Laboratory Biorisk Management

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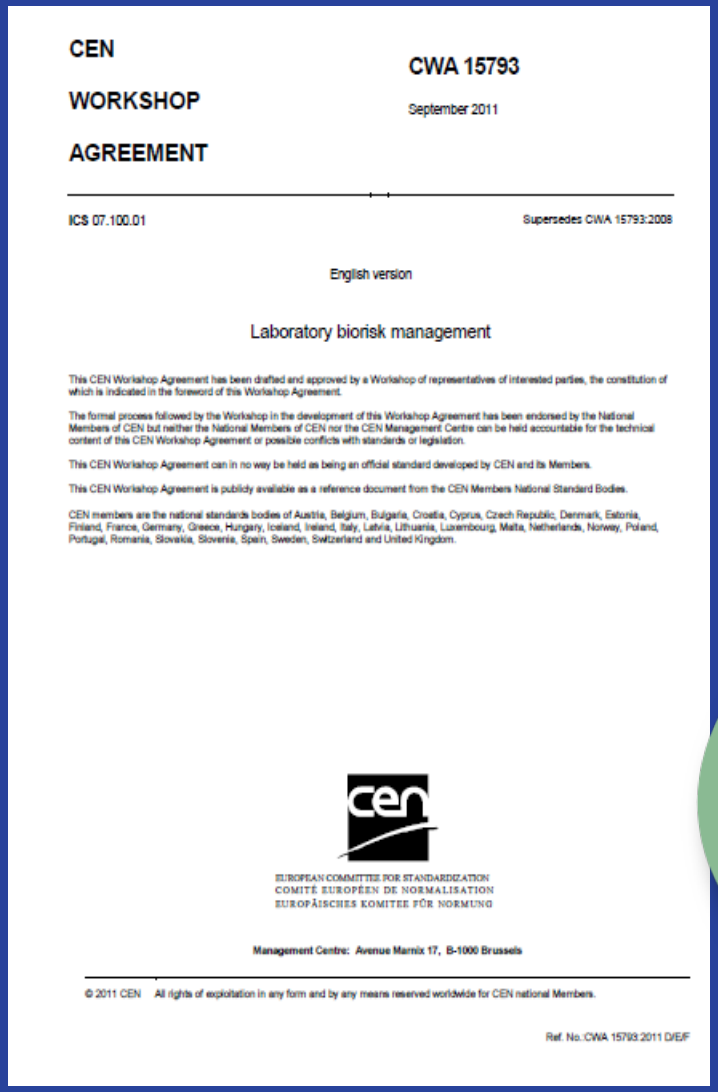
LABORATORY BIORISK MANAGEMENT

Biosafety AND Biosecurity

Origins of Biorisk Management



CEN

WORKSHOP

AGREEMENT

CWA 15793

September 2011

ICS 07.100.01

Supersedes CWA 15793:2008

English version

Laboratory biorisk management

This CEN Workshop Agreement has been drafted and approved by a Workshop of representatives of interested parties, the constitution of which is indicated in the foreword of this Workshop Agreement.

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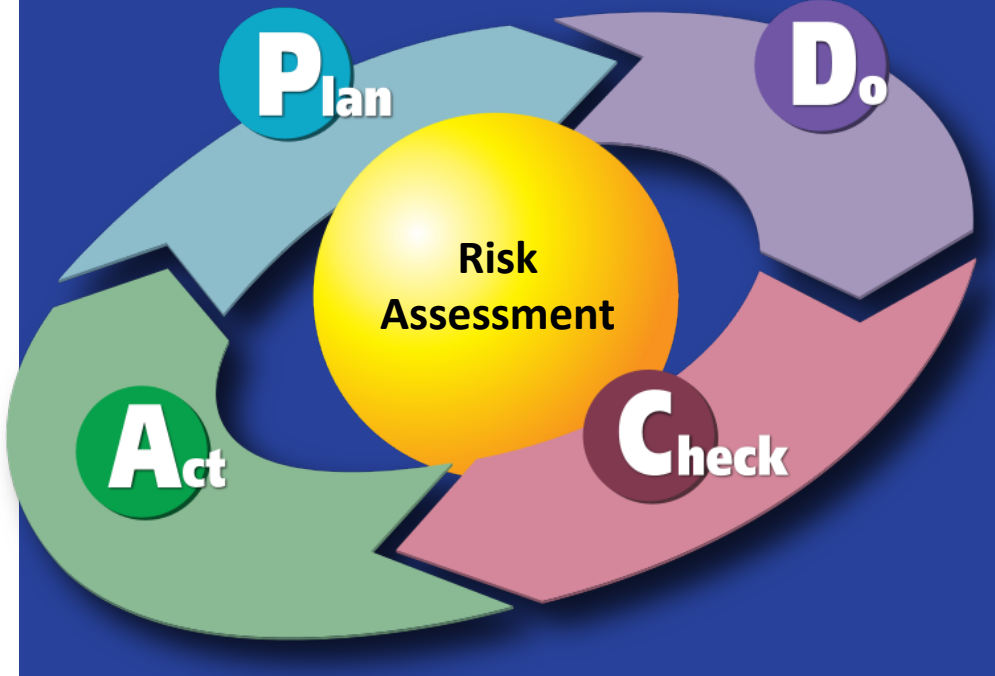
cen

EUROPEAN COMMITTEE FOR STANDARDIZATION
COMITÉ EUROPÉEN DE NORMALISATION
EUROPÄISCHES KOMITEE FÜR NORMUNG

Management Centre: Avenue Marnix 17, B-1000 Brussels

Ref. No. CWA 15793:2011 D/E/F

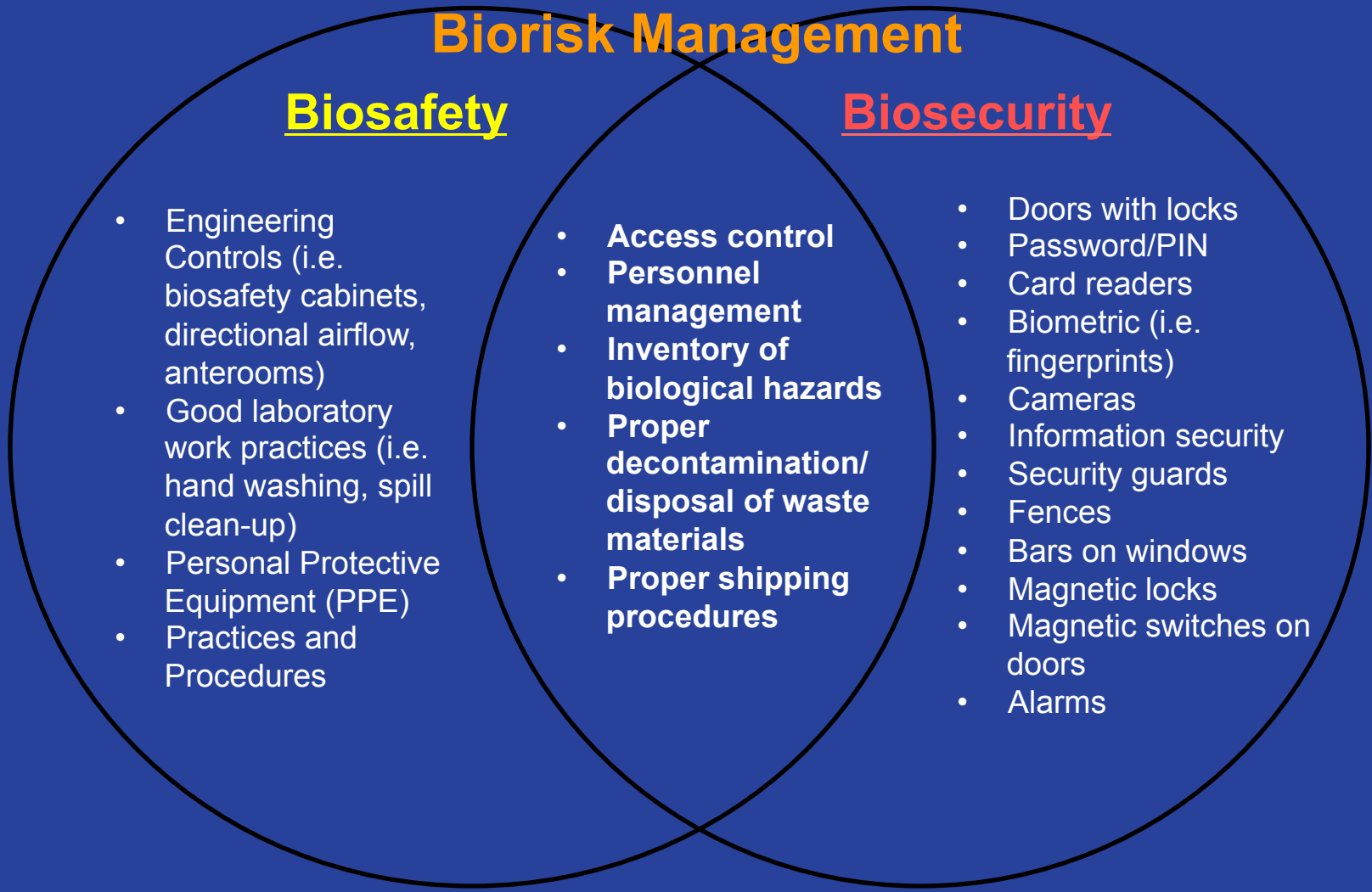
- CWA 15793 (2008, 2011)
- ISO standard now under development



Definitions in CWA 15793

- **Biosafety (adapted from WHO/CDS/EPR/2006.6)**
  - Containment principles, technologies, and practices that are implemented to prevent the unintentional exposure to biological agents and toxins, or their accidental release
- **Biosecurity (adapted from WHO/CDS/EPR/2006.6)**
  - Protection, control, and accountability for biological agents and toxins within laboratories in order to prevent their loss, theft, misuse, diversion of, unauthorized access, or intentional unauthorized release
- **Biorisk (adapted from ISO/IEC Guide 51:1999)**
  - Combination of the probability of occurrence of harm and the severity of that harm where the source of harm is a biological agent or toxin

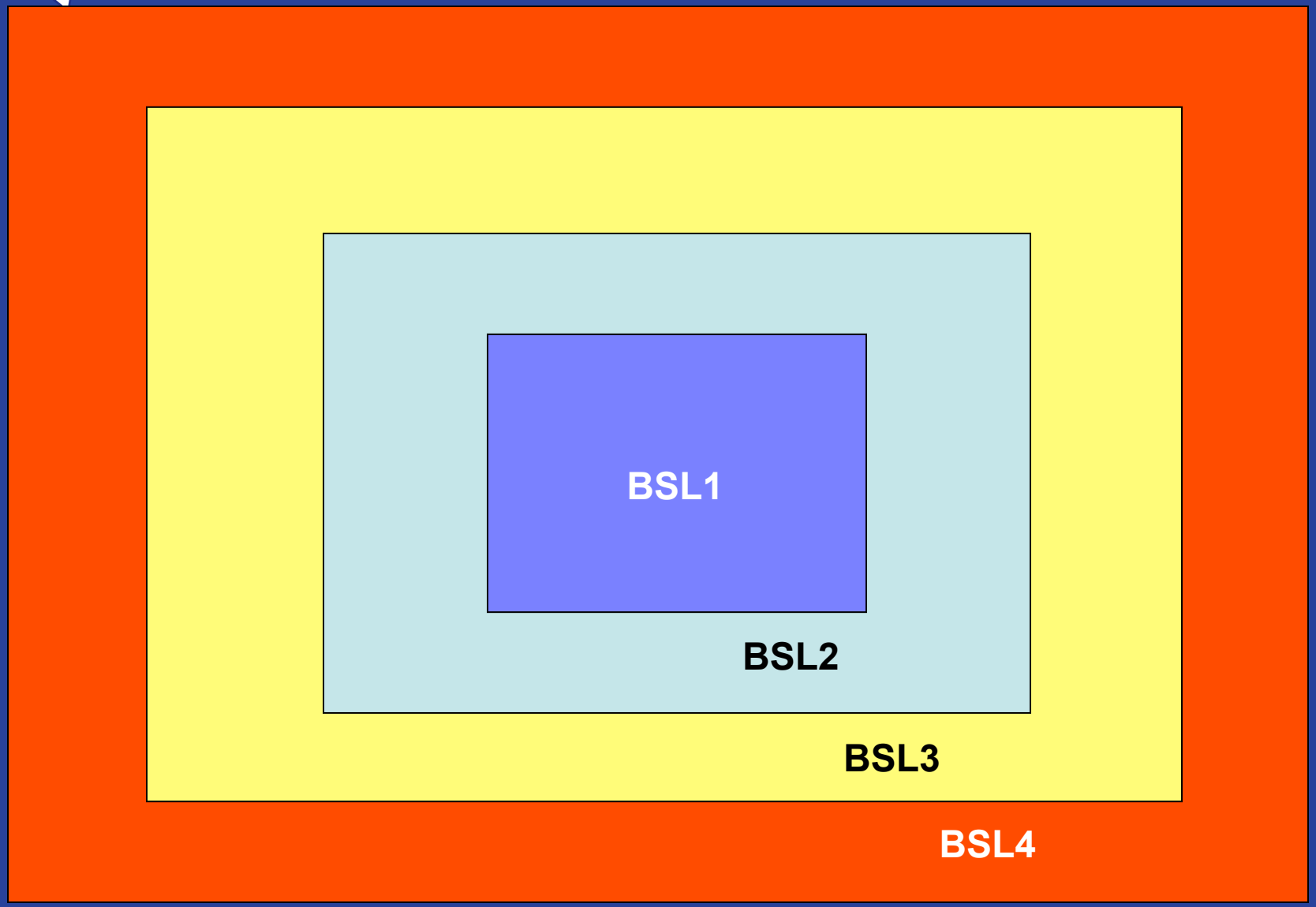
Biosafety, Biosecurity…



Agent Risk Groups

RG 1	RG 2	RG 3	RG 4
Agents that are not associated with disease in healthy adult humans	Agents that are associated with human disease which is rarely serious and for which preventive or therapeutic interventions are *often* available	Agents that are associated with serious or lethal human disease for which preventive or therapeutic interventions *may be* available (high individual risk but low community risk)	Agents that are 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)

