Practical Training Exercise

ANALYZING AND MANAGING RISKS IN LIFE SCIENCES RESEARCH

Based on the article by Ahmed, H.A. et al. “Emergence of Foot-and-Mouth Disease Virus SAT 2 in Egypt During 2012.” Transboundary and Emerging Diseases. 2012; 59; 476-481.

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ADVANCING SCIENCE, SERVING SOCIETY

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.

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Biorisk Glossary

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

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

<u>Additional concepts:</u>

- Protection of human subjects
- Protection of animal subjects
- Responsible research/responsible conduct of research

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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

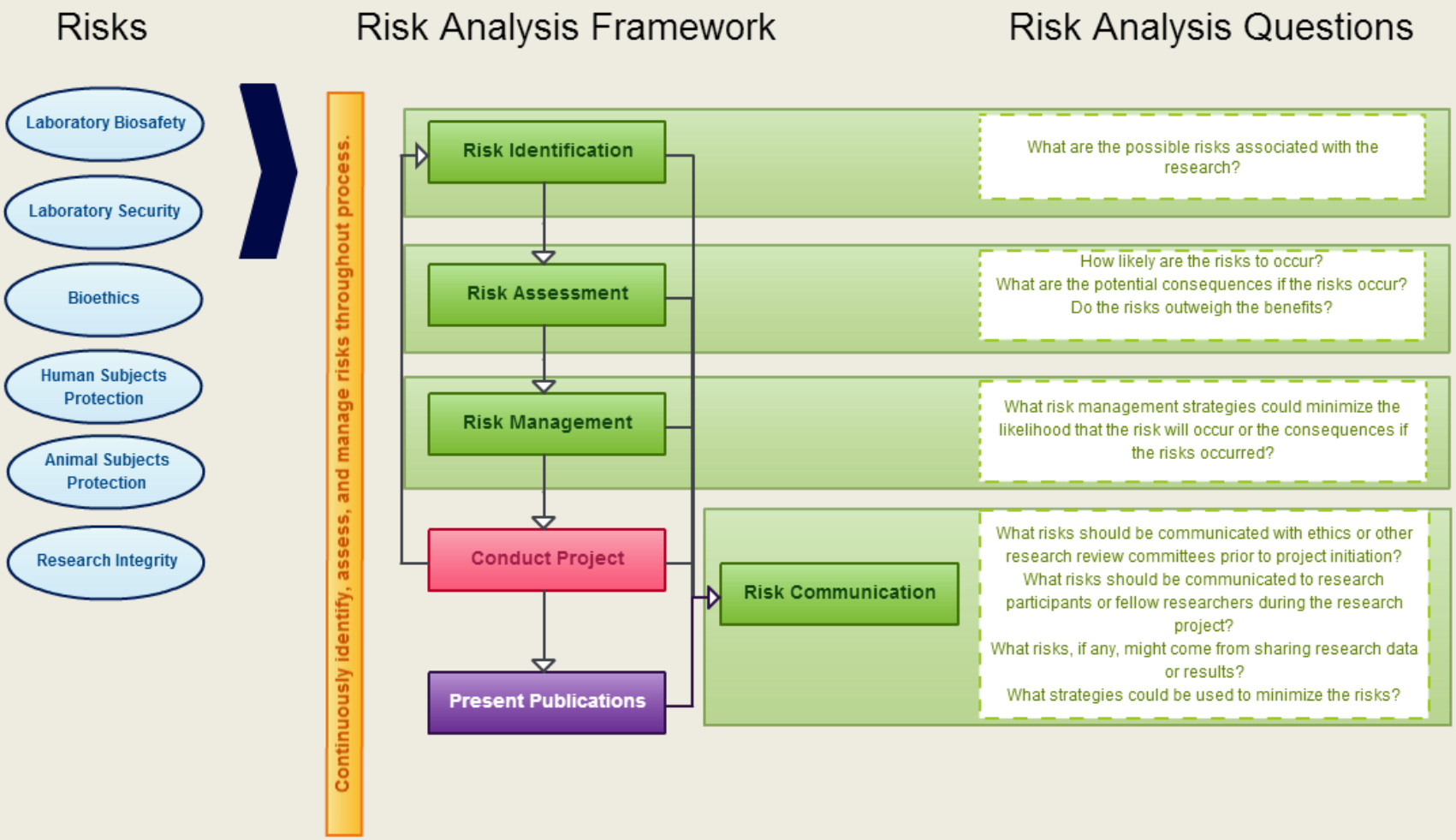
4. Risk Communication

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



CASE
STUDY

Emergence of Foot-and-Mouth Disease Virus SAT 2 in Egypt During 2012

Ahmed, H.A. et al. “Emergence of Foot-and-Mouth Disease Virus SAT 2 in Egypt During 2012.” Transbound and Emerg Dis. 2012; 59; 476-481.

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

Foot-and-mouth disease (FMD) virus is a devastating and highly contagious disease in cloven-hoved animals.

Of the seven serological types of FMD virus, type O was the most prevalent viral subtype in Egypt until 2012. Subtype A emerged in Egypt twice – in 1972 and 2006.

In 2012, Egypt experienced several outbreaks of FMD virus, all caused by the serotype SAT 2 (Southern African Territories 2). This outbreak caused severe disease in cattle, water buffalo and small ruminants.

