Enhancement and application of a risk assessment technique for research and teaching laboratories

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Je planmäßiger der Mensch vorgeht,
um so wirkungsvoller trifft ihn der Zufall.
— Friedrich Dürrenmatt

Meinen lieben Eltern

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Abstract

Risk management became an important element of the modern society. Being aware of risks and take appropriate actions to handle them are crucial elements in most industries, especially the ones for which the consequences of undesired events reach disastrous extents. To do this, risk management techniques were developed to systematically identify hazardous elements and assess the related risks.

Accidents occurring at universities can lead to serious consequences, even though their scale is often smaller when compared to industry. However, most of the well-established risk management techniques are not applicable for the research and teaching environment. These techniques require clearly defined processes and resources, which are not easily provided for the academic setting. Moreover, the research setting differs significantly from the industrial due to its peculiarities (high turnover of personnel, scarce statistical data, equipment in experimental state, etc.).

The intention of this dissertation is to further investigate these topics and to present a solution to fill the gaps. Thus, different risk management approaches are reviewed and the demands of an ideal method for risk management applicable to research setting are postulated. These requirements are met by development of the Laboratory Assessment and Risk Analysis (LARA), a method that was enhanced and tested at different Swiss Universities in the framework of this dissertation.

The results of the LARA use in the field suggest that this technique leads to suitable results and allows managing risks at universities, regardless of the character of hazard met. Used in an existing safety framework, LARA can help to allocate resources in an optimal way by taking into account the specificities of research environment and therefore help to improve the occupational safety level significantly.

Key words: Hazard, risk, occupational safety, risk analysis, risk assessment, risk management, resource allocation, risk mitigation.

Zusammenfassung

Risikomanagement gewann in den letzten Jahrzehnten immer mehr an Bedeutung. Für die meisten Bereiche der Wirtschaft ist das Erkennen möglicher Risiken und die Erarbeitung von Abwehrdispositiven überlebensnotwendig geworden, insbesondere wenn der mögliche Schaden desaströse Ausmasse annehmen könnte. Um Risiken zu erkennen und daraus resultierende Gefahren zu evaluieren, wurden in den letzten Jahrzehnten verschiedenste systematische Methoden entwickelt.

Auch wenn Unfälle an Universitäten nicht die gleichen Ausmasse haben wie in der Industrie, können sie doch zu ernsten Konsequenzen führen. Die meisten Risikomanagementmethoden sind im universitären Umfeld jedoch kaum anwendbar. Die Voraussetzungen sind zu unterschiedlich; denn die Methoden benötigen klar definierte Prozesse und Ressourcen, welche an Universitäten kaum verfügbar sind. Auch weitere Faktoren sind sehr unterschiedlich, wie beispielsweise die hohe Fluktuationsraten, kaum verfügbare Statistiken, Gerätschaften in experimentellem Zustand, und weiteres.

Ziel dieser Dissertation ist es, diese Problematik zu untersuchen und Lösungsansätze zu entwickeln. Dazu werden verschiedene gängige Risikomanagementmethoden besprochen und die optimalen Eigenschaften einer Methode für Universitätslabore postuliert. Diese werden mit der Entwicklung der Laboratory Assessment and Risk Analysis (LARA) erfüllt, einer Methode, die im Rahmen dieser Dissertation erweitert und getestet wurde.

Die Resultate dieser Tests lassen darauf schliessen, dass diese Methode tauglich ist, Risiken an Universitäten zweckmässig zu analysieren, unabhängig in welchem Forschungsgebiet sie angewendet wird. In Verbindung mit einem umfassenden Sicherheitskonzept kann die LARA Methode knappe Ressourcen optimal verteilen, indem sie die vorhandenen Eigenheiten berücksichtigt. Dadurch können die Risiken an Universitäten deutlich gesenkt und damit das allgemeine Sicherheitsniveau verbessert werden

Stichwörter: Gefährdungen, Risiko, Arbeitssicherheit, Risikoanalyse, Risikobewertung, Risikomanagement, Ressourcenverteilung, Risikoverminderung.

Résumé

La gestion du risque est devenue un élément important de la société d'aujourd'hui. Il est crucial d'être conscient des risques afin de prendre les mesures appropriées afin de les gérer dans la plupart des industries, et plus particulièrement dans celles où les conséquences d'évènements néfastes peuvent prendre des dimensions désastreuses. Ainsi, les techniques de gestion du risque ont été développées afin d'identifier systématiquement les éléments dangereux et évaluer les risques qui leur sont liés.

Les accidents survenant dans les universités peuvent avoir de graves conséquences, bien qu'a une échelle moindre que ceux survenant en milieu industriel. Toutefois, la plupart des techniques classiques de gestion du risque ne sont pas applicables au milieu de la recherche et de l'enseignement. Ces techniques reposent sur des procédures clairement établies, et nécessitent des ressources qu'il est difficile de pourvoir en milieu académique du fait de ses spécificités intrinsèques (changements fréquents du personnel, données statistiques insuffisantes, équipement au stade expérimental, etc.)

Cette dissertation a pour but d'approfondir cette problématique et de proposer les solutions qui répondraient aux besoins identifiés. Ainsi plusieurs approches de gestion du risque sont analysées. Cette étude aboutira à la proposition de critères idéaux en vue de développer une méthode d'analyse du risque spécifique au milieu académique. Ces critères ont alors été rassemblés au sein de la méthode Laboratory Assessment and Risk Analysis (LARA). En plus de son développement, LARA a pu être optimisée et testée dans différentes universités suisses. Les résultats de l'utilisation de LARA sur le terrain ont démontré l'adéquation de cette méthode qui permet de mieux gérer les risques au sein des universités, et ce indépendamment du type de dangers considères. Intégrée a une organisation existante de sécurité, LARA permet d'allouer les ressources de manière optimisée en tenant en compte des spécificités du milieu de la recherche et donc aider à améliorer le niveau de la sécurité au travail.

Mots clefs : Danger, risque, sécurité, analyse de risque, priorisation des risques, gestion des risques, allocation de resources.

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Introduction

With the technical progress during the industrial revolution in the 18th Century, humans got hold of the instruments to increase the size of accidents to disastrous extents. Especially the chemical industry is responsible for numerous catastrophes, claiming thousands of lives and polluting the environment on a large scale. Reasons for these accidents to happen were either ignorance or misjudgment of an imminent danger. Some accidents however were severe enough to shake up the public and led to regulations, which forced the industry to manage their risks.

An example of such an accident is the disaster that happened in 1976 in the Italian town Seveso, just 20 km away from Milano [Bertazzi, 1991]. On the 10th of July, an overpressure in a chemical production site of the company ICMESA caused the release of an unknown amount of the compound 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), better known as dioxin. The poisonous gas contaminated a densely populated area of 6 km^2, affecting the villages Seveso, Meda, Desia, and Cesano Maderno. The nature suffered tremendous damages, leaves withered within hours and approximately 3'300 cadavers were found in the surrounding area. Until today, the dimension of the human damage is unknown; the public authorities failed to provide evidence in order to call the chemical company to account. However, experts estimate that thousands have suffered from short and long-term effects of this disaster [Bertazzi, 1991].

This disaster raised the public awareness and the pressure on the industry and legislation began to rise. As a direct consequence of the Seveso disaster, the European Union enacted the Seveso-directive in 1982, successed by the Seveso-II-directive in 1997 [Council of the European Union, 1998]. The Seveso-directive regulates the use of dangerous chemical compounds, for which stipulations need to be met. These include, that the operation has to be registered, regular safety reports, internal and external emergency plans are mandatory, and safety measures need to be published. Since Switzerland is not directly affected by the laws of the European Union, own regulations were introduced in order to avoid such accidents (e.g. the Ordinance on Protection against Major Accidents [Swiss Confederation, 1991]).

Another example of a man-made disaster is the chemical spill in Schweizerhalle in 1986. Near Basel, a storage depot of the pharmaceutical company Sandoz storing 1350 tons of chemicals burned down. The reason for this fire is assumed to be a wrong manipulation during the boxing of a compound. The firefighters managed to get control of the fire, but the forge water

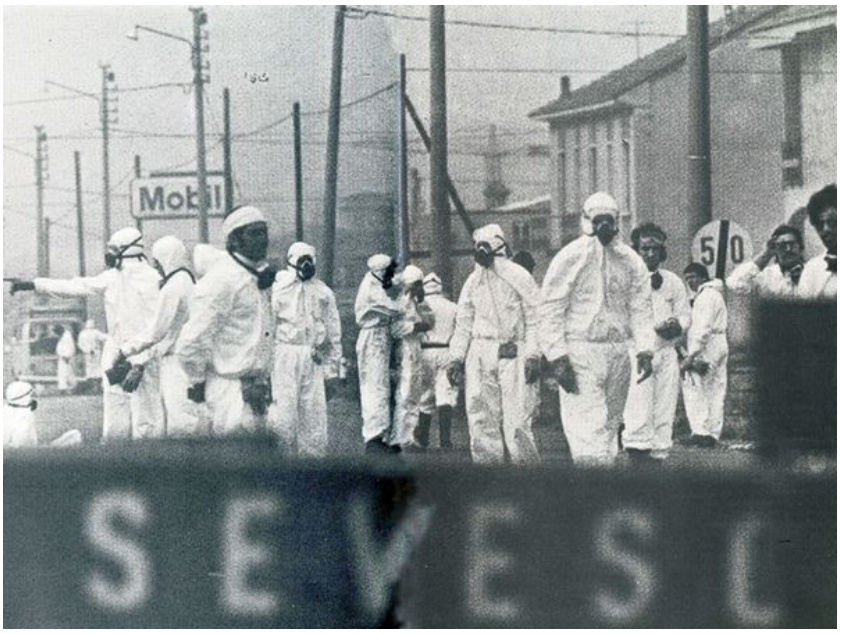


Figure 1 – A scene on the boarder of the evacuated zone in Seveso [Indymedia Ireland, 2013].

containing large quantities of various pesticides entered the river Rhine, which caused severe pollution. The contamination annihilated a large part of the river's fauna on the length of several hundred kilometers and had a serious impact on the ecological system of the river. Some of the effects are still present today.

As the Seveso disaster, the incident in Schweizerhalle shook up the public and authorities, which initiated an extensive program to protect the river Rhine. The International Commission for the Protection of the Rhine (ICPR) has the mandate to avoid these kinds of disasters and to protect the ecological system of the river. This includes strict controls of chemical concentrations and the pursuit of the polluters. The monitoring of the river Rhine also gives valuable insights on ecological effects of chemicals and has important implications on the legislation for the use of chemicals.

However, not only external pressure in form of legal consequences provoke companies to be aware of their risks; also other considerations, such as unacceptable financial losses in case of a disaster increased the importance of accident prevention. Regardless of whether a systematic risk management is the results of legal obligations or other considerations, it became an important aspect of the modern industrial sector.

Risk Management at Universities

What is daily business and widely applied in numerous fields of industries, is uncharted terrain for most universities' research and teaching laboratories. The accidents in this surrounding might not be as disastrous as the ones occurring in the industry, but still take place all over the

world [Marendaz et al., 2013; Ouédraogo, 2011c]:

- Darthmouth college (Hanover, USA), 1996: fatal intoxication of a scientist after a contact with the highly poisonous compound dimethyl mercury.
- University of Mulhouse (France), 2006: one death and several injured due to a blast in the university's chemistry building.
- Technical University of Delft (Netherlands), 2008: a short circuit caused a fire, which completely destroyed the building of the architecture faculty.

These are just a few examples of accidents happening at universities and indicate that the accident potential is present, but might be underestimated. Other than in the industry, universities lack structures to promote a safe environment:

"We find that the accident rate in universities is 10 to 50 times greater than in the chemical industry. In DuPont, if a guy hits his thumb with a hammer in Singapore, the chairman of the board has a report on his desk. Imagine if that happened in academia." –James Kaufmann [Peplow and Marris, 2006]

Figure 2 – As a consequence of a short circuit, a building of the architecture faculty in Delft burned down [Minh, 2008].

It is probably a question of time until an accident happens at a university that has similar implications as the ones described above. It should in each university's interest to actively

avoid such incidents from happening, to be aware of risks in their operations, and to manage them accordingly. However, risk management needs a systematic method and resources. Most existing risk management approaches, such as the Failure Mode, Effect and Criticality Analysis (FMECA) or Hazard and Operability analysis (HAZOP) were designed for a specific application in the industry. HAZOP for example was invented as a tool to analyze processes in the chemical process industry. The scientific research differs from these operations significantly and many times the existing approaches are not feasible. Additionally, the provided resources are often not sufficient to perform such a risk management approach; they require special training, manpower and expertise.

Not only the difference of the processes and the lack of provided resources make an application of widely used techniques difficult; also the peculiarities of the research environment hinder a successful application. Equipment is often only in experimental state, processes are not fully discovered and described, and emerging technologies might involve unknown risks. Other than in the industry, universities can be considered as a conglomerate of micro-companies rather than a single company. Research groups rarely share similar goals and operate with minimal interference between each other. Moreover, responsibilities are often not clearly defined and shared guidelines are not always established. Another important aspect are social factors, which create a challenging environment for safety management: high personnel turnover, a multitude of different cultures, and a culture of disregard when it comes to safety.

Intention and Goal of this Dissertation

Widely used methods are not applicable to manage risks in the research and teaching environment; at the same time, a systematic risk management is necessary in this setting to avoid serious accidents. The goal of this dissertation is to further investigate the topic and to present a solution to fill this gap. In order to do so, this thesis is structured as follows:

Chapter 1: Risk Management explains concepts related to risk and how these concepts can be linked together to manage risks. A basic risk management workflow is explained in detail and the important aspects are discussed. Furthermore, the most common risk assessment techniques used in the industry are explained, their advantages and disadvantages reviewed, and their feasibility for the research environment investigated. Based on this comparison, ideal specifications of a risk management technique for research and teaching laboratories are postulated. Few specific methods for the research environment exist, but none of these methods can be used as a holistic method for all aspects of research laboratories. These methods are explained, their benefits pointed out and assessed based on the postulated specifications.

Chapter 2: LARA – Laboratory Assessment and Risk Analysis presents and discuss the LARA approach. This method was developed by the Group of Chemical and Physical Safety

(GSCP) of EPFL and was enhanced during the studies, on which this dissertation is based on. LARA is a holistic risk management method for research and teaching laboratories. The main goals of LARA are as follows:

- Provide a risk management technique for all types of academic research laboratories.
- Allow a less resource demanding risk management, to fit the provided resources of the research environment.
- Development of a software application, allowing user-friendly and intuitive risk analysis.
- Consideration of the particular setting of the academic research environment.

In this chapter, the development history, cornerstones, and main principles of the LARA method are presented. Based on the general workflow of risk management presented in Chapter 1, the complete workflow of the LARA method is explained in detail with examples.

Chapter 3: Application Examples of LARA shows how the enhanced LARA method can be applied and if this method is capable of introducing adequate risk management to the research environment. In order to do so, a choice of different processes is evaluated in LARA and the strengths and the limitations of this method is discussed. In order to have a broad range of applications, the processes do not only differ in their focus or their branch of study, the evaluations were also performed at different Swiss universities.

The results of these applications suggest that LARA leads to suitable results and allows managing risks at universities, regardless of the specific field of application. Used in an existing safety framework, LARA can help to allocate resources in an optimal way by taking into account the specificities of this environment and therefore improves the occupational safety levels significantly.

1 Risk Management

The concept of risk has been a subject of change during history of mankind and is strongly related to the religious beliefs of an epoch [Bernstein, 1998]. Religion was always used by mankind as an approach to explain the world. Future events were linked to fatalistic beliefs and were often seen as a whim of the gods. Oracles and soothsayers were one manifestation of these beliefs, showing the need of the people to know what they are facing in the future. During the age of enlightenment, cultural and religious changes cleared the way for scientific progress, which influenced the way how western civilizations explained and saw the world. Probability theory, first used as a gambler's tool, linked events with different possible outcomes and their relative probabilities. For a simple game with defined rules and defined possible outcomes, this might be sufficient to predict and estimate the future; for more complex scenarios however, this approach is not enough. For real life situations, one has to determine possible outcomes and estimate how probable these outcomes are. In a similar way how gamblers could think about turning the odds to their favor, it is possible to optimize those probabilities and therefore being better prepared for the future. This approach comes close to the modern conception of risk analysis, which deals with following fundamental questions:

- What can go wrong?
- How likely can it go wrong?
- What can be done about it?

Even though risk analysis has become an important factor in modern society and economy and reached a high level of complexity, it satisfies the basic need of humans to be aware of the unknown, just like the oracles in ancient times did.

Risk Management in Occupational Safety And Health

When applied in occupational safety and health, the main goal of risk management is to reduce the accident rate. Traditional approaches for safety management tend to overlook

some important factors, since they mainly build on experience rather than on a systematic determination of hazards and risks. Especially unusual accidents are rarely determined by the traditional approaches; risk management is more likely capable to detect them, due to the systematic approach. Additionally, risk management is well-established in various fields of application, which gives a certain guarantee about the effectiveness of a method. Furthermore, an adoption into an organization and its workflows can promote different collaborations, which were not existing before. As a results, the method delivers evaluated hazards and risks, a recommendation of safety measures and a better general understanding of processes. This documentation helps to keep track of the safety related issues and gives the management a measurable component.

There are various reasons to adopt risk management into an organization. Knowing about efforts to reduce the risks can have a positive impact on different stakeholders of an organization. This includes the employees, which work in a safer environment, as well as customers, legislators, neighbors of the production site and insurance companies. Furthermore, applying risk management and reducing the accident rate can also be a legal obligation, depending on the local legislation. Risk management also brings economical benefits: even if the reduced accident rate does not bring direct advantages (e.g. less work interruption), the risk management can lead to indirect advantages (e.g. lower insurance premium).

1.1 Definitions

Risk management as a scientific approach lies in the intersection of various different sciences and has countless applications in most sectors of a modern society. It highly benefits from this variety of influences, but it can also lead to misconceptions. Different scientific, cultural and personal backgrounds of involved people are a source of these misconceptions. Due to this, clear definitions of important concepts are crucial for an objective and unbiased risk management. For this thesis, the most important concepts and terms are defined as follows:

Risk

The most important concept for risk management is risk itself. Risk management has countless fields of application and risk might have different uses in these fields, therefore many definitions of this term exist. Attempts to grasp the concept can lead to rather complicated definitions, such as the risk definition of the U.S. Department of Defense:

An expression of the impact and the possibility of a mishap in terms of potential mishap severity and probability of occurrence [U.S. Department of Defense, 2000]

In most basic definitions, risk is a concept containing three aspects: events, their possible outcomes and the their occurrences [Fishkin, 2006]. For a simple gambling example (e.g. flipping a coin), the outcome can be separated into success or failure. Even though not all sources agree on it [Adams, 2012; International Organization for Standardization, 2009], a majority of definitions relate a failure (negative) to risk, whereas the success (positive) is seen as chance. However, outcome is not the only aspect, which leaves room to interpretation: risk can also be defined through the statistical aspect of the occurrences:

Risk is the semi-variance of the distribution of all consequences, taken over negative consequences only, and with respect to some adopted reference value [Vlek and Stallen, 1981]

Other definitions are pointing in a psychological direction and focus on the event aspect of risk. An event can be seen as a conscious decision and therefore risk judgements are:

Intuitive value judgements which express a diffuse negative evaluation of a decision alternative [Singleton and Hovden, 1987].

Aven [2011] classifies the definitions into “risks defined through probabilities" and “risk defined through uncertainties". The first class of definitions includes the three aspects events, consequences and associated probabilities. The second class of risk definitions includes uncertainties, for example:

Risk is uncertainty about and severity of the consequences (or outcomes) of an activity with respect to something that humans value [Aven, 2009]

Uncertainty however is an object of discussion itself [Rogers, 2003] and increases the complexity and the level of abstractness of the concept *risk*. In order to focus on the subject rather than the definitions, for this thesis the risk will be used in its general sense:

Possibility of an undesired consequence [Harms-Ringdahl, 2003]

Hazard

For risk management, the term hazard can hardly be avoided. For most definitions, hazards are the sources for risk [Fishkin, 2006] and the concepts are inseparably linked to each other (see Figure 1.1). Ericson [2005] describes hazards as prerequisite for an accident, where risk acts as a possible route from one to the other. For this thesis, hazards are defined as follows:

A condition that is prerequisite for a risk [Harms-Ringdahl, 2003]

Exposure

Not only a source (hazard) is necessary to establish a risk. Exposure of a possible target is required as well to form a risk situation (see Figure 1.1). If both target and hazard are present, a risk exists, even though it is negligibly small.

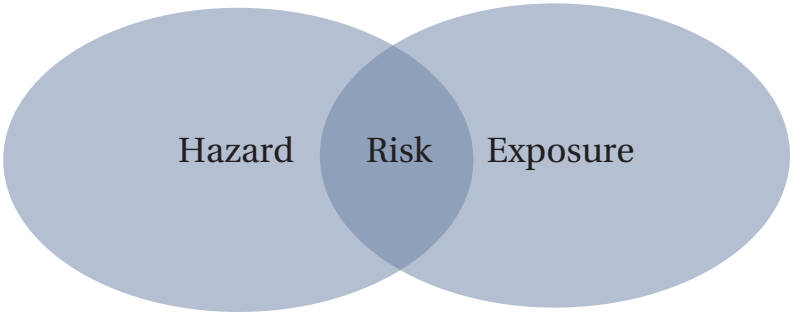


Figure 1.1 – Schematic representation of relation between hazard, risk and exposure.

Uncertainty

Risk management aims to reduce risks and uncertainties about future events. There are several kinds of uncertainties, which origin from different phenomena [Rogers, 2003]:

- Uncertainty in the effect: uncertainty in the realization of the harm that may result from the exposure to the hazard. In this kind of uncertainty, the hazard is known and the possible adverse effect is known as well. There is an uncertainty about the probability of the adverse effect due to the stochastic nature of this process. Taking the harm “infection with the HI virus" and the cause “unprotected intercourse" as an example: the event can lead to an infection or a non-infection, and the uncertainty is related to the probability of these two outcomes.

- Uncertainty in the cause: the adverse effect is known, but several causal relationships are leading to this adverse effect, which generates uncertainty. An example for this kind of uncertainty is the harm “lung cancer" and the cause “smoking". Hardly any source disagrees about a correlation between these two phenomena. However, since other effects can lead to this illness as well, it is impossible to determine with certainty the cause of a specific case.

- Uncertainty in the cause-effect relationship: uncertainty in the degree of correlation between the hazard and the harm. For example, the harm “brain tumor" and the cause “use of cell phones": there are speculations about the causal relationship, but it is not scientifically proven. The uncertainty describes the degree of truth of this postulated relationship.

Additionally to these three types of origins, other influences (e.g. language) can lead to uncertainties as well [Pluess et al., 2013]:

- Lexical uncertainty: caused by different personal interpretation of an expression (e.g. often).

- Informal uncertainty: induced by a subjective interpretation of a concept (e.g. severity).

Other authors describe the concept of uncertainty in a statistical context and distinguish between following types: [Zio and Pedroni, 2012]

- Aleatoric uncertainty describes the relative probability of future events, which are determined by random physical processes. These uncertainties are not reducible by default.

- Epistemic uncertainty describes a lack of knowledge about a phenomena. Other than aleatoric uncertainties, those kind of uncertainties are reducible.

Uncertainty in its basic meaning describes not being sure about something. The concept is not interchangeable with ignorance. Not knowing something is a different phenomena, slightly related to the concept of uncertainty, but important for risk management as well [Paté-Cornell, 2013].

Accident

An accident is an undesired event that causes damage or injury. Harms-Ringdahl [2003] differentiates between four types of accidents:

- Accidents with a direct and sudden consequence, which is triggered off unintentionally. The consequences are observable within a short period of time.
- Accidents, which are giving an increased probability for injury or damage, but without directly observable consequences. An example for this type of accident is cancer due to short-time exposure to carcinogenic chemicals.
- Slow deterioration and degeneration, caused by continuous exposure to a hazard. Sources for this could be chemicals as well, but other than the second type, it is not necessarily a question of probability but severity.
- Sabotage, which can appear in form of the other three types of accidents. The main difference is the intentional triggering of the the event.

The border between these types of accidents can be blurred and the distinction is mainly based on the time passed. The difference between the first type and the third type is the amount of time necessary to lead to the consequences: seconds to hours for the first one, years to decades for the third one.

Accidents are defined as incidents leading to a certain loss or damage. If an incident happens without any loss or damage, the term near miss is used. Different models describe the relationship between near miss and accidents [Meyer and Reniers, 2013]. These models established the connection between near miss, property damaging accidents, minor accidents and major accidents. An often used approach to illustrate the relation is the use of a pyramid form; a less severe level is always prerequisite for a more severe level and the occurrences depend on each other.

1.2 Risk Management Process

The risk management process coordinates activities and efforts to direct and control an organization with regard to risk [International Organization for Standardization, 2009]. Various different approaches were suggested; main differences between these approaches is how they are adopted into existing workflow and safety structures. Figure 1.2 shows a suggestion of a risk management workflow based on the ISO 31000:2009 norm [International Organization for Standardization, 2009]. The workflow has three main parts: the adoption into an existing organization (definition of context and monitoring), risk assessment (identification, analysis and evaluation of risks) and risk treatment.

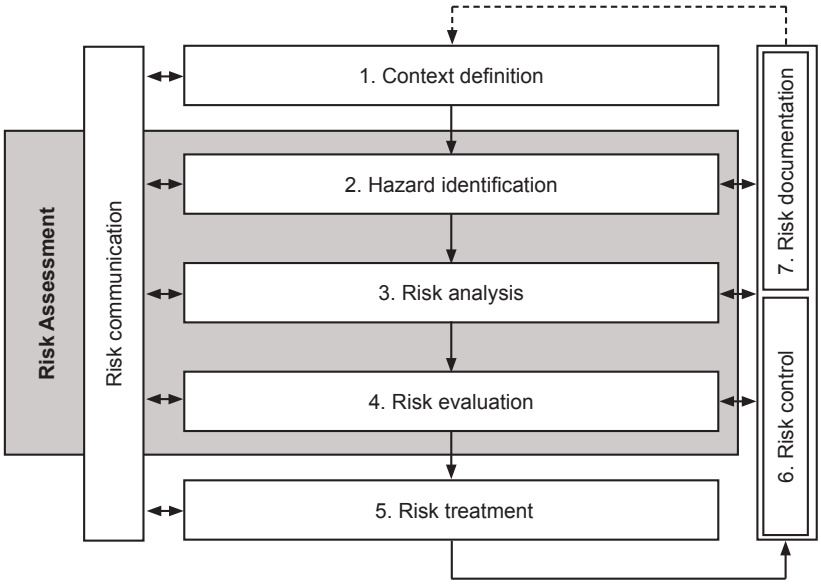


Figure 1.2 – Risk management workflow.

1.2.1 Definition of the Context

The first step of the workflow is the definition of the context for the risk management process. On an organizational level, the framework of the process, the resources, roles and responsibilities need to be delineated. External influences must be taken into account as well; stakeholder's expectations and legal regulations similarly shape the aims of the risk management process.

In order to measure the performance of the processes, quantitative approaches using key indices (e.g. the accident rate) can be used. To reach a high level of effectiveness, clear responsibilities and system limits are a crucial part of the process, independently if it is a single activity or a larger project. Inconsistencies in responsibilities can lead to undetected risks. In order to compare the different risks with each other, the criteria to evaluate them must be determined including the dimension of these criteria. Severity for example might

not be measured in the same dimension for a pharmaceutical supplier as for an aviation enterprise. Once the measure of comparison is defined, limits of acceptability are set before the risk assessment takes place; in order to have an objective tool for decisions, those limits are valid for the defined system.

1.2.2 Hazard Identification

The first step of the sub-workflow risk assessment has the goal to identify possible hazards. Most systematic risk assessment techniques differ mainly in their approach on how to do this. Some might focus more on the components of a system, some examine the activities involved. However, all those systematic techniques rely on information. Statistical data about past accidents and near misses are an important source for those techniques. Standard operation procedures and schematics of the process can help to understand a system and therefore to be aware of the possible hazards occurring when performing an activity. A complete identification of all possible hazards however is not realistic, independently which method is applied. Reasons for this are random effects (aleatoric uncertainty), a lack of knowledge (epistemic uncertainty), or influences from outside of the studied system. These unidentified hazards decrease the significance of a risk assessment and should be eliminated as much as possible.

1.2.3 Risk Analysis

The goal of this step is to understand the risk and to estimate its magnitude. This includes the rating of each single risk present according to the predefined criteria (e.g. severity, probability, detectability). All of those criteria involve a certain amount of uncertainty. The rating of severity for example can be determined in various ways, depending on the assumed consequences. It has to be clearly defined, if the worst case scenarios or the most probable consequence is assumed for this rating. These considerations must be followed for all risks present, otherwise the comparison of them will be biased. Additionally, the already applied corrective measures for a risk must be known in order to analyze the risk correctly.

Once the hazards are described with the predefined criteria, the risk estimation takes place. In order to compare the risks, a common risk scale is established for this step. This can be achieved using quantitative approaches (e.g. probability values as risk dimension), semi-quantitative approaches (e.g. risks values on a predefined scale) or qualitative approaches (e.g. high risk). Since the concept of uncertainty is highly related to the concept of risk, they need to be analyzed as well in this step of the risk assessment. This includes studying the different sources, such as different expert opinions.

1.2.4 Risk Evaluation

Risk evaluation is the last step of the risk assessment process; in this step, decisions are made about how to deal with the specific risks. A basic question needs to be answered for every single risk:

Is it necessary to treat this risk?