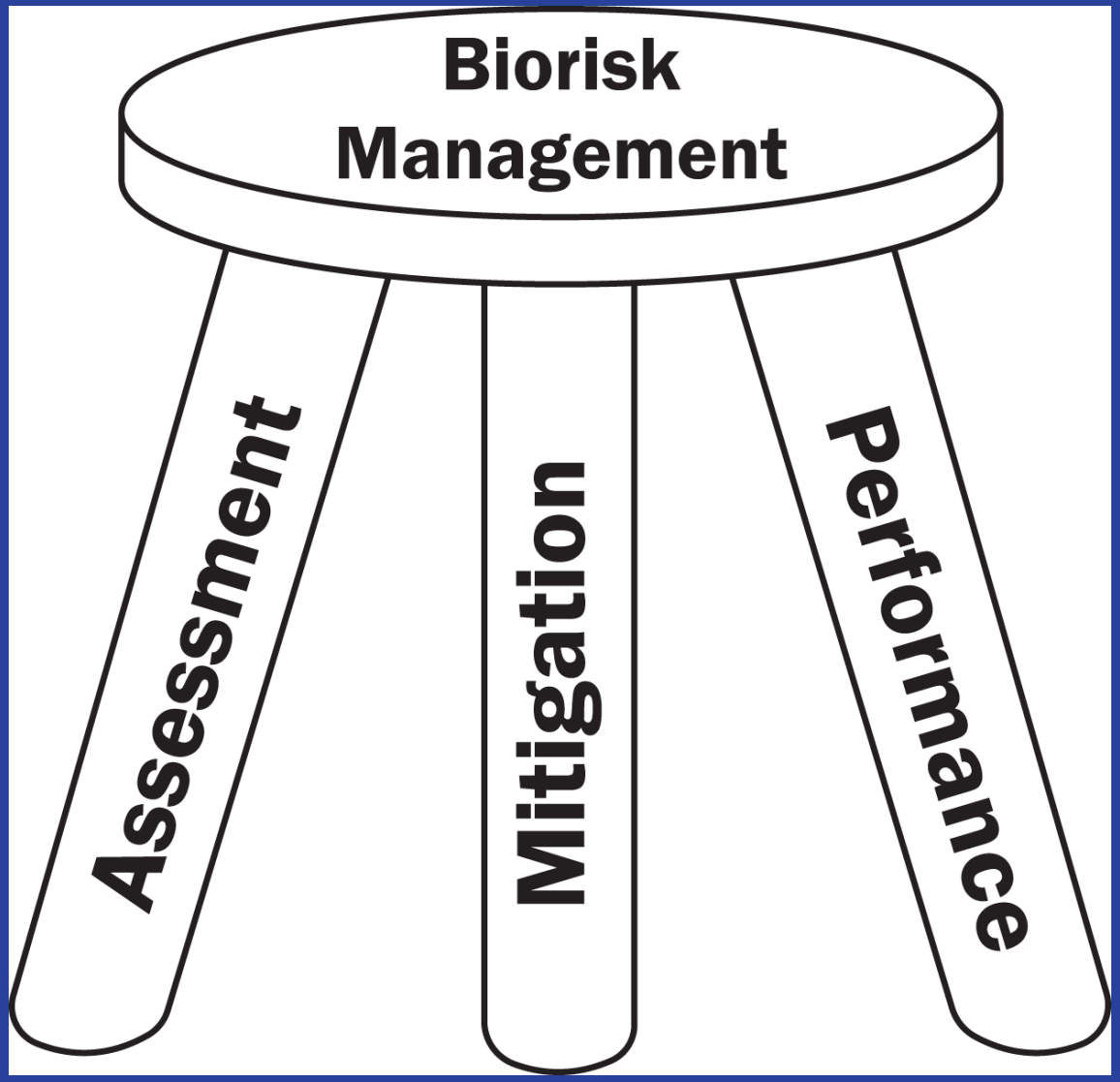
Biosafety Levels



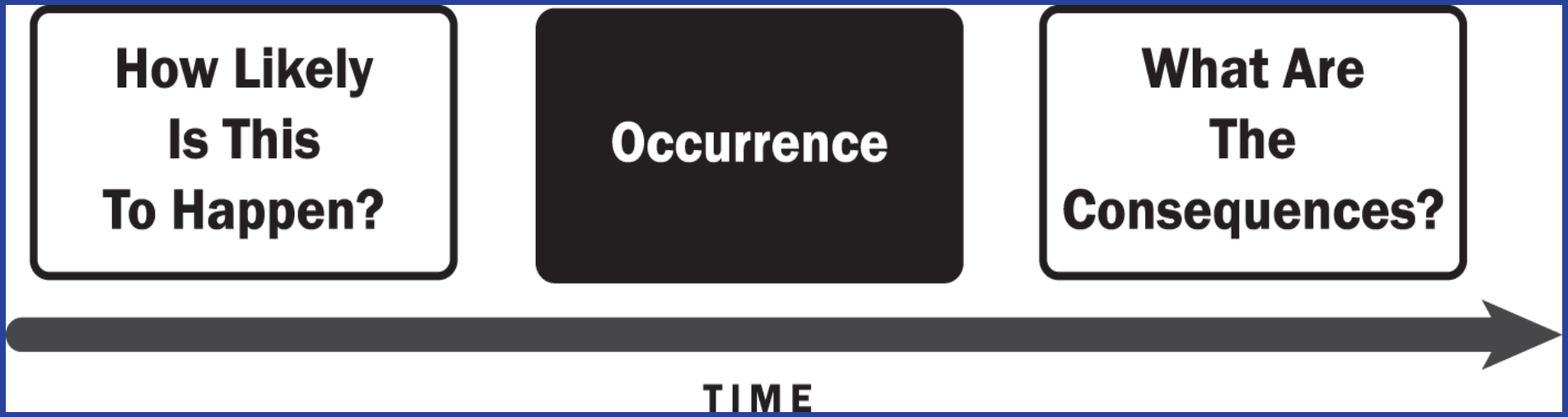
Laboratory Biorisk Management

- Depth of roles and responsibilities
- Intellectually sound, evidence-based decision making
- Substantive risk assessments based on unique operations
- Risk-based control measures
- Constant effectiveness evaluation
- Explicitly scalable

The AMP Model



I. Assessment



Are the Risks the Same?

Should the Mitigation Measures Be the Same?

II. Mitigation

- **Mitigation measures should be drawn directly from the risk assessment, and should target the most unacceptable risks**

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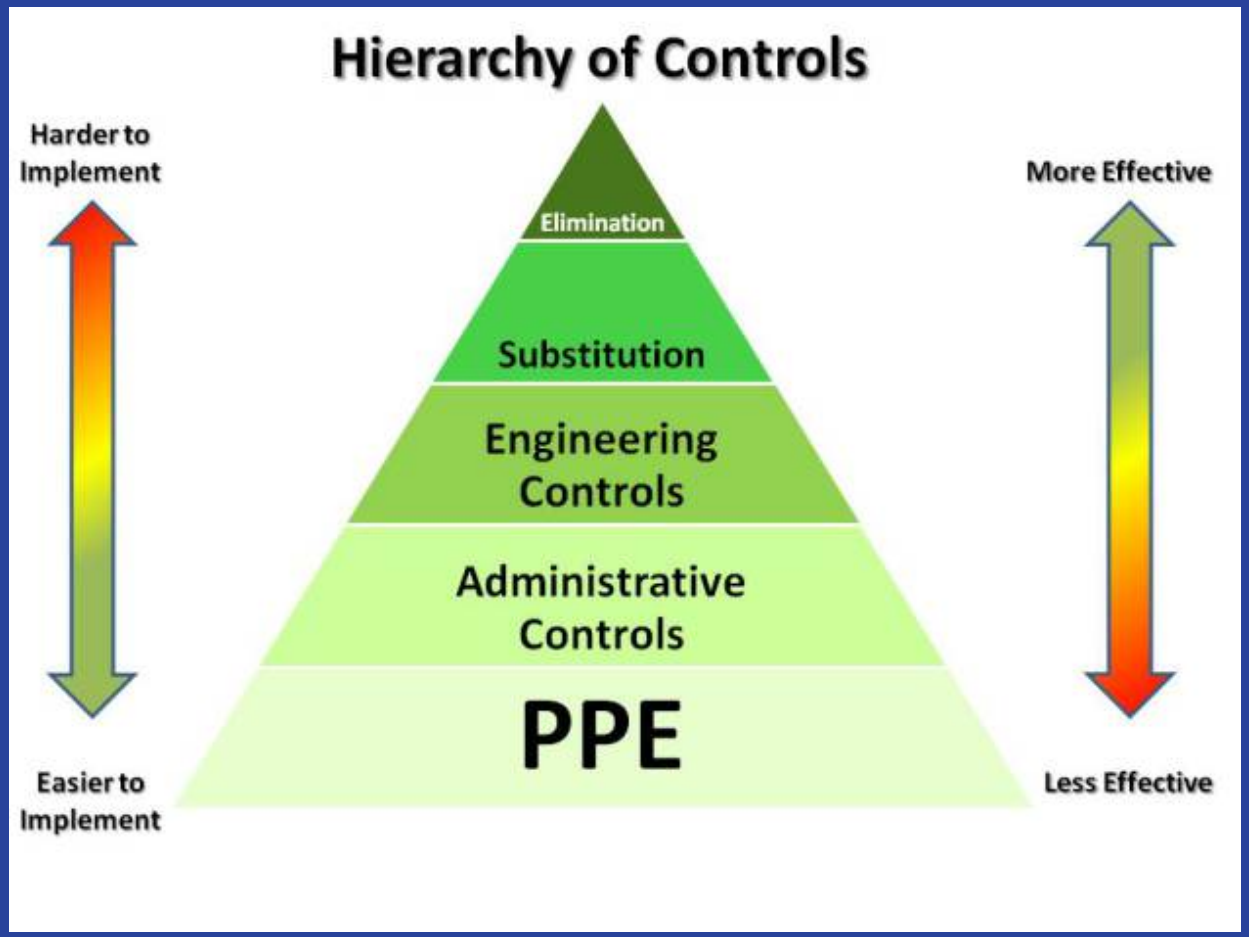
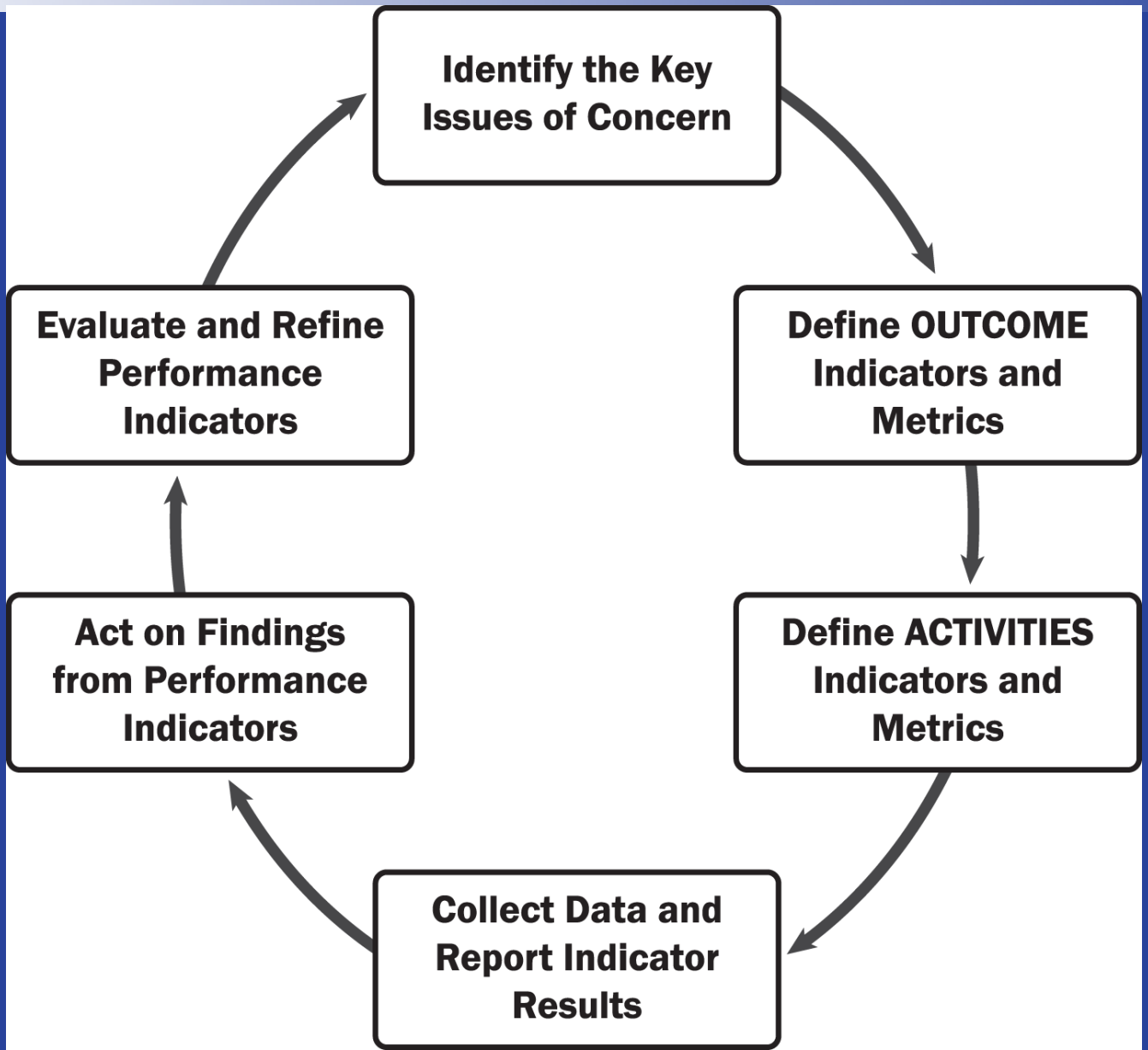
- **Mitigation measures should be drawn directly from the risk assessment, and should target the most unacceptable risks**



III. Performance

III. Performance



Nebraska's Ebola Patient-Specific PPE Checklists

PPE Donning and Doffing

Ebola Patients

These are standard Nebraska Biocontainment Unit Personal Protective Equipment procedures. These are developed to protect against Category A agents. Therefore, they vary slightly from CDC recommendations.

