Practical Training Exercise

ANALYZING AND MANAGING RISKS IN LIFE SCIENCES RESEARCH

This exercise was developed by Center for Science, Technology and Security Policy at the American Association for the Advancement of Science (AAAS).

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Learning Objectives

1. Develop the skills to think critically about risks and risk mitigation strategies needed in your own scientific environment;

2. Enhance your ability to identify risk management strategies and approaches that minimize identified risks and maintain the high-quality and utility of the scientific activity; and

3. Apply the risk analysis framework to your own or your peers’ scientific activities.
Participant Expectations

By the end of this exercise, you will have familiarity with:

1. The definitions of different types of risks associated with laboratory, field, and public health research.
2. The process of risk analysis—risk identification, assessment, management, and communication—including:
   - How to identify and assess risks by considering the possible likelihood and consequences of risks, and the risks versus benefits of a research activity,
   - Strategies for managing risks, and
   - Who, when, and how to communicate risks.
3. How to apply the risk analysis framework to your own scientific activities.
Ground Rules for Participation

1. Prior to starting this exercise, participants should have read the case study article.

2. Ask the facilitator to clarify questions about the case study article.

3. Focus on understanding and analyzing the diverse risks involved in the research rather than on critiquing the methodologies or research choices of the authors.

4. Interact with one another in a way that encourages open communication and exchange of ideas. For example, listen to everyone’s ideas respectfully.

5. You may want to take your own notes to enhance your ability to actively participate in the training activity.
Biorisk Glossary

These definitions are from the WHO’s *Responsible Life Science for Global Health Security: A Guidance Document*.

**Responsible Research Spectrum**

- Deliberate Misconduct
  - Misuse
  - Theft
  - Environmental Release

- Negligence and Bad Practice
  - Accidental Exposure
  - Falsification, Fraud, Plagiarism

- Research Ethics
  - Animal Subjects Care and Use
  - Human Subjects Research

**Additional concepts:**
- Protection of human subjects
- Protection of animal subjects
- Responsible research/responsible conduct of research

- Bioethics
- Biorisk
- Biorisk reduction
- Laboratory biosafety
- Laboratory biosecurity
- Dual-use life sciences research
- Research excellence
Risk Analysis Framework

Your risk review will follow these 4 stages:

1. Risk Identification
2. Risk Assessment
3. Risk Management
4. Risk Communication
1. Risk Identification

process by which researchers consider all possible internal, external, and organizational risks.

Asks the question:
- **What are the possible risks associated with the research?**

2. Risk Assessment

process by which researchers identify needed resources and consider biosafety/biosecurity recommendations.

Also defined as the “process of evaluating the risk(s) arising from a hazard(s), taking into account the adequacy of any existing controls and deciding whether or not the risk(s) is acceptable.” (OHSAS 18001: 2007)

Asks the questions:
- **How likely are the risks to occur?**
- **What are the potential consequences if the risks occur?**
- **Do the risks outweigh the benefits?**
3. Risk Management

Process by which researchers consider regulations/guidelines, training, and SOP compliance issues.

Asks the question:

- **What risk management strategies could minimize the likelihood that the risk will occur or the consequences if the risks occurred?**

Possible strategies: physical barriers, personnel training or vetting, regulations and laws, and/or alternative experiments.

4. Risk Communication

Process by which researchers consider communication strategies, non-compliance issues and approval/modification processes.

Asks the questions:

- **What risks should be communicated with ethics or other research review committees prior to project initiation?**
- **What risks should be communicated to research participants or fellow researchers during the research project?**
- **What risks, if any, might come from sharing research data or results?**
- **What strategies could be used to minimize the risks?**
Risk Analysis Chart

Risks

- Laboratory Biocatety
- Laboratory Security
- Bioethics
- Human Subjects Protection
- Animal Subjects Protection
- Research Integrity

Risk Analysis Framework

- Risk Identification
- Risk Assessment
- Risk Management

Risk Analysis Questions

- What are the possible risks associated with the research?
- How likely are the risks to occur?
- What are the potential consequences if the risks occur?
- Do the risks outweigh the benefits?
- What risk management strategies could minimize the likelihood that the risk will occur or the consequences if the risks occurred?
- What risks should be communicated with ethics or other research review committees prior to project initiation?
- What risks should be communicated to research participants or fellow researchers during the research project?
- What risks, if any, might come from sharing research data or results?
- What strategies could be used to minimize the risks?

