oriented biosafety system. Typical outcomes of such a biological risk assessment are the identification of risks that require immediate attention and management, as well as the determination of appropriate biosafety levels, which by definition are a combination of different controls and not limited to the physical barriers, practices, and/or the use of personal protective equipment.

Although the biosafety community has been exposed to this process for decades and is apparently practicing it, there has not been a true consensus-building effort on documenting the actual procedures and outcomes of risk assessments. To make matters worse, the process is often viewed as too cumbersome, not quantifiable, and

just not practical. Recent review of postings on the ABSA "Biosafety Mailing" list, a common information exchange forum for biosafety professionals, revealed some dangerous trends. Too many in the community are just asking for copies of existing procedures, often lacking a clear understanding of the fundamental differences between "Risk Groups" and "Biosafety Levels" and/or seeking a quick and easy alignment between certain biological agents and their proposed biosafety level.

Although risk assessments are currently performed, the lack of a unified approach and appropriate tools makes such assessments unnecessarily difficult. The current lack of clearly quantifiable processes makes the biological risk assessment a predominantly qualitative approach and, as such, potentially highly subjective, variable, and inconsistent.

At the same time, as the biosafety community is struggling with a necessary and useful process, **we see an overall increasing tendency towards a zero-risk mentality based on perception as it relates to containment facilities.** This tendency is compounded by the fact that we are currently experiencing an unprecedented growth in new facilities within communities that are questioning the facility's safety, management, and research, which are essential foundations of successful work with infectious agents.

### Biological Risk Assessment in Laboratories—Discussion

In the beginning of the discussion, the group outlined some basic steps that would comprise a risk assessment process for biological agents.

#### What is risk and how is it addressed?

Risk might be commonly defined as the probability of an adverse outcome occurring (i.e., a consequence). In the case of a biological agent in the laboratory, that would mean the probability or chance that one or more

persons might become infected. However, caution is necessary. For example, we might address the risk of exposure simply as the probability of a laboratory worker becoming exposed to an agent based on a certain procedure. It is important to note that the risk of exposure says nothing about the consequence, which could be infection followed by severe morbidity, mortality, and/or a severe impact on public health. In contrast, the risk of infection would address the probability of becoming infected given that exposure to an infectious agent has already occurred. In both scenarios the hazard is the agent with unique intrinsic properties and the probability of something harmful occurring (consequence), leading to the actual risk. In general terms, the risk is a function of probability and consequence.

By itself, the risk assessment process can be broken down into three steps that start with the identification of the biological agent (hazard). Once the hazard has been identified and its unique properties researched and established, the second step is normally the assessment of the probability that such a hazard will cause an undesired event or consequence (e.g., exposure, disease, etc.). The probability will vary significantly based on the handling of the agent (e.g., procedures performed) as well as the control measures in place. The third step is the management of the risk through established control measures and reassessment if necessary.

Any successful risk assessment depends on the knowledge and information feeding into it. At the minimum, the hazard has to be identified and characterized and the procedures and practices applied have to be defined. During the discussion process, the group identified a number of characteristics or “good to know things” about an agent that help to characterize the hazard. Some of these characteristics will have an effect on the probability and/or the consequence. For example, an agent with an increased host range will result in an increased overall probability that an infection might

occur upon exposure. At the same time, the pathogenicity/virulence of the agent will certainly affect the consequence (infection might result in death). That assumes that the terms “pathogenicity” and/or “virulence” are clearly defined.

A listing of inherent agent characteristics (which is by no means complete) is included in Table 1.