UNMC
UNIVERSITY OF NEBRASKA

GBRMC

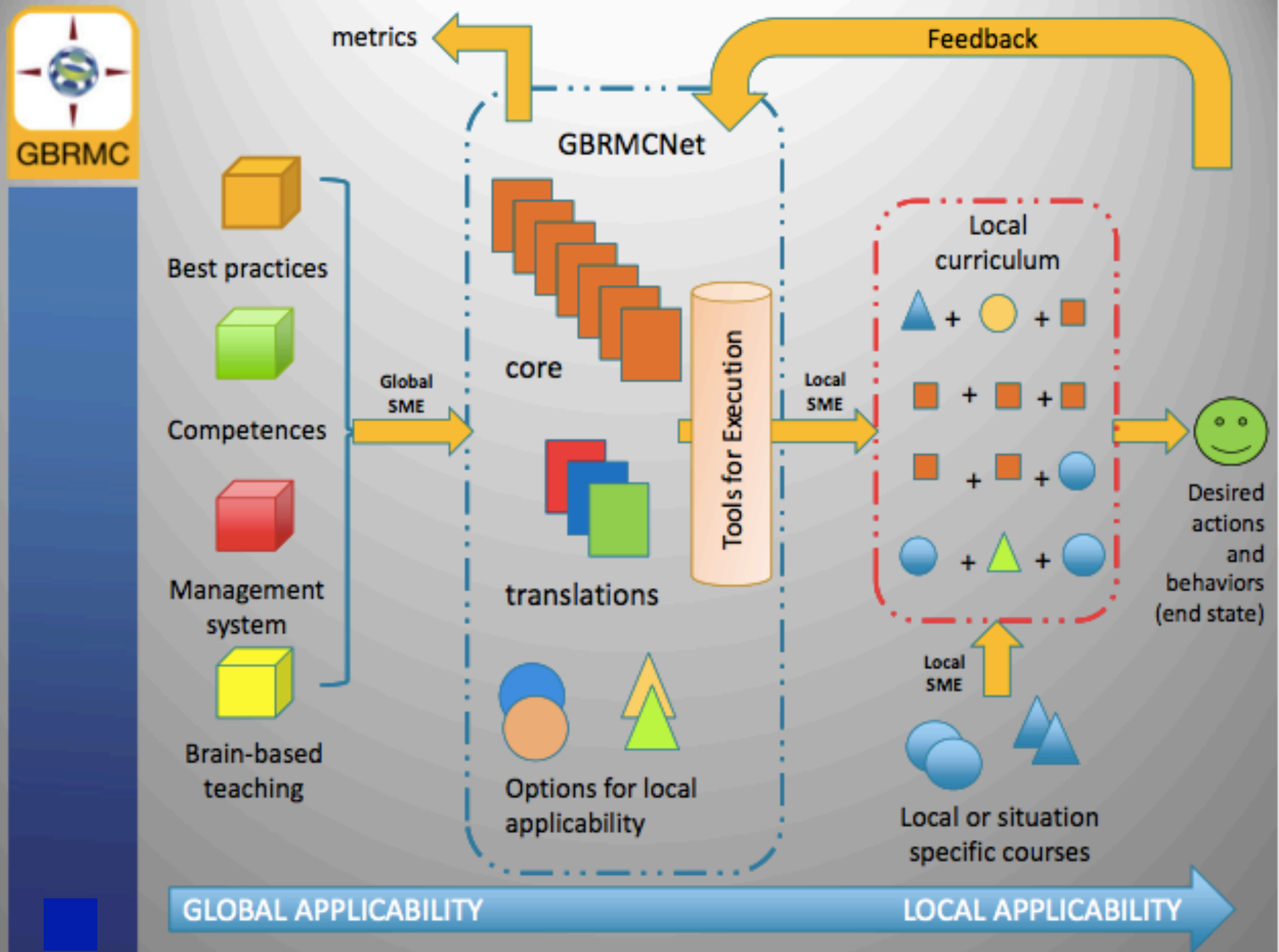
GBRMC

Global Biorisk Management Curriculum (GBRMC)

Catalog of Courses

GLOBAL BIORISK MANAGEMENT CURRICULUM


GBRMC Courses
(by CWA 15793 Domain)
Review & Revise
Measurement and Analysis of Biorisk Management System Performance
Conducting Audits and Inspections to Assess Biorisk Management Performance
Revising and Improving a Biorisk Management System based on Performance Results
Establishing and Using Performance Indicators
Drills, audits, and inspections (lab-level)
Policy & General Management
Orientation to biorisk management
Bioethics
Dual-use and responsible conduct of research
Writing and communicating biorisk management policy
Establishing and communicating BRM roles, responsibilities, objectives, and goals
Developing, conducting, and maintaining a hazard inventory
Identifying legal requirements that impact BRM
Planning & Assessment
Risk Characterization & Evaluation
Biosafety Risk Assessment
Biosecurity Risk Assessment
Work Program Review and Approval
Incident Response Planning and Preparation
Administrative Controls
Human Performance for Biorisk Management in the Laboratory
Laboratory level hazard and risk communication
Developing, evaluating, validating, and communicating standard operating procedures
Developing, implementing, and evaluating training and other methods to assure BRM competence
Developing roles & responsibilities for risk-based access to and accountability for biological agents and toxins
Establishing and maintaining formal and informal BRM mentoring programs
Managing human performance in the BRM workforce
Establishing and maintaining Worker Health Programs
Operational Controls
Risk mitigation strategies
Developing, evaluating, validating, and communicating standard operating procedures
Facility features
Engineering Controls and Equipment
Good laboratory practices
Personal protective equipment
Shipping Infectious Substances and Biological Specimens
Understanding and maintaining facilities & equipment for biorisk management
Basic features & maintenance for physical and information security measures
Field biosecurity
Decontamination
Biosecurity
Disposal
Reporting, Monitoring & Response
Introduction to Incident Management & Response
Incident recognition and response in the laboratory
Drills, audits, and inspections (lab-level)
Incident Response & Investigation
Incident Response Evaluation & Improvement
Basic Biorisk Management Track
Lab-Level Track
Management & Leadership Track


GBRMC
metrics
Feedback
GBRMCNet
Best practices
Competences
Management system
Brain-based teaching
Global SME
core
translations
Tools for Execution
Local SME
Local curriculum
Desired actions and behaviors (end state)
Local SME
Options for local applicability
Local or situation specific courses
GLOBAL APPLICABILITY
LOCAL APPLICABILITY

GBRMC

Trainers with Access*

- Algeria
- Argentina
- Armenia
- Australia
- Azerbaijan
- Belgium
- Brazil
- Cameroon
- Canada
- Cote D'Ivorie
- DRC
- Egypt
- Ethiopia
- Georgia
- Hong Kong
- India
- Indonesia
- Iran
- Iraq
- Jordan
- Kazakhstan
- Kenya
- Kyrgyzstan
- Malaysia
- Mexico
- Mongolia
- Morocco
- Mozambique
- Nigeria
- Peru
- Philippines
- Russia
- Rwanda
- Saudi Arabia
- Singapore
- South Africa
- Swaziland
- Tajikistan
- Tanzania
- Trinidad & Tobago
- Uganda
- Ukraine
- UK
- USA
- Uzbekistan
- Vietnam
- Yemen
- Zambia
- Zimbabwe

*TDP or Trainers' Orientation

Risk Assessment

Risk Assessment Definitions

Hazard

- *Something* that has potential to do harm

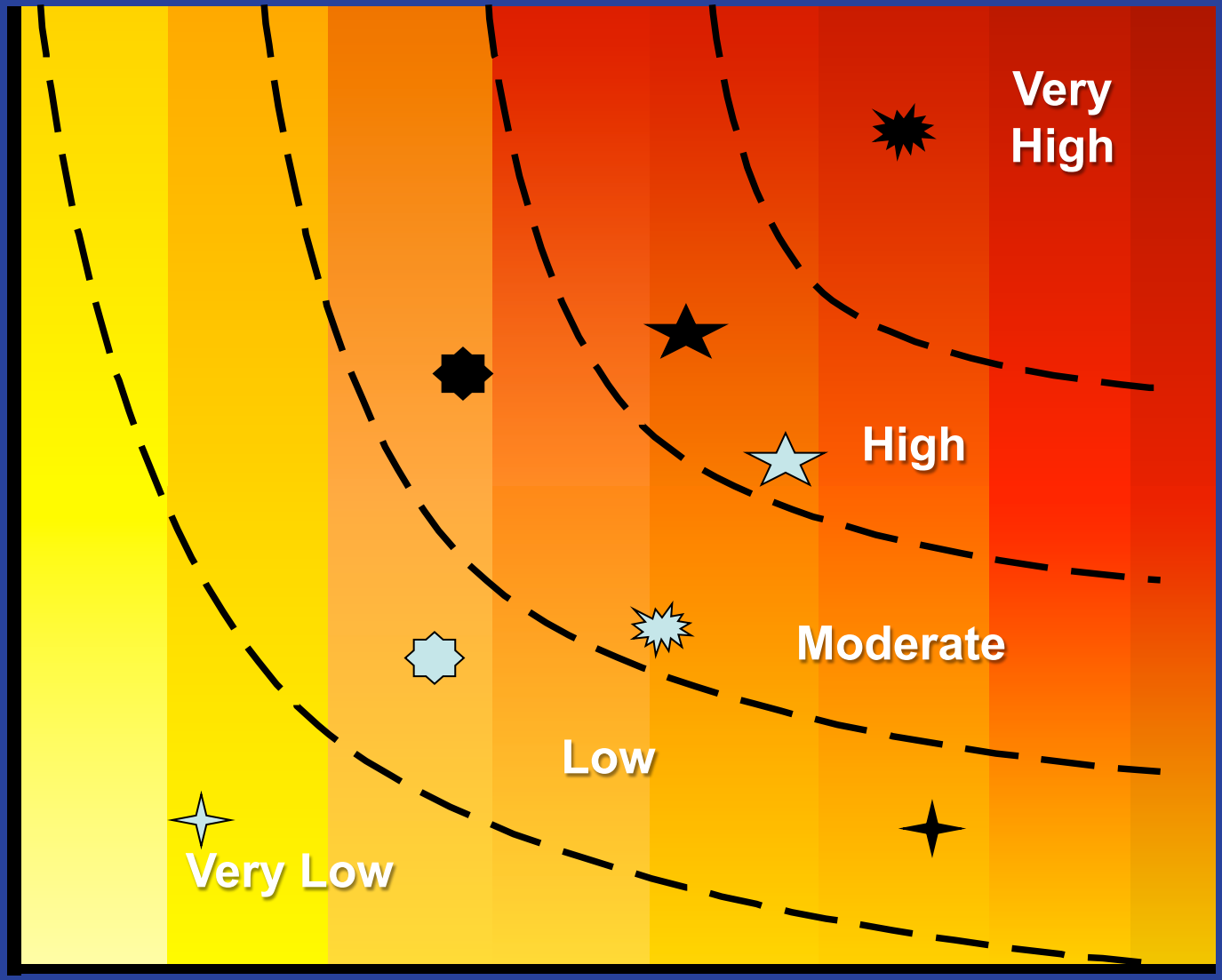
Threat

- *Someone* who has potential to do harm using a specific hazard

Risk

- In an event involving a specific hazard and/or threat, the likelihood and consequences of a *particular outcome*

Risk: What Can Go Wrong?



How to Assess Risk…

Many different ways to assess risk.

But it needs to be

- ***Structured,***
- ***Repeatable, and***
- ***Documented.***

And it needs to acknowledge that any activity has many, many risks.

The real value in a risk assessment is in comparing risks against each other, and prioritizing some risks over others.