An emergency team from the United Nations' Food and Agricultural Organization (FAO) to "characterize the FMD strain responsible and assess the field situation…[as well as] to establish primary containment measures through a national FMD control strategy."

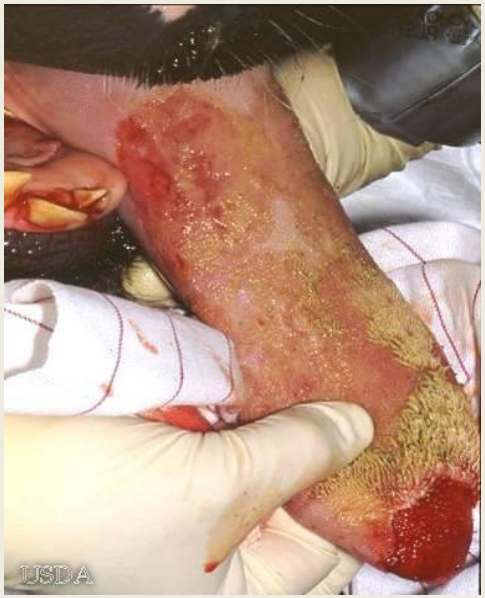
The authors proposed to characterize the viral strains from the FMD virus SAT2 outbreaks using analysis of sequence data.

Background Information Overview

Foot-and-Mouth Disease

- Foot-and-mouth disease (FMD), often called hoof-and-mouth disease, is a highly contagious viral diseases that affects animals with cloven hooves.
- The FMD virus spreads between animals through close contact with infected animals, inhalation of aerosolized virus, and contact with contaminated surfaces (fomites).
- The virus causes fever and blisters and sores on the feet, mouth and area in and around the mouth, and teats. The painful blisters can cause animals to become listless and lead to weight loss.
- FMD does not infect humans.
- Seven distinct types of FMD exist – O, A, C, Asia 1, SAT 1, SAT 2, and SAT 3.
- Culling (killing of infected animals) is the most common disease control method, though this approach has significant impacts on farmers and the economy. Other measures of control include quarantine and movement restrictions, and disinfection of affected areas and equipment.
- A vaccine for FMD exists. It can be used to prevent infection with the FMD virus. The decision to vaccinate animals involves scientific, economic, political, and societal factors.