A risk does not necessarily need to be treated, accepting it might be an option as well. If it is treated or not, cannot be answered by the analyst alone, the board of an institution needs to be involved as well. Usually, acceptability levels are set independently from a single analysis when defining the context of the risk management process. For risks, which are not unacceptable, the as low as reasonably practicable (ALARP) principle can be used:

ALARP is a widely used principle in risk management [Melchers, 2001]. When a risk level is neither unacceptable nor acceptable (Fig. 1.3), it should be reduced as low as reasonably practicable; this means that the costs to reduce a risk should not be grossly disproportional to the gains obtained [Aven, 2011]. However, neither disproportion nor gains of a measure are a clearly defined term. The limits for these regions (acceptable, ALARP, unacceptable) are usually predefined by the board of an institution in order to have the same scale for all risk analyses.

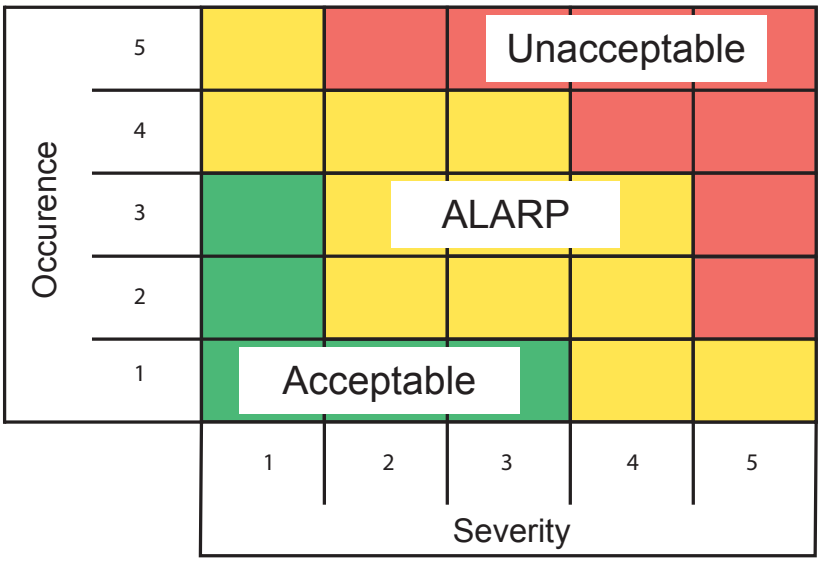


Figure 1.3 – A sample risk matrix illustrating the three regions of risk treatment.

1.2.5 Risk Treatment

As a result of the risk assessment procedure, priorities are set in which order the different risks need to be treated. As a next step of the risk management workflow, possible corrective measures are identified and the resources for risk treatment are allocated.

When the decision is made to treat a risk, possible corrective measures must be determined and evaluated. How numerous the alternatives of measures are relies highly on what moment the risk assessment is performed: if the assessment is done in an early design stage, different alternatives exist compared to a late assessment. Usually, a prevention of an accident is more favorable than the protection from possible consequences. Corrective measures try to influence one factor contributing to the risk, for example lower the probability or reducing the severity of an unwanted event. A systematical determination of the factors can be achieved by the Strategical, Technical, Organizational and Personal (STOP) approach:

STOP is a systematic approach to determine possible corrective measures for a hazard [SUVA, 2004]. Four different classes of measures help to find possible alternatives:

- Strategical measures aim to modify a process to reduce a risk (e.g. substitute a hazardous element of a process to a less hazardous one).
- Technical measures can be applied to protect an exposed target against the consequences of a hazard (e.g. sprinkler system against fire) or to reduce the occurrence of an adverse event by technical installations.
- Organizational measures modifying the organizational elements around a certain process; evacuation plans, response techniques, work instructions and training can lower the occurrences of unwanted events and their possible consequences.
- Personal measures are directly applied to the persons involved in a process. This could be personal protective equipment or training of the exposed personnel.

Once the alternatives for all risks are found, the allocation of the resources is done. A common approach to do so is to decide based on the risk scores and reduce the most important risks present. However, a risk reduction only based on risk scores is not leading to ideal results; financial concerns need to be considered as well to have a optimal resource allocation [Aven, 2011]. Additionally, the risk reduction potential of every corrective measure can be taken into account to reach a better allocation of measures [Cox, 2012]. Other approaches are using optimization algorithms to achieve an optimal resource allocation [Reniers and Sörensen, 2013]. A more detailed discussion about resource allocation can be found in Chapter 2.6.

1.2.6 Risk Control

In order to ensure that the corrective measures are effective and efficient, they must be controlled regularly. This includes obtaining further information about the hazard, the risk, and the control itself. This information can improve further risk assessments and show if the measure works as intended. Accident data and especially near misses are of high importance to do so. The results must be periodically analyzed and the insights recorded in a systematic way.

1.2.7 Risk Documentation

Risk documentation is a central element in the iterative risk management process. On one side, the documentation is necessary for giving information to all roles involved in the process. This includes all the details of the evaluation and the action plan to implement corrective measures. On the other side, an effective documentation helps to re-use information for future analyses, training, and helps keeing track about costs and efforts.

1.2.8 Risk Communication

Risk communication is of high importance for every risk management approach and has a superior function. By communicating evaluations results to all the involved roles, it helps them to understand the decisions made and to include the expertise of all stakeholders. However, the communication is not only limited to the distribution of information, but also allows external knowledge to influence the context of a risk management approach.

1.2.9 Continuous Improvement

As for most management approaches, continuous improvement is an integral part of risk management. A widely applied principle of continuous improvement is the Deming wheel (see Figure 1.4), also known as PDCA cycle (Plan – Do – Check – Act). This principle describes process optimization based on following four iterative steps:

- Plan: development of objectives and actions necessary to achieve these objectives.
- Do: execution of the planed actions and collection of data.
- Check: monitoring of the actions to check their effectiveness (e.g. with audits and inspections) and evaluation of the results.
- Act: carrying out of improvements, if the results of the planed process and the results differ.

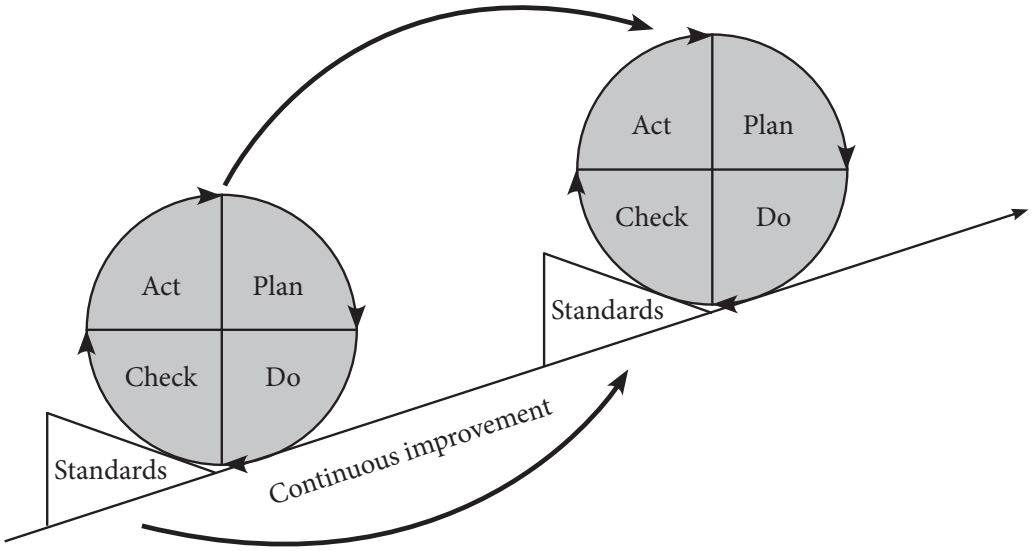


Figure 1.4 – Continuous improvement can be achieved by iteration of the Deming wheel and consolidating through standardization.

The continuous improvement is achieved by iterating the steps of the Deming cycle and consolidating the achieved results through standardization. For risk management, the results are of the procedure are analyzed and decisions to improve the process are defined. According to the PCDA principle, the optimization is performed in an iterative process and guarantees the suitability of a risk management approach.

1.3 Risk Assessment Methods

Most steps of the risk management process are important on an organizational level only: how to define the system, how the risks are treated and monitored. These steps are not bound to a specific application and are interchangeable on many levels. In contrary, the risk assessment acts as a core part and should be suited for a specific application. Many approaches have been suggested to perform this process; they mainly differ in their focus. Some methods concentrate on components of a system, whereas others point out possible deviations. Most of these risk assessment approaches were specifically created for a certain field of application; the use in another environment was not intentioned. However, most methods spread from one field to other fields of application and were successfully applied. In this section, various widely used approaches will be discussed and their feasibility for the research environment is explained in detail.

1.3.1 Classification of Methods

Even though most risk assessment approaches share similar goals, the approaches differ significantly. This includes not only the result obtained by the different methods, it also includes the inputs, requirements, workflows, and other aspects. Some methods focus on the consequences of an event (inductive), where other methods are are trying to determine the influence factors leading to this specific unwanted event (deductive). Some use statistical reliability data to calculate possible scenarios (quantitative), others rely on linguistic expert judgements (qualitative). The qualitative approaches require more data, but usually provide a higher level of detail. Thus, the complexity of the analysis and the demands for the analyst are increasing. Most factors are somehow connected, but not all of them are necessarily dependent. A method can provide a high level of detail without giving exact probability estimations. Besides of the mentioned attributes, the methods differ as well in their scope: some target components of a process, others aim to find hazards and risks in the activities involved. The required performance or level of detail can also vary depending on other considerations: either the method is used as a primary safety tool or is used as a backup to find unknown hazards. Another important factor is in which phase the risk assessment method is involved during the development cycle of a process; in the initial design phase, corrective measures can be applied much more effective than in the operation phase.

To characterize the different methods, they are compared using the criteria represented in Table 1.1.

1.3.2 Hazard and Operability Analysis (HAZOP)

Overview The HAZOP was introduced by the Imperial Chemical Industry (ICI) in the late 1960s to assess safety risks in chemical process plants. The method as it is known today was published by Lawley of ICI Petrochemicals in 1974 and became a widely used technique in

Table 1.1 – Criteria to compare the different risk assessment methods.

Requirements	Approach
Data	*Form*
Difficulty	*Level of detail*
Complexity	*Direction*
Expertise	*Focus*
Time	*Phase*

the chemical process industry worldwide after the Flixborough disaster in 1974 [Meyer and Reniers, 2013]. Due to the popularity in the chemical industry, other industries adopted this technique, such as the petroleum industry, the food industry and many others [Ericson, 2005; Hashemi-Tilehnoee et al., 2009].

Since the technique is widely used in different fields of industry, commercial software is available and research is performed to improve the results. Publications about applications of HAZOP reaches from nuclear engineering to computational methods [Dunjó et al., 2010]. The research mainly focusses on quantification of the different risks, extending the identification scope or the integration of human factors in the analysis [Dunjó et al., 2010].

Table 1.2 shows the classification attributes of the HAZOP approach. The main characteristics are the low amount of data necessary and the low difficulty; on the contrary, a high level of system expertise is necessary. The effect of the deviations are difficult to estimate and much expertise is necessary to do so. The strict and systematic approach can lead to a high complexity level and is therefore relatively time consuming. The approach focusses on the function of system elements and their possible deviations. It is usually applied in the system design or in the detailed design phase.

Table 1.2 – HAZOP specifications.

Requirements		Approach	
Data	Moderate	*Form*	Qualitative
Difficulty	Low	*Level of detail*	Moderate
Complexity	High	*Direction*	Inductive
Expertise	System/technique	*Focus*	Functional deviations
Time	High	*Phase*	System/detailed design

Principles HAZOP analysis is a technique developed for identifying and analyzing hazards and operational concerns of a system [Ericson, 2005]. If a system works as intended, the

situation is expected to be safe and therefore no accidents will occur. In contrast to this, system deviations are seen as sources of hazards. To systematically determine those deviations, the system is divided into the different system parameters, such as measurable physical quantities, operations or actions (e.g. temperature, stirring, stop). Those parameters are combined with predefined keywords (more, less, no) to find possible deviations of the normal operation. The basic principle of every HAZOP analysis therefore is:

parameter + keyword = deviation

These conditions will be analyzed for possible causes and consequences and corrective measures will be defined to avoid the hazardous condition. Usually, most combinations of parameters and keywords are not making sense and can be discarded.

Advantages and disadvantages The basic principle of HAZOP can easily be learned and performed. The application to a system however needs deep knowledge of the system to estimate the impact of possible deviations. The system needs to be studied with a team of experts and a HAZOP moderator to reach a complete analysis. This team effort can bring many different points of view on one hand, but is very resource-demanding on the other hand. Even though the technique is able to identify a high amount of possible hazards, these hazards lie in the predefined system boundaries and hazards unrelated to deviations can be overseen.

Table 1.3 – Advantages and disadvantages of HAZOP (from Ericson [2005], p.376).

Advantages	Disadvantages
Easily learned and performed	Focusses only on single events
Does not require technical expertise for application	Possible overlook of hazards unrelated to a key word
Rigor focussing on system elements and hazards	Training is essential for optimal results
Team effort with many viewpoints	Time consuming und thus expensive
Commercial software available	

Application at the research environment Even though HAZOP is a very systematic and widely used approach, it cannot be applied to the academic research environment without limitations. Some specifications would fit the academic environment well: the moderate amount of required data and the low difficulty, which makes it easy to learn and perform. On the other hand, the concept of deviations, which is crucial for the HAZOP procedure is hardly applicable to the research environment. The equipment is often only in experimental state and knowledge about possible deviations is often not existing. Additionally, the high demands

for both manpower and time would not fit the limited resources of this environment. The focus on key words and single events are another problem when applying this method to research laboratories, since the accidents are often caused by complex sequences of independent events.

1.3.3 Failure Modes, Effects and Criticality Analysis (FMECA)

Overview The technique originates from the US Army and was first published as a Military procedure MIL-P-1629 U.S. Department of Defense [1949] under the name “Procedures for Performing a Failure Mode, Effects and Criticality Analysis". From a Military use, the Failure Modes, Effects and Criticality Analysis (FMECA) made its way to the National Aeronautics and Space Administration (NASA), where it was used for aerospace and rocket development [Ericson, 2005]. In the 1970s, FMECA was introduced in the automobile industry by Ford Motor Company; today, general guidelines developed by the three U.S. auto makers are used worldwide in various fields of industry [Meyer and Reniers, 2013]. Depending if the approach is explicitly including the criticality or not, it is called FMECA or Failure Modes and Effects Analysis (FMEA). Since the basic structure is similar, most statements in this section are valid for both approaches.

FMECA is applied in numerous fields, such as the food industry [Scipioni et al., 2002] and nuclear engineering [Guimarães and Lapa, 2007]. As for HAZOP, this technique is widely used and commercial and non-commercial software is available. Most research concerning FMECA goes in the direction of improving the quantification approach, for example with the implementation of a Fuzzy Logic calculation method [Keskin and Özkan, 2009; Zaili et al., 2009] or other mathematical improvements [Bluvband et al., 2004].

As represented in Table 1.4, the FMECA approach is a relatively flexible approach, still capable of providing an in-depth analysis of a system. The complexity and the difficulty of the method are moderate; however, a high level of system expertise is necessary. Other than HAZOP, FMECA includes the criticality as a quantitative element; nevertheless, the estimation enables only rough estimations rather than precise analyses and is therefore a semi-quantitative method. A main characteristic of the method is the variability of the scope: it is possible to focus on components, on functions or on both. It is usually applied in the detailed design phase.

Principles The main interest of a FMECA procedure is what elements of a system can fail, how they will fail and how frequently these failures will occur. After the system and its limits are determined, it will be divided into all relevant elements. In a functional approach, the division is based on the specific functionalities and sub-functionalities. In a structural approach, the division is focused on the structures of the system, e.g. components and parts, regardless of their specific function group. Which approach to chose depends on the development progress and the knowledge of the system: if the function of a specific group of components is not

Table 1.4 – FMECA specifications.

Requirements		Approach	
Data	Moderate	*Form*	Semi-quantitative
Difficulty	Moderate	*Level of detail*	In-depth
Complexity	Moderate	*Direction*	Inductive
Expertise	System (high level)	*Focus*	Variable
Time	High	*Phase*	Detailed design

known, a functional approach is not possible. After the system elements are determined, they are usually transcribed into a matrix-like worksheet. Many different FMECA worksheet formats have been proposed, depending on what field of application the procedure will be applied. An example of such a worksheet can be found in Table 1.5.

Table 1.5 – Example FMECA worksheet.

Component	**Failure mode**	**Failure rate**	**Causal factors**	**Immediate effect**	**System effect**	**RPN**	**Method of detection**

Depending on the specific worksheet, different information is collected or estimated for each single element of the system. This includes possible failure modes, causal factors, immediate effects and effects on the whole. Once the hazard scenarios are collected, the risks are evaluated. The prioritization of the risks can be done using the Risk Priority Number (RPN), which is a multiplication of the risk dimension values (Severity, Occurrence and Detection). This value however, is more suited for reliability analyses than system safety and has certain limitations (see Chapter 2.4.2). Another way of expressing the system's failure probability in this approach is the failure rate of an element. As a last step, possible corrective measures are suggested.

Advantages and disadvantages The FMECA approach is easily understood and inexpensive to perform; nevertheless, it can lead to meaningful results. It can predict the reliability of the analyzed item by focussing on the different system elements and their influence on the system itself. Due to the simplicity, various software applications that allow FMECA analysis exist. Like many other risk analysis techniques, FMECA declines to analyze a combination of failures. Additionally, hazards that are not related to failure modes are not detected. Since human errors and other external influences are not considered as failure modes, all hazards

resulting form those influences are not considered either. Even though the procedure itself can easily be learned, it requires a certain expertise about the system to be analyzed.

Table 1.6 – Advantages and disadvantages of FMECA (from Ericson [2005], p.255).

Advantages	Disadvantages
Easily understood and performed	Focuses on single failure rather than failure mode combinations
Inexpensive to perform, yet provides meaningful results	Not designed to identify hazards unrelated to failure modes
Provides rigor for focusing the analysis	Provides limited examination of human error
Provides a reliability prediction of the item being analyzed	Provides limited examination of external influences and interfaces
Commercial software available	Requires expertise on the product or process under analysis

Application at the research environment As the HAZOP procedure, the FMECA would fit the academic environment due to the ease of use and the low complexity of the process itself, while still producing meaningful results. Additionally, the semi-quantitative character could be applied in a beneficial way in this environment, since statistical data about accidents or reliability data are only hardly available for this setting. Even though the approach is not complex, the requirements are relatively high in terms of time and expertise, which would make an application in research laboratories difficult. Furthermore, the FMECA approach is not designed to identify hazards unrelated to failure modes, human error, and external influences. Human errors however are an important source for accidents in research laboratories. Other than clearly defined processes, scientific research is often connected to experimental equipment, unknown processes and other unknown variables.

1.3.4 Fault Tree Analysis (FTA)

Overview The Fault Tree Analysis (FTA) approach was developed by Bell Laboratories for use on the Minuteman Guidance System (intercontinental ballistic missile) [Ericson, 2005]. Boeing realized the potential of the FTA approach and applied it on the whole development of the Minutemen Weapon System. The technique was so successful in this application, that it spread to the non-military sector of Boeing and from there to various other fields of industry, such as the nuclear power industry.

Due to the quantitative aspect of the FTA approach, it is used mainly in industries, where reliability data is available and a high safety level must be achieved, e.g. nuclear power industry, aeronautical industry, chemical industry and military industry. The method itself does not

leave room for substantial changes, therefore the research done concerning FTA is either about applications [Park and Lee, 2009] or about enhancements [Doytchev and Szwillus, 2009]. A main characteristic of the approach is the need for quantitative data; for making the method accessible for less data-based applications, the use of Fuzzy Logic [Markowski et al., 2009] or semi-quantitative approaches [Hauptmanns, 2004] were suggested.

Table 1.7 – FTA specifications.

Requirements		**Approach**	
Data	High	*Form*	Quantitative
Difficulty	Moderate	*Level of detail*	Moderate to in-depth
Complexity	High	*Direction*	Deductive
Expertise	System (high level)	*Focus*	Events
Time	Very high	*Phase*	System design

Table 1.7 gives an overview of the main characteristics of the FTA approach. A main attribute is the quantitative part of the approach. This requires a high amount of data and system expertise, and is therefore able to provide an in-depth analysis of the system. Another crucial element of the FTA approach is the focussing on events, rather than components or functions. It is usually applied in the system design phase.

Principles As a first step for the FTA procedure, an undesired top event is defined. In a treelike structure, events that can lead to this top event are defined and linked via Boolean logic (e.g. AND, OR, etc.). In the same manner, these events are explained via sub-events, until a basic level of events is reached. For each basic event, a probability value is assigned and the probabilities of every event in the tree are calculated. In a next step cut sets are defined. Cut sets are combinations of independent basic events, which might lead to the undesired top event. This is the main delivery of the FTA procedure: by knowing the cut sets, an analyst has a good overview about possible failure paths, can detect weak elements in the system and can apply corrective measures. In Figure 1.5, a short example of a FTA is given.

Advantages and disadvantages The FTA procedure has numerous advantages and is therefore a very solid and widely used method for risk analysis. The approach itself is methodical, rigorous, structured, and can be learned relatively easily. Even though having clear structures, the technique allows to perform analysis on various levels of processes and systems. Another advantage is the visual presentation of the results, which allows to model complex relationships in an understandable manner. The technique is not limited to process boundaries; therefore, it supports to factor in human errors and other influences. Additionally, it is scientifically sound, since it is based on widely applied mathematical approaches, such as Boolean algebra and probability theory. On the other hand, the method can easily be-

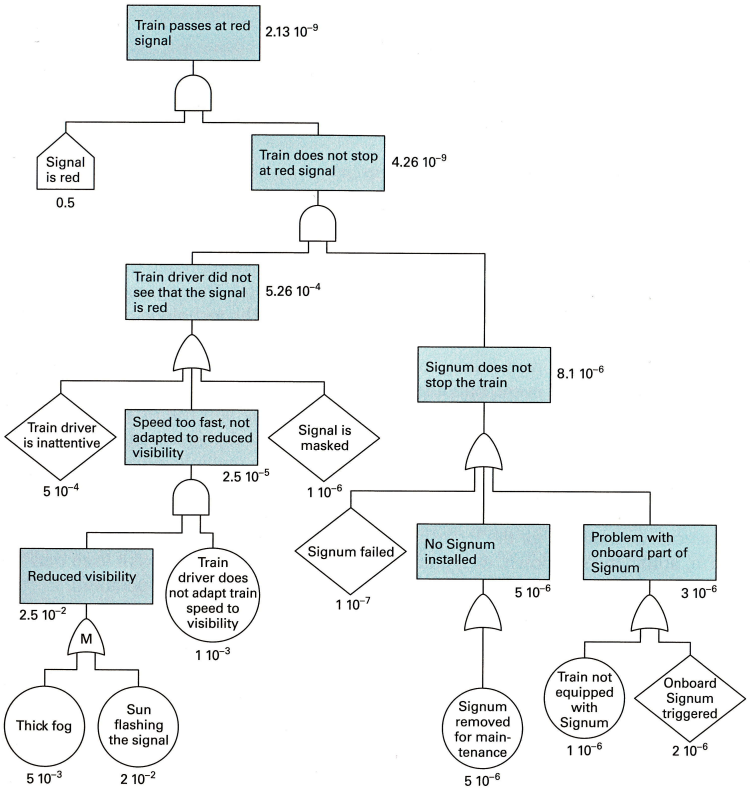


Figure 1.5 – Example of a FTA tree including probability calculations (from Meyer and Reniers [2013], Fig. 4.22, p. 125).

come time consuming and rather the goal than the tool. Additionally, it requires training and practical experiences to perform the analysis.

Application at the research environment A main reason to apply FTA to the research environment is its focus on events and the possibility to include hardware, software, environment and human interactions. Another benefit of the method is the clear and rigorous structure of the approach, which would facilitate an adoption into academic safety framework. On the other hand, the method demands resources, which are usually not available in this environment. The amount of data which is required does not fit the provided information for this setting. Furthermore, causal event paths might not be obvious in laboratories, which makes it hard to generate a fault tree diagram.

1.3.5 Event Tree Analysis (ETA)

Overview The Event Tree Analysis (ETA) most probably originates from the nuclear power industry as a side product of a complex FTA analysis [Ericson, 2005]. This analysis became too cumbersome and the new ETA approach was established to lower the level of complexity.

Table 1.8 – Advantages and disadvantages of FTA (shortened version of Ericson [2005], p.219).

Advantages	Disadvantages
Structured, rigorous and methodical approach	Can easily become time consuming
Can be effectively performed on varying levels of design detail	Can become the goal rather than the tool
Visual model displays cause - effect relationship	Modeling sequential timing and repair is more difficult
Relatively easy to learn, do and follow	Modeling multiple phases is more difficult
Models complex system relationships in an understandable manner	Requires an analyst with some training and practical experience
Combines hardware, software, environment, and human interactions	
Scientifically sound: based on probability theory and Boolean algebra	

Therefore, the ETA approach is often coupled with the FTA approach, also called bow tie approach.

Due to the relation to the FTA approach, ETA is used in similar industries: for example nuclear power industry, aeronautical industry, chemical industry and military industry. ETA in general has applications in fields, where consequence modeling or corrective measure design is of high importance. As FTA, the method does not leave room for substantial changes. As for many other quantitative risk assessment techniques, the research is aiming to make the approach accessible to applications with fewer available data, e.g. with uncertainty improvements and the use of Fuzzy Logic [You and Tonon, 2012; Ferdous et al., 2011].

Table 1.9 – ETA specifications.

Requirements		Approach	
Data	High	*Form*	Quantitative
Difficulty	Moderate	*Level of detail*	Moderate to in-depth
Complexity	Moderate	*Direction*	Inductive
Expertise	Technique (high level)	*Focus*	Consequences
Time	Moderate	*Phase*	Detailed design

Table 1.9 shows the main attributes of the ETA approach. The technique uses an inductive approach and focuses on consequences of events. As FTA, ETA provides a high flexibility concerning the level of detail. However, the method requires a high level of expertise and a

high amount of data, due to the quantitative estimation of consequence probability.

Principles The ETA approach starts at the point, where a FTA ends: the undesired event. In a binary mode, possible consequences of this event and further consequences are determined. After the initiating event is defined, pivotal events are identified (see Figure 1.6). Those pivotal events are often related to safety barriers and describe function or disfunction of them. In this manner, the event tree is built and probabilities for the pivotal events are determined. When knowing all the scenarios, the possible outcomes are judged according to their probability and their severity in oder to estimate the risk. Based on this evaluation, possible improvements of the safety barriers are suggested and the process is documented.

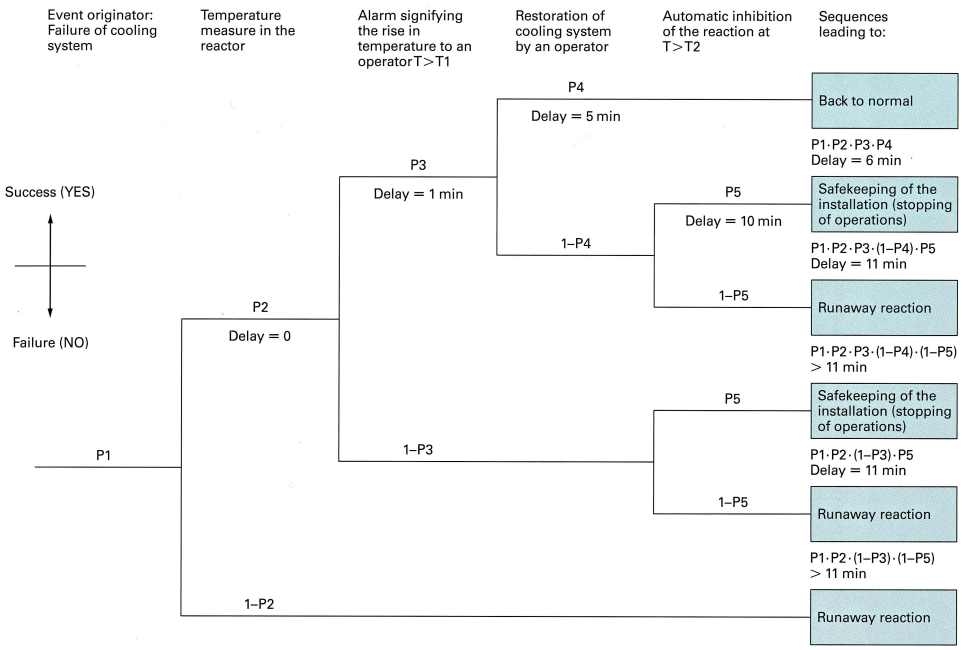


Figure 1.6 – Example of an ETA tree (from Meyer and Reniers [2013], Fig. 4.23, p. 128).

Advantages and disadvantages The FTA procedure shares many advantages with the related ETA approach: a logical, structured approach that is able to display cause and effect relationships. Like FTA, it is relatively easy to learn and understand, but requires a certain amount of experience to be applied. It provides a solid probability assessment and is able to combine hardware, software, environment and human interactions. On the other hand, it models only single events, which makes it impossible to evaluate consequences that originate from a combination of events.

Application at the research environment The ETA technique has the same benefits for the research setting as the related FTA approach: it is a highly structured approach, relatively

Table 1.10 – Advantages and disadvantages of ETA (shortened version of Ericson [2005], p.233).

