Practical Training Exercise

ANALYZING AND MANAGING RISKS IN LIFE SCIENCES RESEARCH

Ali, A, et al. “Prevalence of HBV infection in suspected population of conflict-affected area of war against terrorism in North Waziristan FATA Pakistan.” Infection, Genetics and Evolution. 2013 Aug 30; 12: 1865-1869.

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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.

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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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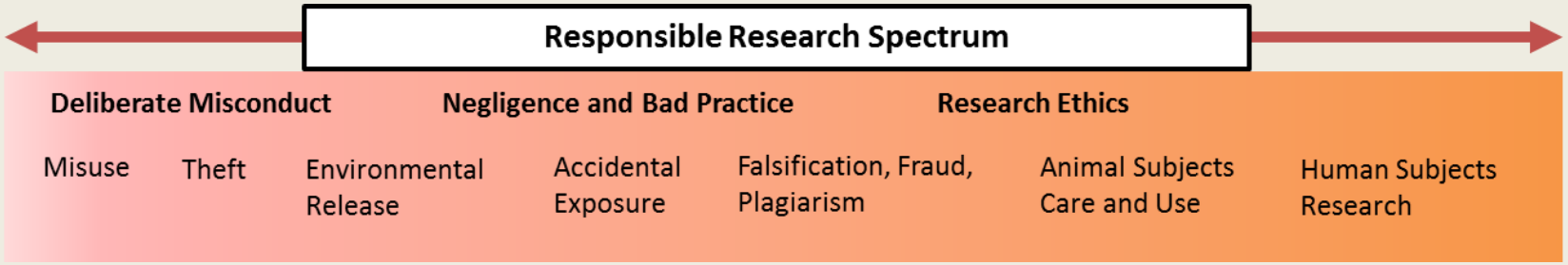
Biorisk Glossary