FMD Infection
Photo Credit: Texas A&M University

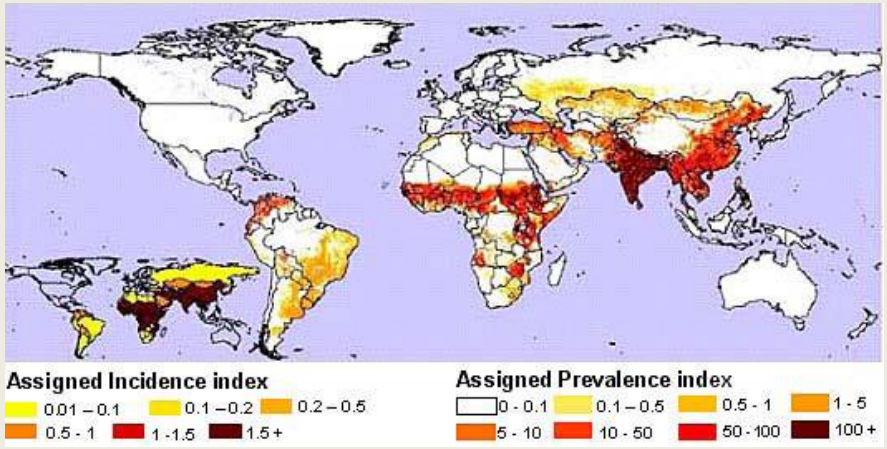


FMD Infection
Photo Credit: Texas A&M University

Background Information Overview

Geographic Distribution of FMD

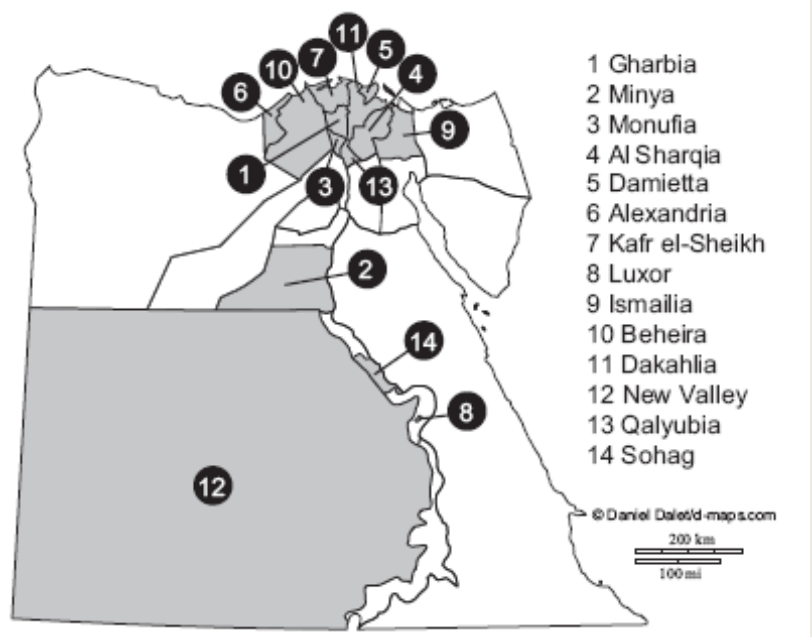
- FMD is endemic in Africa, Asia, and parts of South America, though periodic outbreaks occur elsewhere.
- FMD types O, A, and Asia 1 are endemic in the Middle East.
- FMD types O and A are endemic in North Africa.
- FMD types O, A, C, and SAT are endemic in Sub-Saharan Africa.



FMD Incidence and Prevalence Indices, 2000-2004
Photo Credit: Sumption, Keith et al.

Background Information Overview

- Between 1964 and 2005, FMD virus type O was the predominant subtype found in Egypt.
- In 1972: FMD virus type A was introduced into Egypt.
- In 2006: Egypt had a large outbreak of FMD type A
- 2012: Egypt had numerous outbreaks of FMD SAT 2.
  - Cattle, water buffalo and small ruminants (such as sheep and goats) displayed clinical signs.
  - The mortality rate in young animals was 50%.



Emergence of Food-and-Mouth Disease Virus SAT 2 in Egypt During 2012
Photo Credit: Ahmed, H.A. et al. 2012.

Research Methodology

- **Sample collection:** Samples of vesicular epithelial tissue from 14 FMD outbreaks, which were submitted to the Animal Health Research Institute of the Egyptian National Reference Laboratory, were used in this study. Tissue suspensions were prepared from the samples.
- **Virus isolation:** Samples were used to inoculate tissue culture cells. Viable FMD virus would be released in the cell culture supernatants.
- **FMD virus type identification:** An antigen-detection sandwich enzyme-Linked Immunosorbant Assay (ELISA) was used to identify which FMD types (O, A, C, Asia 1, or SAT 2) were found in the tissue suspensions or cell culture supernatants.
- **Viral RNA extraction**: Viral RNA was extracted and amplified using real-time reverse Transcription Polymerase Chain Reaction (RT-PCR). RT-PCR was conducted using two methods: 1) a one-step method ; and 2) the more conventional, two-step method and gel electrophoresis.
- **Genotyping for SAT 2 serotype:** Viral RNA was amplified using RT-PCR and primer sets for the SAT2 specific sequences. The positive PT-PCR product was sequenced using commercial sequencing technologies. The resulting DNA sequence, which was a partial sequence of the VP1 gene, was compared to other FMD virus VP1 genes using the online BLAST algorithm.