Advantages	Disadvantages
Structured, rigorous and methodical approach	Unable to model multiple, dependent events
Can be effectively performed on varying levels of design detail	Possible overlook of system dependencies
Visual model displays cause - effect relationship	Partial successes/failures are not distinguishable
Relatively easy to learn, do and follow	Requires an analyst with some training and practical experience
Models complex system relationships in an understandable manner	
Combines hardware, software, environment, and human interactions	
Permits probability assessment	

easy to perform and learn and able to factor in human interactions into the analysis. Other than the FTA it is less complex and the requirements are lower, which would suit the provided resources at universities. Additionally, the focus on consequences and on safety barriers could bring advantages in this result-oriented environment. However, other characteristics makes the method less suited for research laboratories, such as the quantitative risk estimation or the fact that is not possible to model dependent events.

1.3.6 Job Safety Analysis (JSA)

Overview Job Safety Analysis (JSA), which is also known as Job Hazard Analysis (JHA), is a simple risk assessment technique originating from the construction industry [Rozenfeld et al., 2010]. It is widely used in fields where tasks are standardized and influence factors are limited, such as construction industry or the steel industry. The simplicity of the method makes it hardly applicable to complex systems and therefore only few enhancements exist. Checklist based risk assessment approaches are closely related to this approach.

An overview of the characteristics is given in Table 1.11. Due to the low level of detail provided by the analysis, the complexity is kept low and the requirements in general are limited as well. However, the method does require a certain amount of knowledge of the studied system. The focus is very variable and not limited to a certain systematic approach. It is usually applied in the operation phase.

Principles The main idea of the JSA approach is to use existing procedures to assign hazards to a specific job. It is important to develop a complete job portfolio and not only focus on

Table 1.11 – JSA specifications.

Requirements		Approach	
Data	Low to moderate	*Form*	Qualitative
Difficulty	Low	*Level of detail*	Low
Complexity	Low	*Direction*	Deductive
Expertise	System (moderate)	*Focus*	Variable
Time	Low	*Phase*	Operation

single activities. This includes peripheral activities related to a job, such as maintenance, interruptions, planing and other related tasks. As a first step, different resources are consulted to list all activities, equipment and materials related to a job. These resources are for example Standard Operating Procedure (SOP), worker information, accident data, and insurance information. Once all the components are defined, possible hazards are found using a brainstorming procedure with certain questions (e.g. “Can special deviations occur caused by this type of equipment?"). The hazards are then analyzed, the risks evaluated and possible corrective measures are suggested.

Advantages and disadvantages The main advantage of the JSA is the simplicity of the approach. Therefore it is inexpensive to perform, but still provides valuable information gathered from different influences. The method highly relies on experience. On one side, this can be an advantage, since it is able to focus on more important aspects of safety. On the other hand, this might be a disadvantage as well: it could happen, that the analysis brings no new information and it is only done to achieve an illusion of safety.

Table 1.12 – Advantages and disadvantages of JSA [Harms-Ringdahl, 2003].

Advantages	Disadvantages
Easily understood and performed	No systematic approach to identify hazards
Inexpensive to perform	Possible that it provides no new information
Based on experience	
Inclusion of various influences	

Application at the research environment Other than the other methods presented in this section, the JSA approach fits the available resources of the academic research environment: it is easily understood and learned, inexpensive to perform and not time consuming. Furthermore, it is very flexible concerning the included variables, which would fit the experimental nature of most processes. On the other hand, the lack of systematics and the fact that it is

based on experience could make an application cumbersome. A qualitative approach might not be enough for the complexity of the risks which scientist are facing in the laboratories.

1.4 Methodological Overview

The selected and discussed approaches differ significantly in how they assess risks. In order to characterize the methods, the following dimensions are used: inputs (requirements) and outputs (results). These inputs and outputs are depending on and affecting each other. A method which requires more data and is more difficult to perform usually leads to a more detailed analysis; however, a linear relation between these dimensions cannot be established.

They way the approaches deal with the data makes them more or less favorable for a specific area of application application. In order to evaluate which characteristics suits the academic research environment, the different aspects of the inputs and outputs are discussed in detail in this chapter. As a conclusion, the requirements for a risk assessment technique for research and teaching laboratories are postulated.

1.4.1 Inputs

The first part of the methodological analysis deals with the input of a method. The requirements differ significantly and define if the method is suited for a specific environment. Table 1.13 gives an overview of the requirements of the presented methods. The requirements are interdependent and overlap to some extent.

Table 1.13 – Different risk assessment approaches compared based on their resource requirement.

Method	Data	Difficulty	Complexity	Expertise	Time
HAZOP	Moderate	Low	High	System/technique	High
FMECA	Moderate	Moderate	Moderate	System (high level)	High
FTA	High	Moderate	High	System (high level)	Very High
ETA	High	Moderate	Moderate	Technique (high level)	Moderate
JSA	Low/moderate	Low	Low	System (moderate)	Low

A first type of requirements is the information necessary for an analysis. Each method requires information about the process (data, expertise): for example workflows, SOP, accident data, or schemes of systems. Some methods require more information, such as the FTA or the ETA approach, others require less, such as the JSA. The academic research environment does not provide a high amount of data due to its specificities, such as the experimental state of the equipment and the use of not completely investigated technologies. For this reason, approaches such as FTA and ETA are not suitable for this environment a less information demanding technique should be used.

A second type of requirements includes the qualification of an analyst performing the assessments (difficulty, complexity and expertise). Even if a method is easy to learn and to perform, it might require a certain amount of experience to detect the most of the possible hazards. An example of this kind of approaches is the HAZOP technique: the combination of system

parameters and key words is easy to execute, but it needs experience to estimate the impact on a system. Usually, the safety related issues in a laboratory are done by scientists as side tasks. Therefore, training of complex and difficult methods is not realistic in this environment and a high level of experience in a method is most likely not obtainable by an individual scientist. A suitable method should be simple to learn and to perform, while not needing too much experience in performing the method.

A last type of requirements indicates how much time an analysis needs in order to be performed. Most presented techniques require a high amount of time. An estimation of time required for a single analysis for these methods can be found in Table 1.14 [Harms-Ringdahl, 2003]. For an industrial process, it might be appropriate to use several weeks for a risk assessment, since the process is most likely to be operated for years. In scientific research laboratories however, processes underlie rapid developments and are constantly changing their scopes. Therefore, a risk assessment method for this environment should be performable in a reasonable amount of time.

Table 1.14 – Different risk assessment methods, their time and their information requirements [Harms-Ringdahl, 2003].

Method	**Time for analysis** (rough indication)	**Information needed**
HAZOP	1-2w	Detailed
FMECA	1d-2w	Detailed
FTA	1d-4w	Detailed
ETA	4d-2w	Detailed
JSA	2h-2d	Moderate

1.4.2 Outputs

The second part of the methodological analysis deals with the output of a method. This includes not only the result of a method but also the way how they identify the hazards and assess the risks. A first characteristic is the direction of an analysis: approaches are either performed in a inductive or in a deductive way. Inductive methods begin with an initiating event and evaluate possible consequences of this event. On the contrary, deductive approaches start with an undesired event and detect possible causes leading to it. For the academic research setting, an deductive method could be more advantageous, since consequences might be difficult to determine in this environment. On the other hand, inductive methods facilitate the application of corrective measures. The most favorable solution is a hybrid-method, combining both inductive and deductive approaches.

Quantitative aspects are not only related to the inputs of an approach but also to the outputs. They are interdependent and quantitative results cannot be achieved with qualitative inputs only. A method such as the FTA approach can be applied without quantitative data; it still

shows causal relationships between events, but loses the main advantage of delivering accident probabilities. For the academic research settings, quantitative data (e.g. reliability studies) is often not available. A method for risk assessment should therefore focus on less quantitative aspects in order to avoid a lack of data. An ideal compromise is the use of a semi-quantitative approach, like the FMECA method is using.

The level of detail and the focus of an assessment are the last aspects related to the results of a technique. The focus defines how the system is divided into its different elements and has a high impact on what is identified and how this is done. In terms of hazard identification, the focus of an approach is the most important aspect, since it determines the yield of identified hazards. Techniques which are too inflexible about their focus can overlook existing hazards. HAZOP for example is not able to identify hazards outside of the defined system. Such functional deviations are difficult to determine for research laboratories, since functions are often not clearly defined for experimental processes. On the other hand, approaches with no systematic hazard identification are often experience driven, such as the JSA approach, and tend to overlook hazards as well. An optimal hazard identification process for the research setting is structured, but flexible, such as the hazard identification approach of FMECA. The level of detail is affected by the choice of focus and depends on the available information of a system.

Table 1.15 – Different risk assessment approaches compared based on their technical specifications.

Method	Form	Level of detail	Direction	Focus	Phase
HAZOP	Qualitative	Moderate	Inductive	Deviations	Design
FMECA	Semi-quantitative	In-depth	Inductive	Variable	Design
FTA	Quantitative	Mod./in-depth	Deductive	Events	Design
ETA	Quantitative	Mod./in-depth	Inductive	Consequences	Design
JSA	Qualitative	Low	Deductive	Variable	Operation

1.4.3 Requirements of the Research Environment

None of the presented methods can be directly applied to the academic research environment without limitations. Most of them have characteristics which would fit to this environment, but each of them has drawbacks which makes an application hardly possible. Table 1.16 gives an overview of the most important advantages and disadvantages of the presented methods for the use in the research setting. The HAZOP approach has the advantage of having a structured and systematical approach, while not being complicated to learn and to apply. The method however can become very resource demanding: a trained and experienced expert is necessary as well as a relatively high amount of time per process. The structured FMECA approach uses a semi-quantitative scale for risk estimation, which would suit the lack of data in this environment. Unfortunately, the approach focusses on failure modes and single events and is therefore not suitable, since failure modes can be hardly determinable for experimental

equipment. Both FTA and ETA visualize complex relationships and focus on events rather than components or functions. Nevertheless, both methods demand a high amount of resources and are not capable of model dependent events, which is crucial for a risk assessment in the research environment. Concerning the demands of resources, the JSA approach suits this environment best: it is easy to learn, to apply, and flexible about the focus of the analysis. However, the method is not very profound and the analysis might lack the required level of detail.

Table 1.16 – Advantages and disadvantages of the presented risk assessment techniques for the use in the research environment.

Method	**Advantages**	**Disadvantages**
HAZOP	Structured and easy to learn approach	Ressource demanding
FMECA	Semi-quantitative approach	Limited to failure modes
FTA	Visualizes complex relationships	Resource demanding
ETA	Consequence focussed	Unable to model dependent events
JSA	Flexible and easy approach	Superficial

In order to perform a risk assessment in the research environment, an adaption of an existing method or a development of a new method is necessary. As a deduction of the discussion in this chapter, the ideal specifications for such a method are represented in Table 1.17. However, these specifications are interdependent; a method usually requires a certain input for delivering a specific output. Those considerations influenc the specifications and should be acquirable by an appropriate method.

The method should be relatively undemanding in terms of resources. For most processes and pieces of equipment, statistical data only hardly exists due to their experimental disposition. Additionally, not all the effects on a system originating from these components are fully determined. The method should therefore deliver meaningful results while not requiring to much data. The demands for manpower should also be low, since experts are hardly available and most scientists are not experienced in performing risk assessments. Thus, the complexity of the the analysis should stay on a lower level; higher levels of complexity are usually time demanding and often linked to intensive analyses. The required expertise regarding the system however should be high enough to produce meaningful results, but low enough to fit the available system expertise in this setting. Scientific research often underlies rapid changes and is very flexible in terms of reorientation. Due to this, the risk assessment procedure should be performable in a reasonable amount of time.

The requirements define the results of a method; a quantitative approach is hardly possible with the amount of delivered data. A semi-quantitative approach is an ideal solution for this dilemma: delivering a sound base for decision making while not being too resource demanding. A high level of details is not absolutely necessary for this environment. Procedures and equipment can change constantly and the level of detail has to be kept low and focused on the most important components rather than going too much into detail. Since the procedures,

the equipment, and the material vary depending on the fields of research, the approach needs a certain flexibility in the focus. This affects the way how the processes are divided into their components: depending on the situation, the causal chain or the consequences of an event need to be modeled. Therefore, an ideal approach allows to adapt the focus and to perform an analysis in an inductive or a deductive way. Additionally, the technique should be effective when applied in the operation phase, since most processes in this setting are not examined in a design phase.

Table 1.17 – Ideal specifications of a risk assessment approach for the academic research environment.

Requirements		**Approach**	
Data	Low to moderate	*Form*	Semi-quantitative
Difficulty	Low	*Level of detail*	Moderate
Complexity	Low	*Direction*	Hybrid
Expertise	System (moderate)	*Focus*	Variable
Time	Low	*Phase*	Operation

1.5 Risk Management for the Research Environment

For the industrial sector, many risk management techniques have been presented, discussed and widely applied in different fields. For the academic research environment however, hardly any method has been suggested and none of them has gained wide acceptance. Universities as employers have legal obligations to take care of the health of their employees. In most cases, this is achieved by Occupational Safety and Health (OSH) services and by regulations matching the particular legislation of a country. As a development of these internal regulations, different impulses were presented in the literature to systematize safety intentions and to decrease the accident rates [Foster, 2004; Ferjencik and Jalovy, 2009]. Nevertheless, some impulses point in the direction of a systematic risk management approach for this environment. In the following section, these approaches are discussed and their feasibility according to the postulated specifications is assessed.

1.5.1 Hazard Identification Algorithm (HIA)

Specifications The method originates from the Ohio Coal Research Center and was presented by Kremer et al. [2009]. The authors locate a problematic combination in the fact, that there is a necessity for risk analysis due to newly developed processes and the absence of experience concerning common risk analysis techniques. The main motivation to develop this method was to give the scientists a simple tool to perform risk analyses without the need of being trained as safety specialists. The approach is developed for the field of chemical engineering.

The technique is a checklist-based algorithm, which guides the scientist through a set of questions. The scope of an evaluation is a new process and the hazards are assessed not as single hazards, but as a set of hazards. The questions are categorized into five categories based on Occupational Safety and Health Act (OSHA) guidelines, safety manuals, industry guidelines, and the existing operational experience:

1. Ergonomics and mechanical hazards
2. Physical hazards
3. Chemical hazards
4. Psychological and organizational hazards
5. Biological hazard

The questions are posed in a general way, such as “Is there any equipment that needs voltage greater than or equal to 120 Volts?" for the category physical hazards. The algorithm assigns values to the answers and they are weighted according to predefined prioritizations. The

mechanism of the algorithm is not visible to the researcher, but the weighting criteria can be changed according to the needs of a specific institution. The results show critical parts of a process and point out possible hazards.

Feasibility The approach fits mosts specifications of an ideal risk management technique for the research environment (1.18). The amount of data required is moderate, the expertise is limited to the systemic knowledge, and it does not require technical expertise. A scientist with basic safety knowledge should be able to perform the analysis in a reasonable amount of time. Additionally, the method delivers a semi-quantitative risk estimation with a reasonable level of detail. However, the hazard identification is based on regulations and experience in system safety. Since it is not a systematical approach and based on knowledge, unknown hazards are hard to determine. The method originates from chemical engineering and is therefore focused on the application in this field. It should be possible to extend it and apply it in other fields; this requires changes in the question set according to regulations and experience in these fields. Important factors, which are implemented in this approach are the psychological and organizational components. These can become crucial elements, indicating an important relation between safety culture and hazards.

Table 1.18 – HIA specifications.

Requirements		**Approach**	
Data	Low to moderate	*Form*	Semi-quantitative
Difficulty	Low	*Level of detail*	Moderate
Complexity	Low	*Direction*	-
Expertise	System (moderate)	*Focus*	Hazardous properties
Time	Low	*Phase*	Operation

1.5.2 Lab-HIRA

Specifications The Lab-HIRA method was presented by Leggett [2012] as a method for risk management in chemical research laboratories. The main procedure consist of three step: a preliminary hazard analysis called Chemical Hazard Review (CHR), an optional formal risk review based on the identified hazards, and the development and execution of risk mitigation measures.

The CHR is a characterization sheet based on properties of the chemicals and the synthesis involved. As a first part, the physical properties of each single chemical involved are determined, such as boiling point, legal exposure limits, toxicology information, or the autoignition temperature. A second part characterizes potentially hazardous conditions related to the synthesis. This includes not only physical conditions but also other aspects, such as formation of

hazardous functional groups, which are known to lead to an increased instability of a molecule. According to the information provided in this part, hazardous elements are determined and thus a basic risk assessment is achieved.

The second step of the approach is an optional formal risk review. This is only recommended for hazardous elements from the CHR step, which fall into a predefined risk category *unacceptable*. Lab-HIRA suggest checklist-based methods or HAZOP to do an in-depth analysis of these elements. The last step of the process is the development of corrective measures, which are based on the results of the simplified or the enhanced risk assessment.

Feasibility The Lab-HIRA approach has higher requirements than the ones postulated as ideal for the research setting (Table 1.19). The requirements for the analyst are moderate, even though the expertise mainly focuses on system knowledge and expertise in the field of chemistry. The data however is a crucial element of this approach. For basic chemicals data is widely available, but for intermediate steps of chemical reactions, this data can only be estimated very roughly. An advantageous characteristic of this approach is the preliminary hazard analysis which draws attention to potentially more hazardous elements of the system. A more in-depth risk assessment can evaluate the risks of these elements. The main drawback of the method is the fact, that it is only focused on and specifically made for laboratory scale chemical syntheses.

Table 1.19 – Lab-HIRA specifications.

Requirements		**Approach**	
Data	Moderate to high	*Form*	Qualitative
Difficulty	Moderate	*Level of detail*	Moderate
Complexity	Moderate	*Direction*	Deductive
Expertise	System (moderate)	*Focus*	Hazardous properties
Time	Moderate	*Phase*	Operation

1.5.3 Guidelines by the American Chemical Society (ACS)

Specifications The most extensive risk management program for research laboratories was published by the American Chemical Society [2013] with the title “Identifying and evaluating hazards in research laboratories". The U.S. Chemical Safety and Hazard Investigation Board, also known as the Chemical Safety Board (CSB) realized the need for an improved risk assessment in research laboratories due to several severe accidents at universities. They asked the American Chemical Society (ACS) for assistance with developing guidance that would address this gap. Several factors were considered for this guide, such as follows:

- To provide techniques to ensure hazard information is gathered and analyzed.
- To aid researchers in recognizing the value of input from others with varying experiences.
- To provide techniques that can be used for a variety of different types of activities.
- To allow for the variable nature of research tasks by providing tools that help researcher to recognize and response to change - both large and small.

The approach covers the whole risk management process, including the definition of roles and responsibilities. It also shows the importance of change management in this environment, since change can be a possible source of hazards. As risk assessment technique, the approach gives a choice of several methods, which should be applied according to the situation in a laboratory. The risk assessment methods presented are:

- Control banding: a systematic, qualitative approach which is banding together hazards and treats them as type of hazards. Chemical safety levels are defined and treated according to their hazard level. An advantage of this method is the structure which guides the scientist through the analysis. On the other hand, unknown hazards are hardly identified with this technique.
- JSA: see subsection 1.3.6.
- What-if analysis: a question-based approach, which guides the risk assessment via intuitive answering of possible “what-if" questions. To apply some structure to this approach, a set of questions is provided by the ACS guidelines. The advantage of this method is the ease of use, while still providing meaningful results for the risk assessment.
- HAZOP: see subsection 1.3.2.
- Checklists: this kind of approach is related to the use of informational job aids called checklists. The advantage is the ease of use, due to the simple concept of the approach. On the other hand, the approach highly depends on the quality of the checklists.

The guide gives various templates for risk assessment for these methods, but leaves the decision, which method to use, to the analyst.

Feasibility The characterization of this method cannot be done in analog way like the other techniques, since the requirements and the results differ depending on which method is applied. The risk management from ACS is rather a guidance than a specific risk management approach. On one hand, this helps the scientist to implement a specific risk assessment technique according to his needs and gives an overview about the available methods. On the other hand, the application of industrial risk assessment approaches does not lead to satisfying results and does not regard the specificities of the research environment.

Table 1.20 – ACS guidelines specifications.

Requirements		**Approach**	
Data	Moderate	*Form*	Variable
Difficulty	Moderate	*Level of detail*	Variable
Complexity	Moderate	*Direction*	Variable
Expertise	Technique and system	*Focus*	Variable
Time	Moderate	*Phase*	Variable

1.5.4 Conclusions

The risk management techniques differ significantly not only in their approach but also in their scope. Most techniques focus on a specific field and leave most of the other fields of academic research unstudied. For the specific field, the methods might work depending on the available data; however, other fields of the academic research setting are hardly analyzable by the presented methods. A holistic risk management technique for the research environment should include all type of laboratories. This is of high importance for the resource allocation: only if results are comparable, the most important risk of an institution can be evaluated and the budget can be distributed in an optimal way. Nevertheless, the methods presented in this section feature important developments which allow the use in this environment. One example for these development is the use of checklist-like structures for hazard identification and structuring of the processes. However, a further development is necessary to allow the identification of unknown hazards.

The existing techniques do not fit the postulated requirements for the research setting. As a consequence, a holistic risk management method was developed within the framework of this PhD thesis. This method aims to meet the postulated specifications and includes the most important features of the methods presented in this chapter.

2 LARA - Laboratory Assessment and Risk Analysis

In the previous chapter, the necessity of a risk management technique for the research environment was explained and the ideal characteristics of such a method were postulated. A possible solution to fill this gap is the LARA approach. In this chapter, the LARA method will be explained in detail, including main mechanisms, the cornerstones, and development history. Supporting information about the method can be found in Appendix B.

2.1 Introduction

Part of the setting for safety management in the research environment is a lack of resources for safety related issues, no adequate risk management technique, missing statistical data, and a specific situation, unlike the one in most industries. This specific situation arises from various influences, which are typical for this environment: constantly evolving processes, equipment in experimental states, quick changes in research orientation, but also human factors, such as rapid personnel turnover or a multitude of cultural backgrounds. Furthermore, universities are not organized like a company in the industry, but rather a conglomerate of micro-companies; the research groups are not sharing similar objectives and the responsibilities are often not organized on a mutual base. These organizational peculiarities can make safety efforts cumbersome and less effective. Due to this, a comparison of safety standards and risks in this environment is complicated and often unsuccessful. To provide a tool for risk management for universities, the LARA method was initiated and developed. The main goals of this method are:

- Provide a risk management technique for all types of academic research laboratories.
- Allow a less resource demanding risk management, to fit the provided resources of the research environment.
- Development of a software application, allowing user-friendly and intuitive risk analysis.
- Consideration of the particular setting of the academic research environment.

In order to achieve these goals, existing risk management techniques were analyzed and detailed characteristics for this risk assessment approach were elaborated (see Chapter 1). The method needs to provide relatively moderate requirements, since data and manpower are not abound in this environment. Additionally, the provided features should involve flexibility in level of details and the focus of the analysis.

A fundament for this method was elaborated in previous PhD studies [Ouédraogo, 2011c; Ouédraogo et al., 2011a,b]. Since the original calculation method was biased from uncertain expert judgments, a calculation method based on Bayesian networks was introduced and tested with various examples [Pluess et al., 2013]. Additionally, the resource allocation was enhanced using a more flexible approach, which is independent from financial considerations and includes the feasibility of measures [Pluess et al., 2014a]. Furthermore, the LARA method was tested at different universities in comparison with established risk management techniques [Plu].

The LARA method orientates on the general risk management approach presented in the previous chapter (Section 1.2). An overview of the workflow is given in Figure 2.1 and every step will be explained in detail in this chapter. To illustrate the workflow, a step-by-step demonstration with a brief example is given in Chapter 3.1.

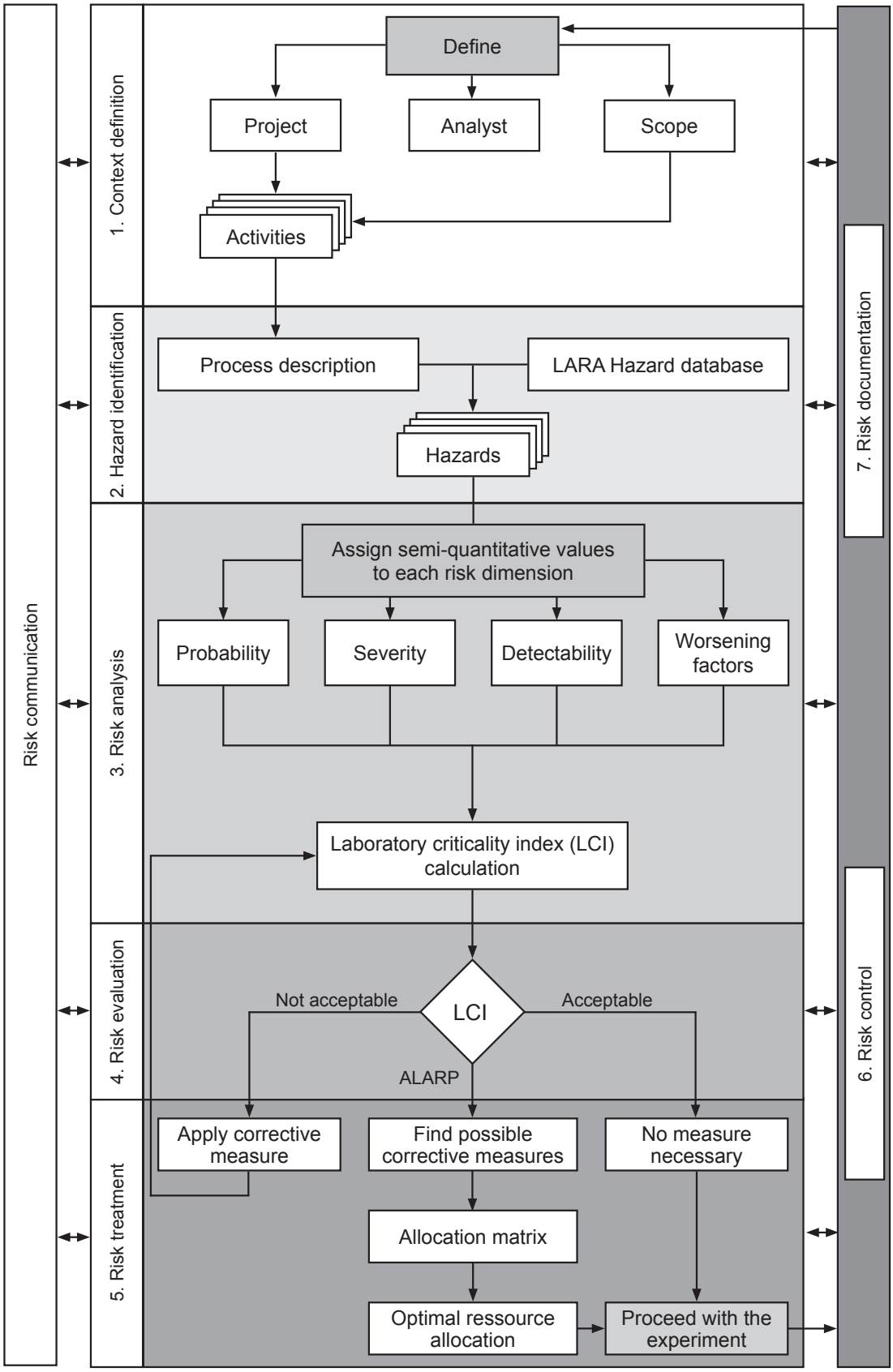


Figure 2.1 – The detailed workflow of the LARA method.

2.2 Definition of the Context

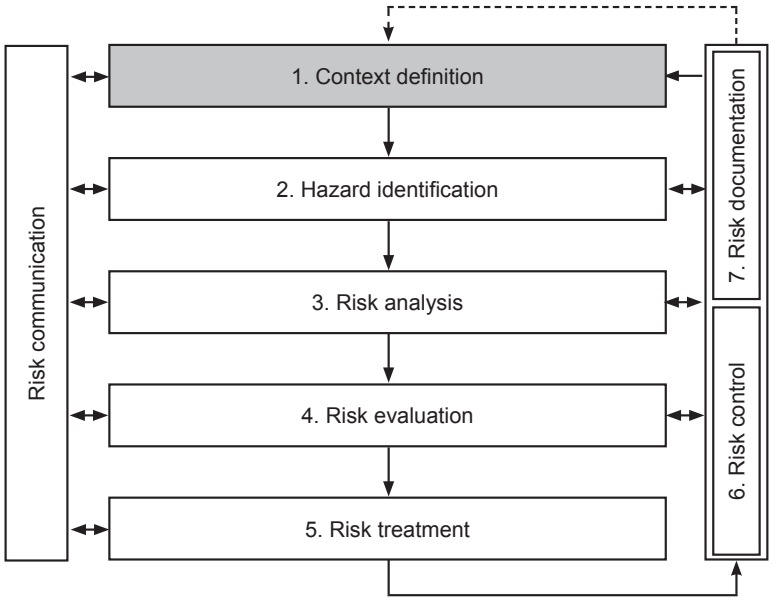


Figure 2.2 – Condensed LARA workflow: definition of the context.

As a first step of the risk management workflow, the context on several levels needs to be established (Figure 2.2). External and internal influences, organizational details, and technical parameters define a risk management method in different degrees. The broader context defines the goals and the cornerstones of the risk management approach. Microscopic details (material, equipment, techniques, etc.) influence a specific situation and need to taken into account for the risk assessment approach. However, the boarders between the influences are blurred lines; external, macroscopic influences are able to change the details of an approach in a similar way as the microscopic fact can change the basic structure of a method. An ideal risk management method leaves room for these changes, while having clearly defined structures, which are necessary for to objective and rigorous results. In this section, different aspects of the context having an influence on the risk management approach LARA is explained in detail.