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

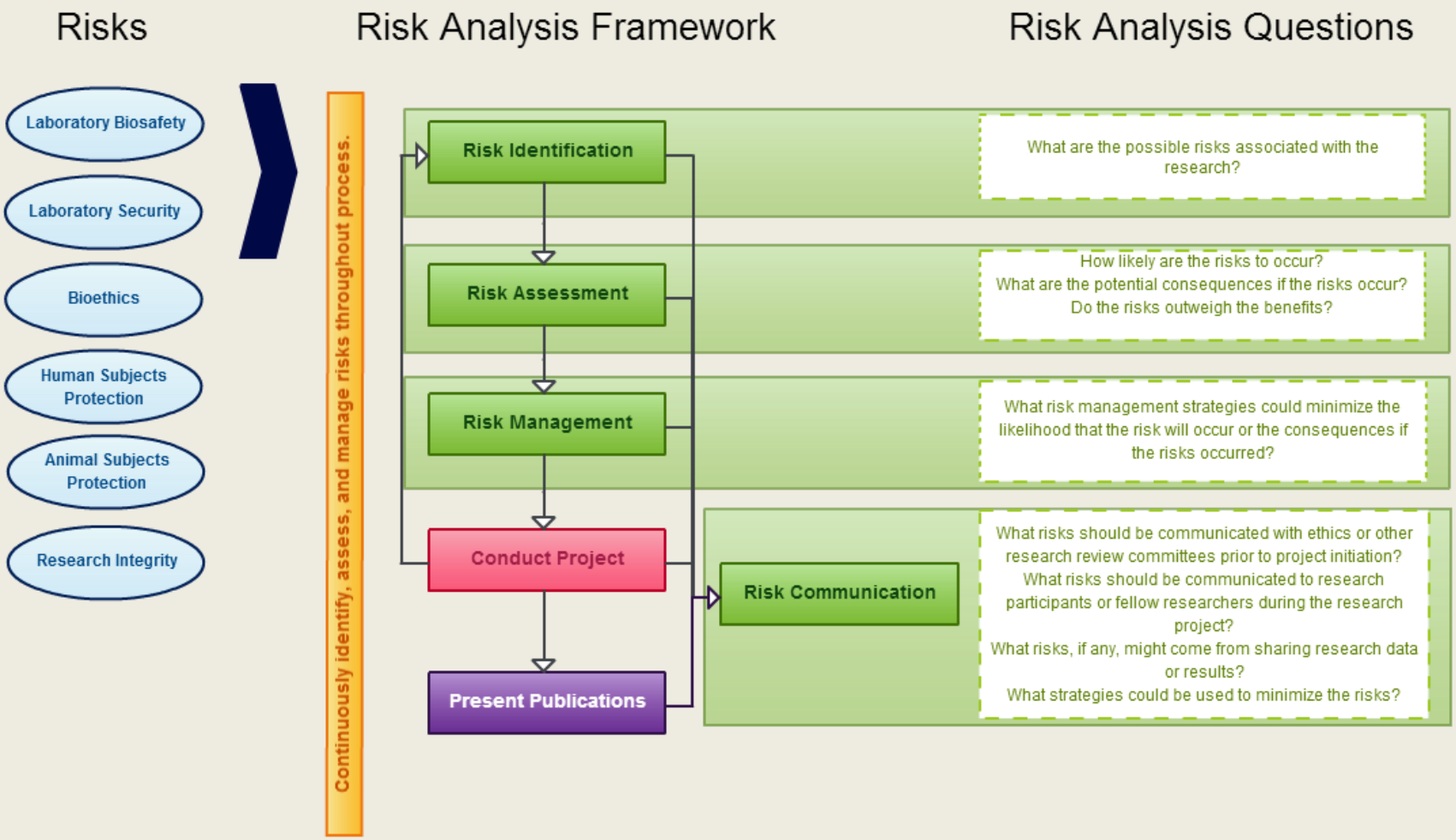
4. Risk Communication

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

Prevalence of HBV infection in suspected population of conflict-affected area of war against terrorism in North Waziristan FATA Pakistan

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Ali, A, et al. “Prevalence of HBV infection in suspected population of conflict-affected area of war against terrorism in North Waziristan FATA Pakistan.” Infection, Genetics and Evolution. 2013 Aug 30; 12: 1865-1869.

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

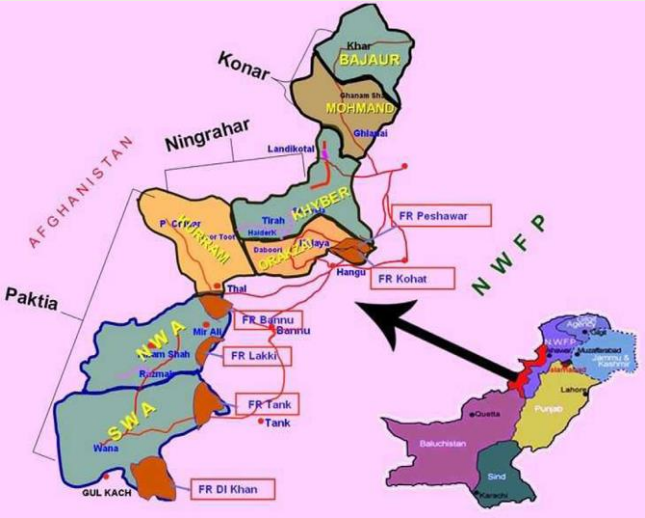
Hepatitis B virus infects 7-9 million people in Pakistan with a prevalence ratio of nearly 3-5%.

Waziristan agency Federally Administered Tribal Area (FATA) borders Afghanistan and is “drastically affected by terrorist and anti-terrorist activities”. It is divided into the North Waziristan and South Waziristan.

The FATA region has a population of 3.4 million with “low socioeconomic status and literacy rate.” “The terrorist actions completely destroyed the social infrastructures, health and education centers, consequently the health facilities and literacy rate is infinitesimal in agency.”

No data or documented studies have been reported on the prevalence of Hepatitis B virus among conflict-ridden people, including those in North Waziristan.

The authors proposed “to estimate the prevalence of HBV infection and the possible risk factors among conflict-affected people of North Waziristan.”



Map of North Waziristan, Pakistan
Photo Credit: Ali et al, 2012

Background Information Overview

Hepatitis B Virus (HBV) Infection

- Hepatitis B virus is blood borne pathogen that affects 2 billion people worldwide. Approximately 400 million people are chronic hepatitis B carriers.
- Hepatitis B virus infects the liver and can cause acute and chronic disease.
  - Acute symptoms of infection include jaundice, dark urine, extreme fatigue, nausea, vomiting, and abdominal pain.
  - Chronic disease includes liver disease, cirrhosis, and liver cancer.
- Hepatitis B virus is "most commonly spread from mother to child at birth, or from person to person in early childhood." Other transmission routes include through sexual transmission and sharing of contaminated needles. (WHO, 2013)
- Hepatitis B virus can survive outside the body for 7 days.
- More than 240 million people have chronic liver infections.
- "About 600,000 people die every year due to the consequences of hepatitis B." (WHO, 2013)
- The "hepatitis B vaccine is 95% effective in preventing infection and its chronic consequences". (WHO, HBV, 2013)

Background Information Overview

HBV Epidemiology

- HBV is endemic in Pakistan with 7-9 million carriers—a prevalence rate of 3-5%.
- More than 95% of adults with acute infection successfully clear the infection.
- People “born with chronic HBV infections have a 15% to 30% lifetime risk of developing complications” that lead to death. (Hiu Gong, 2007)

Pakistani Boy Receiving HBV vaccine
Photo Credit: Foreign Policy, 2011

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Background Information Overview

