DETAILED DESCRIPTION OF RESEARCH PROPOSAL

Title: **Biorisk Management system: Using a Risk-based approach in clinical laboratories**

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Introduction

Clinical laboratories play a key role in the identification, diagnosis, treatment, and management of illnesses in all health care systems (Brown et al., 2015). In almost all aspects of health services, laboratory results are vital for health decision-making, since roughly 60-70% of medical decisions based on laboratory diagnostic test results (Kessel, 2014).

However Clinical laboratories are full of various biological hazards, due to:

- the nature of the diagnostic samples and the uncertainty of any microbiological agent that could be present in these samples.
- the ever-present risk of contracting a laboratory acquired infection (LAI) from unknown diagnostic samples and various isolated / propagated microbiological agents derived from clinical samples.

It is therefore necessary for all clinical laboratories to identify, assess, and control, these risks, in order to prevent incidents, accidents, laboratory infections (LAIs) and loss of lives, and improve the overall safety, security and quality within the laboratory setting.

One aspect of laboratory safety is the Biosafety, a term used to describe the unintentional exposure to pathogens, thus: “the containment principles, technologies and practices that are implemented to prevent unintentional exposure to pathogens and toxins, or their accidental release” (WHO, 2004). Biosafety is a Multi-sectoral area requiring the involvement and cooperation of all interested various stakeholders including governmental authorities, institutional management and laboratory professionals all collaborating toward the goal of safer laboratories. It is not only a list of guidelines , but mostly what we do with these guidelines and how to implement them and how we apply that in our local laboratory environment.

Besides laboratory Biosafety some laboratories also need laboratory Biosecurity, based on the agents processed in the lab. Biosecurity is the term used to describe “institutional and personal security measures designed to prevent the loss, theft, misuse, diversion or intentional release of pathogens and toxins” (WHO, 2004). Biosecurity is therefore the processes implemented to safeguard hazardous biological agents from persons wanting to divert them for malicious purposes; Biosecurity also extends to the protection of sensitive information and technologies from possible misuse.

These two concepts (Biosafety and Biosecurity) complement each other, but there is no Biosecurity without a proper Biosafety regime. Additionally, Biosafety and biosecurity are central aspects with regard to the global protection of human and animal health and safety against hazardous biological agents and they are of continuously growing interest as a result of globalization, technological progress and the rapid increase in communication, transport, and trade. Risks related to outbreaks of emerging and highly infectious diseases in an international context emphasize the need for effective prevention, detection, and response of outbreaks and other public health hazards as defined by the International Health Regulations (IHR) (WHO 2005).

In this context, clinical laboratories play a key role in ensuring that biological agents are identified, safely stored, and controlled in adequately equipped facilities according to best practices. Controlling these biological risks in the laboratory requires the identification of these risks with a risk assessment, following by the implementation of mitigation strategies proportionate to the risks determined and in line with resource availability. Using the hierarchy of controls, which is a combination of engineering and administrative controls, good microbiological practices and procedures and the appropriate personal protective equipment (CDC 2015) the management of biological risks can be achieved more effectively.

A Biorisk Management system must be put in place, in order to sufficiently develop and implement the risk management policy, the procedures and the responsibilities in the laboratory, with the objective to eliminate or to minimize to an acceptable level the biological risks for the laboratory professionals working with them, the community and the environment. Having an established Biorisk Management system in a clinical laboratory is very important, because it improves the laboratory processes and manages the risks more efficiently :

➢ There would be a continuous cycle of review and improvement for the laboratory’s effectiveness and efficiency, by identifying, understanding, and managing the interrelated processes, in which Biosafety plays a big (integral) role. For a long-term effectiveness and sustainability, the concept of a risk-based approach in the biological risk management system needs to be integrated.

➢ Clear guidance would be established, by describing the roles and responsibilities for those who work with or have access to biological materials in the laboratory setting

➢ The number and the severity of incidents, accidents and the occupational exposures and infections would potentially be reduced

➢ The appropriate training of laboratory professionals, supervisors and other personnel of laboratory facilities would create awareness of the potential risks and their contributory factors, so that they could adequately addressed and mitigated to an acceptable level. Enhanced knowledge and awareness of the risks would aide improved an emergency response measures (Bathula and Rakhimol, 2017).