2.2.1 Macroscopic Context

The broader context provides the base for the LARA method and defines the goals of the method. Cultural and moral conceptions aim to avoid loss, especially in the form of human lives. Manifestations of these conceptions are for example regulations related to occupational health and safety, which are a main influence. Stakeholders' expectations (internal and external) are influencing a risk management method and determine what is considered as possible loss. Not only human beings can be affected by unwanted events, other values are targets for possible impacts as well: reputation, funding, recruitment, and others. The peculiarities in this environment originate from the broader context and are an important

factor for the development of LARA. This context defines the goals for the development of LARA, the ideal specifications of such a method and technical details, for example what dimensions are important to consider when analyzing a risk.

2.2.2 Organizational Context

The organizational setting is a second kind of context that influences a risk management method. Other than the broader context, which influences the basic mechanism of a method, this context influences organizational details, the roles and responsibilities. An existing safety framework is an important surrounding for a risk management technique as LARA. At most universities, an occupational health and safety service defines the safety rules at the laboratories based on legal regulations, gives safety courses, provides support in technical questions, and controls all laboratories on regular bases. These existing structures can be used in a beneficial way for the LARA procedure. For risk management, clear responsibilities and information flow are crucial for a successful application; due to this LARA is implemented in this existing framework and uses the responsibilities provided by it. Following roles and responsibilities are defined and used in the LARA framework (see Figure 2.3):

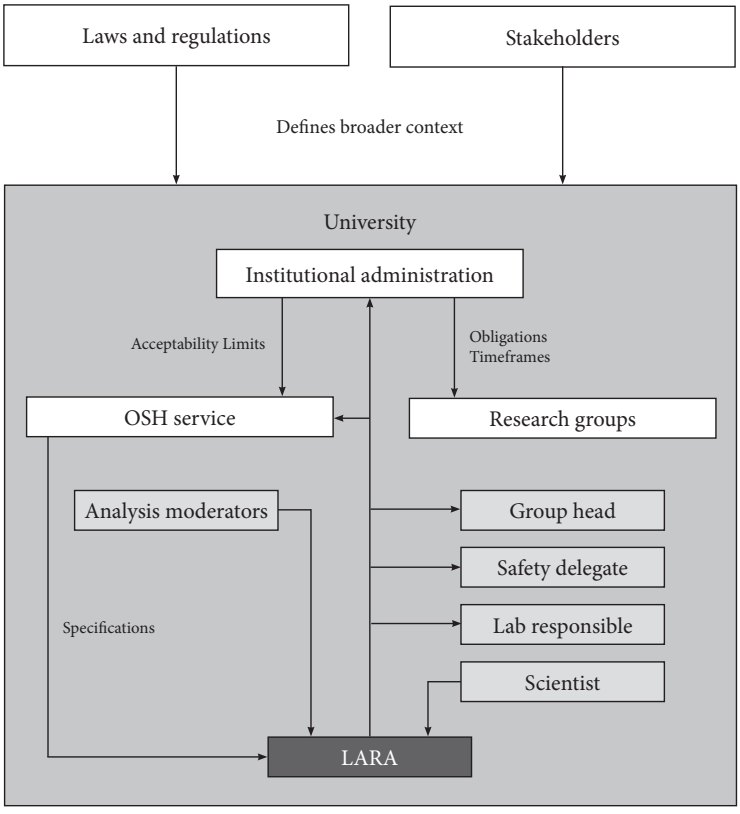


Figure 2.3 – Schematic overview of the roles and responsibilities in the LARA framework.

Institutional Administration

The institutional administration is the main authority and appoints most parts of the organizational framework. The willingness of the this role is crucial to set a functioning safety framework and risk management approach into place and helps to provide a culture of self-critique in this context. It sets the obligations for the involved roles, validates regulations, defines timeframes for risk management cycles and the levels of acceptability. The results of the risk evaluations are reported to the administration for informational purposes.

Occupational Safety and Health Service

Besides of the normal tasks of this service, the support and maintenance of LARA is part of this service. This includes keeping the databases up-to-date, giving instructions in using LARA, and adjusting details for optimal performance of the risk management. The service also practically implements obligations, regulations and timeframes from the institutional administration; schedules for evaluations and revisions are settled in collaboration with the research groups. Furthermore, the service keeps track about the risk evaluations, assesses the progress periodically, and is responsible for the information flow in the system. As a part of this service, the analysis moderators help users to understand the main principles of LARA and assist them in doing analyses, when help is needed.

Research Groups

Different roles and responsibilities are present in a research group. At the top of the hierarchy, the research group head receives the obligations from the institutional administration and implements them into the structures of the research group; he appoints safety delegates and laboratory responsible. He is responsible that the regulations are met and receives risk evaluations for processes performed in the group. The safety delegate is the direct contact person for the OSH and keeps track about the existing and upcoming projects in the different laboratories. In collaboration with the OSH service, analyses are scheduled and discussed in case of irregularities. The last role considered in a research group is the scientist performing the processes, which makes him the main risk owner in this system. After an introduction in the use of LARA, he is considered to perform regular risk assessments for his project. The change management is an important factor; changes in the system should be overviewed and the risks analyzed accordingly.

2.2.3 Technical Context

Technical context defines the details of LARA, mainly found in the risk assessment. A variety of different elements can be counted to this context: materials, procedures, infrastructure, and many others. These elements are represented in the databases used in LARA for classifying the hazards, possible corrective measures and worsening factors, but also in the risk factors and

other elements of the risk assessment (see further Sections of this Chapter for more details). A crucial part of the technical context is the definition of the studied subject. In LARA, a project is the object of an evaluation (see Figure 2.4). The different activities of a project are analyzed separately. In practice, a certain flexibility in the definition of these terms is intended in LARA to fit as many different scenarios as possible.

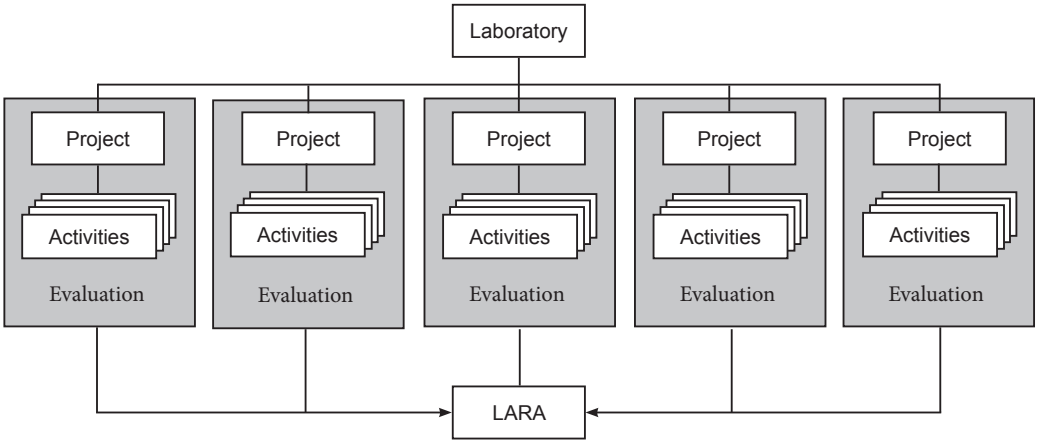


Figure 2.4 – Overview of the relationship between project, activity and evaluation in LARA.

1. Definition of the context	
Intention	**Example (as in Chapter 3.1)**
• Selection of the *process*	• Synthesis of ethyl-(E)-3-(3-nitrophenyl) acrylate
• *Context description*	• *Analysis moderator*: David Pluess • *Lab responsible*: Niklaus Hostettler • *Date*: 11.12.2014 • *Organization unit*: EPFL GSCP
• Selection of *General worsening factors* (see Chapter 2.4)	• Missing safety training • Blocked emergency exits • Missing safety awareness • Responsibilities unclear • Overloaded fume hoods → General worsening factors: 2

Figure 2.5 – An illustrative example of the steps performed in the LARA workflow. A more detailed explanation of this example can be found in Chapter 3.1.

2.3 Hazard Identification

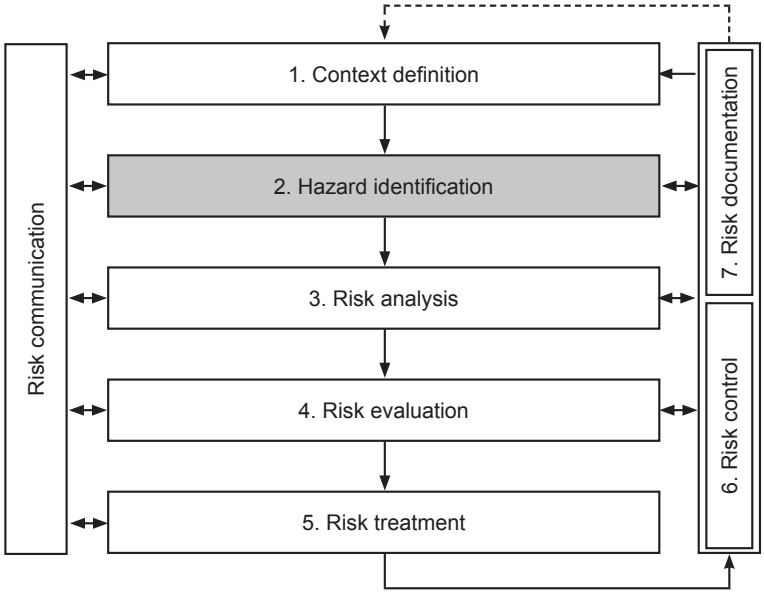


Figure 2.6 – Condensed LARA workflow: hazard identification.

The second step of the LARA workflow aims to identify possible hazards (Figure 2.6). Besides an exposed target, hazards are *a condition that is prerequisite for a risk* (see the hazard definition in Chapter 1.1). A main factor that is influencing the hazard identification is focus of an analysis. Based on the methodological overview in Chapter 1.4, following types three types of focuses can be classified:

Characteristics

The characteristics of the involved entities and activities can generate hazards. For objects, such properties are mostly physical attributes (e.g. flammability, weight for materials, etc.). For activities however, the hazard is located in the characteristic of it (e.g. jumping can lead to falling). A crucial part of the focus on characteristics is the decomposition of the process into the different elements and activities; a method that is aimed at the properties is JSA (see chapter 1.4). When hazards are assigned to the characteristics of elements and activities, their specific function in the process is not relevant. An example for this is the use of a flammable solvent in a chemical reaction: the use of it is due to the solvability, whereas the flammability is accepted, but not desired.

Function

A different point of view is the focus on functionalities of system elements. For most processes, deviations from the intended functionalities can lead to hazards. HAZOP (see chapter 1.4) is a

technique which analyzes the effects of deviations. In this technique, system parameters are matched with keywords, which are indicating a possible deviation (e.g. “pressure” and “more”). However, for performing analyses with this kind of focus a high level of system knowledge is required. Not only knowledge about functionalities of system elements are important, but also deviations of these functionalities need to be predicted, which is not always obvious.

Event

The last type of hazard analysis focus is aimed at events and their possible outcomes. The FTA and the related ETA technique are both techniques, which are applying this focus in the risk assessment. This point of view is not completely separated from the focus on characteristics or functions; for certain scenarios, the expected consequences are an extrapolation of characteristics in combination with functions in a system. Additionally, hazard in its basic meaning as a condition as prerequisite for a risk cannot be met without limitations: events are incorporating some concepts which are also related to risks (e.g. consequences).

2.3.1 Hazard Identification in LARA

The focus of the hazard identification in LARA needs to be coordinated with the studied activities and processes. A focus on the function is hardly applicable in the research environment: functions in experimental processes are not always determinable and experience is necessary to predict possible deviations. The same aspects also limits the possibility to focus on events and consequences. Moreover, human interactions and resulting errors are often difficult to foresee. A focus on characteristic of involved activities is less dependent of experience, determinable without personal interpretation and can be applied in this environment more easily than the other approaches.

A tool for analyzing characteristic and matching them with hazards is the checklist approach, which is used in the JSA procedure and proposed by ACS as one possible method for hazard identification (see Chapter1). The simplicity allows non-experienced users to perform hazard identification. However, checklists rely on efforts previously done by experienced analysts and is not applicable for all scenarios. In addition, the lacking flexibility does not match the requirements for the research setting. To improve this lack of flexibility, the checklist approach is enhanced with a database structure to act as a hazard identification tool in LARA. In this database approach, the determined attributes and characteristics of process elements are matched with known hazards (see Figure 2.7). In LARA, the user integration is an important factor; therefore, a suggestion of hazards and possible relations is possible and acts as constant enhancement of the hazard database.

For this system to work as intended, the database needs to be developed in a logical and comprehensible manner. Finding hazards and the resulting risks can be an intellectual game without limitations and even only remotely possible scenarios can be imagined. To keep the

hazard identification related to the actual tasks and procedures present in laboratories, the hazards in these are only related to materials, procedures, activities and equipment. Therefore, possible risks originate from characteristics (flammability, sharp edges, high temperature), whereas Indirect effects, such as social and psychological hazards are left out in the hazard database. However, since they can have a important impact on the risk level and on other hazards, they are integrated as worsening factors (see Chapter 2.4).

A hazard characterization system is developed on following main classes of hazards: biological hazards, chemical hazards, physical hazards and mechanical hazards. These main classes are divided into hazards groups, where hazards with similar characteristics are classified. Since the hazard group *non-ionizing and ionizing rays* would be a hazard group in a specific hazard class (*physical hazards*) but exceed the practicable size of such a group, it is counted as a hazard class in LARA. The classification is done according to considerations explained in the further subsection of this chapter.

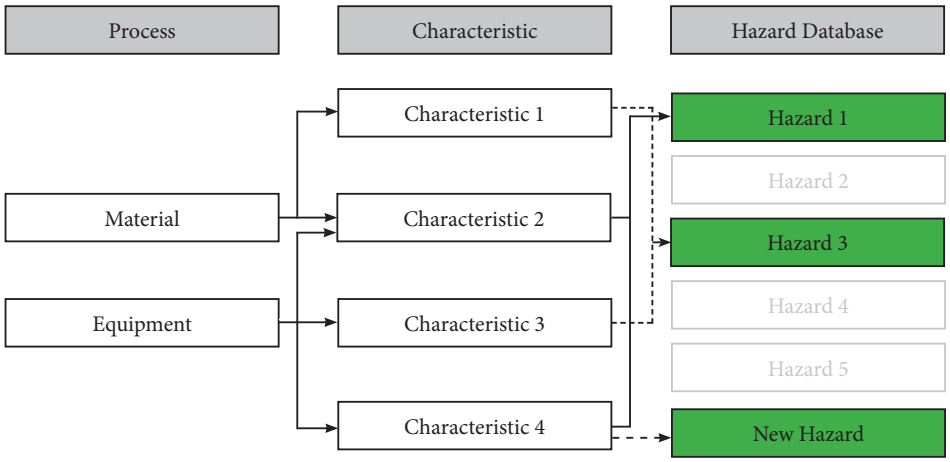


Figure 2.7 – Overview of the matching between the characteristics and the hazard using a database.

2.3.2 Chemical Hazards

Millions of chemicals substances are known and used worldwide for a multitude of purposes. Connected to this use is an exposition to hazards related to these substances. To inform about these hazards, a united system of labeling of chemical products for safe use, transport and disposal began its development at the United Nations Rio Conference in 1992. The result is the Globally Harmonized System of Classification, Labeling and Packaging of Chemicals (GHS) [United Nations, 2007], which is implemented in the European Union as regulation for Classification, Labelling, and Packing (CLP). In CLP, the hazards are classified in to three main groups: physical, health and environmental hazards. The system uses three ways of signalizing these hazards: pictograms, signal word, and hazard statements. Additionally to

these easily accessible hazards informations, a detailed Material Safety Data Sheets (MSDS) gives information about hazard, risks and precautionary statements. For LARA, the hazard classification for chemical hazard is based on the GHS principles.

The GHS gives all the possibilities to classify chemicals according to their hazards; however, for some specific types of chemicals, the properties are not well enough discovered to give information about possible hazards. Nanoparticles are such a type of chemicals: effects on the human body are not yet determined for a lot of these compounds. A way of dealing with nanoparticles is control banding [Groso et al., 2010]. This approach focuses rather on application of corrective measures and applies them to groups of hazards. Compounds which are assumed to have certain similar properties are treated in a similar way. The nanoparticles are added as hazard group in the hazard class *chemicals* in LARA according to the classification from Groso et al. [2010]. Table 2.1 gives an overview of this hazard class *chemical hazards*.

Table 2.1 – Chemical hazards in LARA: hazard groups and hazard examples.

Hazard group	**Hazard example**
Explosives	H205: May explode in fire
Flammability	H226: Flammable liquid and vapor
Oxidizer	H272: May intensify fire; oxidizer
Gases under pressure	H280: Contains gas under pressure; may explode if heated
Instability	H250: Catches fire spontaneously if exposed to air
Corrosive to metal	H290: May be corrosive to metals
Inhalation hazard	H336: May cause drowsiness or dizziness
Oral hazard	H303: May be harmful if swallowed
Skin hazard	H310: Fatal in contact with skin
Eye Irritation	H318: Causes serious eye damage
Germ cell mutagenicity	H341: Suspected of causing genetic defects
Carcinogenicity	H351: Suspected of causing cancer
Reproductive toxicity	H362: May cause harm to breast-fed children
Specific target organ toxicity	H370: Causes damage to organs
Environmental hazards	H411: Toxic to aquatic life with long lasting effects
Nanoparticles	Nanoparticles in suspension

2.3.3 Physical Hazards

Hazard originating from physical effects do not have a similar, unified classification system as the chemical hazards. Following effects are considered to cause physical hazards in LARA: energy transfer, mechanical waves, electromagnetic waves, and pressure. Energy transfer forms hazards related to electricity and thermic effects. Mechanical waves include noise, vibrations, supersonic and infrasonic waves. Pressure is partially overlapping with the GHS classification, but in the physical hazard context it aims at also at hazards originating from hypobaric or hyperbaric environments. According to this classification, electromagnetic waves and fields should be part of the hazard class *physical hazards*, but due the amount of hazards

related to electromagnetic waves and fields, they do not fit the classification structure of LARA and are considered as a separate hazard class. An overview of the hazard class *physical hazard* is given in Table 2.2.

Table 2.2 – Physical hazards in LARA: hazard groups and hazard examples.

Hazard group	**Hazard example**
Noise	Occasional impulsive noise (Peak ≥ 135 dB)
Ultrasonic & Infrasonic	Ultrasonic force
Vibrations	Vibrations on hands (Acceleration a ≤ $5m/s^2$)
Hypobaric environment	Hypobaric or hyperbaric environment
Electricity	Accessible energized objects
Thermic Hazards	Exposition to cold temperatures ($T \leq 15°C$)
Pressure hazards	Vacuum

2.3.4 Electromagnetic Waves and Fields

Electromagnetic waves can be classified according to their wavelength: at a certain wavelength, the radiation carries enough energy to liberate electrons from atoms and molecules, thereby ionizing them. However, the distinction between ionizing and non-ionizing rays is not enough for hazard classification, since the properties in this group is still too widespread. Non-ionizing rays includes the visible spectrum, infrared radiation, UV-radiation and higher wavelengths forming electromagnetic fields. Lasers, which are possible to establish in different spectra are grouped separately due to their special characteristics. The second part of the electromagnetic waves is the ones who are able to liberate electrons: the ionizing rays, which are a hazard group in this category. An overview of the hazard class *electromagnetic waves* is given in Table 2.3.

Table 2.3 – Electromagnetic waves and fields hazards in LARA: hazard groups and hazard examples.

Hazard group	**Hazard example**
Laser	Laser Class 3B
Radio-frequency microwaves	Radiation (frequency ≤ 100 kHz)
Static Magnetic Field	Magnetic field with 0.5 mT line (distance ≥ 50 cm)
UV-IR non-coherent radiation	Unshielded UV-A (320 nm - 400 nm) source
Ionizing rays	Alpha particles

2.3.5 Biological Hazards

Biological hazard originate from biological substances that pose a threat to living organisms. This can include the diseases caused by viruses and microorganisms but also toxic or allergenic substances with biological origin. The mechanisms of these hazards are more complicated

and less known than with the other hazard classes. For safety reasons, a similar procedure than for nanoparticles is applied: control banding. For most research facilities worldwide, following bands are used:

- Biosafety level 1: working with well-characterized agents, which are unlikely to cause serious diseases to healthy adult humans. The hazard potential is low.
- Biosafety level 2: working with well-characterized agents, which can cause light to medium diseases to healthy adult humans. The hazard potential is moderate.
- Biosafety level 3: working with exotic and indigenous agents, which can cause serious to lethal diseases. The hazard potential is high.
- Biosafety level 4: working with exotic and indigenous agents, which can cause serious to lethal diseases for which vaccines or other treatments are not available. The hazard potential is extremely high.

In LARA, these levels are used for further classifying biological hazards originating from microorganisms and viruses. Other biological hazards (contact with animals, toxins) are treated differently, unless they are not related to a possible infection with a disease. The hazard class *biological hazards* is presented in Table 2.4.

Table 2.4 – Biological hazards in LARA: hazard groups and hazard examples.

Hazard group	**Hazard example**
Microorganisms	Bio-Safety Level 2
Genetically modified microorganisms	Bio-Safety Level 2
Viruses	Bio-Safety Level 1
Contact with Animals	Bites
Allergenic or toxic substances of MO	Inhalation hazard

2.3.6 Mechanical Hazards

Probably the most common source of accidents is not related to chemical, biological, or physical effects; mechanical impact can lead to serious or fatal injuries. In general, mechanical hazards originated from the interaction of two or more objects, at which one is often a human body. The cause of the movement of can be used for classification reasons. For example, the an injury caused by a dangerous surface is due to the movement of the harmed person, whereas pinching in a moving machine part is due to the movement of the machine. Another factor for the classification is, if a movement is intended or not and if the movement is controlled or not (e.g. ejecting of object due to a malfunction of a machine). According to this considerations and based on based on OSH guidelines [SUVA, 2004; Bundesverband der Unfallkassen, 2006] are classed in to following hazard groups (Table 2.5).

Table 2.5 – Mechanical hazards in LARA: hazard groups and hazard examples.

Hazard group	**Hazard example**
Moving machine parts	Pinch points
Dangerous surfaces	Sharp edges
Moving tools/objects	Overrunning of an object
Uncontrolled moving objects	Oscillating objects
Work in height	Ladders

2. Hazard identification	
Intention	**Example (as in Chapter 3.1)**
• Subdivision of the process into *process steps*	1. Dissolution of the reactants 2. Addition of Et_3N 3. Stirring overnight under nitrogen 4. ...
• Identification of *hazardous components*	• Toluene • Palladium acetate • Heating • Reduced pressure • ...
• Matching of the possible hazards of every component with the *hazard database* of LARA	**Toluene** • H225: highly flammable liquid and vapor • H315: Causes skin irritation • H336: May cause drowsiness and dizziness • ...

Figure 2.8 – An illustrative example of the steps performed in the LARA workflow. A more detailed explanation of this example can be found in Chapter 3.1.

2.4 Risk Analysis

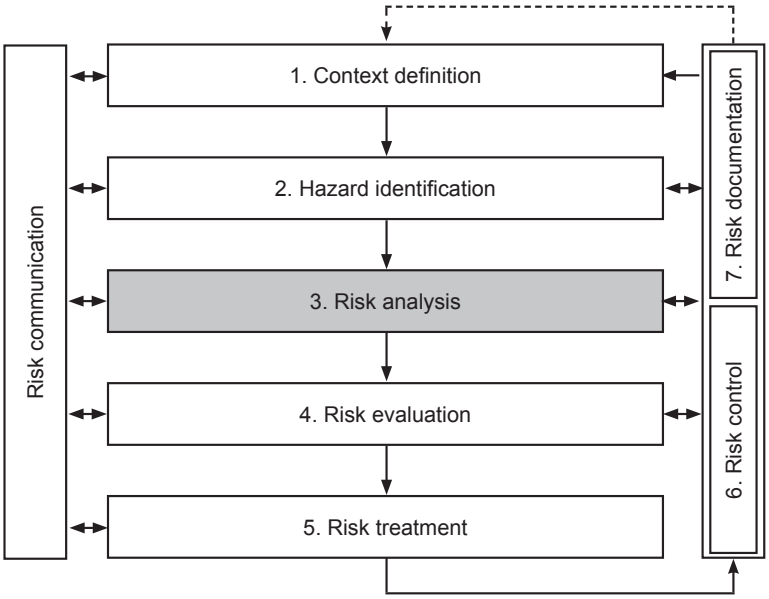


Figure 2.9 – Condensed LARA workflow: risk analysis.

The goal of the risk analysis is to analyze the hazard, describe the resulting risk and to evaluate its magnitude (Figure 2.9). In Chapter 1, the requirements for a method suiting the research environment were postulated; the risk analysis is the part of the risk management workflow, where most of these requirements are either met or not. For the risk description, an ideal method manages on a low amount of data, as statistical data is hardly available for this environment. Additionally, the demands for both expertise and difficulty should be low to moderate, since scientists are rarely trained safety specialists. Quantitative methods are not practicable in this environment due to the requirements, qualitative methods are often not detailed enough; for this reasons, LARA is designed as a semi-quantitative approach. For this kind of methods, qualitative scales and corresponding quantitative values for each dimension are defined. The underlying general scale is valid for all dimensions and represents the magnitude of influence on the risk resulting from a hazard. The corresponding values are integer numbers from one to five and are used for the risk estimation in LARA. Table 2.6 gives an overview of the underlying general scale and the corresponding quantitative values.

In this section, the risk dimensions used in LARA and the risk calculation will be explained in detail. To estimate the magnitude of each risk, the Laboratory Criticality Index (LCI) is calculated according to the risk scores of the risk dimensions. Additionally, the calculation method is compared to other semi-quantitative risk calculation approaches.

Table 2.6 – The general semi-quantitative scale used in LARA.

General qualitative description	Assigned value
Very minor	1
Minor	2
Moderate	3
Serious	4
Very serious	5

2.4.1 Dimensions in Risk Estimation

Risk is a multifaceted concept and has countless definitions. When the risk originating from a specific hazard is described, different dimensions can be used for the characterization. The level of abstractness can vary significantly depending on the specific approach. Simple approaches as the risk matrix approaches use the dimensions severity and probability, often expressed in a qualitative way. Quantitative approaches use statistical concepts as risk dimensions, which are not easily transferable to other methods. In LARA, four dimensions are applied to describe risks (Figure 2.10).

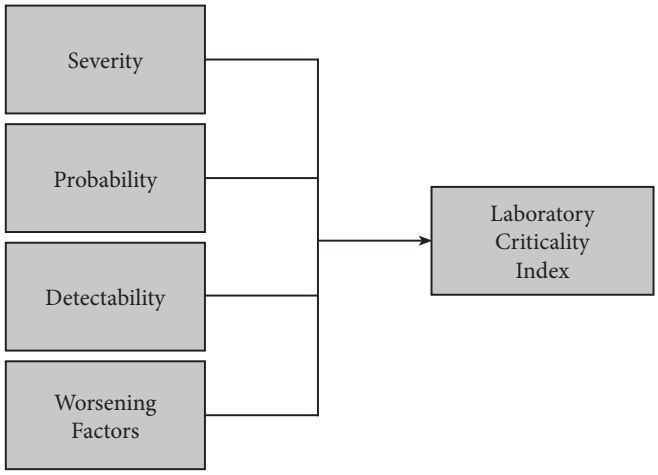


Figure 2.10 – Four dimensions are used in LARA to describe a risk and to calculate the LCI value.

Severity

The first dimension used for risk estimation in LARA is the severity of unwanted events' consequences. Even if the undesired event is easily determined, the consequences are perceived subjectively. In most risk management approaches, the financial impact is used as a gen-

eral scale for the severity. For damages to buildings and equipment, these values are easily determinable. The first scale of Table 2.7 shows the impact rating based on financial aspects.

Table 2.7 – Impact rating scales used in LARA for unwanted events.

	General qualitative description	**Assigned value**	**Specific qualitative description**
Financial	Very minor	1	< 1'000 CHF
	Minor	2	1'000 - 5'000 CHF
	Moderate	3	5'000 - 25'000 CHF
	Serious	4	25'000 - 125'00 CHF
	Very serious	5	> 125'000 CHF
Human	Very minor	1	Injury without work interruption
	Minor	2	Injury with work interruption (> 2 d)
	Moderate	3	Light handicap
	Serious	4	Serious handicap
	Very serious	5	Death
Environment	Very minor	1	Negligible
	Minor	2	Marginal
	Moderate	3	Important
	Serious	4	Critical
	Very serious	5	Catastrophic
Reputation	Very minor	1	Awareness at the laboratory
	Minor	2	Awareness at the unit
	Moderate	3	Awareness at the institute
	Serious	4	Awareness outside the institute
	Very serious	5	Claims against the university
Perception level	Very minor	1	Laboratory
	Minor	2	Faculty
	Moderate	3	University
	Serious	4	Regional
	Very serious	5	National

Estimations of costs for damages on humans exist as well; insurance companies worldwide estimate these kinds of costs to be prepared for claims. These values are based on various influence factors, for example the loss of manpower during the sick leave. For the academic research setting, this point of view is not applicable without limitations. Since universities are not profit seeking, the severity of accidents leading to injuries is more complicated to determine. Assigning costs to these kinds of accidents is a subjective task: a scientist who loses eyesight is most likely not assigning the same value as the insurance company does. In LARA, financial considerations for human loss is avoided by using the second scale of Table 2.7.