Research Methodology Continued

- **Prepare samples for comparison test:** Tissue samples from 10 Egyptian Governorates were sent to the FAO World Reference Laboratory for FMD for confirmation and comparison to other existing strains.
  - The analysis included samples from Libya, Bahrain, Palestine, Kenya and Cameroon.
  - Samples were tested using viral isolation in cultured cells, antigen-detection ELISA, and real-time RT-PCR techniques.
  - Sequence analysis was conducted on the VP1 gene from viral isolates.
    - Viral RNA was extracted from the virus isolates and amplified using RT-PCR.
    - The PCR products, which were overlapping segments of the VP1 gene, were sequenced using commercial sequencing techniques.
    - The resulting DNA sequences were assembled into complete VP1 sequences.
    - The complete VP1 gene sequences were aligned and analyzed using commercially available bioinformatics software.
- **New diagnostic assay:** A specific real time RT-PCR assay was developed to distinguish the new FMD SAT 2 viruses with endemic FMD viruses in the region. The assay was validated using RNA prepared from previously characterized FMDV-positive clinical samples and FMD viruses from other lineages from the region.

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

Emergence of Food-and-Mouth Disease Virus SAT 2 in Egypt

Questions
What, if any, are the potential biosafety risks? What, if any, are the potential biosecurity risks?
Does this research pose any additional risks to FMD-susceptible animal populations or the economy?
What, if any, are the risks involved in transportation of infected animal samples?
Could the research activities and/or results be used to cause harm?

Risk Assessment

Emergence of Food-and-Mouth Disease Virus SAT 2 in Egypt

Questions
What, if any, are the potential consequences of the environmental and animal population risks associated with this research? How likely are these risks to occur?
What, if any, are the potential consequences of the biosafety risks associated with this research project? How likely are these risks to occur?
What are the resources, expertise, training, and tools that could be useful in assessing the risks identified for this research project?

Risk Management

Emergence of Food-and-Mouth Disease Virus SAT 2 in Egypt

Questions
What international, national, or institutional regulations, laws, or best practices could be used to mitigate potential biosafety and biosecurity risks?
What, if any, specialized competencies, skills, and training are needed to successfully carry out this research project?
What additional scientific approaches or methodologies, if any, could be used to further minimize the identified biosafety and biosecurity risks?
What could be done to manage the risks of an unintended result, such as mutation of a FMD viral isolate in the laboratory?
What policies and protocols should be in place to prevent accidental or intentional release of the FMD viral isolates?

Research Results and Conclusions

Results

- The FMD SAT 2 viruses that caused the 2012 outbreaks in Egypt were genetically distinct from viruses recovered in Libya in 2003.
- The FMD SAT 2 outbreak viruses fell into two different lineages, suggesting " either two independent introductions or a single introduction of two lineages" occurred in Egypt.
- At the nucleotide sequence level, these two lineages differed by 10% suggesting that they are not directly related to each other even though they "share a close evolutionary history".
- The authors state that the origin of the FMD outbreaks in 2012 cannot be determined because "sparse sampling of closely related viruses".
- The diagnostic assay developed in the study detected the FMD SAT2 viruses from the recent outbreaks in Egypt and Libya, but it "did not cross react with other five FMDV lineages that might be present in livestock in the region…: serotype O… serotype A", and the FMD virus isolates from the 2012 outbreak in Bahrain.

Conclusions

Coordination and sharing of sequence data is needed to identify transboundary transmission of FMD viruses and links of viral isolates in different countries.

The authors concluded that close monitoring of FMD viruses in North Africa and the Middle East is needed to "define the risks of future outbreaks" and ensure that appropriate control measures are used.