Biosafety RAM

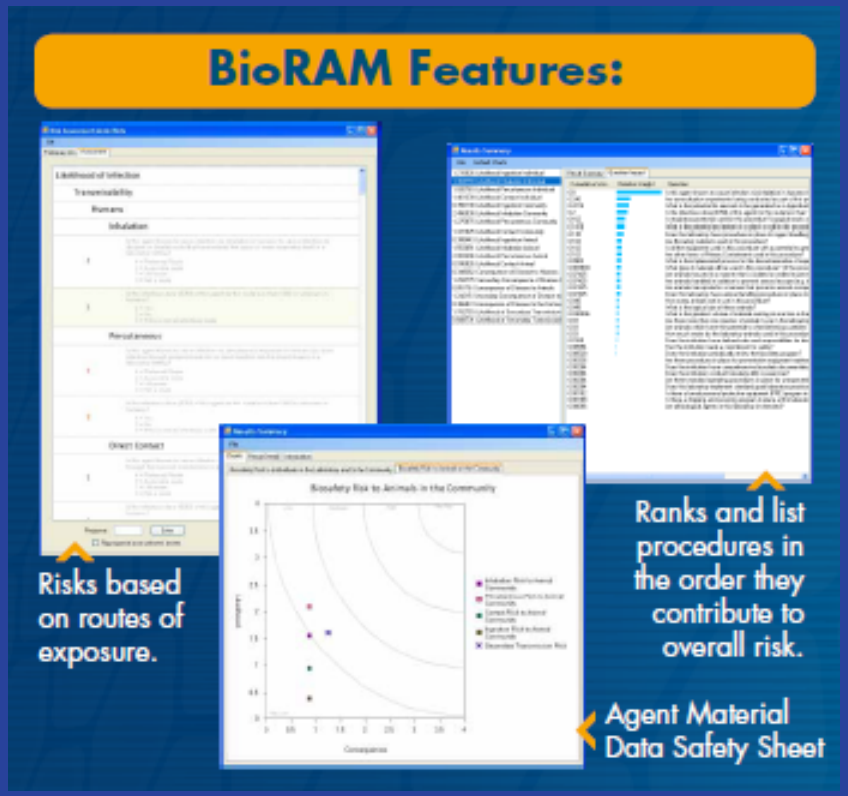
Safety risks based on routes of exposure

- Inhalation
- Ingestion
- Contact
- Percutaneous

Agent properties

Activity-specific procedures

Activity-specific mitigation measures



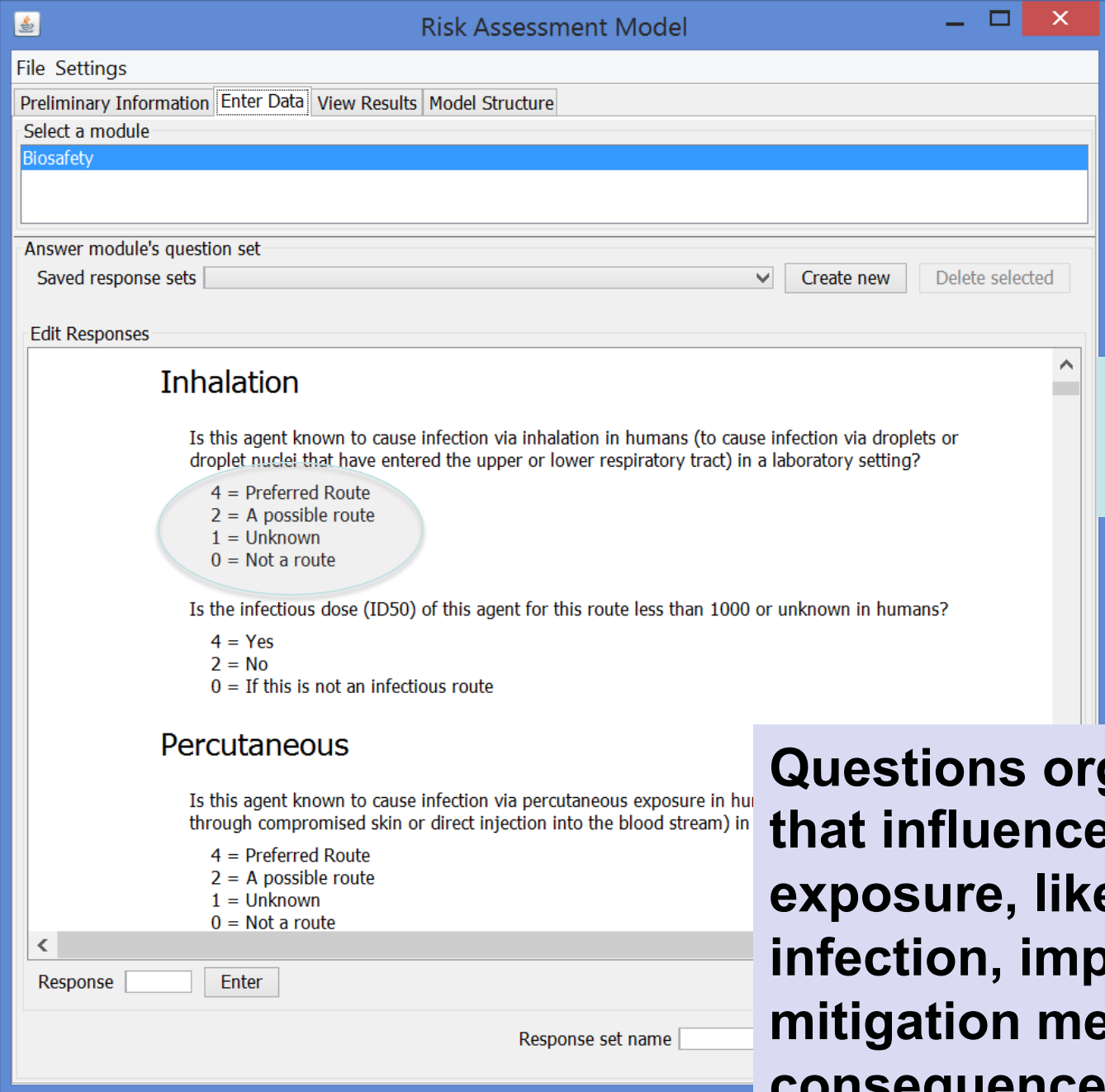
Biosafety RAM Structure

Factors that may increase the likelihood of an exposure and an infection, and the consequences of an infection

Properties of Agent and Laboratory Procedures

Implemented Biosafety Measures

Factors that reduce the likelihood of exposure or the consequences of infection



Answers captured as numerical values ranging from zero to four

Questions organized by factors that influence likelihood of an exposure, likelihood of an infection, implementation of mitigation measures, and consequences of an infection to a human and/or animal host

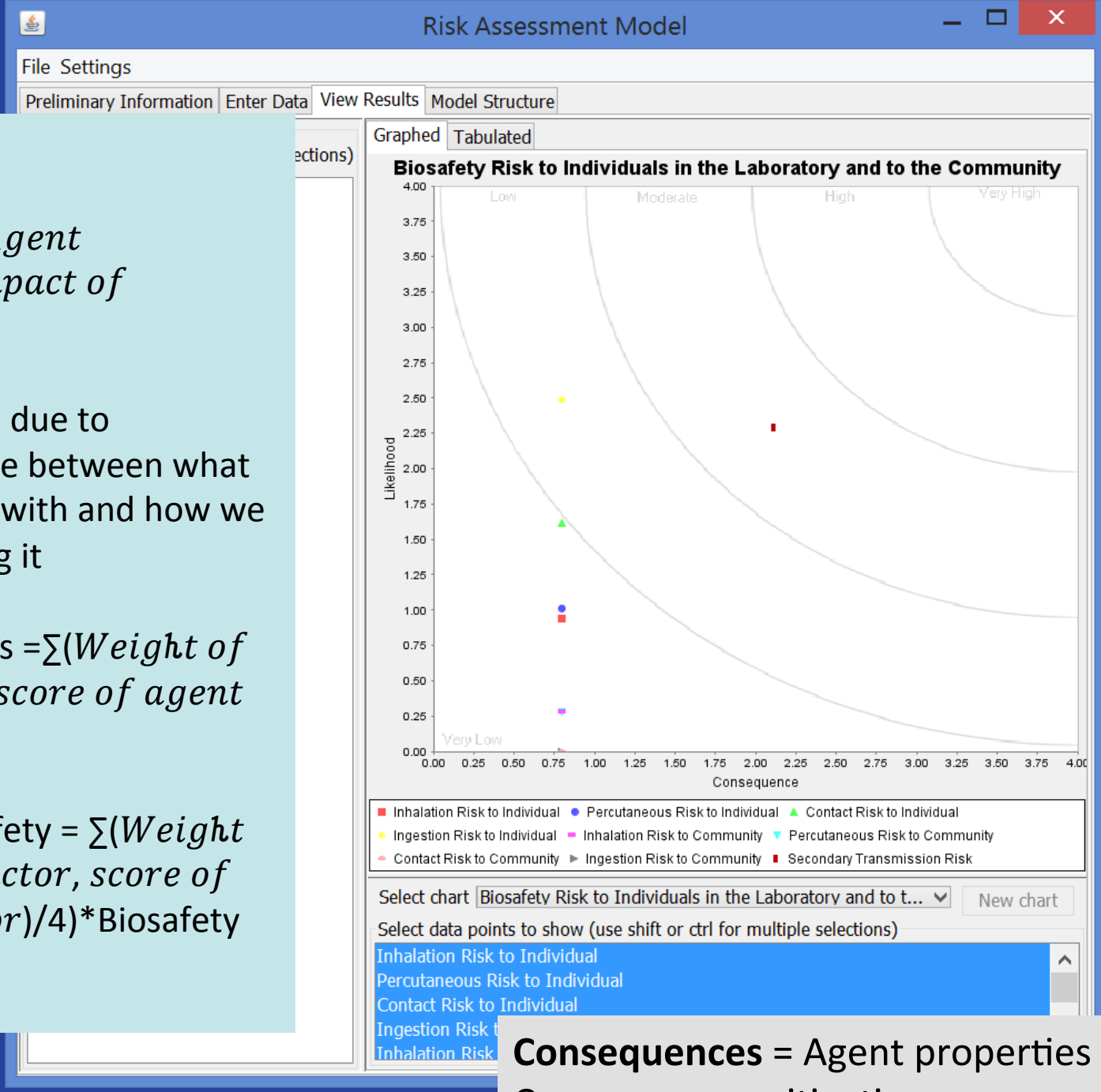
LIKELIHOOD:

Likelihood = √(*Agent Properties*Impact of Biosafety)*

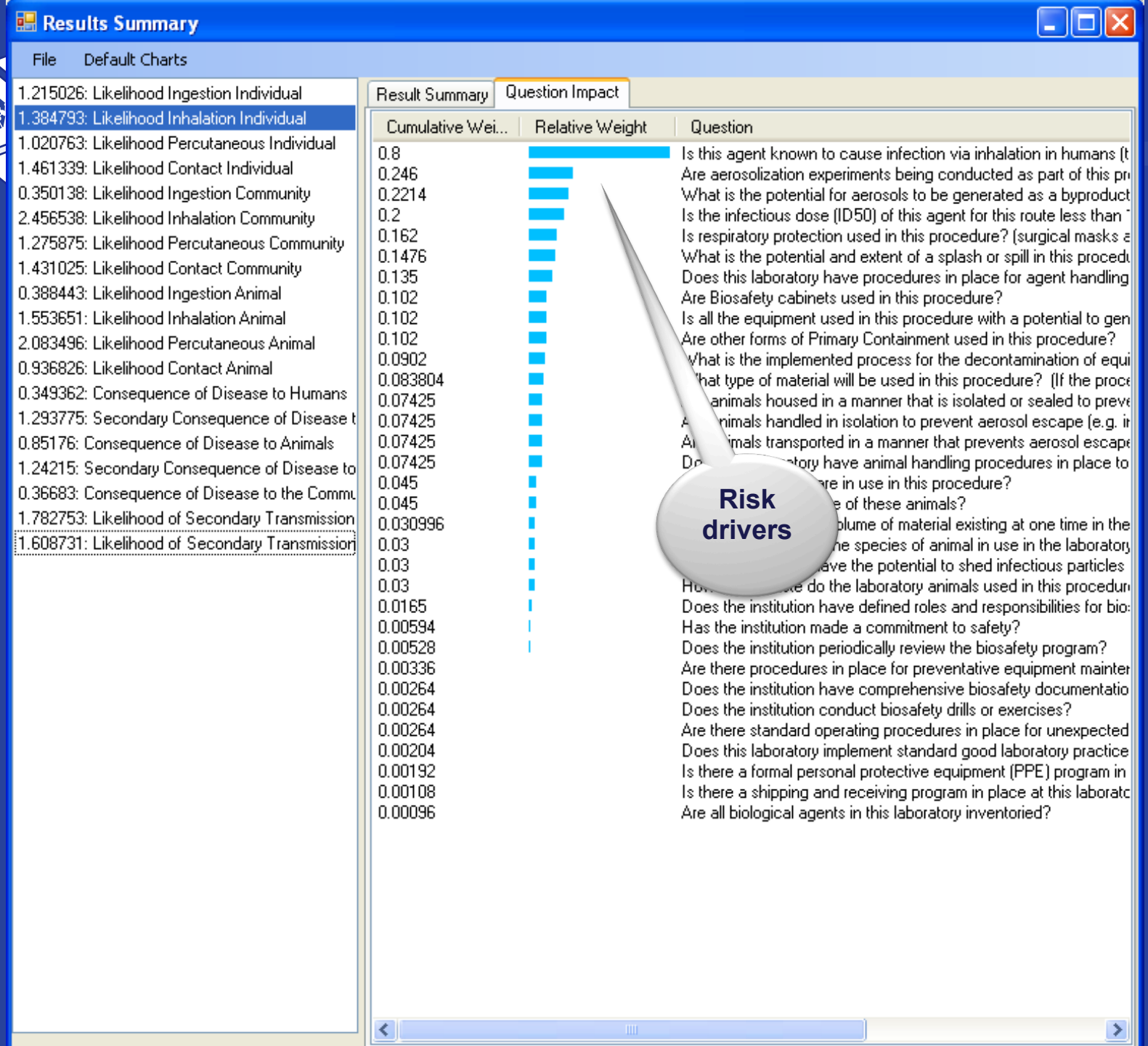
GEOMEAN used due to interdependence between what we are working with and how we are safeguarding it