Human beings, buildings and equipment are not the only targets for consequences of undesired events. Environmental damages are likely to occur for chemical facilities and happened

numerous times in the past decades. Industrial facilities are strictly monitored and controlled regularly by the authorities, but for academic research facilities these controls are not as rigorous. In LARA, accidents with environmental damages are considered using the third scale from Table 2.7.

For universities, their reputation is of high importance and is often cultivated with various kinds of efforts. Independently if they are causing any kind of damage to humans, buildings or the environment, major accidents can have a tremendous impact on the reputation of an institute. For industrial companies, a value can be assigned for the brand image, whereas this is hardly possible for universities. To measure the impact on the brand image, the fourth scale of Table 2.7 is used to estimate the impact on the reputation.

Finally, accidents can have an impact that is of more fuzzy nature than the other ones. Perception is often not linked to a rational constant and media are capable of drawing an unproportional amount of attention to a specific event. This kind of impact is often linked to reputational damages, but can be independent from it as well as from the other kinds of impacts. In order to grasp the impact related with this concept, the last scale of Table 2.7 is used.

The scales of five impact fields are used in LARA to describe the impact of an unwanted event (Figure 2.11). None of the scales is of higher importance than another one, they are all based on the underlying general description and lead to the similar values on the semi-quantitative scale. An impact of an unwanted event is rarely only limited to one of these scales. More likely, it has manifestations on each of these scales. For risk estimation, these combinations can lead to complex scenarios and involve subjective moral judgements. In order to have a stringent impact estimation in LARA, the impact rating is not a combination of the different scales' values, only one the highest value is used for risk estimation. The worst-case scenario might lead to a different impact rating than the best-case scenario. In order to keep a clear policy for risk estimation, the most likely outcome of an unwanted event is taken as a reference for this estimation. However, for certain situations the worst-case scenario can be a more preferable option than the baseline scenario: if there is a lack of knowledge about hazardous properties or most-likely outcomes (e.g. nanoparticles) , the analyst has to take this into account with a higher judgement.

Probability

The second dimension of risk estimation in LARA is the probability of an accident. This dimension is challenging to define due to the fuzzy nature of the term *exposure*. Someone who is doing a task related to a risk is not necessarily permanent exposed to this risk. Exact probability values might be valid in a statistical context, but are often not meaningful for specific situations. Nevertheless, efforts were made in the framework of these PhD studies to base the probability values of LARA on statistical values; this was done with support of the Statistical Service of Swiss Insurance Companies (SSUV) which is part of the Swiss National

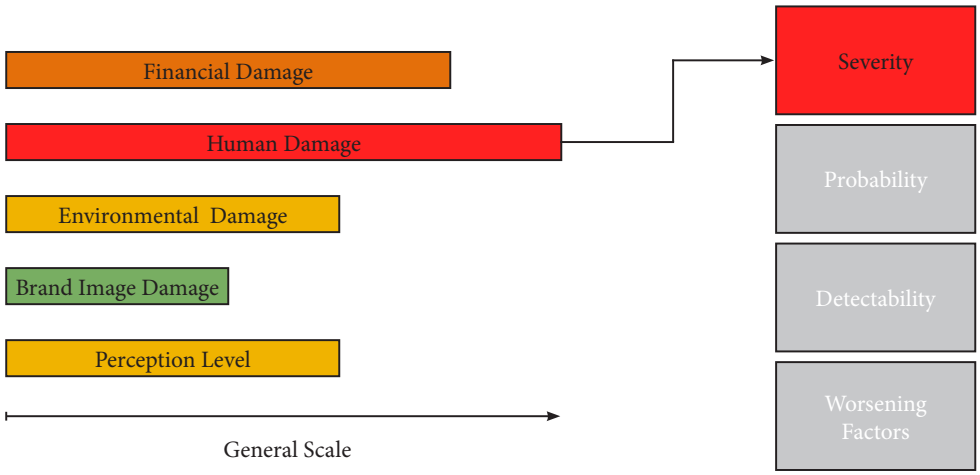


Figure 2.11 – Schematic overview of the scales used for describing the impact of an unwanted event in LARA.

Accident Insurance Fund (SUVA). The statistical data provided by SSUV is the most detailed accident statistics available for Switzerland. However, they focus on type of injuries rather than causes of events. This makes it challenging to assign the data to the different kinds of hazards present in LARA, since the causal chains are unknown. Additionally, laboratory accidents are fortunately not common accidents and the statistical significance of the data is not given. Based on this and the fact that LARA is intended as a semi-quantitative approach, estimations of occurrences are used to describe indirectly, how probable an accident is. Table 2.8 gives an overview of the occurrence rating scale, the assigned values and the qualitative description.

Table 2.8 – Occurrence rating for accidents.

General qualitative description	Assigned value	Occurrence
Accident is unlikely	1	1 / 10 years
Few accidents	2	1 / year
Occasional accident	3	1 / month
Frequent accident	4	1 / week
Accident is almost inevitable	5	1 / day

Not only the occurrence describes the probability of an accident, how often an activity related to a risk is done influences it as well. In LARA, activities are the object of analyses, and these activities are afflicted with risks. In order to estimate the commonness and the duration of an activity, the values from Table 2.9 are used. This scale was developed using effective working hours in relation the commonness of an activity [Ouédraogo et al., 2011a]. If for example an activity takes 60 % of a daily work time and is performed monthly, the resulting value is 3.

Table 2.9 – Commonness and duration rating for an activity.

Period	Daily work in %				
	20	40	60	80	100
Weekly	4	5	5	5	5
Monthly	3	3	3	4	4
Trimesterly	2	3	3	3	3
Semesterly	2	2	3	3	3
Yearly	1	1	1	2	2

Activities can involve hazardous elements, but not all risks take part in a similar way in an activity. An activity might be done on daily bases and last several hours, but a specific risk is only present short-termed in an activity. To take this factor into account, each single hazard is rated according to its involvement in an activity. This rating is shown in Table 2.10.

Table 2.10 – Rating for hazard involvement in an activity relative to the total process duration.

General qualitative description	Assigned value	Hazard involvement in activity
Very little	1	20%
Little	2	40%
Moderate	3	60%
High	4	80%
Very high	5	100%

The values for commonness and duration are specified for a certain activity and are valid for all hazards related to this activity. The assigned values for occurrence and the hazard involvement are used to describe the risk of a single hazard. Other than the impact dimension, where the most important value was taken into account, the probability has three influencing sub-factors, which are combined to express this dimension (Figure 2.12). How they are integrated in the risk estimation will be explained in Subsection 2.4.2.

Detectability

The detectability of an unwanted event acts as a third dimension of risk estimation in LARA. Whether one is able to detect an upcoming unwanted event or not, has a significant effect of the magnitude of a risk. Detection can improve preparedness and lower both impact and probability. Ways of detecting range from human senses to technical devices, for example oxygen sensors used in laboratories to warn from a lack of oxygen. Various factors are influencing the feasibility of a detector and are taken into account in the LARA method.

A first factor is the selectivity of a detector, which describes in what degree a detector is able to distinguish between different risks. Human senses for example can have different degrees of selectivity: the olfactory perception is much more selective than the gustatory perception.

Technical sensors underlie limitations as well and can be more or less selective. A second factor is the availability of a detector, which describes in which degree the detector is available in case of an accident. A last factor influencing the dimension detectability is the reliability of a detector. This factor describes if the detector is reliable in its functionality.

Table 2.11 – Rating of the detectability sub-factors.

Specific qualitative description	Availability	Reliability	Selectivity
Low	5	5	5
Moderate	3	3	3
High	1	1	1

In order to estimate the detectability, all three factors are judged in LARA separately (see Table 2.11). LARA is designed as a semi-quantitative method and an quantitative scale with values ranging from one to five is used for the other risk dimensions; however, the intervals are increased for the detectability. This is due the fact that the qualitative description is fuzzier and the concept is more widespread than the other dimensions. For consistency reasons, the scale for detectability is inverted: a low detectability stands for a high risk is assigned to a high value and vice versa. Similar to the probability dimension of LARA, detectability has three sub-factors which are combined to express the detectability dimension.

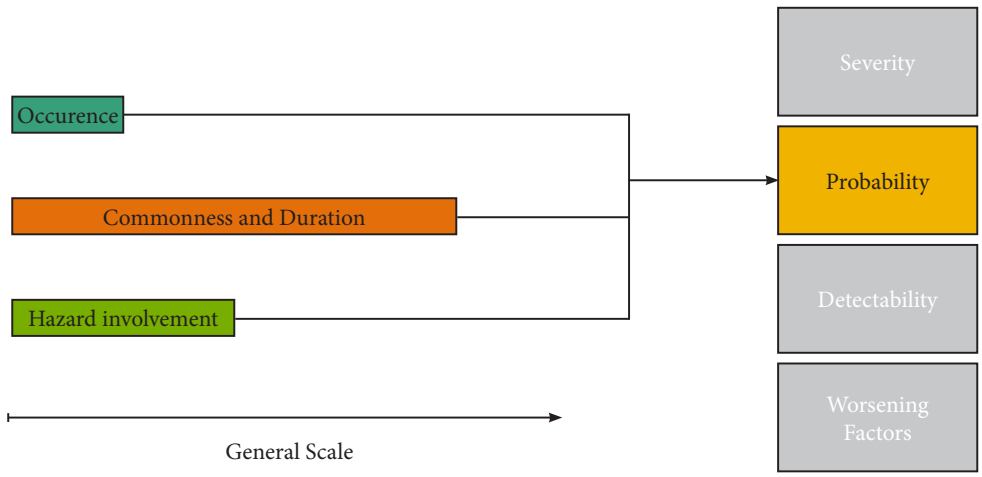


Figure 2.12 – Schematic overview of the influence factors used for describing the probability of an unwanted event in LARA.

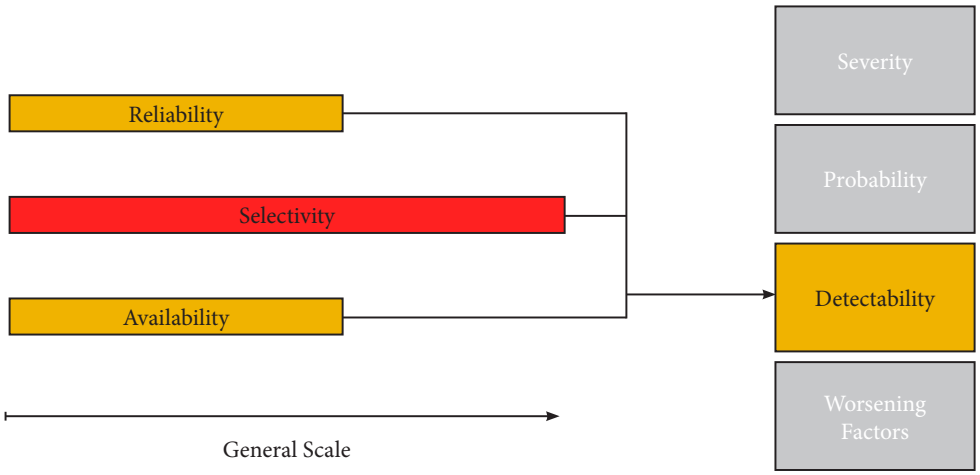


Figure 2.13 – Schematic overview of the influence factors used for describing the detectability of an unwanted event in LARA.

Worsening Factors

In an simplified model, risks can be analyzed based on their impact, their probability and detectability. However, reality is often more complicated and other influences need to be taken into account as well. Especially for an academic research setting, it is important to consider its peculiarities: quick turnover of personnel, lack of written procedures, experimental equipment, along with others. These influences are a breeding ground for risks and cannot be neglected when analyzing them. In order to deal with these factors in LARA, the concept of worsening factors was introduced [Ouédraogo et al., 2011a] in addition to the other risk dimensions. In general, this concept unifies all factors that are able to influence one of the other risk dimensions in a negative way. By expanding the commonly used risk dimensions with the worsening factors dimension, LARA is capable of describing the risks more accurately and to integrate interdependencies; in other methods, such relations are often overlooked and the risks therefore underestimated. The underlying mechanisms are not always similar; the worsening factors are classified as follows [Pluess et al., 2013]:

General Worsening Factors (GWF) These kind of worsening factors are not directly related to one specific hazard, but are increasing the risk level for all hazards in a similar manner. An example for such a factor is a information overload: it is not worsening a specific hazard, but can promote unawareness in a laboratory and increase all the risks present. Due to their fuzzy nature, they are not implemented in safety regulations. An example is the different languages spoken in a laboratory: it is almost impossible to regulate this in practice, but they can lead to misconceptions and therefore amplify risks. In general, these kinds of influences can be

Table 2.12 – General worsening factors categories and examples for each category.

Category	Worsening factor example	Effect
Climate	Humid climate	Malaise
Ergonomics	Respiratory personal protection equipment	Exhaustion
Electrical	Old electrical system	Short circuits
Lighting	Inadequate distribution of light	Misconceptions
Safety	Information signs not visible	Unawareness
Work organization	Unclear responsibilities	Misunderstanding
Social conditions	Risk prone climate	Risk taking
Work related	Permanent attention necessary	Exhaustion

described as a basic risk level, independently from hazards, exposure and risks. In order to group them, categories shown in Table 2.12 are used.

Hazard-Specific Worsening Factors (HSWF) Other than the GWF, these kinds of factors are specific for a hazard and are directly influencing it (see Table 2.13). In principle, considerations what can worsen a specific risk or what is able to trigger an accident, is implemented in existing safety guidelines. This kind of factor often originates in deviations from safety guidelines, for example not wearing adequate personal protective equipment, the absence of mandatory preventive tools, or the failure of a possible hazard detection tool.

Table 2.13 – Hazard-specific worsening factors examples for some hazards.

Hazard	Worsening factor example	Effect
Flammable vapors	Unideal electrical equipment	Ignition
Laser	No adequate PPE	Eye damage
Toxic vapors	Insufficient ventilation	Intoxication
High pressure	No shielding	More severe impact

Synergetic Worsening Factors (SWF) The last kind of worsening factors integrated in LARA derive from interdependencies between hazards. In particular situations, a risk can be worsened or even enabled by the presence of another risk. Various combinations are possible to form this kind of situations, for example the presence of non-ionizing radiations sources and flammable material without any kind of safety measure, which could prevent an ignition.

In LARA, the analyst begins the evaluation by choosing from the database of GWF which ones of them are actually present for this evaluation. This choice is valid for all the involved activities in the evaluation. In contrast, the HSWF and the SWF are specifically assigned to a single hazard and therefore only valid for this hazard. When the hazards from an activity are evaluated, the analyst decides using the database which SWF and HSWF are significant for the analysis.

Table 2.14 – Synergetic worsening factors scale to assign a semi-quantitative value used for risk estimation.

General qualitative description	Assigned value	Sum of selected SWF scores
Very minor	1	< 5
Minor	2	5- 15
Moderate	3	15 - 25
Serious	4	25 - 35
Very serious	5	> 35

Every single worsening factor, independently of what type it is, has a score assigned. These scores are indicating to what degree a single worsening factor is capable of increasing a risk. Based on the sum of these scores for each worsening factor category, a semi-quantitative value is determined using a predefined scale (see Table 2.14 for an example). The scale used for GWF indicates a relation between the sum of the selected worsening factors and the total possible worsening factors: a sum of zero is assigned to one and the maximum possible worsening factor sum is assigned to five. On the other side, the HSWF and the SWF scales are not related to a maximum score of possible worsening factors and the maximal semi-quantitative value can be reached using different combinations of worsening factors.

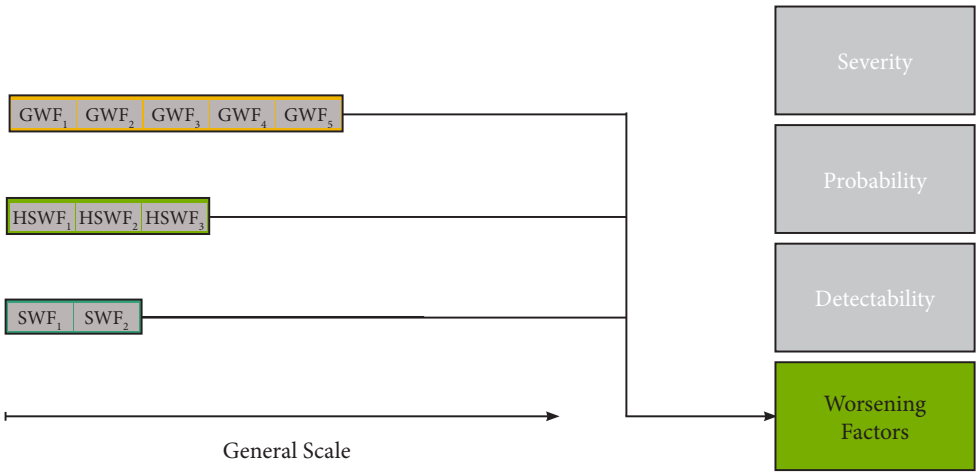


Figure 2.14 – Schematic overview of the worsening factors dimension and how they accumulate in LARA.

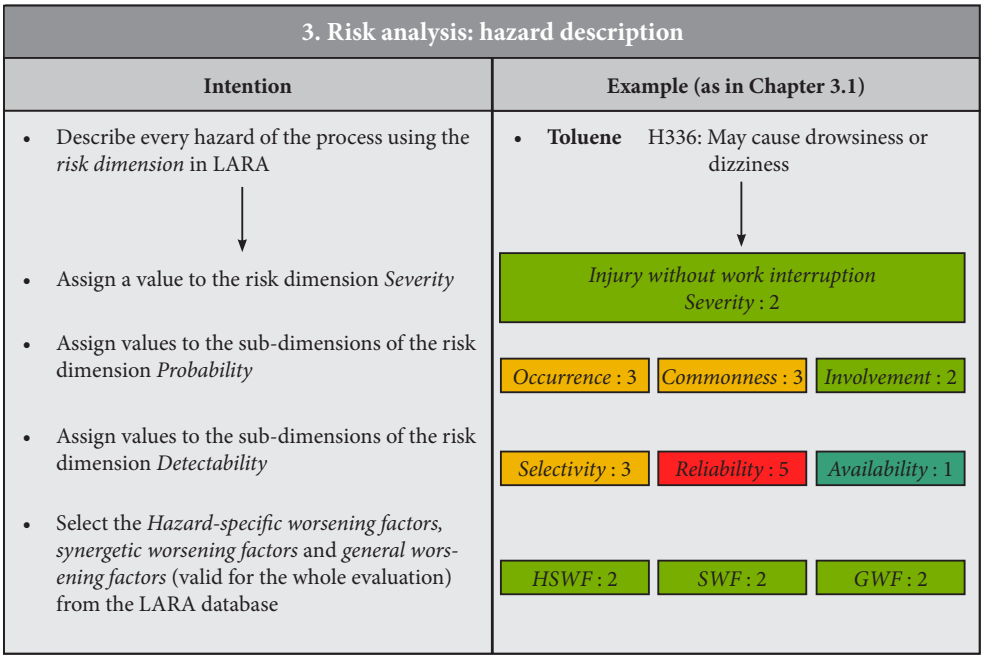


Figure 2.15 – An illustrative example of the steps performed in the LARA workflow. A more detailed explanation of this example can be found in Chapter 3.1.

2.4.2 Risk Estimation

(Parts of this subsection are a modified version of the article: *Expert Judgements in Risk Analysis: a Strategy to Overcome Uncertainties* [Pluess et al., 2013].)

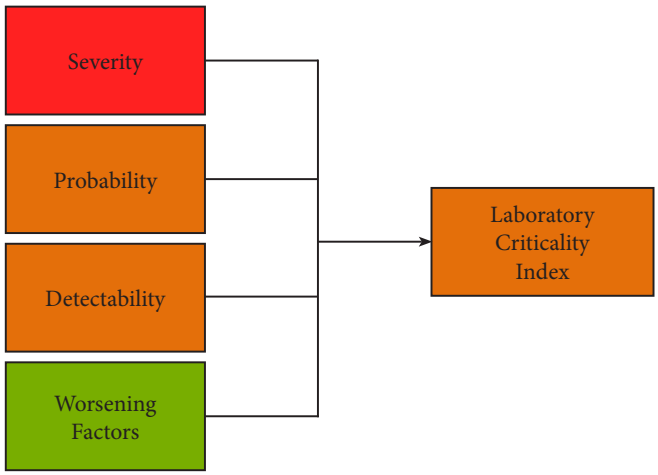


Figure 2.16 – For risk comparison, the four risk dimension values are combined to the LCI value for each risk.

One of the main challenges when developing a risk analysis technique for the research environment is the risk estimation. The latter is important in order to correctly prioritize risks and to apply adequate corrective measures. Most of the existing techniques depend on accurate statistical data, e.g. studies on reliability [Yun et al., 2009]. Due to the investigational nature of scientific research, statistical data on reliability for substances or equipment are hardly available. An often-used approach to deal with this is the use of semi-quantitative estimation methods, which rely on linguistic judgments of experts (e.g. often, rarely, significant financial loss). However, these linguistic terms are related to three different kinds of uncertainties:

- Stochastic uncertainty.
- Lexical uncertainty: different personal interpretation, e.g. often.
- Informal uncertainty: subjective interpretation of what an element means, e.g. severity.

Since linguistic judgements are used to estimate the risk of a hazard, these uncertainties are significantly minimizing the informative value of a risk analysis. Analyses performed by different experts can lead to different results for the same risk. In order to propose a reliable method for research environment it is necessary to improve the value of these judgments. Various approaches have been presented in the literature to decrease the uncertainties in

different fields of risk analysis; one popular solution is the use of Fuzzy Logic [Darbra and Casal, 2009]. The use of Bayesian networks is another promising strategy to improve the significance of semi-quantitative risk analyses [Ren J., 2007]. Based on Bayesian probability, Bayesian networks are not only capable of improving the uncertainty of both lingual and numerical expressions [Wang et al., 2009]; they have other advantages (visualization, easiness) when used to perform risk analyses [Zaili et al., 2008].

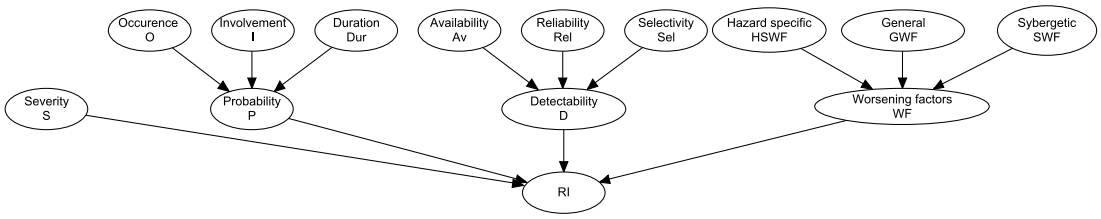


Figure 2.17 – The Bayesian network used for the calculation of the LCI.

In semi-quantitative risk analysis techniques, verbal statements are used to describe the risk factors. According to these linguistic variables a value on a numerical scale is assigned. This approach is used for all LARA's risk estimation factors. Table 2.8 exhibits a possible relation between qualitative statements, quantitative values and corresponding numerical values of the occurrence of an accident. For the variables and the sub-variables of severity (S), probability (P) and worsening factors (WF), a scale of integer numbers between one and five is used. Since the detectability (D) is more challenging to determine, a scale from one to three was used. In various risk analysis techniques, a multiplication-based formula (Eq. 2.1) similar to the one in FMECA technique is used to calculate the RPN (for the comparison of the different calculation methods, the values of the variables having sub-variables were determined using the average of the sub-variables):

$$RPN = S \cdot P \cdot WF \cdot D \tag{2.1}$$

This method has however some important drawbacks for prioritizing the risks [Braband, 2003], e.g. the results are not uniformly distributed over the scale. In order to overcome these drawbacks, Braband [2003] proposed to use a logarithm-sum-based formula (Eq. 2.2) in order to calculate an improved risk priority index (iRPN); this calculation method was adapted in LARA and is used to prioritize and compare the different risks: if a risk has a higher iRPN value, corrective measures must be applied with a higher priority [Ouédraogo et al., 2011a; Ouédraogo, 2011c]. A weighting process performed with an Analytic Hierarchy Process (AHP) suggested the use of a = 1.66, b = 5.78, c = 6.06, and d = 17.24 [Ouédraogo et al., 2011b] as bases

for the logarithms of the factors.

$$iRPN = log_a(S) + log_b(P) + log_c(WF) + log_d(D) \tag{2.2}$$

Still, the logarithm-sum based calculation method remains sensitive to uncertainties of the semi-quantitative judgements; the variance of the results obtained by different experts being too high for the comparison of the different risks evaluated. The implementation of new risk dimension even amplifies this problem. To overcome this, a new method using Bayesian networks to calculate the LCI was developed in the framework of these PhD studies. This calculation is a modified version of a method presented by Zaili et al. [2008], which uses Bayesian networks to model Fuzzy rule bases with belief structures.

Fuzzy logic is a widely applied calculation approach in risk management to deal with imprecise qualitative information. It uses linguistic variables in form of IF-THEN rules to model a reasoning process without employing imprecise quantitative information. However, due to several peculiarities of the calculation, the Fuzzy calculation method can lead to a significant loss of information [Zaili et al., 2008]. To overcome this limitation in LARA, the Fuzzy rule base structure is combined with a Bayesian network approach [Zaili et al., 2009]. Rule bases in general allow linking qualitative statements for input variables with a predefined value (quantitative or qualitative) of the output variable. An example of such a rule in the context of LARA can be expressed as (see Figure 2.19a) for a schematic representation):

$Rule$: IF

$serious$ (4) ($Impact$)
$AND\ moderate$ (3) ($Detectability$)
$AND\ unlikely$ (2) ($Probability$)
$AND\ very\ serious$ (4) ($Worsening\ Factors$)

$THEN$

$moderate$ (3) ($Risk\ Index$).

A complete rule base consists of one single IF-THEN rule for each possible combination of input variables. For this example with four variables and five different qualitative statements, the rule base contains 625 rules. This rule base is usually gathered through evaluations with experts, reflecting their judgement of interdependencies between input and output of such a system. However, such a rule base is not able to reflect slight changes in the input variables and is prone for inconsistencies; the expression of the output variable possesses only degrees of belief. In Fuzzy logic approaches, this is taken into account by extending each single IF-THEN

rule to a belief rule with associated with belief degrees (see Figure 2.19b) for a schematic representation). In the LARA calculation method, such a rule could be expressed as follows:

$Rule: IF$

$serious\,(4)\,(Impact)$
$AND\ moderate\,(3)\,(Detectability)$
$AND\ unlikely\,(2)\,(Probability)$
$AND\ very\ serious\,(4)\,(Worsening\ Factors)$

$THEN$

$$\{(0.0\ very\ low), (0.02\ low), (0.88\ moderate), (0.1\ high), (0.0\ very\ high)\ Risk\ Index\}.$$

This can be further expressed in the form of conditional probabilities as follows:

Given Impact (4), and Detectability (3), and Probability (2), and Worsening Factors (4),
the probability of Risk Index$_h$ ($h = 1,...,5$) is (0.0, 0.02, 0.88, 0.1, 0.0)
or $p(RI_h|S(4), D(3), P(2), WF(4)) = (0.0, 0.02, 0.88, 0.1, 0.0)$

By expressing the output variable as a distribution over the states of an output instead of a singe crisp value, this Fuzzy rule base provides a more informative and realistic representation than a simple IF-THEN rule base. For the further calculation examples in LARA, the rule base was generated using a truncated normal distribution with the variance of 0.5 for the output variable *Risk Index*. The mean value of each rule's distribution is based on the average semi-quantitative input value of the four risk dimensions. To allow the adaptation of LARA to changes in the context the risk management framework, the weighting of these input parameters and the distribution can be adjusted.

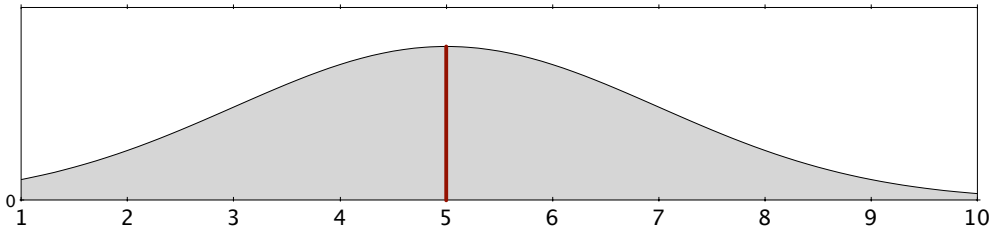


Figure 2.18 – An example of a truncated distribution: mean 5.0, variance 0.5, truncated between 1 and 10.

In a simplified version of the calculation approach of LARA, this rule base would be sufficient to deliver an output distribution for each for each input scenario. However, not only the outputs are afflicted with errors due to imprecise information; also the input variables can be biased

Table 2.15 – A part of the Fuzzy rule base used in LARA for calculation of the risk index.

Rule	Input (risk dimensions)				Risk index				
Nr.	S	P	D	WF	Very low	Low	Moderate	High	Very high
1	1	1	1	1	0.40	0.24	0.06		
2	1	1	1	2	0.39	0.30	0.09		
3	1	1	1	3	0.35	0.35	0.13		
...	...	...	...	...	...	...	...	...	...
378	4	3	2	4		0.02	0.88	0.1	
...	...	...	...	...	...	...	...	...	...
623	5	5	5	3			0.13	0.35	0.35
624	5	5	5	4			0.09	0.30	0.39
625	5	5	5	5			0.06	0.24	0.40

due to uncertainties in expert judgements. To overcome this limitation, the input value for each risk dimension is expressed as a distribution instead of a crisp value (see Figure 2.19c) for a schematic representation). As for the output parameters of the rule base, a truncated normal distribution with the variance of 0.5 was used 2.18. Other than regular normal distributions, this kind of distributions do have finite endpoints (for LARA, the scale of the inputs: 1 to 5). This enables to model a variety of shapes, for example a uniform distribution and allows higher flexibility for the model [Fenton et al., 2007]. The mean value is given by the choice of the analyst judging the risk dimension with the semi-quantitative scales presented in Chapter 2.4.1.