A laboratory management team performing a risk assessment might have to look at all (or many) of these characteristics and establish a baseline of required information on the specific agent (hazard). The group considered this an important task and if documented would set the foundation for the next step in the risk assessment process. At the same time, the group also discussed under what circumstances these characteristics would change. The common conclusion was that if one establishes baseline agent-specific criteria, these criteria would not necessarily change and would actually be the unique properties of the agent independent of its use, location, etc. The only time the characteristics would change is if the agent itself changes. The group recognized this assumption as very important because it leads to the compilation of information on agents that can be used in every laboratory. Does this mean that everyone doing a risk assessment has to compile all of this information on a particular agent? The answer is both Yes and No. Yes, because we need the information on the laboratory/procedure level to perform a risk assessment, and No, because the biosafety and medical community can establish such a baseline set of data and put it into the public domain. Interestingly, a similar approach is taken by the Public Health Agency of Canada’s Material Safety Data Sheets (MSDS) for infectious agents, which are currently under revision.

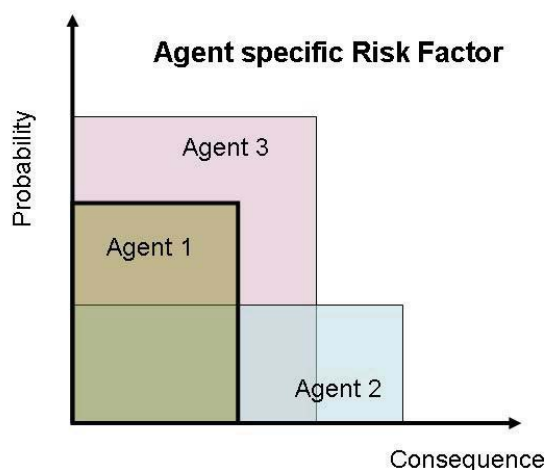
Because agent-specific characteristics have a probability factor and a consequence factor associated with them, establishing an agent-specific risk value (factor) that is independent of its use, laboratory procedure, lo-

**Table 1**

Agent characteristics and effect on probability and/or consequence.

Agent strain (unique properties)	None
Drug resistance	Consequences
Host range	Probability and consequences
Environmental stability/survivability • Ease of storage (biosecurity)	Probability and consequences
Infectious dose	Probability and consequences
Route of transmission or infection	Probability and consequences
Pathogenicity/virulence	Probability and consequences
Sensitivity to disinfectants	Probability
Ability to be grown at high titre	Probability and consequences
Vectors	Probability
Agent life cycle	Probability
Agent state (e.g., vegetative, spore)	Probability and consequences

**Figure 1**  
Agent specific risk factor.



cation, etc., (Figure 1) can be accomplished.

However, the group recognized that the establishment of such a risk factor requires the actual assessment of each characteristic property according to its impact on probability as well as consequence and then assessing or scoring these characteristics in comparison to each other. In the end, a unified system for determining the unique agent risk factor could be established.

This proposed model is similar to a biosecurity risk model established by Sandia National Laboratories (Salerno & Gaudioso, 2007) which was presented and discussed during the workshop. At the same time, it was realized that this scoring process can easily become very complicated and needs to be as simple as possible without sacrificing important input.

A suggestion by the group was to possibly limit the agent-specific traits to the following six factors:

1. Infectious dose
2. Lethality
3. Morbidity
4. Environmental stability
5. Availability of treatment
6. Transmission/transmissibility

This discussion led to the question of if, when, and how "Risk Groups" are to be incorporated into the current risk assessment process.

## Risk Groups

Historically, starting in 1983 with the first edition of the WHO *Laboratory Biosafety Manual*, countries were encouraged to develop their own risk group classification system based on the agents encountered in that country and using the following factors:

- Pathogenicity of the agent
- Modes of transmission and host range of the agent
- Availability of effective preventive measures

- Availability of effective treatment

Another important factor considered were the prevailing conditions in the geographical area in which the microorganisms are handled (e.g., endemic vs. non-endemic pathogens, which vary from country to country).