Agent Properties =∑(*Weight of agent factor, score of agent factor*)

Impact of biosafety = ∑(*Weight of biosafety factor, score of biosafety factor*)/4)*Biosafety Weight



Consequences = Agent properties * Consequence mitigation measures


Results Summary
File
Default Charts
1.215026: Likelihood Ingestion Individual
1.384793: Likelihood Inhalation Individual
1.020763: Likelihood Percutaneous Individual
1.461339: Likelihood Contact Individual
0.350138: Likelihood Ingestion Community
2.456538: Likelihood Inhalation Community
1.275875: Likelihood Percutaneous Community
1.431025: Likelihood Contact Community
0.388443: Likelihood Ingestion Animal
1.553651: Likelihood Inhalation Animal
2.083496: Likelihood Percutaneous Animal
0.936826: Likelihood Contact Animal
0.349362: Consequence of Disease to Humans
1.293775: Secondary Consequence of Disease t
0.85176: Consequence of Disease to Animals
1.24215: Secondary Consequence of Disease to
0.36683: Consequence of Disease to the Commu
1.782753: Likelihood of Secondary Transmission
1.608731: Likelihood of Secondary Transmission
Result Summary
Question Impact
Cumulative Wei...
Relative Weight
Question
0.8
Is this agent known to cause infection via inhalation in humans (t
0.246
Are aerosolization experiments being conducted as part of this pr
0.2214
What is the potential for aerosols to be generated as a byproduct
0.2
Is the infectious dose (ID50) of this agent for this route less than
0.162
Is respiratory protection used in this procedure? (surgical masks a
0.1476
What is the potential and extent of a splash or spill in this procedu
0.135
Does this laboratory have procedures in place for agent handling
0.102
Are Biosafety cabinets used in this procedure?
0.102
Is all the equipment used in this procedure with a potential to gen
0.102
Are other forms of Primary Containment used in this procedure?
0.0902
What is the implemented process for the decontamination of equi
0.083804
hat type of material will be used in this procedure? (If the proce
0.07425
animals housed in a manner that is isolated or sealed to preve
0.07425
nimals handled in isolation to prevent aerosol escape (e.g. ir
0.07425
imals transported in a manner that prevents aerosol escape
0.07425
tory have animal handling procedures in place to
0.045
re in use in this procedure?
0.045
e of these animals?
0.030996
olume of material existing at one time in the
0.03
he species of animal in use in the laboratory
0.03
ave the potential to shed infectious particles
0.03
do the laboratory animals used in this procedur
0.0165
Does the institution have defined roles and responsibilities for bio
0.00594
Has the institution made a commitment to safety?
0.00528
Does the institution periodically review the biosafety program?
0.00336
Are there procedures in place for preventative equipment mainter
0.00264
Does the institution have comprehensive biosafety documentatio
0.00264
Does the institution conduct biosafety drills or exercises?
0.00264
Are there standard operating procedures in place for unexpected
0.00204
Does this laboratory implement standard good laboratory practice
0.00192
Is there a formal personal protective equipment (PPE) program in
0.00108
Is there a shipping and receiving program in place at this laboratc
0.00096
Are all biological agents in this laboratory inventoried?
Risk drivers

Biosecurity RAM

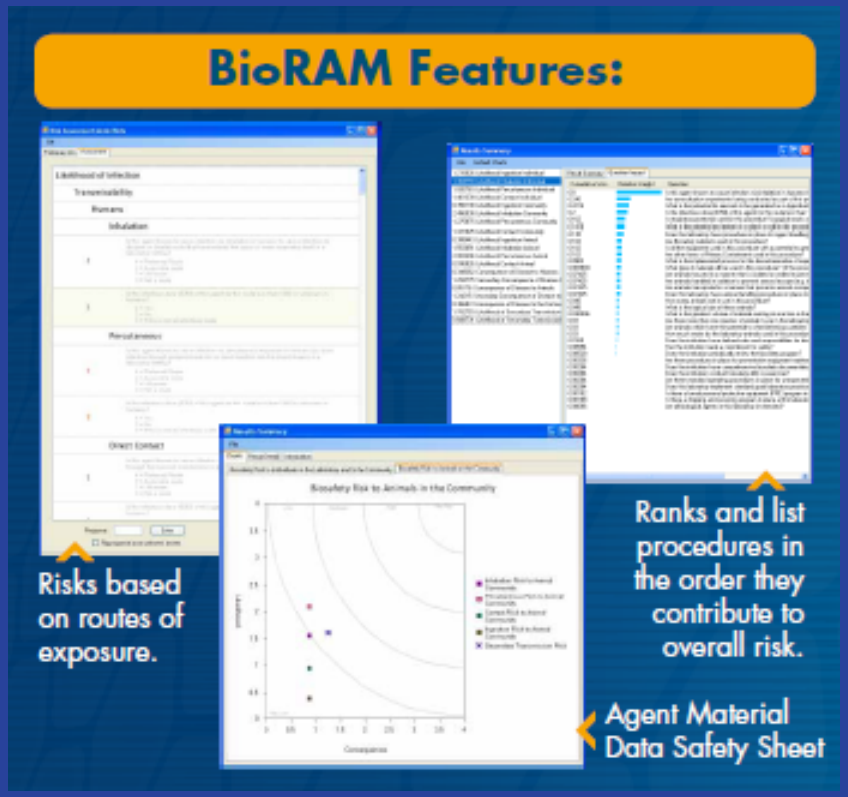
Security risks based on the motives, means, and opportunities of the threats

- Insider
- Outsider

Agent properties

Activity-specific procedures

Activity-specific mitigation measures



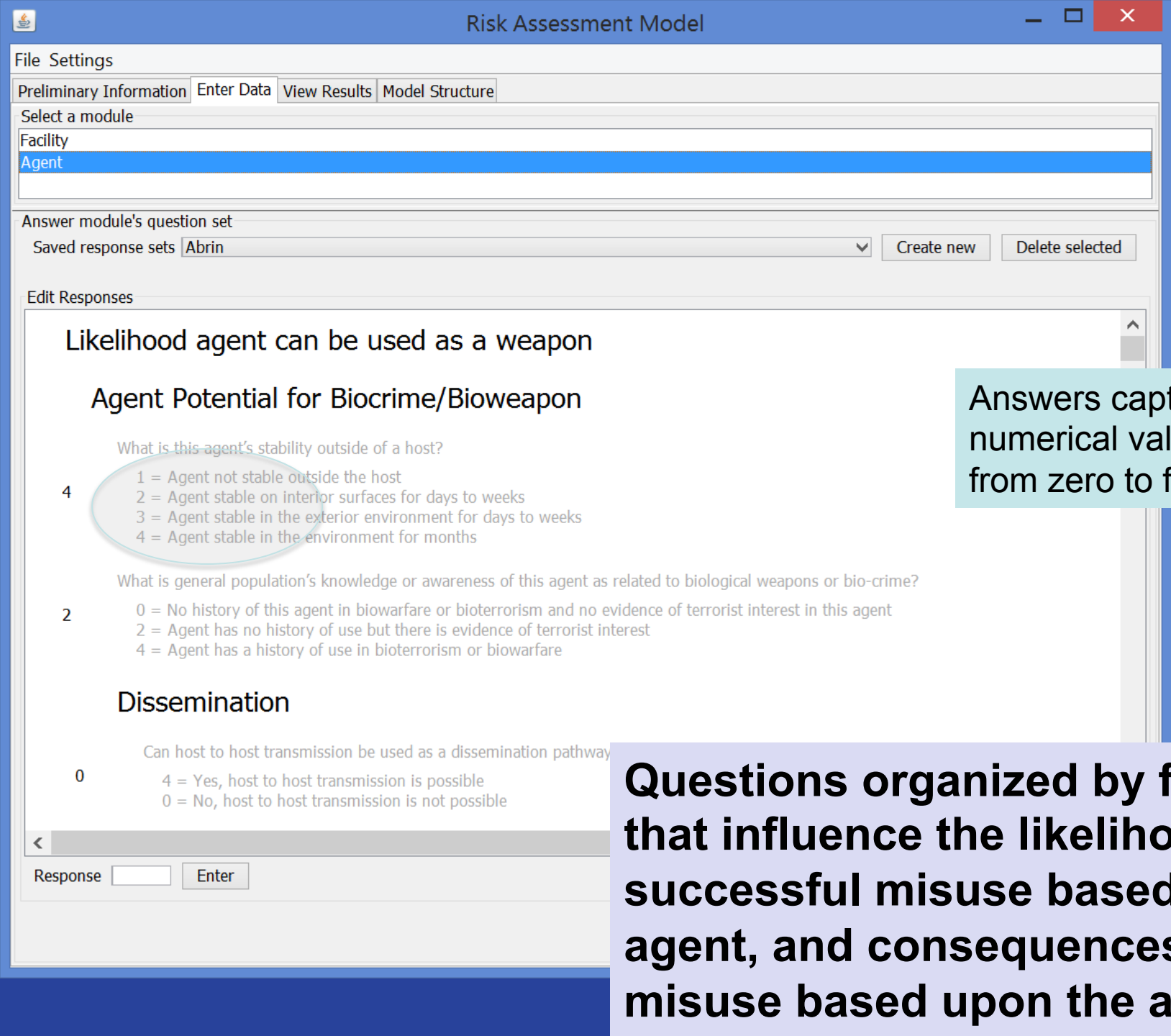
Biosecurity RAM Structure

Factors that may increase the likelihood of successful malicious use, and the consequences of malicious use

Properties of Agent and Laboratory Procedures

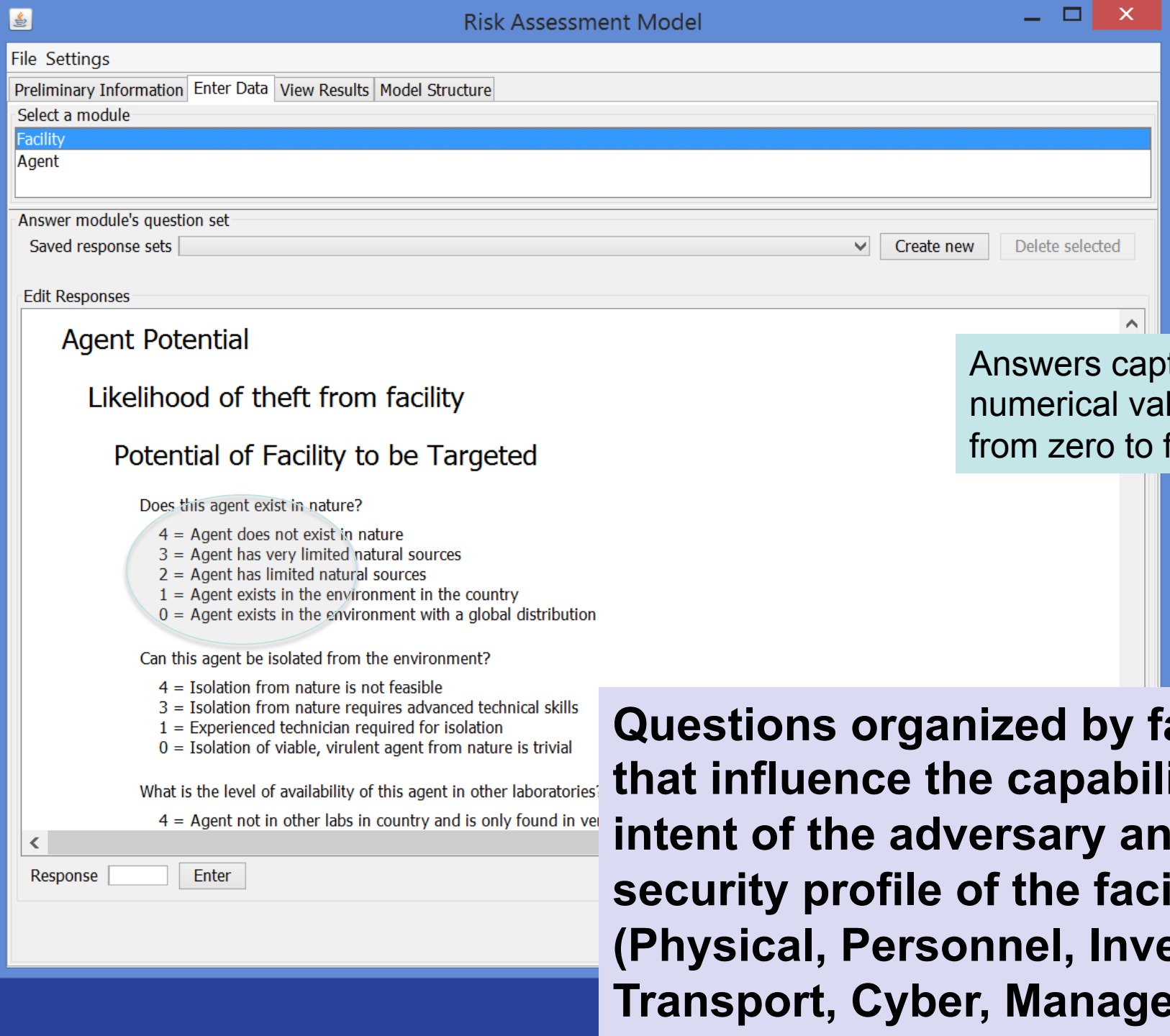
Implemented Biosecurity Measures

Factors that reduce the likelihood of successful malicious use



Answers captured as numerical values ranging from zero to four

Questions organized by factors that influence the likelihood of successful misuse based on the agent, and consequences of misuse based upon the agent