In the calculation method used in LARA, the Fuzzy rule base is combined with this kind of input by using a Bayesian network to model the calculation. This improved method is based on Bayesian statistics, being used in different branches of risk management [Marhavilas et al., 2011]. Bayesian networks are using probability tables [Fenton and Neil, 2012] with different states for each single node of the network. For LARA, the probability tables for each basic node is given by the input distribution (depending on the risk judgement). The different probability tables were created using a ranked node concept described by Fenton et al. [2007]. This concept facilitates the generation of the probability tables using truncated Gaussian probability distributions. The Fuzzy rule base is used as probability table for the parent node. Figure 2.17 gives an overview of the Bayesian network used for the calculation.

When an expert gives judgements on the different input parameters, the states of the risk index (RI) node can be calculated using following Eq. 2.3:

$$p(RI_h) = \sum_{i=1}^{5}\sum_{j=1}^{5}\sum_{k=1}^{5}\sum_{l=1}^{5} p(RI_h \,|\, S_i, P_j, D_k, WF_l) \cdot p(S_i) \cdot p(P_j) \cdot p(D_k) \cdot p(WF_l) \tag{2.3}$$

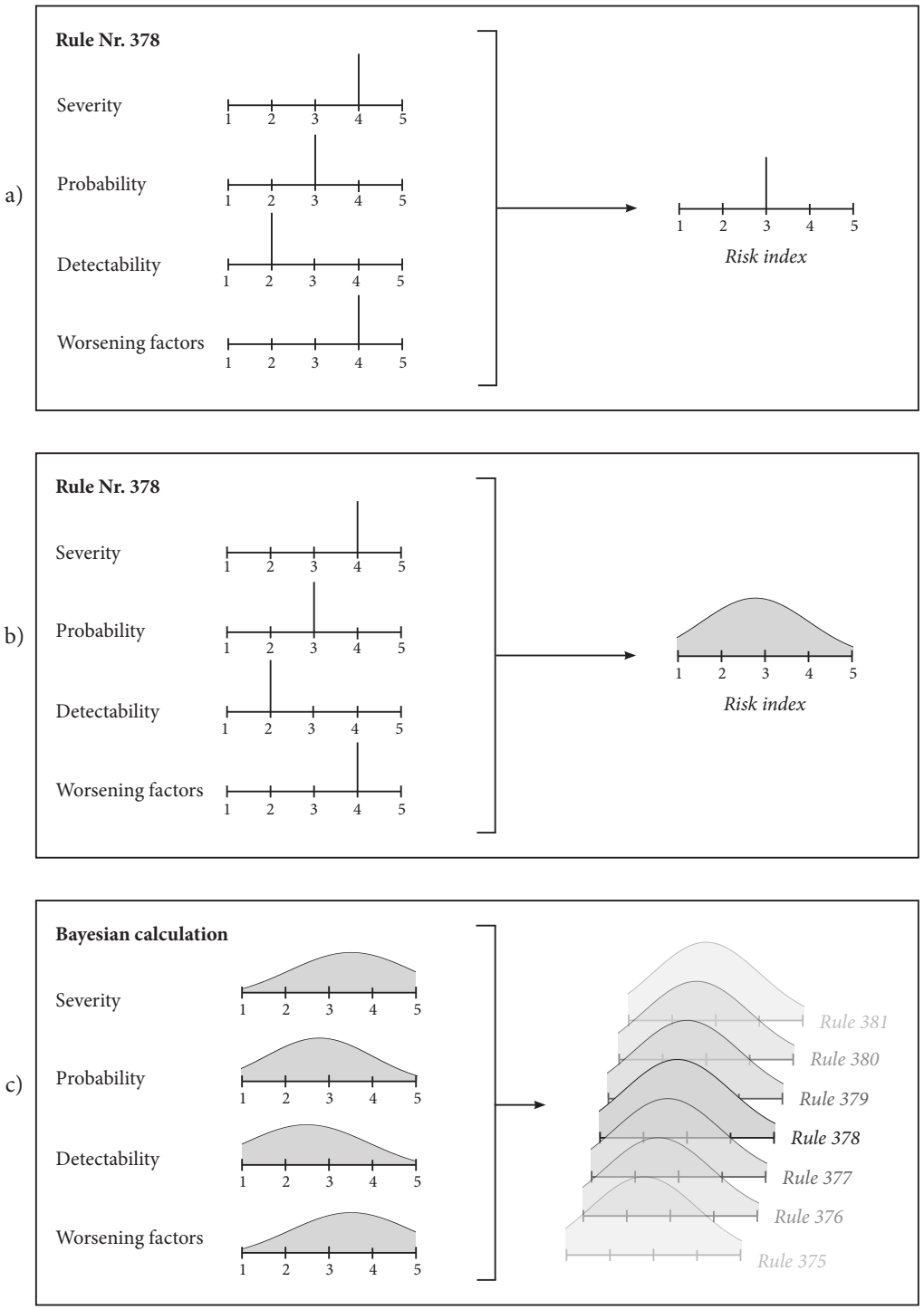


Figure 2.19 – A schematic representation of the Bayesian calculation approach: a) a simple rule base. b) a Fuzzy rule base as used in LARA. c) the calculation in LARA by using the Fuzzy rule base with fuzzified inputs.

The above calculation is an aggregation of the complete rule base for a specific input; depending if an input is close to a rule in the Fuzzy rule base, it can gather information or not (0.0, 0.0, 0.0, 0.0, 0.0). The calculation can be modeled in the software *Hugin* [Hugin Expert A/S, 2015], which was used to perform the calculations in LARA. Since the *Risk Index* node represents a probability distribution, for better comparison of the different risks, a single crisp number called LCI is calculated with the following Eq. 2.4 (see Figure 2.20). The adversity factor (A) for each state of the risk index node allows to differently weight the different states and further allow a high flexibility in the calculation system. As a last step, the resulting range of values are normalized to a scale ranging from one to ten (2.5):

$$LCI = \sum_{h=1}^{5} p(RI_h) \cdot A_h \tag{2.4}$$

$$LCI_{normalized} = \frac{(LCI - 4.51) \cdot 9}{3.18} + 1 \tag{2.5}$$

The actual calculation used in LARA has some minor modifications comparing to the model proposed in this Chapter:

- The risk dimensions Probability, Detectability and Worsening factors are not chosen directly by the analyst, but are combinations of different sub-factors (occurrence, duration, availability etc.). The values of these dimensions are therefore calculated in such a way that each dimension forms a subsystem with an own Fuzzy rule base. The parent nodes in these systems are calculated as the Risk Index in the main system
- Additionally the Detectability is reduced to three different states for the input variables (as explained in Chapter 2.4.1).

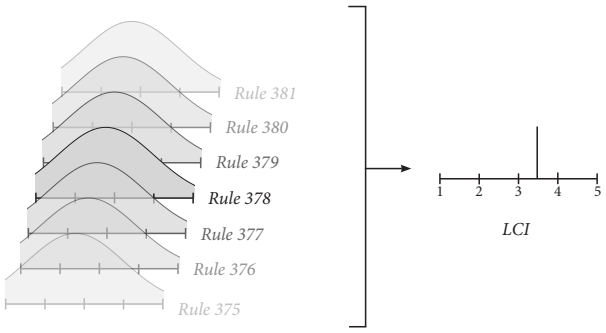


Figure 2.20 – After the Bayesian calculation, the results are defuzzified using Eq. 2.4 to form a crisp LCI value.

Comparison of the calculation methods As described above, LARA is using expert judgements to estimate the risk score. Due to the uncertainties connected to these judgements, different experts may have different opinions when estimating the factor of a single risk. This leads to a situation, where different experts are producing different results in the risk estimation for the same risk. To illustrate this influence for a fictional hazard, Table 2.16 exhibits raw data judgements given by different experts for each factor and the corresponding risk scores.

Table 2.16 – Comparison of the "correct" risk factors (as defined in Figure 2.17) of a sample hazard and the different expert judgments for this hazard.

	S	**O**	**I**	**Dur**	**Av**	**Rel**	**Sel**	**HSWF**	**GWF**	**SWF**	**RPN**	**iRPN**	**LCI**
Correct	4	3	4	2	3	3	1	3	3	2	2.8	7.5	6.3
Expert 1	4	4	4	2	3	3	2	4	2	1	3.0	7.7	6.6
Expert 2	3	2	3	3	3	3	1	2	3	1	1.9	6.5	4.9
Expert 3	4	2	3	1	3	2	1	2	2	1	1.6	6.0	4.6
Expert 4	3	2	5	2	2	3	2	4	2	2	2.3	7.1	5.6
Expert 5	5	3	5	1	3	3	2	4	3	3	4.2	8.4	7.6

Even though the used "correct" value is hypothetical, this example reveals the impact of uncertainties: all three calculations methods are giving a certain range of risk scores. For a better comparison of the used calculation methods (RPN, iRPN, LCI), all results were normalized to a scale ranging from one to ten. Assuming a correct value (2.8 for RPN, 7.5 for iRPN, 6.3 for LCI), the risk scores based on expert judgements have a maximum difference of 1.4 for the RPN method, 1.5 for the iRPN method and 1.7 for the LCI method. This effect strongly biases the risk estimation and can lead to false judgements when treating the risk. When comparing this biased risk score with other risks, and depending on the scenario, risk might be underestimated. Therefore, resources needed to implement corrective measures may not be correctly allocated.

To further investigate these uncertainties, more examples with more variations of expert judgements were generated. For 32 different risks with fixed "correct" values, we calculated every possible combination of expert judgments. For these judgements, a maximum difference of 1.0 to the corresponding "correct" risk factor was set. When using only integer values for expert judgement, depending on the combination (one and five give fewer combinations, since zero and six are no valid judgements) a data set can include up to 60,000 different expert judgements for one single risk. Figure 2.21 indicates the distribution of the risk scores for six different random risks (two for each of the three different calculation methods). To illustrate the difference of the distributions' variances, the risk score with the lowest and the risk score with the highest variance were chosen for each calculation method. Figure 2.21a displays the two RPN values for the two selected hazards. The first risk score calculated with the RPN method leads to an average risk score of 1.31 with a variance of 0.03. This means that all possible expert judgements are closely distributed around the "correct" value. The second example leads to an average risk score of 2.28 with a variance of 0.49. Other than the first

example, the possible combinations for expert judgements are distributed more broadly. For the risk comparison this implies that if the judgement from the expert is slightly different, the risk score changes differently depending on the range in which the resulting risk score lies in. Taking all 32 examples into account (Table 2.17), the average variance is 0.26 with a relative standard deviation of 52.6%. Considering the risk scores and the corresponding variances, the RPN calculation method shows the tendency of having a rapidly increasing variance with increasing risk score. When performing risk analyses, this makes the risks with higher risks scores nearly incomparable.

Table 2.17 – Comparison of the variances shown in Figure 2.21, and the variances of all the calculated samples.

	Variance 1 (Figure 2.21)	**Variance 2** (Figure 2.21)	**Mean variance** (32 samples)	**Relative standard deviation** (32 samples)
RPN	0.03	0.49	0.26	52.6 %
iRPN	0.18	0.70	0.41	39.9 %
LCI	0.28	0.71	0.50	27.5 %

Using the iRPN approach (Figure 2.21b), more constant variances are observed. The example with the lowest variance leads to a risk score of 7.56 with a variance of 0.18, which is significantly higher than with the RPN method. The upper variance example leads to risk score of 6.74 with a variance of 0.70, which is also higher than the first method. The average variance for the IRPN method is 0.41 is higher too, but the has a lower relative standard deviation (39.9%) than the RPN method. For the risk comparison this means that a different judgement leads to different changes in the risk score depending on where the result is found on the scale; other than with the RPN method the changes are not as different through the whole scale. Even though the mean variance is larger (Table 2.17) than with the RPN method, the lower relative standard deviation makes this method more reliable for the risk estimation. Risks in different regions of the risk scale can be compared in order to apply corrective measures. However, the logarithm-addition based formula iRPN has some significant drawbacks, e.g. it is less flexible in using different probability distributions for input parameters.

The use of Bayesian networks is a possible solution to overcome these drawbacks and having a reliable risk estimation method. The variances observed (Figure 2.21c) are more constant even with larger risk scores. For the example with the lowest variance of the 32 example hazards the risk score is 6.16 with a variance is 0.28, whereas for the example with the highest variance leads to a risk score of 5.41 with a variance 0.71. For all 32 examples the mean variance is 0.50 with a relative standard deviation of 27.5 %. As the iRPN method, the LCI approach has a higher mean variance (Table 2.17) than the RPN method. Yet, the relative standard deviation is lower than for the two other calculation methods. Additionally, the variance appears to be independent of the result's magnitude. This allows reliable risk estimations and a meaningful comparison of different risks.

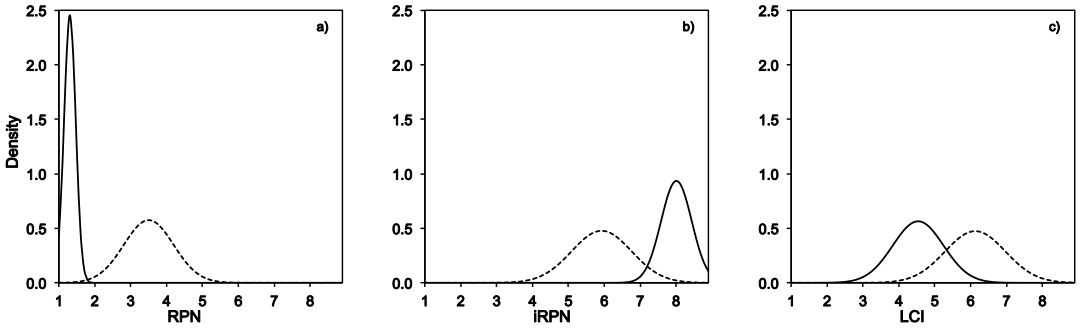


Figure 2.21 – Distributions of the risk values based different expert judgements of two different hazards: a) RPN method, b) iRPN method and c) LCI method.

This comparison reveals that the uncertainties in expert judgements do have a significant impact on the semi-quantitative risk estimation. This impact is amplified depending on the risk estimation method used. The comparison of three different estimation methods suggests that the use of a Bayesian network approach can lead to more consistent risk estimation with respect to other methods. When using a numerical scale to compare risks related to different hazards, the scale should represent a linear relationship between the risk scores; otherwise, the comparison will be biased. This is why a reliable and constant calculation method is of crucial importance. Uncertainties are not only resulting due to experts' judgements, but they are also caused and amplified by calculations. As consequence, uncertainties in expert judgement and the resulting variance of the risk calculation cannot be entirely eliminated. The analysis of the results obtained by the RPN method has shown that this method exhibits a changing variance, depending on the magnitude of the risk score. In order to have a constant scale of the risk score, a risk estimation method should have a constant variance through the whole spectrum of results. The iRPN method gives more constant results, but other aspects of this approach reveal drawbacks when performing risk analysis. The approach of calculating the LCI based on Bayesian network is capable of overcoming these drawbacks giving reliable results with a constant variance through the whole spectrum of the results. Due to this consideration, as well as the easier illustration of risk factors' dependencies, Bayesian networks method is an important alternative to other calculation methods in semi-quantitative risk analyses. If this calculation method is applied for academic research laboratories, the risks of different hazards can be estimated more precisely and therefore resources can be better allocated when implementing corrective measures.

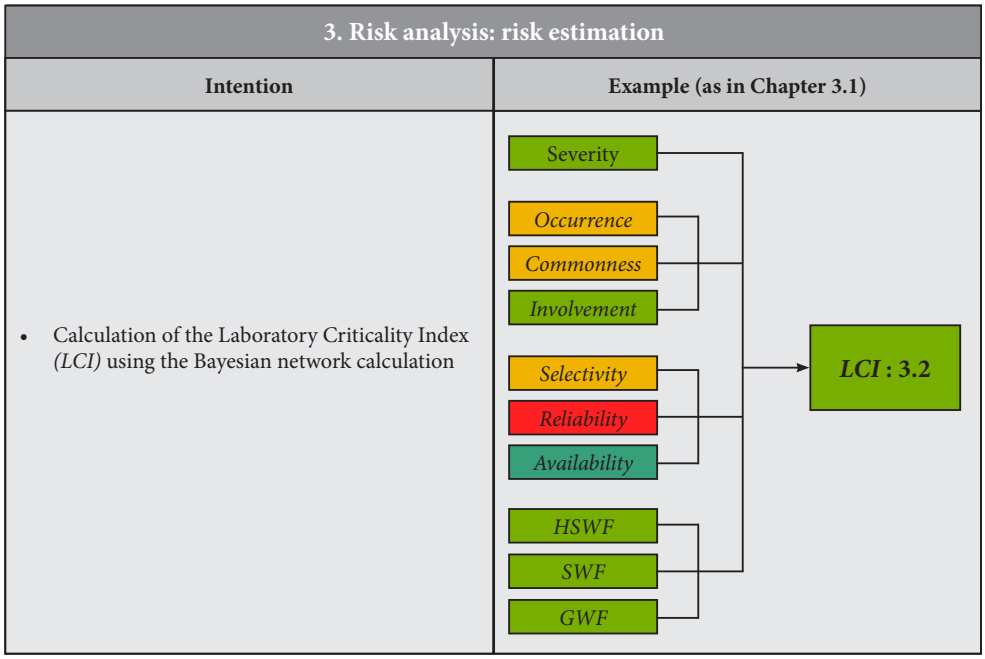


Figure 2.22 – An illustrative example of the steps performed in the LARA workflow. A more detailed explanation of this example can be found in Chapter 3.1.

2.5 Risk Evaluation

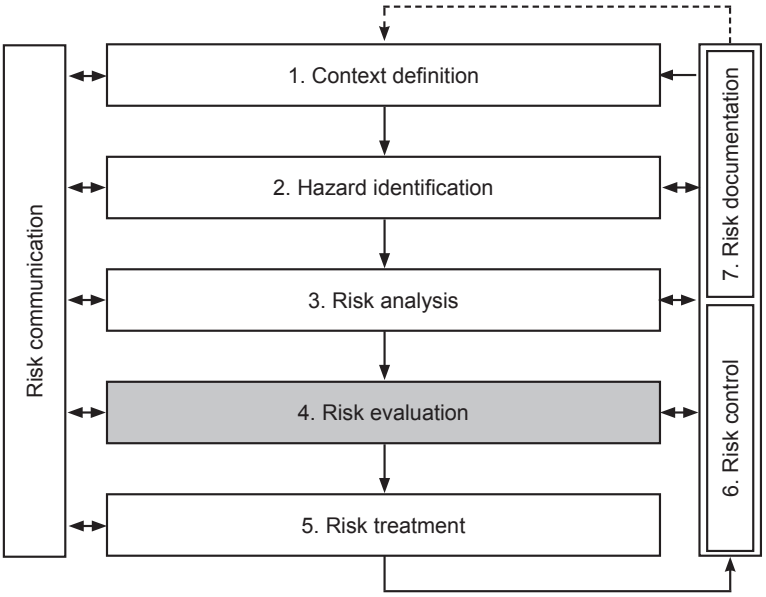


Figure 2.23 – Condensed LARA workflow: risk evaluation.

Once the magnitudes of the different risks are determined, decisions are made what to do about them. A basic question that needs to be answered for each risk is:

Is it necessary to treat this risk?

This question introduces the concept of acceptability into the risk management process. What is acceptable or not is defined by the context of the risk management approach, for example societal norms. The field of application influences the acceptability as well: 300 road casualties per year are acceptable for most societies, whereas 300 casualties from nuclear power plants are most likely not. For some industrial applications, the limits are exactly set and defined by national regulations [Melchers, 2001]. This requires precise calculations, which only quantitative risk management approaches can provide. The result of these calculations can deliver estimations about the magnitude of a possible loss in terms of casualties or financial loss (relative to the probability of an event). These results provide a high accessibility due to the comprehensive scale and allow discussion about the issue of acceptability. If a risk is above a defined acceptability limit, measures should be applied in order to lower this risk. However, the remaining risks cannot necessarily be considered as acceptable. In most risk management approaches, an ALARP region acts as a transition between the acceptable and the unacceptable risk levels [Melchers, 2001].

The ALARP region is conceptually illustrated in Figure 2.24. If a risk is above a certain probability limit, it cannot be tolerated under any circumstances. On the other side of the scale, the risks are either acceptable or even negligible for practical interest. In between of these limits,

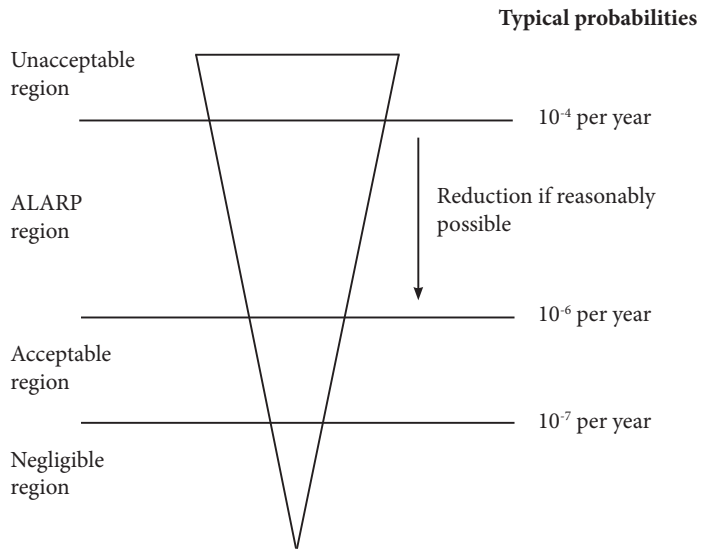


Figure 2.24 – Conceptualization of the ALARP approach [Melchers, 2001].

the ALARP region indicates risks which should be reduced, if the effort to do so is not grossly disproportionate to the gain obtained (i.e. reasonable). ALARP implies therefore subjective approaches and lingual concepts (*reasonable*), which are biased with similar uncertainties than the calculation approach using expert judgments. How the LARA method approaches this challenge is explained in Chapter 2.6, whereas the setting of the limits is explained in this Chapter.

Figure 2.24 reduces acceptability to a one-dimensional concept by only regarding the probability of an event. However, the possible impact is an important factor to determine the magnitude of a risk and needs to be taken into account for the decision-making. A widely used illustration of this two-dimensional risk concept is the risk matrix (Figure 2.25).

Similar to the limits in Figure 2.24, the possible scenarios are distinguished with the use of acceptability limits into three different regions (acceptable, ALARP, unacceptable). However, the two-dimensional risk concept allows a more detailed distinction between risk scenarios. It allows defining exact and comprehensible limits by applying logical rules (if the severity is above 4, then the risk is considered to be unacceptable) and shows how the factors contributed to a risk score.

In LARA, a semi-quantitative calculation method is used. As the risk matrix, this method does not provide an exact estimation of possible loss, but allows a relative comparison between the risks on a fixed scale. The calculation method integrates four different risk factors and unifies them into a one-dimensional scale. As a consequence of this simplification, the resulting risk scores do not indicate how the factors contributed to a score as in the risk matrix. However, similar rules can be applied, as it is possible in the risk matrix approach. Figure 2.26a shows a

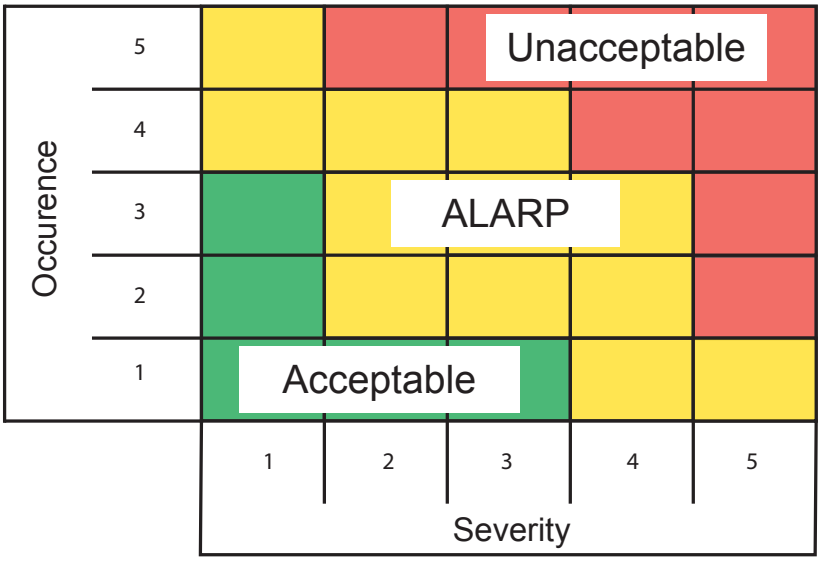


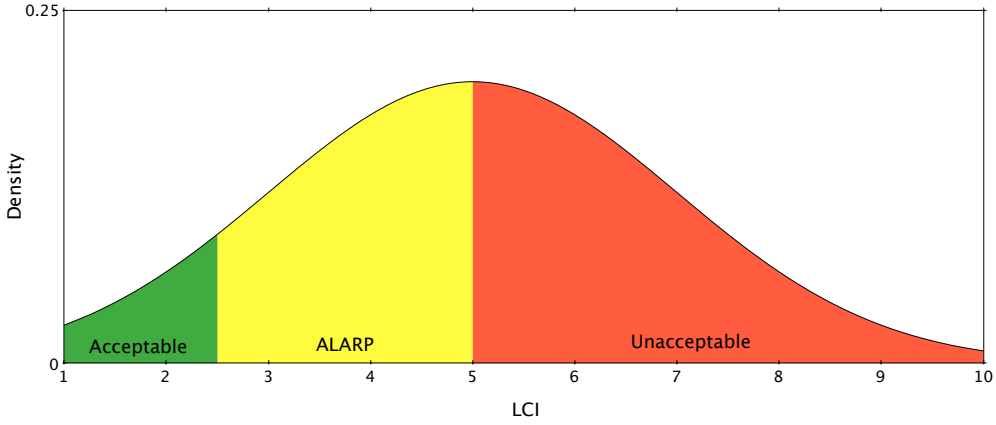
Figure 2.25 – A sample risk matrix illustrating the three regions of risk evaluation.

possible acceptability scenario, where the presence of a maximum input of one risk factor (all other factors remain on a minimum level) defines a lower limit and the presence of a second maximum input defines the upper limit. For the LCI scale from 1 to 10 and with similarly weighted factors, the lower limit is set at 2.5 and the upper limit at 5. Taking into account all possible risk scenarios, about 10% of the risk score are considered as acceptable, whereas around 50% are considered as unacceptable.

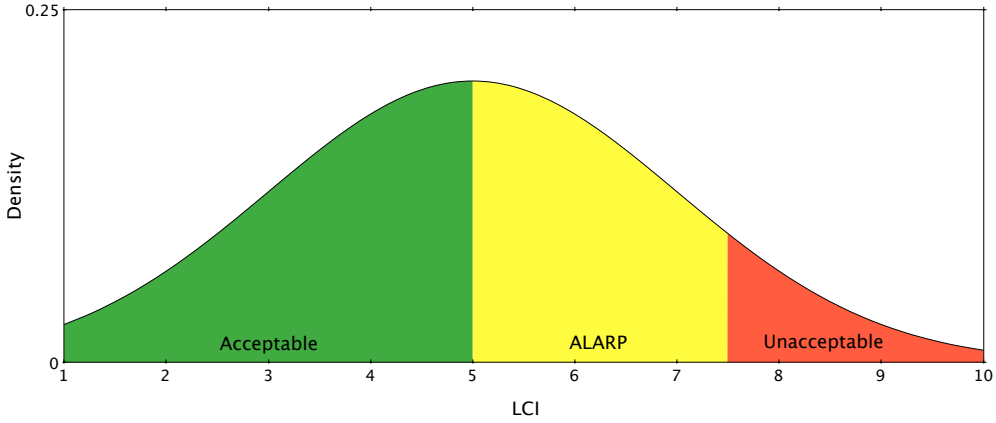
A less conservative scenarios is shown in Figure 2.26b and allows accepting higher risks. For this scenario, the lower limit is set for a risk having two maximum inputs (as the upper limit in the first scenario), whereas the upper limit is defined by risks having three maximum inputs. For the LCI scale from 1 to 10 and with similarly weighted factors, the lower limit is set at 5 and the upper limit at 7.5. Taking into account all possible risk scenarios, about 50% of the risk score are considered as acceptable, whereas around 10% are considered as unacceptable. A more balanced scenario is the one presented in Figure 2.26c, where the lower limit is taken as in the first scenario and the upper limit is defined as the one in the second scenario. For the LCI scale from 1 to 10 and with similarly weighted factors, the lower limit is set at 2.5 and the upper limit at 7.5. Taking into account all possible risk scenarios, about 10% of the risk score are considered as acceptable, whereas around 1% are considered as unacceptable.

Another approach to define these limits is not via such rules, but by taking into account the distribution of possible risk scenarios. A possible scenario is shown in Figure 2.27. The acceptability limits are determined mathematically: the lower 25% of all possible risk scenarios are considered as acceptable, the upper 25% considered as unacceptable. This leads to a lower limit of acceptability of 3.6 and a upper acceptability limit of 6.3.