At that time, risk groups were directly linked to certain laboratory classifications (from basic to maximum containment), and if procedures changed, for example the use of larger quantities, the risk group level typically changed, resulting in a higher laboratory classification (containment) being assigned. This system actually based the risk group classification on not only agent characteristics but also procedures and techniques that would result in certain outcomes. It is also important to recognize that initially the concept of risk groups included both a probability factor and a hazard factor as reflected in the definitions of these risk groups. For example:

*"Risk Group II (moderate individual risk, limited 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 is limited."*  
(WHO, 1983)

As one can see, the definition includes the hazard (pathogen) as well as a probability assessment (unlikely, may cause). But, according to the WHO, the risk group classification was supposed to be based on the factors outlined above and would be country-specific.

Unfortunately, over the years, more and more risk groups were established that were primarily based on agent-relevant information without the input of laboratory procedures and practices. In some cases, organizations eliminated the laboratory aspect within their risk

group definitions. At the same time, other industries increasingly adopted this information; for example, for decades the transportation community used risk groups to decide which packaging system to use for the transport of infectious substances.

Over time, following the WHO recommendation, some countries developed a risk group classification using their own expert judgment and now provide a listing of biological agents according to Risk Groups 1-4. However, the actual assigning process, as well as the decision-making criteria or matrix, is not available and the critical or deciding factors for placing an agent in a specific risk group are unknown or not readily available. Even more important, what might be a Risk Group 3 agent in one country might be a Risk Group 2 agent in another. In addition, over time countries and/or agencies developed their own definitions of risk groups and moved away from the ones originally designed by the WHO. Faced with the situation that risk group classifications vary from country to country, sometimes using different definitions and non-disclosed decision-making information, the group questioned the value and use of current risk groups. Ultimately, the current risk group classification provides only a number from 1 to 4 which is supposedly (ultimately?) a relative risk difference.

The biosafety community has also increasingly adopted the fact that risk groups do not equal biosafety levels. For example, current practice is that higher quantities of an agent might increase the biosafety level but do not do anything to the risk group assignment of that organism. Looking back at the discussion above, it is obvious that this concept is in total opposition to its original design (WHO), where higher quantities actually changed the risk group level.

Interestingly, if one looks at the literature, most approaches to biological risk assessment actually promote the use of risk groups (including the 5th edition of the *Biosafety in Microbiological and Biomedical Laboratories* (BMBL)). However, none of these recommendations give a justification for why to use or how to use them in the actual risk assessment process. At the same time, as discussed initially, the person and/or group performing the risk assessment is challenged to identify the hazard (agent) with its intrinsic characteristics, basically compiling the same and additional information that someone used at one point to assign an agent to a specific risk group.

This brings us back to Table 1 and the information that needs to be compiled and made available to make the process transparent and reproducible. As outlined above and presented in Figure 1, any assignment of a risk factor depends on the scoring of the intrinsic agent characteristics which can then be used to assign a numeric value. As long as the process and the data are not available and are not reproducible, the value of the model is highly questionable. However, a unified approach by the biosafety community discussing and

agreeing on these factors and their scoring will make the model and the process highly transparent, scientifically sound, and reproducible. This is where the real value lies, and this is the reason the group decided to continue in the discussion and development of this model. At the same time, the group concluded that including the existing risk groups within a risk assessment process might not be of real benefit and could cause confusion.

The next step outlined by the group was to look at processes, procedures, and tasks to determine the risk of an undesired event happening. It became obvious that currently this process is highly subjective, primarily based on the lack of sufficient quantitative data. Recent publications have shown that aerosolization can be quantified and together with information on infectious dose can actually lead to some quantification of the process (Bennett & Parks, 2006). At the same time, the group recognized the important need for further work and research in this area. For the time being, it was accepted that most biological risk assessments will be of a more qualitative nature. That does not mean, however, that the process itself and the outcome cannot be made more reproducible.

Continuing the discussion of a new risk assessment tool and model, the group suggested establishing criteria that would allow the scoring of procedures, practices, and equipment, etc., using (again) transparent judgment-making tools and reproducible methods and results. If available, the scoring tables would allow for the establishment of a risk matrix similar to Figure 2, which would include the effect of different laboratory procedures, tasks, and equipment on risk, categorized according to their probability and consequence. Such a list with appropriate scoring tables does not exist for laboratory biosafety but is used for biosecurity risk assessments (Salerno & Gaudioso, 2007). One of the next logical steps for the group, together with other biosafety professionals, is to establish this information.