Risk assessment

As mentioned above Risk assessment is the fundamental process of the risk management system and involves steps for the selection of appropriate biological safety and security measures and other facility safeguards, to mitigate risks to an acceptable or manageable level (Sandia National Laboratories, 2014). There are many methods on how to perform a risk assessment. One of these methods is the 5-step method described in the 4th version of the Biosafety manual of WHO, still in a draft version (World Health Organization, 2019). This method described the following steps (Figure 1) for performing a risk assessment:

Step 1: “Gather information” to identify the hazard and consider the nature of the work.
Step 2: “Evaluate the risks” that exist and calculate the overall risk. Risk = Likelihood x Consequence, a combination of the probability of an incident and the severity of the damage (Perseus, n.d.).
Step 3: “Develop a risk strategy”. Upon determining the risk level, a risk management system needs to be developed.
Step 4: “Select and implement control measures” on basis of the hierarchy of controls system, thus the Engineering and administrative Controls, the Personal Protective Equipment, the Vaccination, and the medical monitoring of the laboratory staff.
Step 5: “Review risks and control measures”. When the risk assessments will be completed, they should be part of a risk management system, and are routinely examined and revised, if necessary.

Figure 1: The risk assessment framework (Adapted from WHO, 2019 and WHO, 2020)

Much can be learned from understanding how different industries approach safety and security. In particular, those industries that have experienced major accidents, involving large-scale loss of lives, have been compelled to reassess their safety programs, and have almost universally recognized deficiencies in risk management as a principal cause in those accidents. As a result, those industries have embraced performance-based, holistic, risk management paradigms and risk assessment tools, e.g.:

- Airline industry, Safety Management Manual (SMM) (https://www.icao.int/safety/SafetyManagement/Pages/GuidanceMaterial.aspx)
- Chemical industry, "Process Safety Management of Highly Hazardous Chemicals" (PSM) (https://www.osha.gov/SLTC/processsafetymanagement/)
- Food industry, Hazard Analysis and Critical Control Points (HACCP) program (https://www.fda.gov/food/hazard-analysis-critical-control-point-haccp/haccp-principles-application-guidelines) and Global Food Safety Initiative (GFSI - https://mygfsi.com/)
- Pharmaceutical industry, ICH Q9 "Quality Risk Management" (https://www.ema.europa.eu/en/ich-q9-quality-risk-management).

Project justification and Goals

Clinical laboratories in Greece need to introduce a biological risk management approach and a Biosafety culture. The goal is to find ways to enhance Biosafety and Biosecurity in Greece and Develop a local system to mitigate the biological risks. Therefore, the main idea of this PhD study is to review different Biomedical laboratories in Greece, to investigate how they examine the biological materials and get a general view on how Biosafety is handled in these laboratories. Using the results of this review, actions can be formulated to improve Biosafety.

All the above should be in connection with the upcoming introduction of the new WHO laboratory biosafety manual 4th edition, which has a risk-based approach by contrast of the risk groups and the biosafety levels of the previous editions. The risk-evidence based approach is technology-neutral, cost effective and dissociates the direct correlation of the pathogen categorization with containment levels and put more emphasis on local risk assessment, good microbiological practices, standard operating procedures (SOPs), and training.

In order to achieve these changes in the biological risk management strategies that urgently needed in Greece:

- Health organizations should adopt best practices and training of laboratory staff based on the WHO laboratory biosafety manual 4th edition, which adopts a risk-based approach
- To update the Greek legislation on Biosafety and Biosecurity, in accordance with current European and international laws. One of the aims of this PhD study will be the "Gap Analysis" of Greek legislation on Biosafety regulations and to submit a report on the findings to policy makers, with recommendations for improvement.

Expected challenges regarding Biorisk management and the relative risk assessment:

- Lack of unified approach and comparability between risk characterization methods and tools
- An urgent need to develop standardized safety and security performance indicators for biorisk management
- A new ISO 35001:2019 (Biorisk management for laboratories and other related organisations) standard
- The rapid technological developments cause new challenges, but also a lot of uncertainty in terms of risks and regulations. To address these challenges, the biorisk management community must continue to improve the tools for biorisk management professionals. This includes more advanced tools for risk assessment and methods to accurate measure and compare the performance of biorisk management systems.
- Lack of understanding in laboratories of how to assess risk and implement the risk-based approach based on their local situation
- Lack of support from the administration of the health organizations and the state
- New resource allocation to Biorisk management systems

The ultimate goal is to create safer laboratory places and to improve the quality of diagnostic tests performed in these laboratories, as the standard operating procedures contribute to both Biosafety and Quality.