Health Landscape in North Waziristan

- In FATA region as a whole and in North Waziristan in particular, health services have deteriorated significantly since 2001.
- Vaccination programs have deteriorated due to attacks on medical personnel and facilities.
- Limited healthcare is currently provided by:
  - Government-funded hospitals, rural health and community health centers
  - Insurgent-funded hospitals and clinics
  - The international aid community

Research Methodology

- **Participant identification.** A total of 790 suspected hepatitis B infected individuals were enrolled in the study. Research scholars asked participants to provide their name, gender, age, socioeconomic status, educational level, and several health questions using a questionnaire.
- **Sample collection and serum preparation.** Research scholars obtain 5ml whole blood from study participants. Serum was separated within 6h of collection, transported to the University, and stored in the freezer until further processing.
- **Serological investigation.** The presence of cross-reacting antibodies to hepatitis B virus in participant sera was analyzed using enzyme-linked Immunosorbent assays (ELISAs).
- **HBV DNA extraction and amplification.** Hepatitis B DNA from sera of ELISA positive participants was extracted using a commercially available kit. Real time polymerase chain reaction was carried out to confirm viral DNA and quantify the level of viral DNA in the samples.
- **Statistical analysis.** The data was analyzed using commercially available software.

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

Prevalence of HBV infection in suspected population

Questions
What, if any, are the potential safety and security risks to “research scholars” and laboratory scientists involved in this experiment?
What, if any, safety, security, or ethical considerations are associated with identifying and taking samples from HBV positive individuals in conflict-affected areas?
What, if any, additional risks or concerns are associated with obtaining samples from disadvantaged and a poorly literate population?
What, if any, are the ethical and security risks to the research subjects of this experiment?

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Risk Assessment

Prevalence of HBV infection in suspected population

Question
What, if any, are the potential consequences of the biosafety risks associated with the research project?
What, if any, are the potential consequences of the biosecurity risks associated with the research project? Which risk is likely to be higher: theft of human sera containing HBV or misuse of research materials and/or results?
What, if any, are the potential consequences of the ethical risks associated with the research project?
What are the resources, expertise, training, and tools that could be useful in assessing the risks identified for this research project?

Risk Management

Prevalence of HBV infection in suspected population

Question
What risk mitigation strategies could researchers use to mitigate the ethical risks to the HBV-positive human subjects in this research project?
What risk mitigation strategies could researchers use to mitigate the laboratory biosafety and potential biosecurity risks of the research project?
What approaches, if any, could be taken to reduce the risks to “research scholars?”
What, if any, specialized competencies, skills, and training are needed to successfully enroll, interview, and collect blood samples from participants, and separate and transport sera in conflict-ridden areas?
Are there any international, domestic, or institutional laws and regulations that could help manage risks from this research project?

Research Results and Conclusions

Results

- Approximately 58.4% of participants tested positive for hepatitis B virus; they had cross-reacting antibodies to HBV.
- Male participants (75.39%) were more susceptible to HBV infection than females (24.6%).
- Illiterate participants appeared to be more susceptible to HBV than literate participants.
- Low socioeconomic participants were affected by HBV infection more than middle class participants.
- Participants who were divers were more susceptible to HBV infection than participants with other occupations, such as farmers.
- HBV prevalence in 21-30 year olds is 38.9%, which is significantly higher than prevalence in children (>10 years, 3.14%) or older adults (<50 years, 7.14%).
- Main routes of transmission are: re-use of needles and disposable syringes, sexual exposure, risks at the barber, and tatooing.

Conclusions

- “High prevalence of HBV infection in young individuals and among the injector medicines users”
- Education, awareness campaign, and preventative measures, and vaccination are needed in these conflict areas.

Risk Communication

Prevalence of HBV infection in suspected population

Question
What are the risks that should be communicated during this research? To whom?
How would you communicate the risks from being involved in the research to a potential research participant that: Is illiterate? Is a child? Lives in a high-conflict area?
What data and information protection measures should be implemented to protect the safety and anonymity of research participants?
What social and cultural sensitivities are associated with the research project?
What, if any, safety and security risks are associated with communication of the study area, research methods, and research results?
What, if any, strategies would you use to minimize identified risks during communication of the research project and results to other researchers, individuals in the conflict areas, and the broader public?