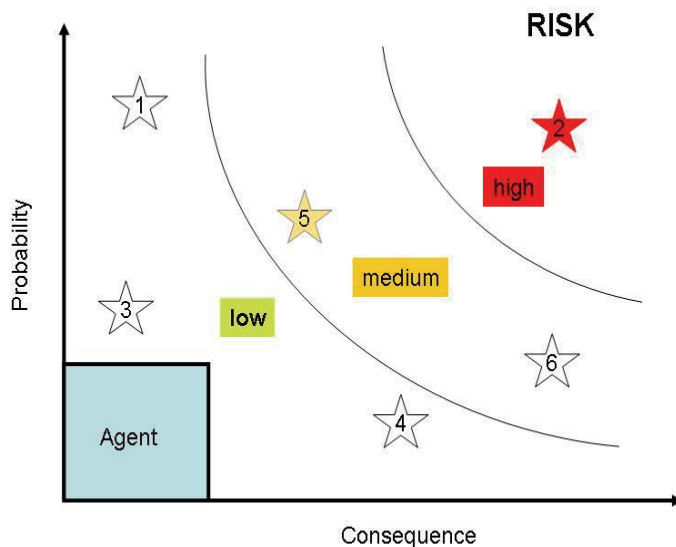
If implemented, the outcome of such a process would allow for a thorough discussion on how to manage the risk and how to allocate resources. For example, a facility might decide to focus on procedures number 2 and 5 (Figure 2) and through the implementation of additional controls significantly reduce the probability part of the equation, assuming that the consequence might not be easy to reduce. Consequently, the overall risk will be reduced (Figure 3).

To establish such a tool, the group discussed the various factors that would be assessed, scored, and incorporated into a formula; this is currently under development and a focus of the next workshop planned for 2008.

Overall, the group is convinced that this model has enough potential to be further explored, developed, and tested. This is by no means the end; for the group it is the beginning of a very useful process, bringing new tools and consensus to the community.

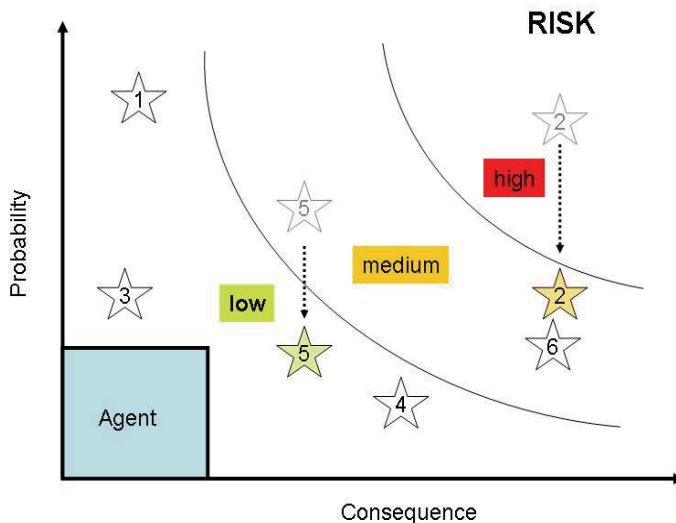
**Figure 2**

Risk Assessment outcome for various tasks (1-6).



**Figure 3**

Implementation of risk control measures reducing the probability and therefore the overall risk (2 and 5).