Answers captured as numerical values ranging from zero to four

Questions organized by factors that influence the capabilities and intent of the adversary and the security profile of the facility (Physical, Personnel, Inventory, Transport, Cyber, Management)

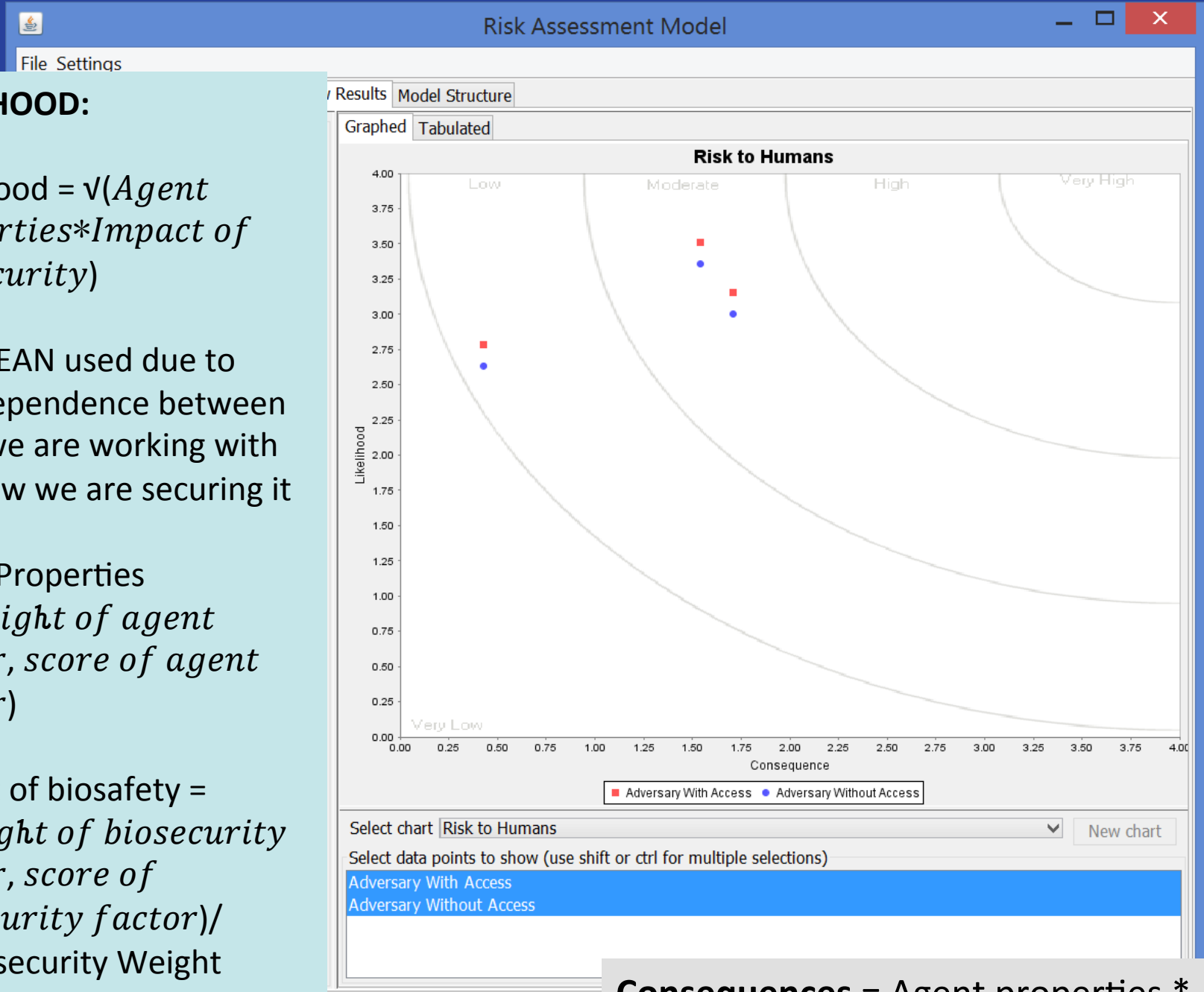
LIKELIHOOD:

Likelihood = √($Agent\ Properties * Impact\ of\ Biosecurity$)

GEOMEAN used due to interdependence between what we are working with and how we are securing it

Agent Properties =∑($Weight\ of\ agent\ factor, score\ of\ agent\ factor$)

Impact of biosafety = ∑($Weight\ of\ biosecurity\ factor, score\ of\ biosecurity\ factor$)/ 4)*Biosecurity Weight



Consequences = Agent properties * Consequence mitigation measures

Data from Spiez Laboratory Review of Biosafety RAM model (Daniel Kumin)

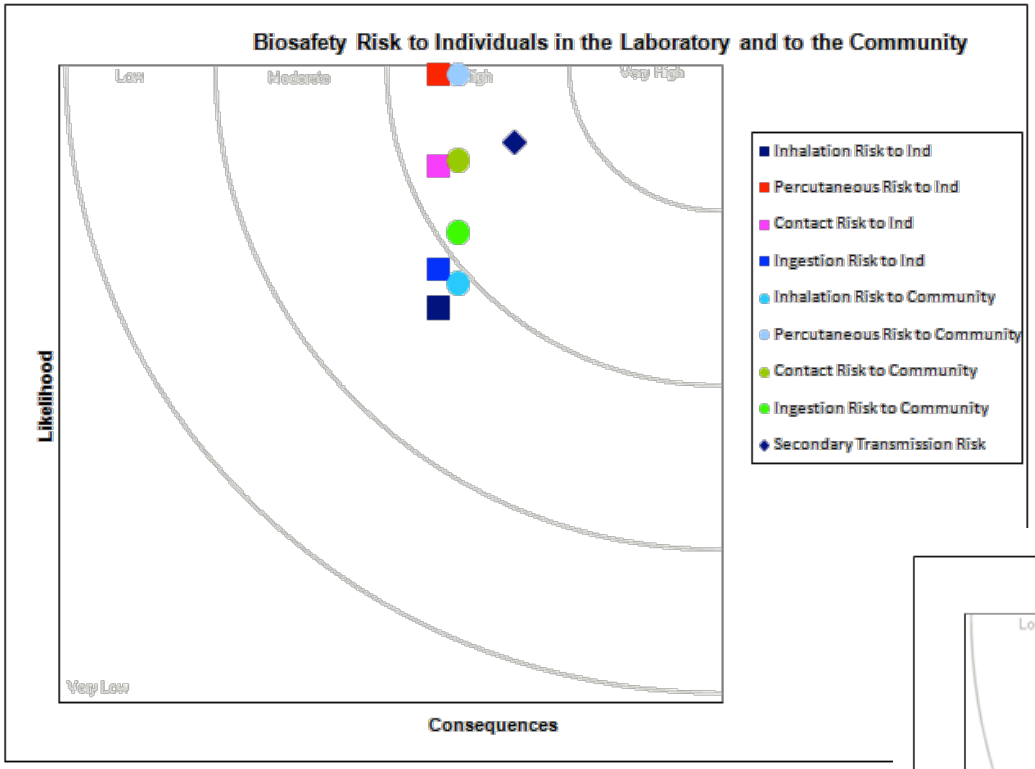


Figure 1: Risks posed by Nipha Virus prior to any implementation of Mitigation Measures

Before mitigation

After mitigation

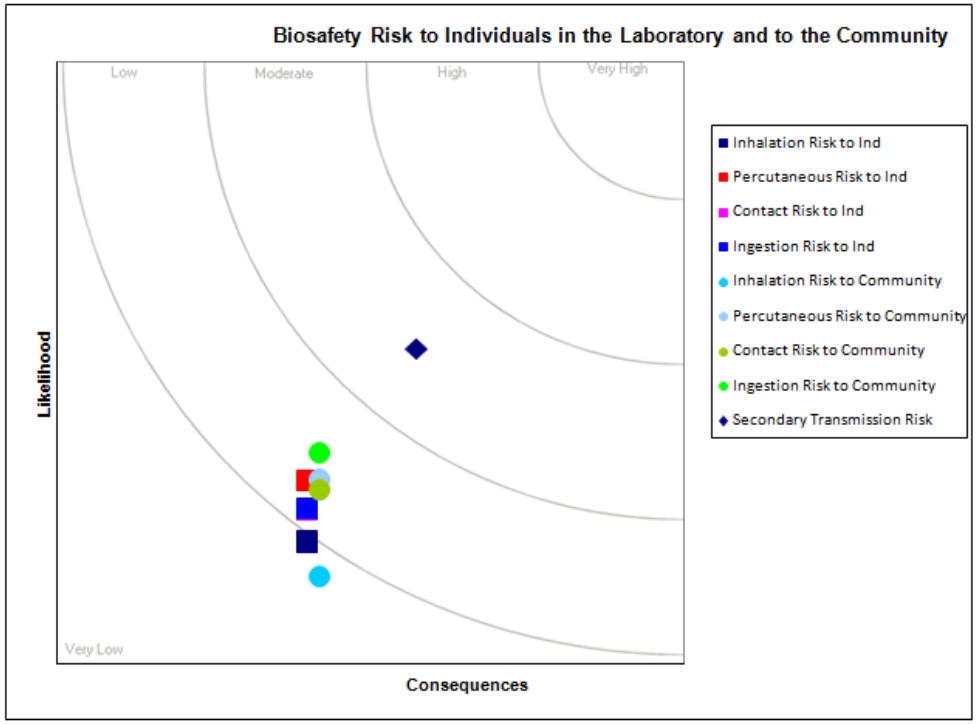


Figure 2 Risks posed by Nipah virus post implementation of procedural, engineering, and ppe control measures