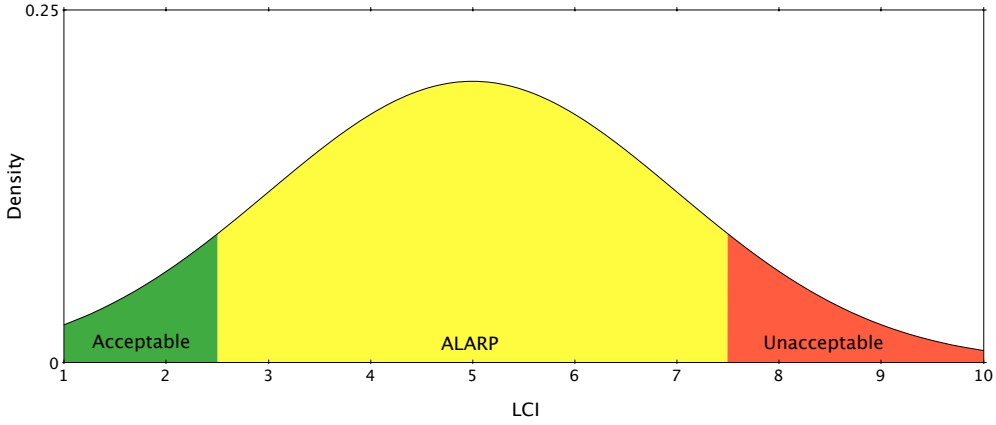
Two systematic ways to determine the acceptability are therefore possible in LARA: a rule-like



(a) Acceptable limit 2.5 and unacceptable limit 5.0.



(b) Acceptable limit 5.0 and unacceptable limit 7.5.



(c) Acceptable limit 2.5 and unacceptable limit 7.5.

Figure 2.26 – Distribution of LCI values and acceptability values: rule-like setting of limits.

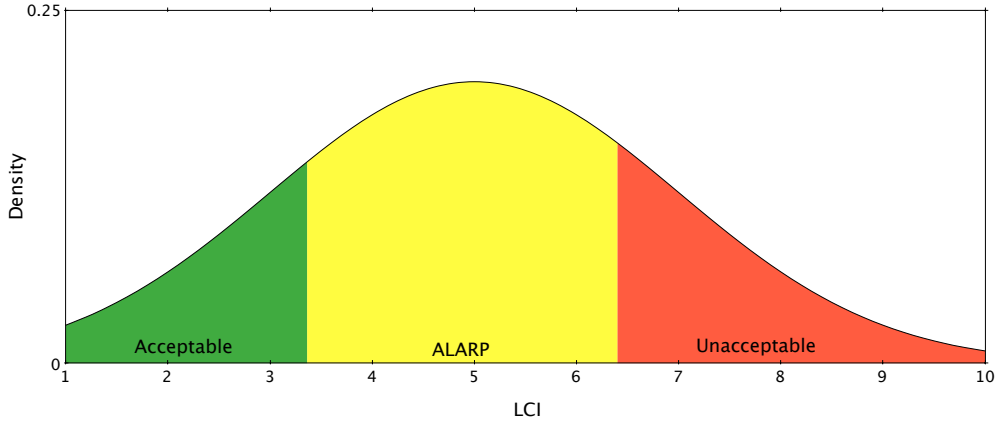


Figure 2.27 – Distribution of LCI values and acceptability values: distribution-dependent setting of limits.

approach as performed in the risk matrices or a more mathematical using the distribution of possible risk scenarios. As an advantage of the Bayesian network calculation approach, the distribution can be set directly and are not related to random mathematical effects. Additionally, the risk estimation approach facilitates the acceptance judgment by offering a constant variance through the risk scale.

Independently what logic lies beneath the setting of the limits, it remains a subjective decision what is acceptable and what is not. This judgements is done by the board of the institution and is usually valid for all organization units of a university. For comparability reasons and in order to have a consistent strategy for risk management, the limits usually remain the same for longer periods. If the context has changed, the occupational service can advice the board of the institution to adjust the limits.

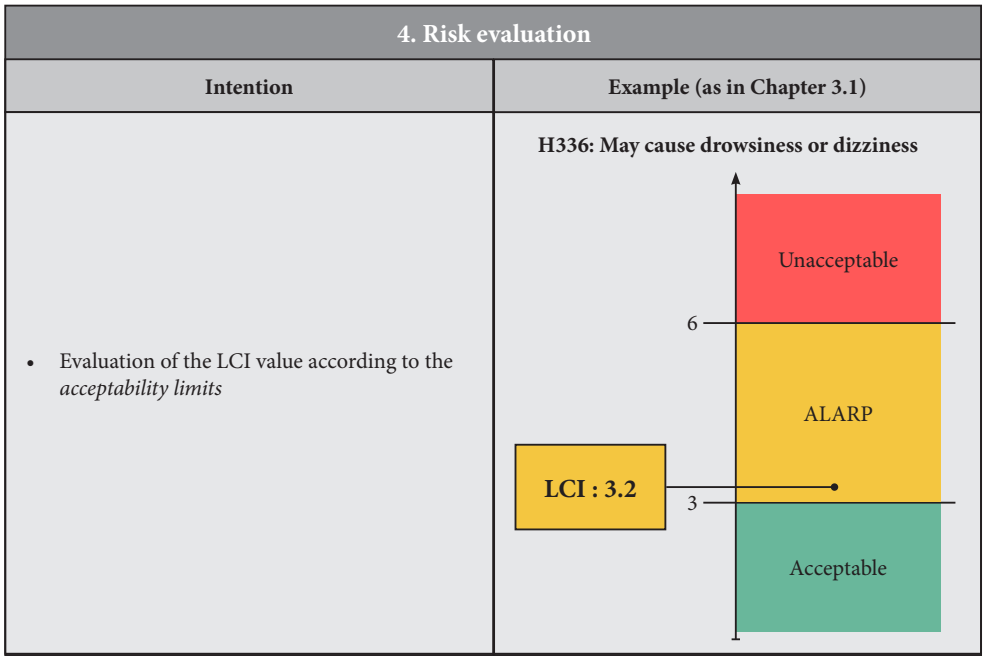


Figure 2.28 – An illustrative example of the steps performed in the LARA workflow. A more detailed explanation of this example can be found in Chapter 3.1.

2.6 Risk Treatment

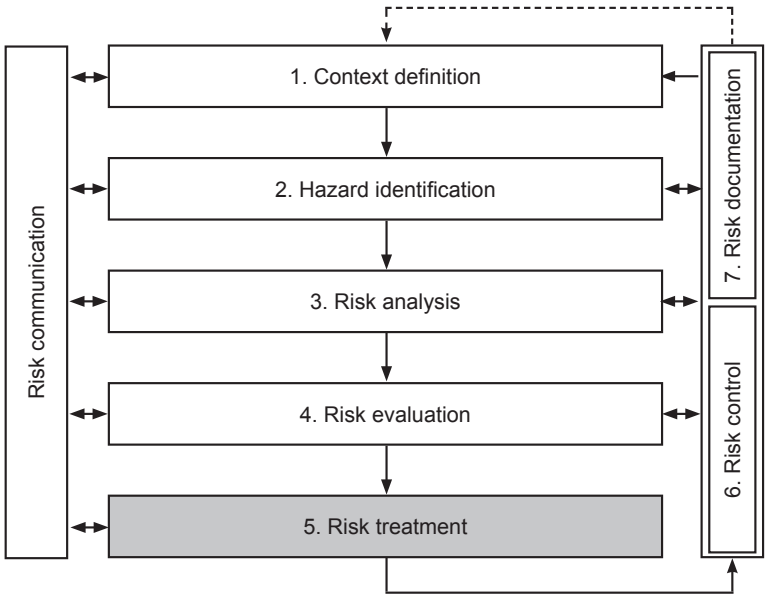


Figure 2.29 – Condensed LARA workflow: risk treatment.

(Parts of this subsection are a modified version of the article: *Resource allocation in risk management: integration of non-financial factors to risk mitigation* [Pluess et al., 2014a].)

Most publications in the field of risk management focus on risk identification and more refined or precise risk quantification rather than on risk treatment. Knowing the relative importance of the different risks present is crucial when deciding about the different possibilities of risk treatment. Moreover, these decisions are not based solely on a risk score; other aspects do have an influence on the decision. A risk might have different ways of treatment; some might be more favorable in financial terms, other might be more feasible for a specific situation. Additionally, a better overall result might be achieved when treating several smaller risks rather than a single, more important one.

Since every process has benefits, the amount of resources used for risk treatment need to be in a relationship with the benefits gained. This limitation makes it necessary to choose between different options of risk treatment in order to achieve an optimal result. Choosing the corrective measures simply based on risk scores independently of financial concerns does not lead to an effective risk management [Aven, 2011]. When lacking of defined financial limitations, deciding about corrective measures by their ability to reduce a risk score is still more favorable than choosing according to a risk score [Cox, 2012]. A better allocation can be achieved when linking the risk reduction potential with the actual costs of the proposed measure; this risk reduction per cost ratio gives the best results when allocating measures when lacking of a defined limitation [Cox, 2012]. When a limited budget comes into play, optimization methods such as the knapsack optimization are giving optimal results [Cox,

2012]. When using this approach, even interactions between the different corrective measures can be taken into account [Reniers and Sörensen, 2013]. However, all these approaches are linked to a financial aspect or a limited budget. For less profit-oriented environments, such as the academic research, the value gained by the basic research can hardly be estimated in direct financial terms and is therefore hardly comparable to the costs of risk treatment. Additionally, other factors may influence the choice of corrective measures, such as the acceptation by the scientists or non-financial requirements.

In the previous step of the LARA workflow, the LCI values (ranging from 1 to 10) are compared and the decision is made, if corrective measures need to be applied. According to predefined limits, the risks are categorized in one of the three regions: acceptable, ALARP or unacceptable. The board of the institution usually sets these limits and their application to all processes is compulsory. For risks in the acceptable LCI range one can proceed with experiment without corrective measure. The risks in the unacceptable region are treated regardless of the costs and the effort necessary and are re-evaluated after setting the mitigation measures. The remaining risks should be reduced as low as reasonably practicable.

To find the most preferable corrective measures in regards of both financial and non-financial aspects, the concept of a resource allocation matrix (Figure 2.30) is introduced in the framework of these PhD studies. This concept is similar to risk matrices, which are widely used in risk management. The size (5x5) and the number of zones (4) of the matrix are chosen in order to have ideal performance in terms of decision making according to Ni et al. [2010] The two dimensions of the matrix, representing financial aspects and non-financial concerns, are described in the following subsections. The zones of the matrix indicate an optimal resource allocation as follows (from the bottom left to the upper right corner):

- Zone 1: risk mitigation measures falling in this zone are not favorable in both financial and non-financial aspects. Such measures should be avoided for an effective resource allocation.

- Zone 2: risk mitigation measures falling in this zone are either not favorable in financial or non-financial aspects. Such measures should not be considered, if better alternatives are available.

- Zone 3: risk mitigation measures falling in this zone are either favorable in financial or non-financial aspects. Such measures should considered, if no better alternatives are available.

- Zone 4: risk mitigation measures falling in this zone are favorable in both financial and non-financial aspects. Such measures should considered in any case.

2.6.1 Corrective Measures

For most risks, a multitude of option exists to identify possible corrective measures. However, the choice is highly dependent on the moment in the design process, when possibilities are assessed (see Chapter 1.4). In the academic research setting, the risk assessment takes place at a moment, when most processes are already designed and most likely already in operation.

The approaches to identify possible corrective measures differ in their focus. What they have in common is the intention to change a factor of the risk context. Either they change the risk itself by substituting an element of the hazard/exposure relation or they are affecting the risk dimension. For the severity, most measures fall into the category protection, since they are aiming to lower consequences of happened accidents. The probability aspect is often related to preventive corrective measures, lowering the chances of an accident to happen. However, the concept of prevention and protection are not linked to a certain risk dimension or risk prerequisite and are sometimes overlapping [Meyer and Reniers, 2013]. The detectability can be increased with various methods, some preventive and some protective. The worsening factors are inducing another important possibility for risk mitigation: avoidance. By avoiding combinations of situations, risks can be reduced in relation to other risks. Therefore, corrective measures are related to hazards or to worsening factors in LARA, since their presence is often independent of the initial risk. If no element in the risk context can be changed, the risk can

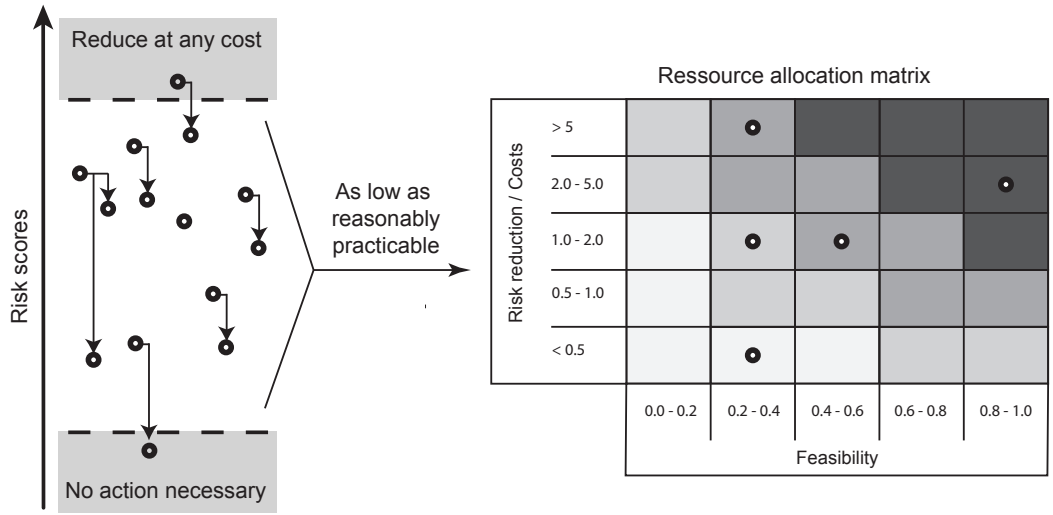


Figure 2.30 – For risks in the ALARP region, a resource allocation matrix is used to decide between the corrective measure options.

either be accepted or insured.

For LARA, various systematic approaches (e.g. STOP principle (see Chapter 1.1)) were used to generate a database of corrective measures. For every corrective measure suggestion are stored in the database, which risk dimension are most probably affected by it; nevertheless, the analyst decides based on the specific situation, which dimensions are affected in which magnitude. Additionally, feasibility values are stored in the database, which are important for the allocation of corrective measures (see Section 2.6.3). Similar as for other factors in the database, the user is able to suggest corrective measures for both hazards and worsening factors. Due to this, the database is constantly increasing and reacting to changes in the environment.

For a specific evaluation, the user chooses corrective measures for each hazard and judges the relative impact on each single risk factor. For an optimal allocation of the resources, the risk is reassessed and the user gives an estimation of the costs. If a corrective measure is chosen in the resource allocation, the user defines clear responsibilities and deadlines for these measures. In the information flow of LARA, this is an important part and the disposition of the corrective measures will be monitored regularly (see Section 2.7).

2.6.2 Financial Aspects

In order to have an optimal approach in resources allocation, one has to take into account, not only the risk score, but also the limited financial resources [Aven, 2011]. For some scenarios however, the risk score is still the most important indicator: risks with scores above an acceptable limit should be reduced below this limit independently of the cost or last resort, the process must be omitted. When the risk reduction stops being a necessity and multiple options are possible, benchmarking becomes important to find the optimal allocation of resources.

One possibility to determine the quality of corrective measures is to compare them based on their ability to reduce the risk score *risk-reduction index*. By adding the financial component, one obtains the relation between the risk reduction potential and the costs of a measure. The *risk reduction per unit cost index* is another possibility to benchmark the measures for resource allocation. Cox [2012] has shown, that for limited budgets (i.e. the budget is lower than the sum of all measures' costs), allocation strategies based on the risk reduction per unit cost index are always favorable compared to the strategies using risk-reduction index or only the risk score. Another way to approach the problem is to treat it as a knapsack problem [Reniers and Sörensen, 2013]. In a knapsack problem, a knapsack is packed with a choice of items with different size and utility value; an optimization algorithm can be used to reach a maximal utility value. The choice of corrective values can be considered as such a problem, with the utility value being the risk reduction potential and the weight being the cost of a measure. These optimization algorithms lead to better results compared to the other allocation strategies [Cox, 2012; Reniers and Sörensen, 2013]. However, they rely on precisely defined budget for risk

mitigation. For the academic research environment, such budgets are often neither defined nor expressed; sometimes they are only planned at a higher organizational level, not at the operational level. Additionally, the main aim of scientific research is not the direct financial gain; this is however an important element in setting a budget for risk mitigation.

Due to the requirement to have a fixed budget for the knapsack approach, the risk *reduction per unit cost index* is used as a benchmark indicator in the LARA method. This ratio is applied only to the risks having a risk score in the ALARP range. All other risks are either unacceptable and treated regardless to their cost (except if it is deemed too high, in this case the same approach as the one used for the ALARP region is applied), or acceptable and therefore untreated. It this case they are monitored to control that they remain in the acceptable region. The index serves as the first dimension of a resource allocation matrix, indicating the performance and the financial aspects of corrective measures. However, the costs of a specific measure needs to be evaluated in relation to the longevity of it and the amortization has to be included. Otherwise, expensive but long-lasting measures are penalized compared to the other measures. For the examples in this chapter, an amortization period of ten years was assumed.

2.6.3 Non-financial Aspects

Financial aspects and the effectiveness of corrective measures to reduce a risk are playing a key role when deciding about the allocation of safety measures. In a research environment however, the gain related to a process is hardly directly measurable in financial terms. This makes a direct assessment of gain, loss and the costs to prevent a loss meaningless. In general, the effectiveness of a corrective measure can also depend on other factors but financial. These factors arise from the specific situation, the personnel involved or other specificities. In order to use them systematically for allocation of safety measures, their definition and quantification is necessary. For LARA, the influencing factors were defined as follows:

Acceptability

Acceptability (A) describes the acceptability of the corrective measure by scientists directly affected by it. If the staff is not accepting the proposed measure, its effectiveness will be reduced and therefore the measure might not be favorable. Reasons for not accepting a corrective measure could be: distrusting the mitigating capability or unwillingness to use it due to distorted perception on cumbersomeness of operation.

Example: A fume hood in a chemistry laboratory is equipped with an alarm, which goes off when the sash is open for too long. If a scientist doesn't accept this measure he might block the mechanism, so he can work without opening and closing it all the time.

Simplicity

Simplicity (*S*) describes the facility of both operation and installation. If there are further requirements for a corrective measure to function or the measure is complicated to operate, it might be less favorable than other ones.

Example: automatic shutdown systems (e.g. blocking systems in case of misuse) can prevent serious accidents. Thanks to their easiness of use these kinds of installations are preferred to manual shutdown systems.

Compatibility

Compatibility (*C*) describes whether the corrective measure interacts with the environment and other measures, both positively and negatively. These interactions need to be considered because they can significantly influence the performance of the measure.

Example: sound alarms do have a low compatibility with noisy environment. On the other hand, visual alarms are well adapted to darkened laboratories.

Versatility

Versatility (*V*) defines the capability of corrective measures to positively affect a higher number of different independent risks. A more versatile measure is more favorable to install compared to specific measure, if the performance is comparable.

Example: installation or improvements of existing ventilation systems can positively affect different hazards present in academic research laboratories.

These four factors do not have the same importance when choosing corrective measures; a quantification of their relative importance is therefore needed. When dealing with choices between different options, the analytical hierarchy process (AHP) has become an important tool. This method was developed by Saaty [1980] to analyze and perform complex decisions and it has found different applications in the field of risk management [Miri Lavasani et al., 2011; Zeng et al., 2007; Ouédraogo et al., 2011b]. The AHP process breaks down the decision making into the different criteria involved and the options to choose from. A decision hierarchy is formed on these elements and a clear goal is defined. The criteria are compared pairwise by the decision maker in order to set an overall weighting for the hierarchy. After comparing the different options according to the criteria and their relative weighting, the most favorable solution is pointed out. In our specific case, a shortened AHP process to determine the weighting of the influencing factors was implemented. This shortened calculation is based on a method already presented by Kariuki and Löwe [2007]. This allows determining the relative influence of each factor on the non-financial feasibility. For the comparison, a numerical judgment scale from 1 to 9 was used. Each attribute is judged how important it

is relative to the other attributes. The question to be asked for each comparison was "*When comparing the different attributes, which is more important for the non-financial feasibility?*" Five occupational health and safety specialists were asked to compare the different factors pairwise according to the AHP procedure. To do so, all identified attributes were compared in a pairwise matrix (n x n square matrix). The weighted eigenvectors of this matrix are added component-wise to obtain an overall scale for priorities, i.e. $\omega_1, \omega_2, \omega_3, \ldots, \omega_n$. The results reflect the relative importance of each factor and are used in the resource allocation approach as weighting for the factors. The obtained weighting factors (ω_x, X = A, S, C, V) are presented in Table 2.18.

Table 2.18 – Resulting weightings of the non-financial factors.

Factor	**Weighting (ω_x)**
Acceptability (ω_A)	0.43
Simplicity (ω_S)	0.30
Compatibility (ω_C)	0.10
Versatility (ω_V)	0.17

In order to express all non-financial aspects with one single value, they are unified into one feasibility factor *F*. When choosing a corrective measure, the analyst will rate its acceptability, simplicity, compatibility, and versatility separately on a scale from 1 to 5 (1 represents an insufficient and 5 an outstanding rating). From the weights ω_x and the rating value r_x (r_{max} = 5), the feasibility factor *F* is calculated using following eq. 2.6:

$$F = \frac{\omega_A \cdot r_A + \omega_S \cdot r_S + \omega_C \cdot r_C + \omega_V \cdot r_V}{r_{max} \cdot (\omega_A + \omega_S + \omega_C + \omega_V)} \tag{2.6}$$

F can attain the maximum value of 100% or 1. More the value *F* approaches the maximal value, the better the feasibility of the corrective measure is in regard of the non-financial aspects. The feasibility factor *F* serves as the second dimension of the resource allocation matrix.

2.6.4 Example of Resource Allocation

The use of solvents is part of almost every activity in a chemistry laboratory. However, the risks originating from solvents were underestimated for a long time. Various solvents, previously considered to be harmless, can have a serious effect on the human health. These effects are often of chronic nature and difficult to assign to a specific source of exposure. To protect exposed persons, most countries have defined legal permissible exposure limits, for both and Time-Weighted Average Exposure (TWA). For the purpose of this study, dichloromethane and chloroform serve as examples. In Switzerland, the following permissible exposure limits are published [SUVA, 2014]:

- Dichloromethane: TWA 50 mL/m^3 and Short-Term Exposure Limit (STEL) 180 mL/m^3.
- Chloroform: TWA 0.5 mL/m^3 and STEL 2.5 mL/m^3.

Even for modern laboratories with adequate ventilation, these limits can be easily reached due to an extensive use of these solvents. Unknown and presumably adverse effects on the health, especially for more vulnerable persons (e.g. pregnancy) make it necessary to comply with these limits and therefore to find and install corrective measures. For the illustration of corrective measures' selection process, we are considering only the risks resulting from aspiration of the solvents dichloromethane and chloroform. Synergetic effects due to other hazards present in the processes are left out for simplicity purpose. A risk analysis using the LARA method has lead to the results expressed in Table 2.19.

According the limits in the LARA procedure, the LCI value ranges between the acceptable and the unacceptable zone and should therefore be reduced as low as reasonably practicable. The choice of the corrective measures using the resource allocation matrix for this example is explained in the next paragraph.

Corrective Measures

Corrective measures can be found using various systematic approaches, e.g. STOP principle (see Subsection1.2), which is organizing the measures into different groups:

Table 2.19 – LARA risk analysis of the use of chlorinated solvents in the laboratory.

Risk factor	Sub-factor	Qualitative description	Assigned value
Severity		Human: serious handicap	4
Probability	Commonness	Weekly, 40% of daily work	5
	Occurrence	Few accidents	2
	Involvement	80%	4
Detectability	Reliability	Moderate reliability	3
	Selectivity	Moderate selectivity	3
	Availability	Moderate availability	3
Worsening factors	Hazard-specific	Wrong handling of the existing ventilation Higher vulnerability (pregnancy) Low perception of the effects (long-term handicap)	2
	General	Lack of procedures Lack of training Too many working hours	2
	Synergetic	(Not considered)	1
Laboratory criticality index (LCI)			**5.45**

- Strategic: if possible, a less toxic solvent should substitute the chlorinated solvents. Since this is not always possible, the use of other products or even other chemical pathways should be considered. For this study, the substitution of the solvents was not considered; substitution can remove a hazard, but can also lead to new hazards related to the new substances. Therefore, the substitution could bias the comparison.
- Technical: improving ventilation (local or general) and removing factors that limit its current performance could reduce the concentration and therefore lower the risk.
- Organizational: training of the personnel can lower the risk significantly, since a misuse of the existing installations can reduce their performance. Additionally, other organizational methods could be applied, such as dislocation of critical processes to less-exposed laboratories, or limiting the exposure time by shortening the maximum work time in the laboratory.
- Personal: as the last option, the adverse affects can be deflected using personal protection equipment (PPE), such a respiratory protection.

In order to find the feasibility value *F*, the corrective measures are judged in regard to its four sub-factors. The results of this judgment (and the derived feasibility values) for the selected corrective measures are expressed in Table 2.20. Improving the ventilation has the highest feasibility value, since this measure is highly accepted by the personnel, simple and versatile. On the other hand, organizational measures have the lowest value, since the measure is very specific and might not be accepted by the staff concerned.

Table 2.20 – Overview of the feasibility values and their sub-factors for different corrective measures .

Nr.	Corrective measure	$\mathbf{r}_A$	$\mathbf{r}_S$	$\mathbf{r}_C$	$\mathbf{r}_V$	F
1	General ventilation	5	5	4	5	**0.98**
2	Training	3	3	5	4	**0.67**
3	Personal Protection Equipment (PPE)	1	5	3	4	**0.58**
4	Organizational measures	2	3	2	2	**0.46**
5	Local ventilation	5	5	4	3	**0.85**

Table 2.21 exhibits the financial aspects of the resource allocation and the values for the second dimension of the resource allocation matrix. Training of the scientist reduces the risk significantly while having relatively low costs. Personal protective equipment has a significantly lower risk reduction potential; even though it lowers the specific risk of inhalation intoxication, due to its cumbersomeness it can also act as a worsening factor.

Combined, these two dimensions form the risk allocation matrix as shown in Figure 2.31. According to this matrix, training of the staff is favorable to all other options. The risk reduction per unit cost ratio is optimal and the measure is accepted and versatile. Improved ventilation

(both local and general) and organizational measures can be found in the next zone of the matrix and should be implemented as second priority; since they differ significantly in both dimensions one can be favored over the other in function of own needs. Personal protection equipment should be the last option to implement, since the risk reduction per costs ratio is relatively low and the feasibility value does not compensate this lack.

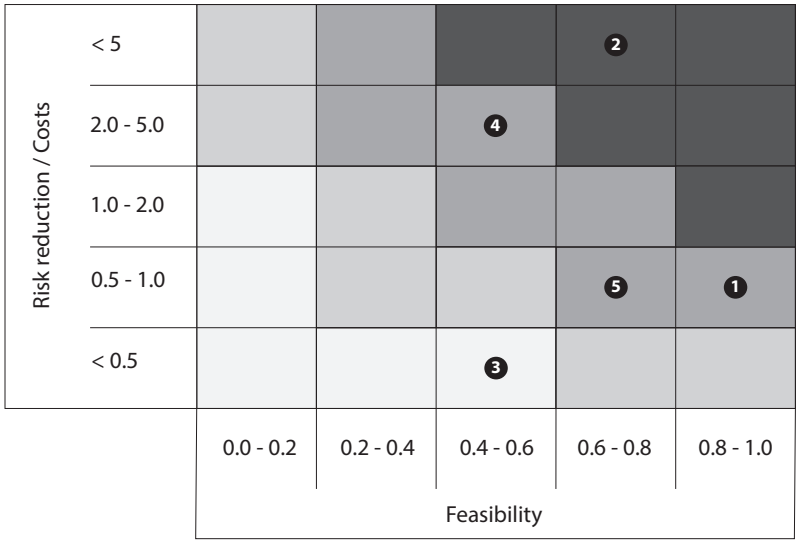


Figure 2.31 – Resource allocation matrix of the different corrective measures.

Table 2.22 only shows a comparison between the different approaches for choosing corrective measures for the same example. Making the choice between the different measures on financial or performance aspects only will lead to other priorities. When the risk reduction potential is the only indicator, the training is the most preferred option. Including the financial aspect, this option is still the most favorable; another change of priority can be observed for organizational measures: even though the risk reduction potential is not as high as other alternatives, this measure is highly favorable when taking into account the costs.

Table 2.21 – Overview of the factors influencing the financial dimension of the resource allocation matrix: the costs, risk reduction and the risk reduction per unit cost ratio.

Nr.	**Corrective measure**	**Costs** [CHF]	**Risk reduction**	**Risk reduction / costs** [10^5]
1	General ventilation	80'000	0.43	0.54
2	Training	10'000	0.59	5.90
3	PPE	12'000	0.02	0.16
4	Organizational measures	20'000	0.46	2.30
5	Local ventilation	40'000	0.43	1.67

Choosing the corrective measures according to this procedure has a significant impact on the involved functions in a laboratory. A main benefit affecting all the actors is the lowered overall risk level. For the user, the scientist performing the experiments, this improvement is made with a minimal interference with his work. Since the user is rarely directly involved in financial considerations, there are no direct disadvantages for him. On the other hand, the laboratory head might face the disadvantage of not achieving the most financially optimal solution for a laboratory. Nevertheless, the lowered overall risk level is beneficial. The analysis moderators and safety delegates, acting as an interface between these groups, will gain flexibility in choosing corrective measures according to the demands of both groups. Additionally, this method allows all the involved functions to access the decision-making due to the simplicity of the approach and therefore its better overall acceptation.