**Gaps**

As part of the overall discussions, the group identified key gaps in information and knowledge that need to be addressed to ensure solid risk assessments. These gaps include the lack of current data on laboratory-acquired infections and the lack of known infectious doses for many agents. The non-existence of these data has led to facility and program solutions which may not necessarily be cost-effective and in some cases may contribute to further risks (i.e., overly stringent containment requirements resulting in increased difficulties for

users to manipulate agents). To begin compiling the necessary information, the group decided to establish a Wikipedia-type web site to contain available information and reference documents useful for biological risk assessment. This web site can be accessed at: [www.biosafetyriskassessment.org](http://www.biosafetyriskassessment.org).

The group also recognized that the international harmonization of risk methodology is a feasible approach. However, end results of “local” risk assessments will vary from country to country and region to region. The level of biosecurity and biosafety training and awareness for those working with dangerous pathogens was

also considered a major factor in assessing risk. Public perception of risk, political structures, disease prevalence, and other issues all contribute to decision making in risk assessment and management.

## Integrating Biosafety, Biosecurity, and Bioterrorism?

Integrating the broader concepts related to biosecurity and bioterrorism into the overall process would result in a comprehensive, overarching toolkit for biological risk assessment. In addition to the criteria described for conducting a biosafety risk assessment, criteria related to safeguarding hazardous biological agents from deliberate theft or diversion for malicious use (bioterrorism, biological weapons) should be identified and scored. Some of these criteria might be established by asking the following questions:

- Can the agent be easily weaponized?
- Is it easy to acquire the agent and from what sources?
- Is there a production capacity?
- What is the ease of storage of the agent?
- What is its dissemination and stability?
- What are the consequences and how would they be mitigated?

The U.S. Centers for Disease Control and Prevention (CDC) has developed a comprehensive categorization scheme for agents based on their potential for posing a bioterrorism risk ([www.bt.cdc.gov/agent/agentlist-category.asp](http://www.bt.cdc.gov/agent/agentlist-category.asp)). The criteria outlined for each of the categories are similar to those listed above, but are different from the criteria used to create biosafety-related Risk Groups of agents. This can result in the same agent being placed in a high bioterrorism category, but a lower Risk Group and vice versa. Ideally, these two systems of categorization could be merged to produce an overall biorisk assessment. This would provide decision makers with a comprehensive understanding of the scope of the

biological risk and would enable them to better provide optimal solutions for the overall biological risk presented.

## Next Steps

The group will continue its effort to facilitate the establishment of a comprehensive toolkit for biological risk assessment as discussed above. The biosecurity model (Salerno & Gaudioso, 2007) is very promising and will be used as guidance to assemble a similar process for biological risk assessment. To continue the work on this model, the group established the following tasks, which will be addressed in the months to come:

- Develop scoring tables for individual agents through expert input.
- Develop scoring procedures for laboratory-based tasks and processes through expert input.
- Establish a first draft of the risk assessment model and test it within a number of institutions and situations.
- Make the toolkit available to the community at large for unrestricted use and further development.

At the same time, the group is planning to reconvene soon for a second workshop on biological risk assessment.

## Acknowledgements

We gratefully acknowledge the funding provided by the Public Health Agency of Canada and the administrative support throughout the workshop by Patti Alexander.

## References

- Bennett, A., & Parks, S. (2006). Microbial aerosol generation during laboratory accidents and subsequent risk assessment. *Journal of Applied Microbiology*, 100(4), 658-663.
- Salerno, R., & Gaudioso, J. (2007). *Laboratory biosecurity handbook*. Boca Raton, Florida: CRC Press.
- World Health Organization (WHO). (1983). *Laboratory biosafety manual* (1st ed.). Geneva: WHO.

## “Immune Attack” Video Game

The Federation of American Scientists has developed a video game entitled “Immune Attack.” The exciting format was designed to introduce high school and entry-level college students to immunological concepts as they send a nanobot through blood vessels and connective tissue and help someone launch an immune response. The game is free to those who will use it for educational purposes, and a fun way to refresh your immunological vocabulary. Perhaps you don’t think you need it, but can you define ICAM, C3a, CXCL8? If not, information and a free download is available at: <http://fas.org/immuneattack/>