Methodology and Timeline

The study is expected to be concluded in 36 months (3 years).

1st Year: Definition and Evaluation

1 Studying and evaluating all existing international regulations, policies, standards and guidelines, the Greek and EU legislation and law, the safety culture in laboratories and the curriculum in the universities, regarding the identification and mitigation of biological risks. Situational analysis of the regulatory framework for biosafety and biosecurity in biomedical laboratories

2. Conducting open or semi-structured interviews with related experts. Open or semi-structured interviews as method of qualitative research are valuable when little is known about a complex topic, and further details need to be explored to identify current challenges (Waldrop 1992)

3.. Evaluate the "biosafety and biosecurity" portion of the WHO JEE tool, to assess what is currently in place

4. Select various clinical laboratories in the following aereas (1. Hospital 2. Primary health care 3. Public health 4. Veterinarian labs 5. Research) with the aim:

a. To collect Laboratory biosafety and biosecurity data (interviews, documentary analysis and observation data) and questionnaires with questions that could be divided into the following categories:

i. General questions to get information on the laboratory
ii. Questions regarding risk assessments, risk mitigation strategies (including the hierarchy of controls, ie. Containment, Administrative procedures, and Personal Protective Equipment) and Performance evaluation, i.e. the AMP model from WHO
iii. Questions regarding good microbiological techniques and practices used

b. Perform audits, by using the recommendations of the 4th WHO Biosafety Manual and the new ISO standard 35001:2019 with custom checklists.

2nd Year: Analysis

1. Gather the information on the status of Biosafety and biorisk management from the above Greek clinical laboratories

a. Analysing the results from the audits and the interviews.

b. Discuss the analysed results with experts working in the Biosafety area. This step adds more perspective to the problem analysis

2. Using user-friendly interactive tools and simulation models like The Analytical Approach for the Development of a National Biosafety and Biosecurity System PHAC (https://training-formation.phac-aspc.gc.ca/course/view.php?id=210#section-0), which is a tool developed to assist countries or regions build, modernize, or strengthen their national or regional biosafety and biosecurity systems, in order to mitigate the risks of a natural, accidental or deliberate release of biological agents, and make proposals

3. Development in collaboration with the directors of the above laboratories the following:

- A Biosafety manual template, Incorporating guidance on performing the local risk assessment under the risk-based approach of the 4th edition of WHO Biosafety Manual
- SOPs and protocol templates for good laboratory practices e.g. entering and exiting the laboratory, PPE donning/doffing, emergency response (spills, incidents, and accidents with biological materials), hand washing and waste management
- Prepare the Biomedical laboratories for the new standard ISO 35001:2019 (International Organization for Standardization, 2019)
- Designate an Appointed Biosafety Officer, responsible for Biosafety in the laboratories with a mandate for this purpose from the management
- Train the laboratory professionals for maintaining the level of safety of the Laboratory, the responsible work with the biological materials and their effective protection. This training should be organized by the management in cooperation with the Biosafety Officer
- Create Awareness of the laboratory management about their responsibilities for the biological hazards in which the laboratory staff are exposed and informing the laboratory professionals about the biological risks during their work,

3rd Year:

1. Measure the change and the improvement of the status of Biosafety and biorisk management in these laboratories with a new set of questionnaires and audits
2. Investigate whether the clinical laboratories will be able to eliminate or minimize to an acceptable level the risks and the possible Laboratory infections and have improved their quality
3. Assist in the implementation of key strategies aimed at improving the Biorisk Management system e.g. – training interventions.
4. Propose changes on the national level.

Expected outcomes

The Biorisk Management System is based on a continuous improvement philosophy through a cycle of planning, implementing, reviewing, and improving the operations and activities that a Biomedical laboratory undertakes in order to meet its objectives. It could enable the Biomedical laboratories to productively is to eliminate or minimize to an acceptable level the risks and the possible Laboratory infections, in order to protect the laboratory professionals, the patients, the community, as well as the environment, from biological agents and toxins that are handled, transferred or stored at the laboratory facilities, and additionally improve the quality of diagnostic testing performed in these laboratories.

Expected outcomes of this study include:

1. At least 2-3 publications

2. 2-3 training interventions / information sharing sessions with Biomedical Laboratories

3. Recommendations to institutions and the government

4. Start the process of implementation and information of the WHO JEE tool on Biosafety.

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