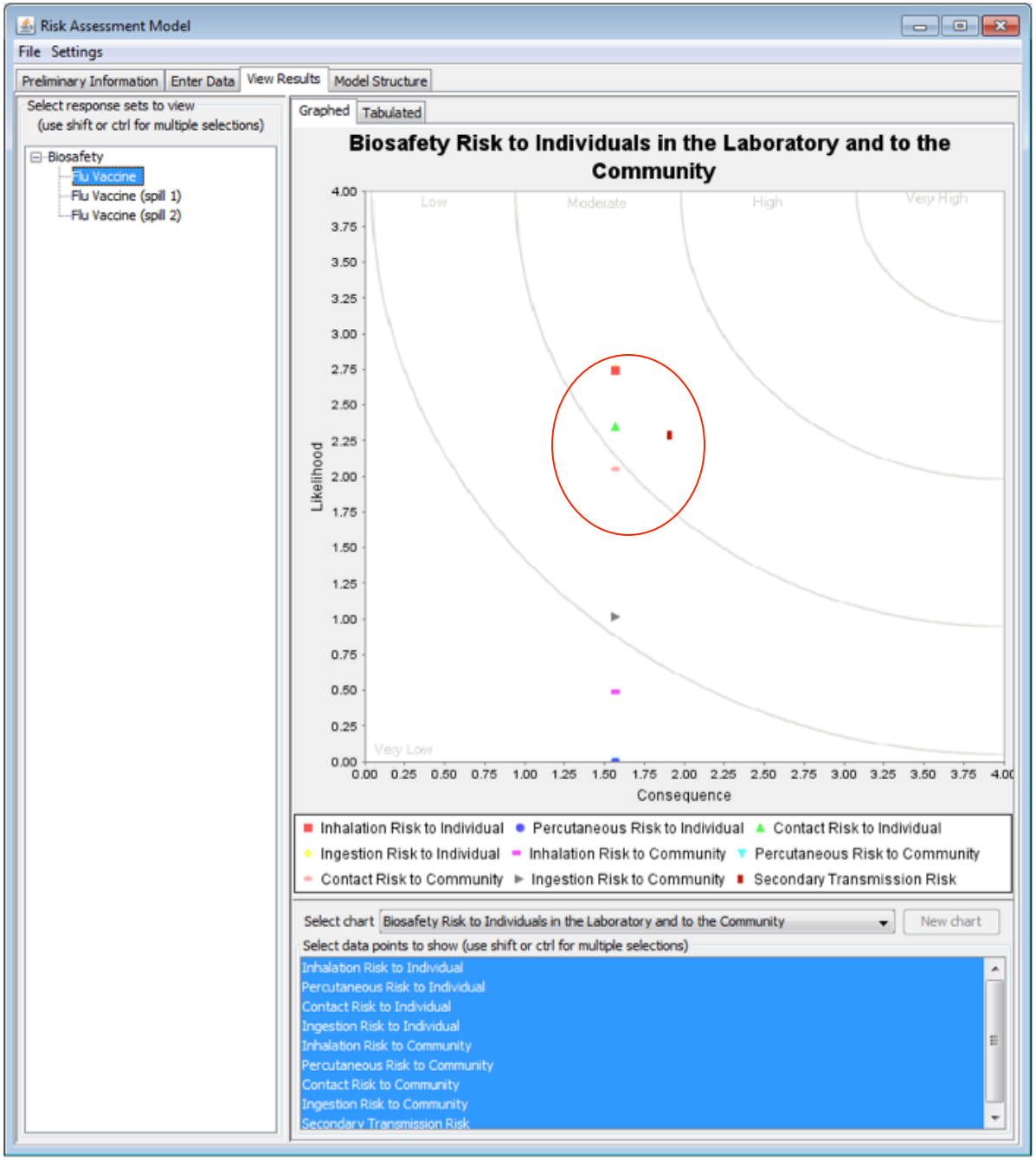
Question	Response Suggestions	Normal Operation Score	Spill (and original SOP)	Cleanup with updated SOP
Likelihood of Exposure				
Potential of Exposure from Laboratory Processes				
Type of Material				
What type of material will be used in this procedure? (If the procedure will have both purified material and diagnostic samples, select the purified material option)	4 = Purified biological materials 2 = Diagnostic samples (e.g. blood, urine, tissue, saliva, etc) 1 = Environmental samples (e.g. soil, water, etc)	4.0	4	4
What is the greatest volume of material existing at one time in the procedure?	4 = Over 10 liters 2 = Up to 10 liters 1 = Milliliter volume	4.0	4	4
Inhalation Exposure				
What is the potential for aerosols to be generated as a byproduct of this procedure (e.g. pipetting, sonication, etc.)?	4 = A notable potential for the generation of aerosols may be produced 1 = A limited quantity of aerosols may be produced 0 = No procedures in use which may generate an aerosol	2.0	4	2
Are aerosolization experiments being conducted as part of this procedure?	4 = Large scale aerosolization experiments are being performed 3 = Small scale aerosolization experiments are being performed 0 = No aerosol experiments are being performed	2.0	4	4
Percutaneous Exposure				
What is the amount of sharps used in this procedure?	4 = A large volume of sharps in use (e.g. scalpels or needles in use at least daily in this procedure) 3 = A small volume of sharps in use (e.g. scalpels or needles rarely used for this procedure) 0 = There are no sharps in use	1.0	1	1
What is the amount of breakable material or items with sharp edges in this laboratory?	4 = A large amount of breakable material (e.g. glassware common in laboratory) 3 = A small amount of breakable material 0 = There is no breakable material in the laboratory	1.0	1	1
Decontamination				
What is the implemented process for the decontamination of equipment prior to maintenance?	4 = There is no decontamination of equipment prior to maintenance or repair 3 = Decontamination of equipment prior to maintenance or repair is performed, but not validated 0 = No equipment is maintained or repaired without decontamination, and the process is documented and validated	2.0	2	2

Question	Response Suggestions	Normal Operation Score	Spill (and original SOP)	Cleanup with updated SOP
Likelihood of Infection				
Transmissibility				
Humans				
Inhalation				
Is this agent known to cause infection via inhalation in humans (to cause infection via droplets or droplet nuclei that have entered the upper or lower respiratory tract) in a laboratory setting?	4 = Preferred Route 2 = A possible route 1 = Unknown 0 = Not a route	4.0	4	4
Is the infectious dose (ID50) of this agent for this route less than 1000 or unknown in humans?	4 = Yes 2 = No 0 = If this is not an infectious route	4.0	4	4
Percutaneous				
Is this agent known to cause infection via percutaneous exposure in humans (to cause infection through compromised skin or direct injection into the blood stream) in a laboratory setting?	4 = Preferred Route 2 = A possible route 1 = Unknown 0 = Not a route	0.0	0	0
Is the infectious dose (ID50) of this agent for this route less than 1000 or unknown in humans?	4 = Yes 2 = No 0 = If this is not an infectious route	0.0	0	0
Direct Contact				
Is this agent known to cause infection via direct contact in humans (to cause infection through the mucosal membranes) in a laboratory setting?	4 = Preferred Route 2 = A possible route 1 = Unknown 0 = Not a route	4.0	4	4
Is the infectious dose (ID50) of this agent for this route less than 1000 or unknown in humans?	4 = Yes 2 = No 0 = If this is not an infectious route	4.0	4	4
Ingestion				
Is this agent known to cause infection via ingestion in humans (to cause infection via contact with the gastrointestinal tract) in a laboratory setting?	4 = Preferred Route 2 = A possible route 1 = Unknown 0 = Not a route	4.0	4	4
Is the infectious dose (ID50) of this agent for this route less than 1000 or unknown in humans?	4 = Yes 2 = No 0 = If this is not an infectious route	4.0	4	4

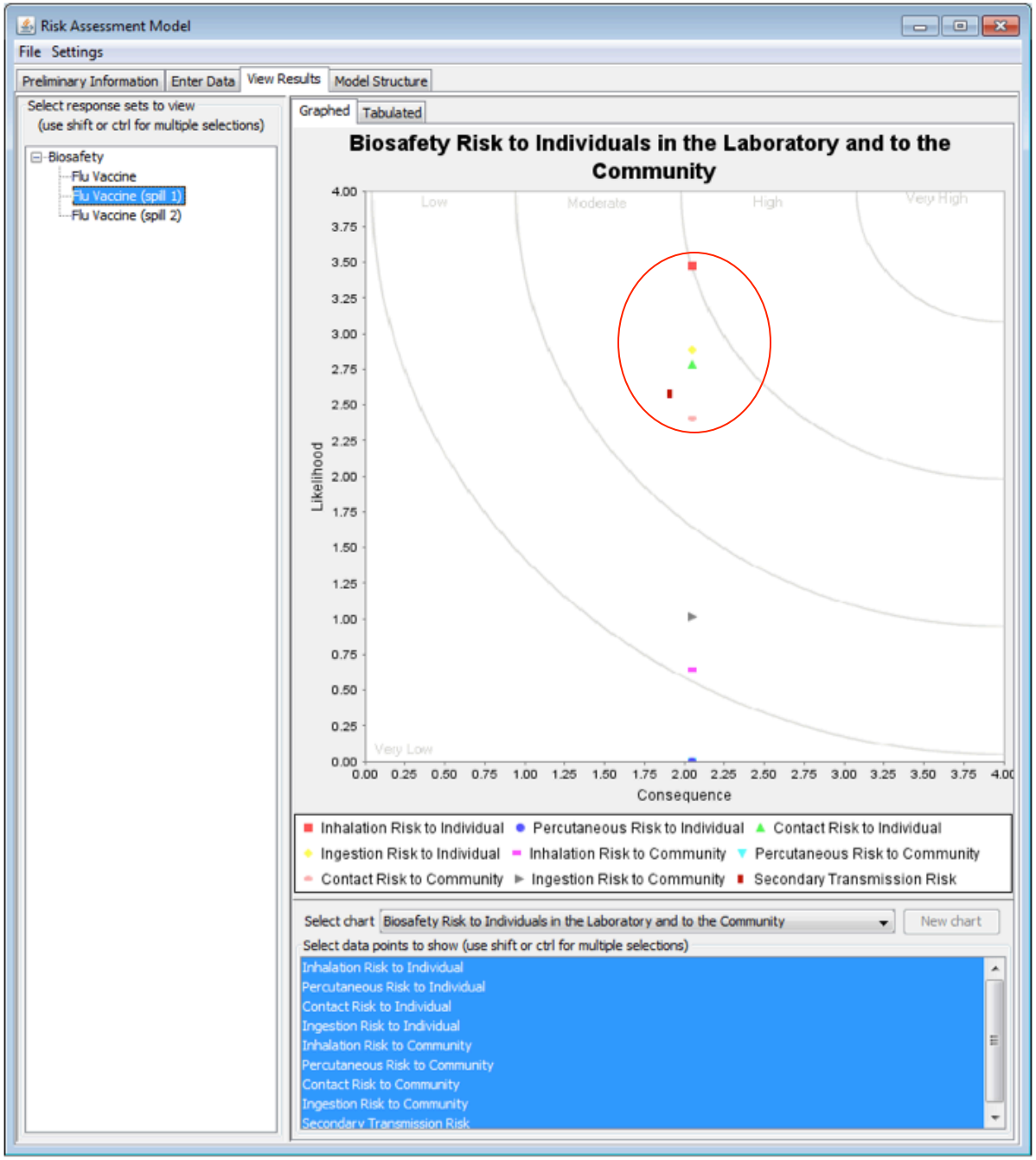
Question	Response Suggestions	Normal Operation Score	Spill (and original SOP)	Cleanup with updated SOP
Main Category: Mitigation Measures				
Standard Procedures				
Are all biological agents in this laboratory inventoried?	0 = There is no inventory system at this laboratory 1 = This laboratory has a limited inventory system 4 = This laboratory has a complete and well-maintained inventory system	3.0	3	3
Is there a shipping and receiving program in place at this laboratory?	0 = There is no shipping and receiving program at this laboratory 1 = This laboratory has limited procedures in place for shipping and receiving 2 = This laboratory has some procedures in place for shipping and receiving, but lacks oversight in implementation 4 = This laboratory has an active shipping and receiving program, and well-defined procedures and plans in place	4.0	4	4
Are there procedures in place for preventative equipment maintenance to reduce/eliminate accidents or equipment failure, which meet defined best practices? These would include equipment calibration, validation, certification, etc.	0 = There is no equipment maintenance program at this laboratory 1 = This laboratory has limited procedures in place for equipment maintenance, but maintenance is generally reactive rather than preventative 2 = This laboratory has some procedures in place for maintenance, but lacks oversight in implementation 4 = This laboratory has an active preventative equipment maintenance program, and well-defined procedures and plans in place	2.0	2	2
Are there standard operating procedures in place for unexpected or catastrophic incidents, including the release of or exposure to an infectious agent (e.g. Incident response plans)?	0 = There is no incident response program at this laboratory 1 = This laboratory has limited procedures in place for incident response, but maintenance is generally reactive rather than preventative 2 = This laboratory has some procedures in place for incident response, but lacks oversight in implementation 4 = This laboratory has an active incident response program, and well-defined procedures and plans in place	2.0	2	2
Is there a formal personal protective equipment (PPE) program in place?	0 = There is no PPE program at this laboratory 1 = This laboratory has a limited PPE program in place 2 = This laboratory has some procedures in place for PPE, but lacks oversight in	1.0	1	3

Question	Response Suggestions	Normal Operation Score	Spill (and original SOP)	Cleanup with updated SOP
Main Category: Consequence				
Consequence of Disease to Humans				
Agent Characteristics				
Does this agent or one of its by-products cause a carcinogenic or mutagenic reaction in a human host?	4 = Yes 2 = Unknown 0 = No	0.0	0	0
Does this agent have toxin or enzyme production which has a negative impact in a healthy human host?	4 = Yes 2 = Unknown 0 = No	0.0	4	4
Does this agent suppress a human host's immune system? (E.g. cause dramatic suppression which renders the host unable to respond to other infections)	4 = Yes 2 = Unknown 0 = No	1.0	4	4
Does this agent have the ability to alter once in a host or in the natural environment to become infectious through new route or new hosts, or to cause increased consequences?	4 = Yes 2 = Unknown 0 = No	4.0	4	4
Morbidity				
What is the duration of illness (the average length of time of clinical signs of infection) in a normally healthy human host?	4 = long duration (months or more) 3 = moderate duration (week(s)) 1 = short duration (days) 0 = No signs of infection	3.0	3	3
What is the severity of illness (the average severity of illness, ranging from no signs of illness to hospitalized in critical condition) in a normal health human host?	4 = Extreme sign of disease (mechanical assistance required to sustain life or death imminent) 3 = High sign of disease (not able to function (hospitalized)) 2 = Moderate sign of disease (able to function in a limited manner (bed rest)) 1 = Low sign of disease (able to function but showing symptoms) 0 = No sign of disease	2.0	2	2
What is the duration of infection (the length of time the host is infected with the organism) in a normal healthy human host?	4 = Infection present for life of host 3 = Infection present post clinical signs for months 2 = Infection present post clinical signs for weeks 1 = Infection present if clinical signs 0 = No sign of disease	2.0	2	2
Does this disease cause any long-term conditions (sequelae) in a normal healthy human host?	4 = High long-term impact which renders the host unable to function normally 2 = Moderate long-term impact which	0.0	0	0