Present Publications
CASE STUDY

Rotavirus and norovirus infections in children in Sana’a, Yemen

Outline of Case Study

Part 1: Research Question/Hypothesis
Part 2: Background Information Overview
Part 3: Research Methodology
Part 4: Risk Analysis in the Research Article
Part 5: Research Results and Conclusions
Research Question/Hypothesis

Research Statement:
As of 2011, no studies have reported the role of rotavirus and norovirus infections in contributing to the high mortality rate for children under five years old in Yemen.

The authors propose to “describe the characteristics of children under 5 years with norovirus and rotavirus infections in Sana’a”.
Rotavirus, Norovirus, and Diarrhea

- Rotaviruses causes gastroenteritis and is the leading cause of severe diarrhea in infants and young children. The virus causes more than 500,000 deaths each year in children under the age of 5.
- Noroviruses is very contagious and causes gastroenteritis leading to stomach pain, nausea, diarrhea, and vomiting.
- Diarrheal illness causes 15% of child mortality globally.
- “Nearly 95% of rotavirus related deaths occur in developing countries.” (GAVI Alliance, 2013)
- “Noroviruses are the leading cause of foodborne disease outbreaks worldwide.” (Koo et al, 2010)
Background Information Overview

Childhood Mortality Resulting from Diarrhea

- WHO lists diarrhea as one of the leading causes of death of children under 5. (WHO, 2012)
- In 2011, diarrhea caused 9% of deaths of children (ages 0-4). (WHO)
- Rotavirus is found in approximately 34-45% of children who had acute gastroenteritis.
- Norovirus infection rates in children with diarrhea range from 4-48%.
Background Information Overview

453,000 global child rotavirus deaths, 2008

Photo Credit: WHO
Research Methodology

- **Participant Inclusion.** Children between the ages of 1 month to 5 years were eligible in the study if they visited outpatient or emergency clinics at two hospitals, had acute diarrhea, and provided fecal samples.

- **Data Collection.** Clinical data was “collected prospectively by a pediatrician who assessed the presence and severity of dehydration.”

- **Fecal analysis.** Fecal samples were sent to the UK partner and tested for the presence of rotavirus and norovirus.
  - Rotavirus was assessed using enzyme-linked immunosorbant assay (ELISA)
  - Samples testing positive for rotavirus were further analyzed through, RNA extraction, reverse-transcriptase polymerase chain reaction (RT-PCR), and sequenced
  - Norovirus was assessed using end-point RT-PCR. The cDNA was sequenced.
  - Phylogenetic analysis was conducted for on rotavirus and norovirus sequences.

- **Statistical Analysis.** The characteristics of the children were compared with the presence of rotavirus and norovirus using standard statistical analyses.
Risk Analysis in this Research Article

While risk analysis is an important part of science, few scientific publications include in-depth descriptions of how the authors assessed and managed risk.

Today your task is to perform a risk analysis based on this research article.

To begin, answer the following question:
Based on your current knowledge of the experimental procedures or research purpose, what risks might be important to consider in designing, carrying out, or communicating this research?
## Risk Identification

Rotavirus and norovirus infections in children in Sana’a, Yemen

<table>
<thead>
<tr>
<th>Questions</th>
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<tbody>
<tr>
<td>What, if any, are the ethical risks associated with involving children as research participants?</td>
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<tr>
<td>What, if any, are the biosafety risks associated with sample collection, transportation, and handling?</td>
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<tr>
<td>What, if any, biosecurity risks are associated with sample collection, transportation, and handling?</td>
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<tr>
<td>What risks would this pose to the researchers both in country and abroad?</td>
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<tr>
<td>Would this research (and shipping overseas) pose any threat to the public?</td>
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</table>
## Risk Assessment