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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? How likely are they to occur? Based on your assessment of the potential consequences, 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? 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

Communicate

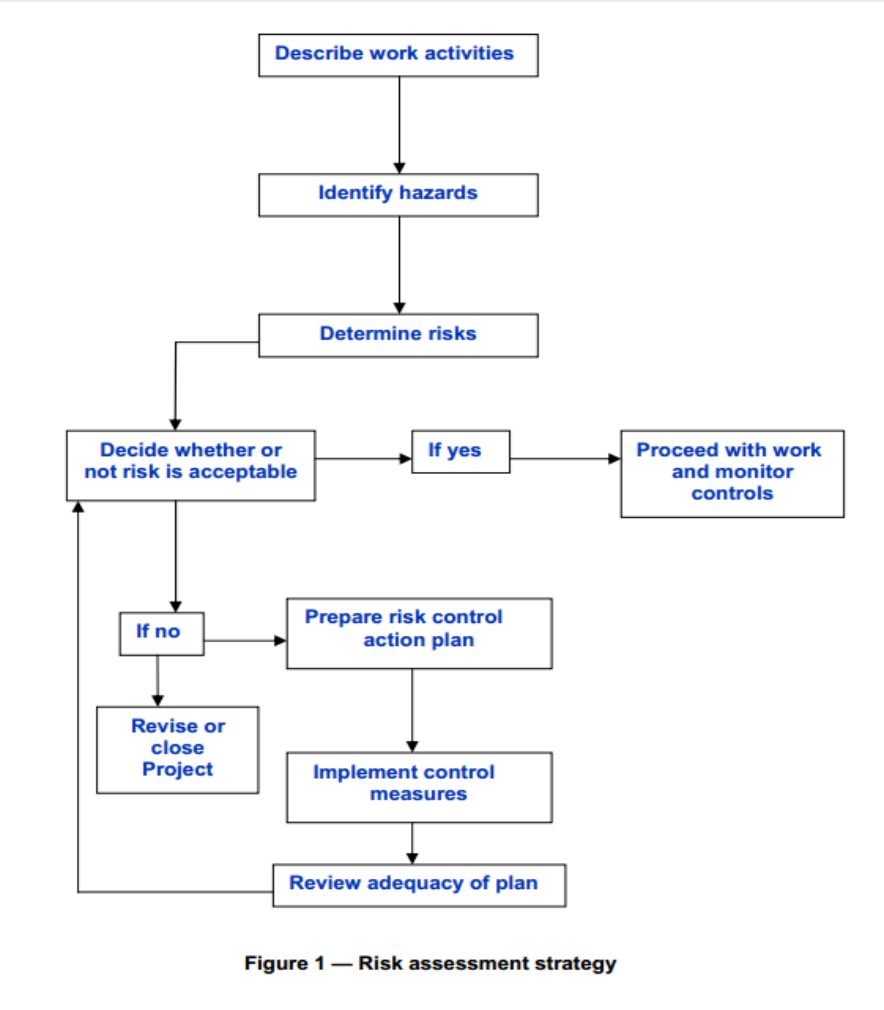

Figure 1 — Risk assessment strategy

"Laboratory risk management." CWA 15793: 2011

Reference List

Background Information

Ali, A, et al. “Prevalence of HBV infection in suspected population of conflict-affected area of war against terrorism in North Waziristan FATA Pakistan.” Infection, Genetics and Evolution. 2013 Aug 30; 12: 1865-1869.

Ali M et al. Hepatitis B virus in Pakistan: A Systematic Review of prevalence, risk factors, awareness status and genotypes. Virol J. 2011 March 6; 8: 102.

Hiu Gong, Hung. Management of Chronic Hepatitis B in Children – Part 1. CME Monthly Self-Study Series; July 2007. Available at: http://www.hkma.org/english/cme/onlinecme/cme200707main.htm.

World Health Organization,. Hepatitis-B Fact Sheet No. 204. Geneva; 2011. Updated 2013. Available at: http://www.who.int/mediacentre/factsheets/fs204/en/.

World Health Organization, Responsible Life Science for Global Health Security: A Guidance Document. 2010; http://whqlibdoc.who.int/hq/2010/WHO_HSE_GAR_BDP_2010.2_eng.pdf.

Diagrams and Images

Ali, A, et al. “Prevalence of HBV infection in suspected population of conflict-affected area of war against terrorism in North Waziristan FATA Pakistan.” Infection, Genetics and Evolution. 2013 Aug 30; 12: 1865-1869.

European Committee for Standardization (CEN). CEN Workshop Agreement: CWA 15793. “Laboratory biorisk management.” Ref. No: CWA 15793:2011 D/E/F. September 2011: 17. Available at: ftp://ftp.cenorm.be/CEN/Sectors/TCandWorkshops/Workshops/CWA15793_September2011.pdf.

Mir, Amir. “Den of Beasts: US trains its guns on the badlands of North Waziristan.” Outlook India, 24 May 2010. Available at: http://www.outlookindia.com/article.aspx?265458

Shaikh, Alanna. “A Shot in the Back.” Foreign Policy, 13 July 2011. Available at: http://www.foreignpolicy.com/articles/2011/07/13/a_shot_in_the_back