Risk Communication

Emergence of Food-and-Mouth Disease Virus SAT 2 in Egypt

Questions
What are the risks that should be communicated during this research? To whom?
How would you communicate the risks and risk management steps to an institutional review committee, other researchers, or other FAO partners?
What are some strategies for communicating these particular research risks to the agricultural community? Do the researchers have an ethical obligation to share their findings with farmers and other livestock stakeholders?
Under what circumstances would the researchers have an ethical, safety, security, or economic obligation to NOT share some aspect their findings with the public? Does such a circumstance exist in this case study?

Final Exercise: Risk in Your Own Research

Perform a risk analysis of your own research. Choose one past, ongoing, or future research project to analyze:

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? Based on your assessment of consequence and probability, are there 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 during the conduct and after completion of the project? What strategies could you use to mitigate the risks? Are there any stakeholders with whom you must share the risks of your research? Your findings?

Example Risk Analysis Strategy

Communicate

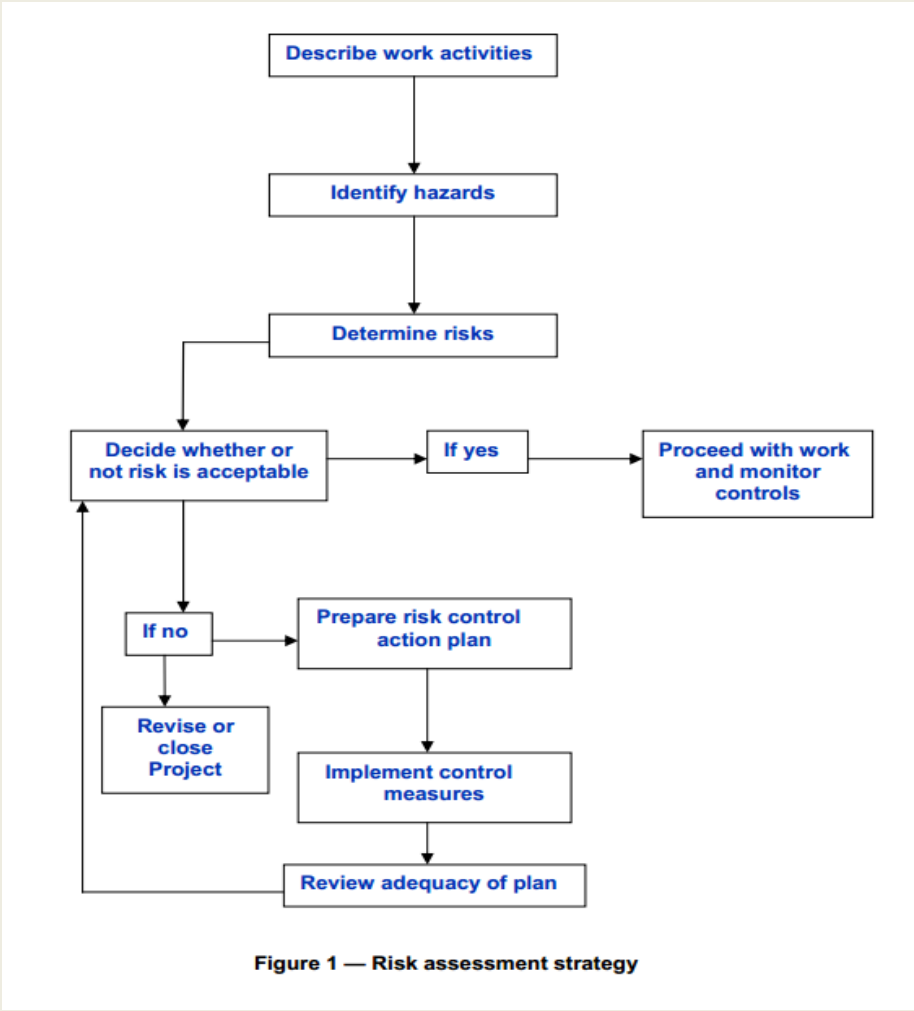


Figure 1 — Risk assessment strategy

"Laboratory risk management." CWA 15793: 2011

Reference List

Background Information

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Diagrams and Images

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