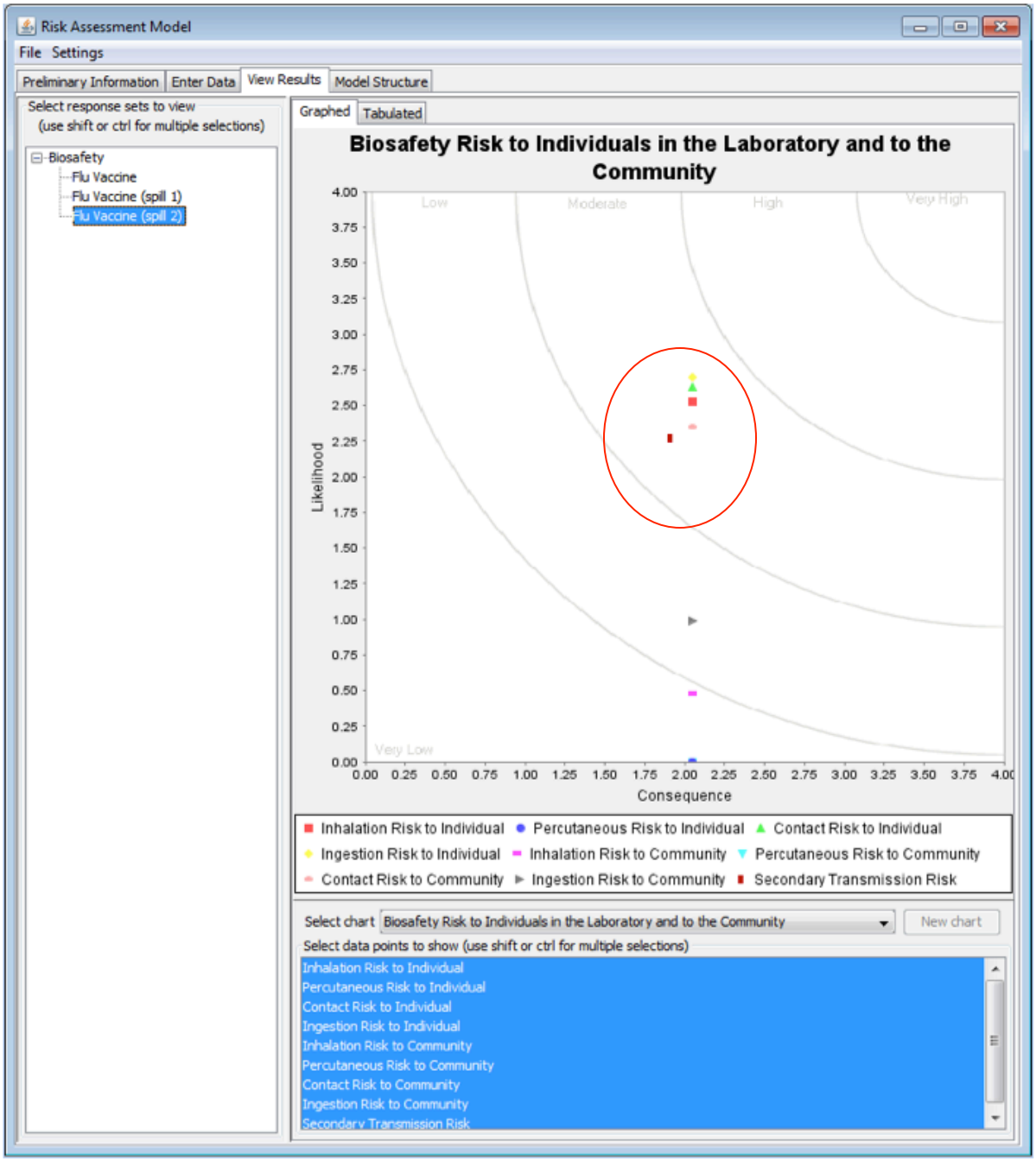
Normal Operation



Spill (and original Clean up procedure)

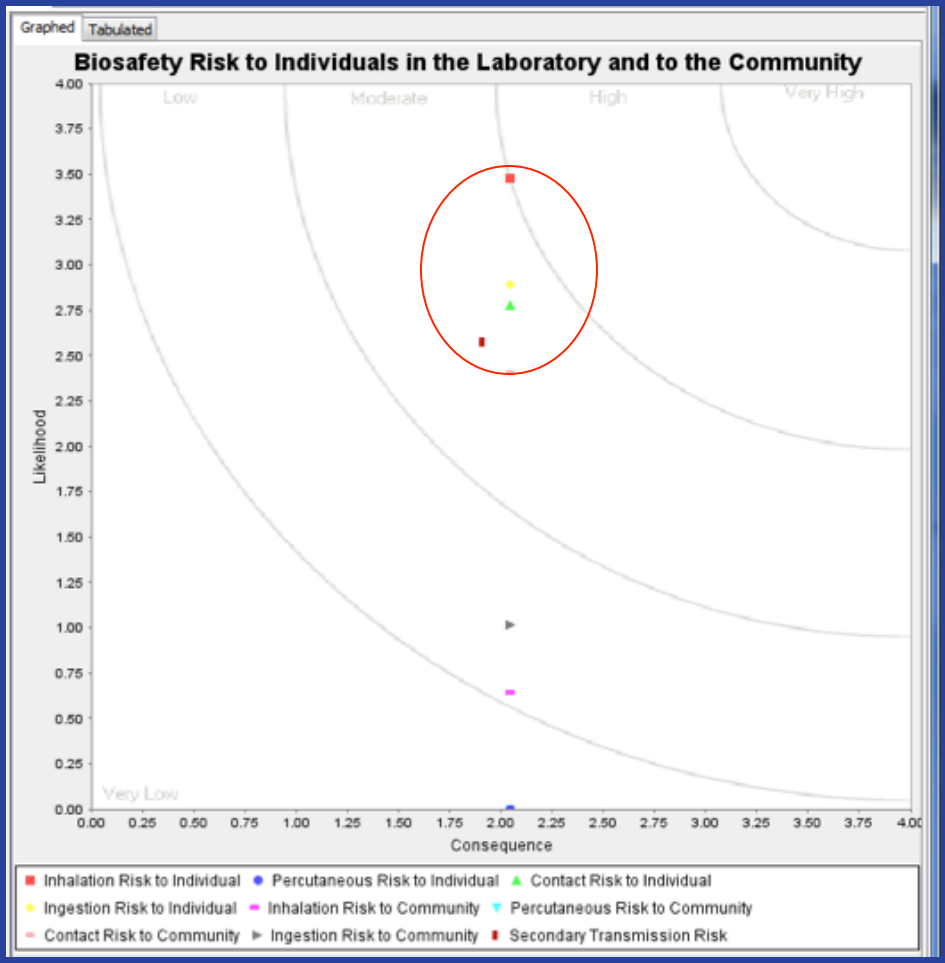


Spill clean-up with new procedure

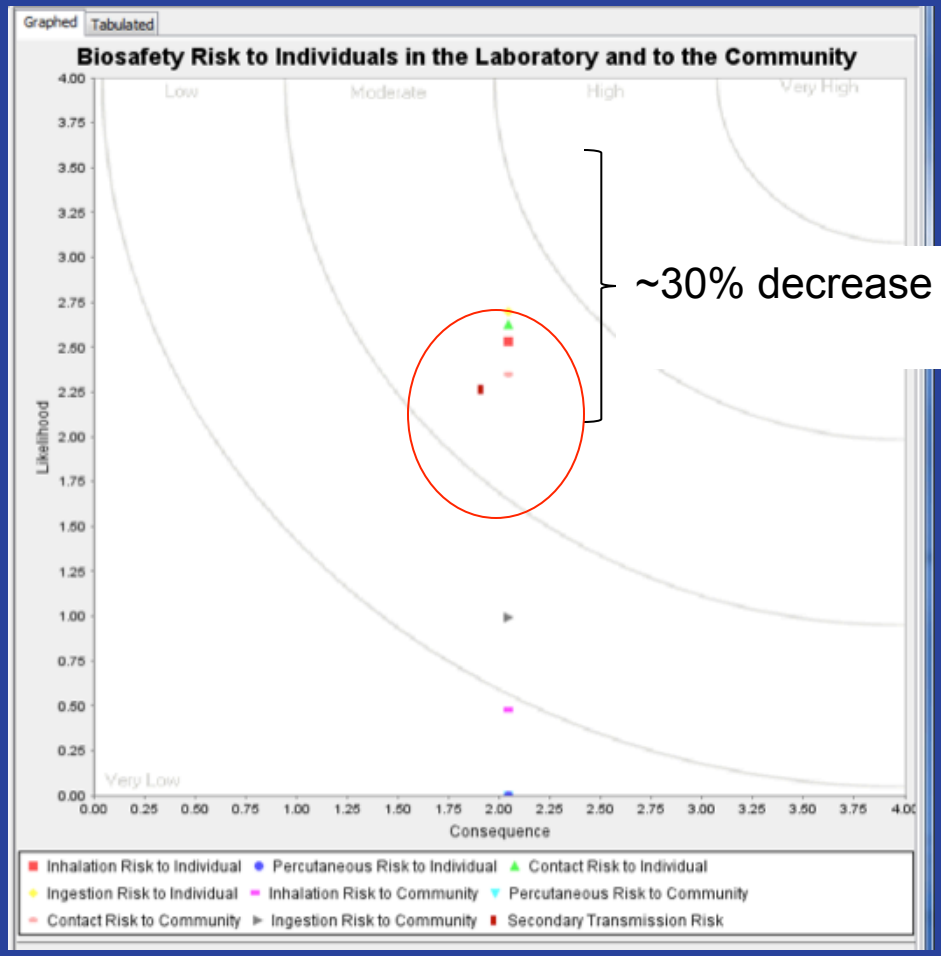


Risk Comparison

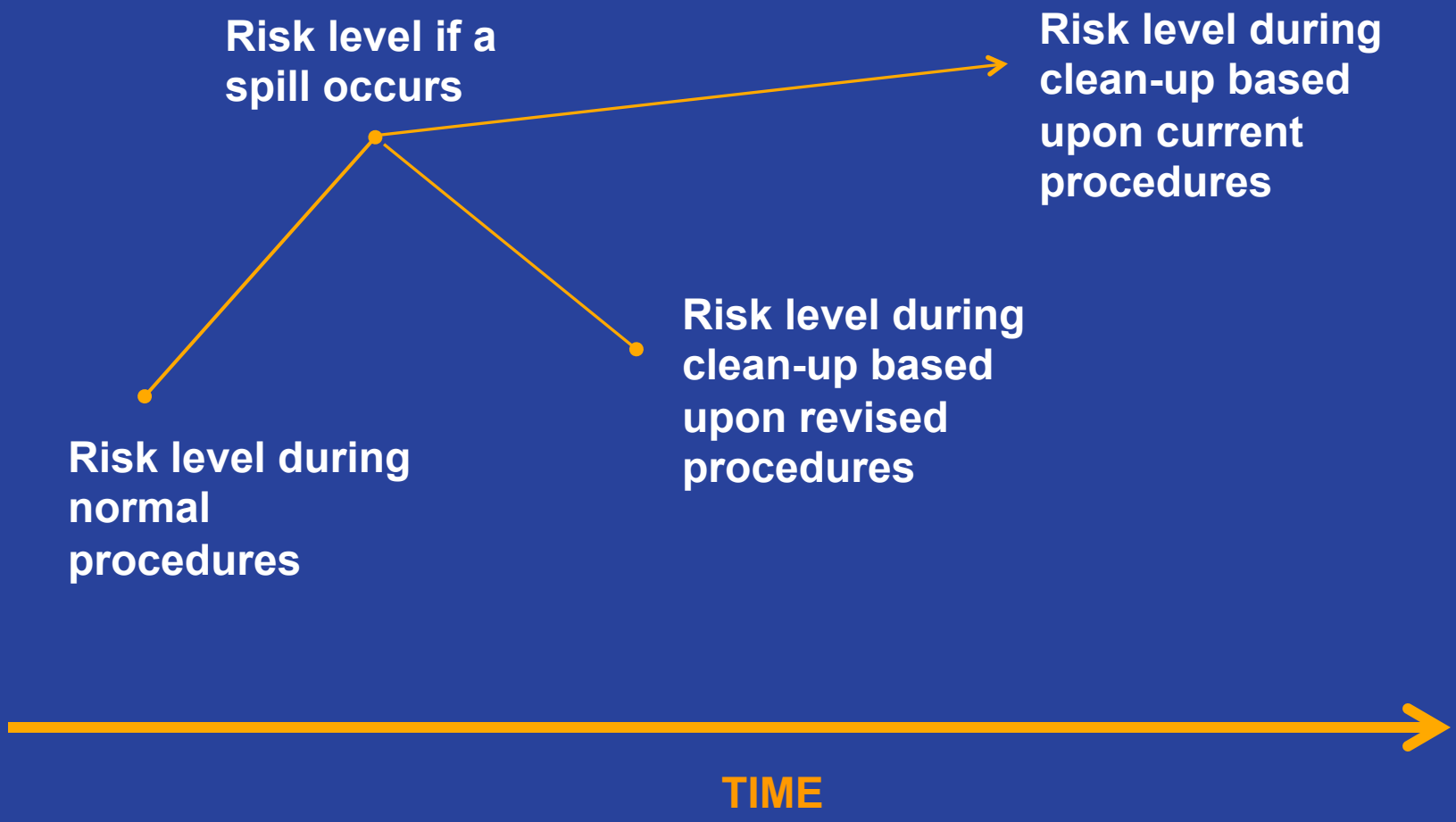
Original Procedures



Revised Procedures



Changes in Risk Over Time



Conclusion

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- **Tremendous value in a structured, repeatable, and documented risk assessment.**
- **Such a method can be applied to any facility, in any country, regardless of nature of work or available resources.**
- **Biorisk management integrates**
  - activity-specific risk assessments,
  - activity-specific mitigation measures, and
  - activity-specific performance evaluations.


Thank you.