### Rotavirus and norovirus infections in children in Sana’a, Yemen

<table>
<thead>
<tr>
<th>Question</th>
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<tbody>
<tr>
<td>What aspect of this research or procedural steps might pose the most severe consequences to patients? What are those consequences and how likely are they?</td>
</tr>
<tr>
<td>What aspect of this research or procedural steps might pose the most severe consequences to researchers? What are those consequences and how likely are they?</td>
</tr>
<tr>
<td>This research team chose to perform the rotavirus and norovirus analysis in the United Kingdom, rather than in Yemen. In your opinion, what are the risks and consequences that most likely prompted the team to make this experimental choice?</td>
</tr>
<tr>
<td>What are the resources, expertise, training, and tools that could be useful in assessing the risks identified for this research project?</td>
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</table>
## Risk Management

### Rotavirus and norovirus infections in children in Sana’a, Yemen

<table>
<thead>
<tr>
<th>Question</th>
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<tbody>
<tr>
<td>What experimental approaches could be used to reduce the identified risks during sample collection, transportation, and processing?</td>
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<tr>
<td>What could be done to prevent and manage the consequences of an accidental laboratory exposure, for example spread of rotavirus or norovirus to a laboratory worker?</td>
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<tr>
<td>What import/export rules and regulations would need to be considered and followed?</td>
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<tr>
<td>What safety precautions should be taken in preparing the biologic material for shipping?</td>
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<tr>
<td>What, if any, are specialized competencies, skills, and training needed to successfully collect, transport, and process these research samples?</td>
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Research Results and Conclusions

Results

• Seventy-eight children (27%) admitted with gastroenteritis had rotavirus and 30 (10%) had norovirus
• 5 children co-infected with both viruses
• “No statistical differences between the demographic or diarrheal episode characteristics of children with norovirus infection…and between norovirus- and rotavirus-infected children”.
• Nine strains of rotavirus (four more common strains) were identified in infected children.
• Two strains of norovirus were identified in infected children. Two children had both strains of norovirus.

Conclusions

• This study was the first to examine rotavirus and norovirus infection in Yemen.
• The results of the study are consistent with global patterns of infection.
• The study allows Yemen to infer the benefits of rotavirus vaccination from global experiences.
• The study provides a baseline of infection data to “initiate extensive surveillance to monitor changes in the epidemiology of these infections”.
## Risk Communication

### Rotavirus and norovirus infections in children in Sana’a, Yemen

<table>
<thead>
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<tbody>
<tr>
<td>What are the risks that should be communicated during this research? To whom?</td>
</tr>
<tr>
<td>What are some strategies for effectively communicating the risks of involving children in the study and the risk mitigation approaches to an IRB or ethics board?</td>
</tr>
<tr>
<td>To ensure that parents of potential child research participants can give informed consent for sample collection, what information do the researchers need to share with parents?</td>
</tr>
<tr>
<td>Are there any individuals or stakeholders in Yemen or in the international community who the researchers are ethically obligated to share their findings with? Why?</td>
</tr>
<tr>
<td>How would you communicate with the public, public health officials, and international scientists the risks and mitigation approaches?</td>
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</table>
Final Exercise: Risk in Your Own Research

Now is the time to think about the risk analysis we just did in the context of your own research:

1. **Identification:** What are the primary risks you face in your research? Think about the risks to you and other researchers and technicians in the field, clinic, and/or lab, the general public, the environment and economy, your institution, and human and animal subjects.

2. **Assessment:** What are the consequences of the identified risks if they occur? How likely are they to occur? Based on your assessment of the potential consequences, are there any risks that could harm people, animals, crops, or the economy?

   What resources, capabilities, and skills are needed to mitigate these risks?

3. **Management:** What strategies could you use or resources you could refer to minimize or mitigate these risks? (These strategies should not decrease the quality of the research.) For ideas of possible strategies and resources, consider those discussed in this practical exercise and from your own experiences.

   Are there any risks associated with your research that cannot be adequately mitigated?

4. **Communication:** What risks, if any, are associated with communicating your research during the design or conduct of the research? What risks, if any, are associated with communicating the research results at scientific conferences and in publications? What strategies could you use to mitigate the risks? Are there any stakeholders with whom you must share or should share the risks of your research? Your findings?
Example Risk Analysis Strategy

“Laboratory risk management.” CWA 15793: 2011
Reference List

Background Information


Diagrams and Images