In the (academic) research environment, other factors than financial do matter when deciding about corrective measures. The resource allocation matrix as proposed in this Section allows taking these non-financial aspects into account. Namely, a possible measure is not only judged by its capability of reducing a risk or the costs of the measure; other aspects, such as acceptation, versatility, the ease of use and compatibility are also considered. These aspects, unified into a single value, are estimated by safety experts in the field and are therefore representing the situation in the laboratories more accurately when compared with other approaches. By expanding the decision making on this additional dimension, the choice of corrective measure can be optimized in several ways. When two corrective measures have similar performance and costs, the decision should be based on other aspects. Additionally, options that might be reasonable financially, but not feasible in the specific situation, can be avoided. Although the risk analysis example presented in this work is a simplified description of a complex situation in research laboratories, it already indicates that making decision between different alternatives of risk mitigation can be very complex. When expanding the resource allocation to a complete process, the number of hazards and the corresponding corrective measures can grow exponentially. Additionally, hazards and corrective measures can interact in several ways. Some hazards might increase other risks; for some scenarios, corrective measures can change a supposedly independent hazard. When facing such complex decisions, an intuitive approach can significantly simplify the choice; the allocation matrix,

Table 2.22 – Comparison of corrective measures' priority rating obtained using different prioritization criteria.

		Priority according to	
Corrective measure	**Risk reduction**	**Reduction/costs**	**Allocation matrix**
Improved ventilation	4	4	2-3
Training	2	1	1
PPE	5	5	5
Organizational measures	3	2	2-3
Biological monitoring	1	3	4

having similar advantages as the well-established risk matrix, is such an intuitive approach. The use of the allocation matrix in the LARA framework can help allocating resources in an optimal way and therefore helps to notably lower the risk in the academic environment.

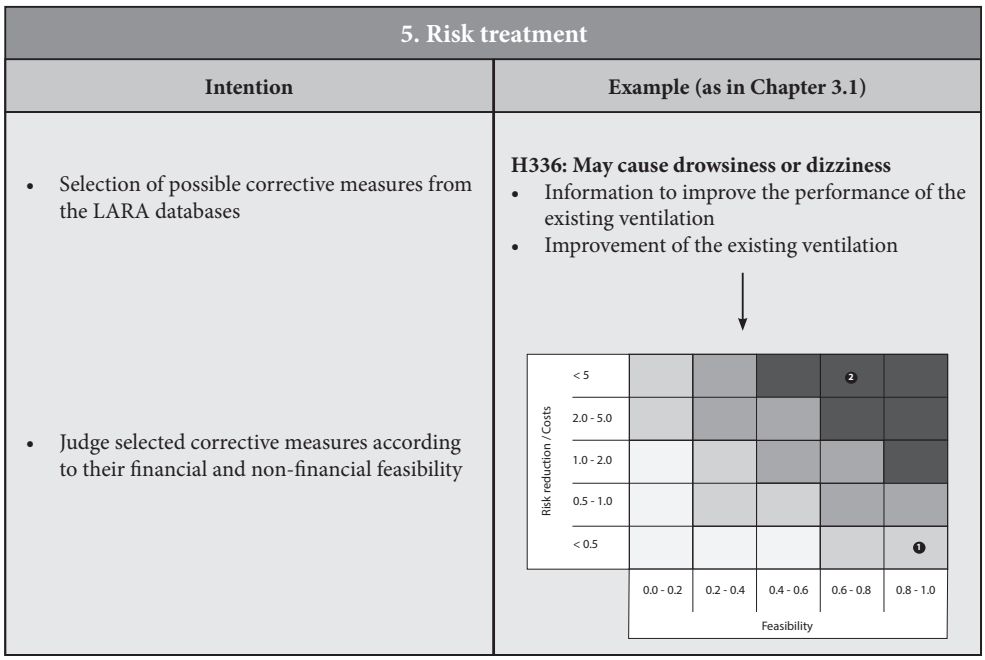


Figure 2.32 – An illustrative example of the steps performed in the LARA workflow. A more detailed explanation of this example can be found in Chapter 3.1.

2.7 Risk Control

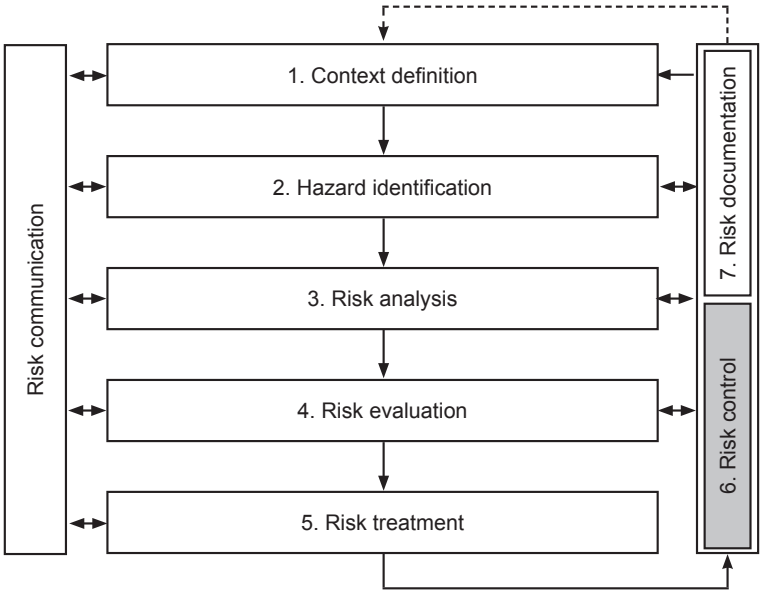


Figure 2.33 – Condensed LARA workflow: risk control.

The next step in the LARA workflow is the risk control. The risk management process in general is an iterative process; it does not end at the implementation of corrective measures. A main responsibility is at the OSH service, which analyzes the results in case of irregularities and control that the proposed correction measures are established as planned. Once the measure is applied, the OSH service ensures, that the measure works as intended, effectively lowers the risks, and provides the robustness of the measure for long-term use. Corrective measures however can be sources of new risks or can help to displace existing risks from one hazard to another; the applied corrective measure need to be checked on such effects regularly.

However, the risk control is not only a simple control effort. In a fast moving environment as the research setting, not only the scope of research is underlying quick changes, hazards and risk are constantly developing as well. Change management is an important factor for risk management and should be applied to a risk management process as LARA. This includes monitor changes and act accordingly. For LARA, changes are mainly related to the context and how they influence the risk management process; yet, the influences are not necessarily limited to the predefined system. However, the changes are not only unidirectional and are different for every step of the risk management framework.

Definition of the Context

Changes in the context can either be on a macroscopic level, on an organizational level or a technical level. The broader context is not underlying rapid changes, but if changes are happening, they can have a tremendous impact on the system. Pressure in form of new

legal obligations of regulations can change the framework completely and therefore it has to change accordingly. For organizational context, the performance of the responsibilities and the information flow needs to be observed and changed, if the system is not efficient enough. This is important as well for the technical context; the risk management workflow needs to be shaped according to the real situation and constantly reconsidered.

Hazard Identification

For LARA, the database structure is a crucial element and is important in almost every step of the risk management workflow. It is designed to let users suggest new entries and therefore to grow constantly. However, the responsibility for the database development should not remain at the user of LARA. Keeping track of near misses and accidents is crucial for having an overview of the risk situation and helps to detect emerging risks. These risks need to be introduced in the database systematically.

Risk Analysis

Constant change is important for the risk analysis step in several ways. The risk dimensions are related to how risk is seen in the context of this framework. Adjustments in reaction to changes can be done as smaller changes: adjustment in the dimensions scales, or changes in the underlying probability distribution (see Chapter 2.4.2). The users can be biased in their judgments; a way of compensating this is to change these distributions. If the changes are more important, the system might even be rearranged in terms of the risk dimensions (adding factors or removing them). The risk calculation is defining how these dimensions are combined and should deliver an accurate impression of the risk. This includes the way, how these factors are weighted and this can be a matter of change due to contextual influences. If one dimension is considered more important than another one, this should be expressed in the calculation. Additionally, the risk calculation method should not remain a static subject and needs to be reconsidered periodically.

Risk Evaluation and Risk Treatment

Changes in the context do have an important impact on the risk evaluation and the risk treatment. The main factors in these step are budgets, acceptability limits, feasibility values, and weighting of these factors. If one of these factors is affected by changes, the system needs to reconstruct to fit the demands of the workflow. Additionally, the choice of corrective measures is a part of the database in LARA and needs to be developed constantly. Lesson learned from past accidents need to be implemented in the corrective measure database.

2.8 Risk Documentation

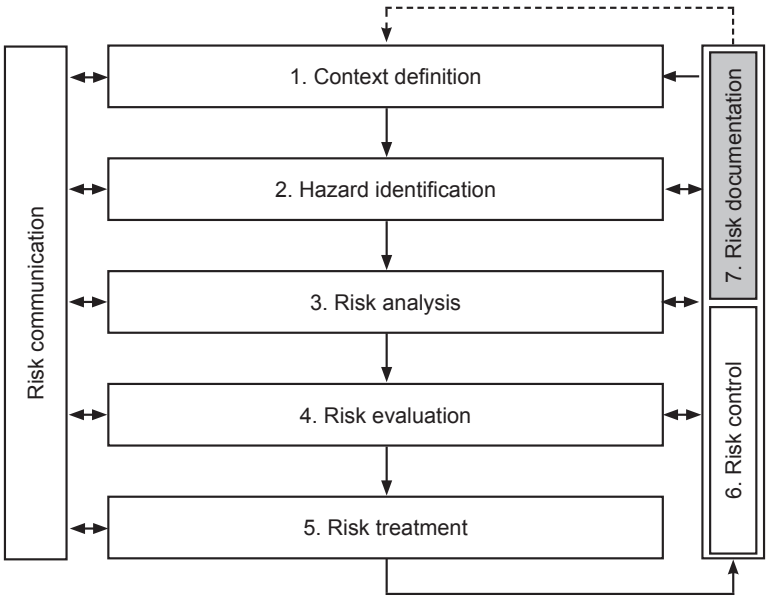


Figure 2.34 – Condensed LARA workflow: risk documentation.

As a last step of the workflow in LARA, the results are documented. Appropriate risk documentation is essential for every risk management approach and supports the continuous learning intended in the iterative process of LARA. Depending on the context, some legislation might require a detailed documentation of the risk management results. In LARA, a detailed risk evaluation report is generated for each evaluation. This allows re-consulting the information for different purposes, for example if a process is evaluated again in the framework of a periodic revision. When the process is carries out as a routine task, a short summary of the risk assessment will be added to the specific SOP. Furthermore, unspecific information is stored in the databases to expand their content and to improve their feasibility. The detailed documentation for each specific step contains following information.

Definition of the Context

The documentation of the context mainly involves the roles and responsibilities at the moment of an evaluation. This assures traceability information and allows to check details if necessary. Another important aspect is to document all factors influencing the evaluation: acceptability limits, general information about the current LARA workflow and information about the specific process of an evaluation.

Hazard Identification

For the hazard identification, all the information available at the moment of the evaluation is recorded in LARA. For later consultations, this allows reproducing the results and might help to improve the risk identification approach. Since the process is described in detail for the documentation, a certain level of confidence needs to be met. However, this is important for the risk communication, described in Chapter 2.9.

Risk Analysis

In LARA, the risk dimensions are used to describe a risk and to estimate the LCI value. However, the scales of these dimensions are not fixed and are intended change regularly to fit the current conditions defined by the context of the risk management. The calculation method of LARA underlies the same principle and is modified according to the situation present. The documentation in LARA keeps record about the current risks dimensions, their scales and the risk calculation method, in order to grant the traceability.

Risk Evaluation

The risk evaluation LARA uses acceptability limits to determine the acceptable, the ALARP and the unacceptable region. An overview about the parameters valid for the risk evaluation is given in the risk documentation.

Risk Treatment

The risk treatment in LARA integrates non-financial and financial aspects in the resource allocation for risk mitigation. As the risk analysis step, this resource allocation uses defined constants, but is intended to allow a dynamic change in the parameters. An overview about the parameters valid for an evaluation is given in the risk documentation. Additionally, all information about the corrective measure options are recorded. For the corrective measures which are about to be applied, the efforts, costs, responsibilities, and deadlines are recorded to allow an effective control of the measures.

Risk Control

The risk control is an element of the change management in the LARA framework. For the documentation of this step, the development of the different system variables is documented: acceptability limits (how and why they are changed), database (coverage, near misses, and adjustments in the structure), and calculation method (how and why the calculation method was adjusted). Additionally, the control of the risk treatment is documented in any revision of an evaluation, since this information is crucial for reconsidering the risk of a project.

2.9 Risk Communication

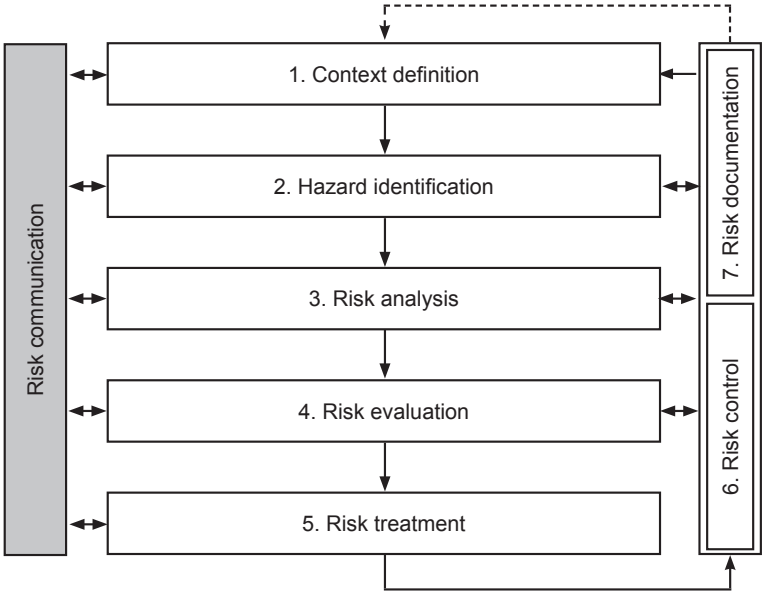


Figure 2.35 – Condensed LARA workflow: risk communication.

Risk communication is a central element of LARA, which stand besides the iterative workflow and has a superior function. Basically, the risk communication affects everything, especially the documentation of the evaluations and the general information about LARA. A main concept of the communication is that every role of the risk management workflow is able to understand decisions made based on the risk evaluations. However, this is also expanded to the stakeholders of an organization. Nevertheless, the information leaving the institution should be revised carefully to avoid misinterpretations or even loss of sensitive information. Confidential handling of the information is essential for this environment, since processes and procedures might not yet been published and leakage of information could be a serious problem. Also internal guidelines are necessary, since disclosure of information could be used for adverse actions (e.g. sabotage or espionage).

However, the communication in LARA is not unidirectional and the information that is entering the system is as important as the information leaving the LARA workflow. Knowledge allows establishing the context of LARA and is important to integrate on every level of application. For a risk management technique such as LARA, it is crucial that all interests are considered and also that the highest amount of expertise possible is used to established the guidelines of the system. For constantly expanding the system with expertise, a widespread application and continuous training and education is a key for achieving the goals of LARA.

In the LARA framework, the results of every evaluation are distributed according to the roles presented in Chapter 2.2. The OSH service is responsible for the distribution of these results. Additionally, it takes care of care of the classification of these results; if the results are extraordi-

nary in any kind of way, the OSH service gives further information to the other roles to ensure the traceability of the results. The institutional administration receives all evaluation results for informational purposes. The OSH service also distributes the results the specific working group where the evaluation was performed. All of the roles present in this group (group head, safety delegate, and scientist) receive the evaluation reports. To ensure the impact of an evaluation, the responsible roles must provide acceptance of the results.

However, the results of LARA are not only of use for risk management purposes. Since the LARA method has also educational intentions, the method and its results might be used this purpose as well. On one side, this includes the application of this risk assessment workflow on processes, which students are actually performing in their practical education. In this case, the communication of the results remains in the closed system of the specific course. These results can be compared to the results gathered from the course responsible and should be discussed to achieve an educational effect. On the other side, LARA evaluation results can be used independently from a practical education course to demonstrate the application of the method or to show different aspects related to occupational health and safety. Furthermore, the results can be used for risk management education due to the simplicity and the traceability of the LARA method.

3 Application Examples of LARA

In the previous chapters, the necessity of a risk management technique for the research and teaching environment was shown, the ideal specifications of such a method proposed, and the LARA risk management technique presented as a possible solution. In order to show the feasibility of LARA, the method has been tested intensively with various examples. The main purpose of these tests was to show that the LARA method is able to reach its goals (Chapter 2.1):

- Provide a risk management technique for all types of academic research laboratories.
- Allow a less resource demanding risk management, that fits the provided resources of the research environment.
- Development of a software application, allowing user-friendly and intuitive risk analysis.
- Consideration of the particular setting of the academic research environment.

To conclusively demonstrate this, the studied subjects were chosen to reproduce a representative image of the research done at universities. This does not only include a broad choice of disciplines (chemistry, biology, etc.), but also a variety of studied procedures from new experiments to routine tasks performed in laboratories.

LARA was developed at EPFL and was mainly influenced by the safety culture of this institution. For other institutions, the different organizational context and safety standards could make an application difficult. Since LARA is intended to be a universal tool for research and teaching laboratories, the feasibility at other institutions was tested as well.

In order to have show the feasibility of the LCI scale and the risk evaluation process, the acceptability values for the different examples are set differently. In a normal risk management system, these values remain the same for all evaluations in order to have an optimal comparability of the different results.

For this test, the complete LARA workflow was questioned and evaluated in detail to show the feasibility, the strengths, and the limitations of the approach. Especially the risk assessment workflow was of interest for the evaluation of LARA. The organizational implications of a risk evaluation will not be discussed to the same extent, since the results are not to be implemented in the organization. However, the suggestions for corrective measures were communicated and the responsibility remains at the institution, were the evaluation took place.

The particular steps of the workflow are probed as follows:

Definition of the context Does the context allow the application of a risk management technique as LARA? Is the responsible scientist capable of performing the evaluation? Is it possible to subdivide an evaluation into activities of reasonable size and to describe them accordingly?

Hazard identification Based on the process description, does the database of LARA give enough options to identify hazards? Is the classification feasible for this purpose? Does the analyst agree with the identified hazards?

Risk analysis Are the risk dimensions appropriate to describe the risks present? Do the single dimension fulfill their intended goal of describing the mentioned aspects? Does the LCI values of the risks represent a plausible image of the risks and the risk level in general?

Risk evaluation Do the defined limits allow classifying the risk in the categories *acceptable, ALARP*, or *unacceptable*? Does the classification of the risk match the conception of the analyst?

Risk treatment Is LARA capable of suggesting possible corrective measures and are they feasible? Does the resource allocation using the allocation matrix allow a more distinct decision for the risk mitigation?

Risk control, risk documentation and risk communication Does the documentation provided by LARA give an adequate overview of the risk situation for the evaluation? How does a change in the context affect the example and the risk assessment results?

By answering these questions and by testing LARA intensively, it will also be shown, that LARA matches the ideal specifications (Table 3.1) of a risk management technique presented in Chapter 1.

Table 3.1 – Ideal specifications of a risk assessment approach for the academic research environment.

Requirements		**Approach**	
Data	Low to moderate	*Form*	Semi-quantitative
Difficulty	Low	*Level of detail*	Moderate
Complexity	Low	*Direction*	Hybrid
Expertise	System (moderate)	*Focus*	Variable
Time	Low	*Phase*	Operation

3.1 Demonstration of the LARA Approach

3.1.1 LARA Procedure

In this section, the LARA approach is illustrated using an example of a short chemical synthesis. For simplification reasons, the example is not discussed to its full extent.

Process

The example synthesis is a two-step synthesis to form ethyl-(E)-3-(3-nitrophenyl) acrylate (Figure 3.1).

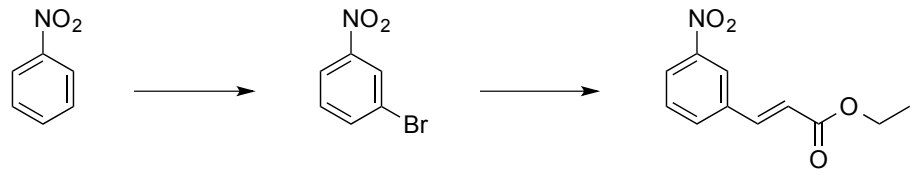


Figure 3.1 – The two-step synthesis of ethyl-(E)-3-(3-nitrophenyl) acrylate is used to illustrate the application of LARA.

Step 1 Nitrobenzene (3.0 g, 3.0 mmol, 1.0 eq) was added to a three-necked flask filled with 24 ml of water and 24 ml of sulfuric acid. The reaction mixture was cooled to 25°C. Potassium bromate (5.5 g, 3.3 mmol, 1.1 eq) was added in portions to keep the temperature between 25-35°C. After the complete addition, the reaction mixture was stirred for 3.5 h, exothermic reactions were cooled with ice. The formed solid was filtered, washed with water (2 x 10 ml) and dried to yield to a yellow solid.

Step 2 m-Bromonitrobenzene (1.07 g, 5.29 mmol, 1.0 eq), ethyl acrylate (6.0 ml, 52.9 mmol, 10.0 eq), palladium acetate (12 mg, 0.05 mmol, 0.01 eq) and triphenylphosphane (28 mg, 0.1 mmol, 0.02 eq) were dissolved in 15 ml of dimethylformamide and 1 ml of Et3N was added. The reaction mixture was stirred overnight at 87°C under nitrogen. The reaction mixture was cooled down to RT and extracted with toluene (13 ml). The organic phase was washed with 1 M HCl (13 ml) and with water (2 x 10 ml). The solvent of the organic phase were removed under reduced pressure and the remaining oil was purified with column chromatography (6 : 1 ; Hexane : Ethyl acetate). Drying yielded to a brown solid.

1. Definition of the Context

As a first step, the evaluation boarders and the related activities are defined. In this example, the evaluation consists of two activities: the first and the second step of this synthesis. Additionally,

the general worsening factors of the laboratory where this synthesis takes place are determined. From the LARA database, the factors presented in Table 3.2 are considered being present and valid for the whole evaluation (*General Worsening Factors*: 2).

Table 3.2 – General worsening factors present for this evaluation.

General Worsening Factor
Missing safety training
Blocked emergency exits
Missing safety awareness
Responsibilities unclear
Overloaded fume hoods

2. Hazard Identification

For each activity, the process is divided into the process steps (Table 3.3) and the components (Table 3.4), regardless if it is an action, material, or equipment. For the second activity, the process is described as follows:

Table 3.3 – Process steps of the second activity.

Process steps
1. Dissolution of the reactants
2. Addition of Et_3N
3. Stirring overnight under nitrogen
4. Cooling down of the reaction mixture
5. Extraction with toluene
6. Washing with 1 M HCl and water
7. Removing of solvent under reduced pressure
8. Column chromatography
9. Drying

Table 3.4 – Hazardous components of the second activity.

Hazardous components	
m-Bromonitrobenzene	Heating
Ethyl acrylate	Toluene
Palladium acetate	HCl
Triphenylphosphane	Reduced pressure
Dimethylformamide	Hexane
Et_3N	Ethyl acetate
Nitrogen	Silica

The components are possibly related with a hazard and are therefore matched with the hazard

database in LARA. For the use of the chemical hexane during the column chromatography, the following hazards are involved:

Table 3.5 – Hazards related to the hazardous component *hexane*.

Hazards
H225: Highly flammable liquid and vapor
H361: Suspected of damaging fertility or the unborn child
H304: May be fatal if swallowed and enters airways
H372: May cause damage to organs through prolonged or repeated exposure
H315: Causes skin irritation
H336: May cause drowsiness or dizziness
H411: Toxic to aquatic life with long lasting effects

The process steps and components are determined for all the activities from this evaluation. Afterwards, all the hazards related to these components are determined.

3. Risk Analysis

The risk analysis in LARA is demonstrated on the bases of the hazard *H336: May cause drowsiness or dizziness* induced by the solvent hexane. To do this, the risk dimensions are evaluated and a value is assigned; Figure 3.2 shows the hazard data sheet generated in LARA. The risk dimensions are assigned based on following considerations:

Severity The impact is limited to human damages. However, since it is a rather unimportant effect, the impact is considered as *injury without work interruption* (*Severity*: 1).

Probability This dimension consists of three sub-dimensions. The first is *occurrence* and is estimated to be an *occasional accident* (*Occurrence*: 3). The second sub-dimension is the *commonness* of this activity, which is assumed for this example as an activity done each semester taking up a high percentage of the daily work (*Commonness*: 3). The last factor for the probability indicates how much the hazard is involved in this activity. Since hexane is only used during the column chromatography and drying, the involvement is rather low (*Involvement*: 2).

Detectability As the probability dimension, the detectability has three sub-dimensions. The detector for this hazard is assumed to be human senses, which means the olfactory perception. A higher concentration of solvent vapors can be detected this way and the hazard avoided, but the performance of this detector is not ideal for each aspect. Therefore, the values are determined as follow: *Availability* 1, *Reliability* 5, and *Selectivity* 3.

H336: MAY CAUSE DROWSINESS OR DIZZINESS

Hazard source: *Hexane.*
Consequences of the hazard: *Drowsiness or dizziness.*

Hazard category	Hazard group	Hazard
Chemical hazards	Inhalation hazard	H336

Presence in steps								
1. Step	2. Step	3. Step	4. Step	5. Step	6. Step	7. Step	8. Step	9. Step

Risk factor	Assigned Value	CM 1	CM 2	CM 3	CM 4	CM 5	CM 6
Severity	1	1	1				
Occurrence	3	2	2				
Commonness	3	3	3				
Involvement	2	2	2				
Availability	1	1	1				
Reliability	5	5	5				
Selectivity	3	3	3				
General WF	2	2	2				
Hazard-specific WF	2	2	2				
Synergetic WF	2	2	2				
LCI	**3.2**	**2.9**	**2.9**				

Nr.	Corrective Measure	Costs [CHF]	A	S	C	V	F
1	Improvement of the existing ventilation	80'000	5	5	4	5	0.98
2	Information to improve the performance of the existing ventilation	1'000	4	1	4	4	0.62

Nr.	Hazard-specific WF	Score
1	Insufficient ventilation	2.3
2	Elevated temperatures	1.6

Nr.	Synergetic WF	Score
1	Evaporation (Heat)	3.9

Figure 3.2 – Hazard data sheet for the hazard *H336: May cause drowsiness or dizziness.*

Worsening Factors The general worsening factors are defined for the whole evaluation (*General worsening factors*: 2). The other factors depend on the hazard. On one side, the *hazard-specific worsening factors* are chosen from the LARA database (*Hazard-specific worsening factors*: 2) as shown in Figure 3.2. On the other hand, the *synergetic worsening factors* depend on the other hazards present in this activity. For this hazard, the evaporation under reduced pressure is considered to worsen the initial hazard (*Synergetic worsening factors*: 2).

Laboratory Criticality Index Using the described values from the hazard data sheet (Figure 3.2) the *LCI* value is calculated with a resulting value of 3.2.

This procedure is repeated with every single hazard identified for the two activities of the synthesis of ethyl-(E)-3-(3-nitrophenyl) acrylate.

4. Risk Treatment

With the levels of acceptability set to 3.0 for acceptable risks and 6.0 for unacceptable risks, the evaluated hazard lies in the ALARP region. Therefore, corrective measures are evaluated with the resource allocation matrix. The hazard data sheet (Figure 3.2) gives an overview of the possible corrective measures available in the LARA database. The resource allocation is demonstrated with the corrective measure *information to improve the performance of the existing ventilation.*

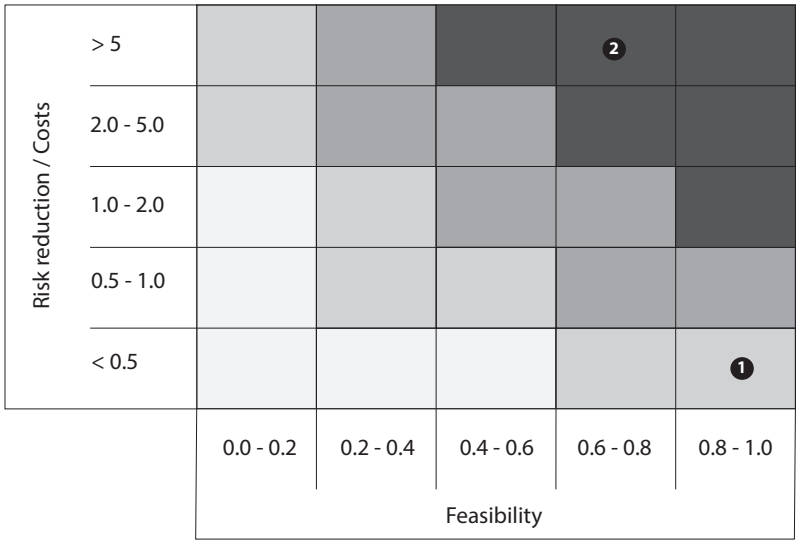


Figure 3.3 – A sample resource allocation matrix based on the corrective measures of the hazard *H336: May cause drowsiness or dizziness.*

First, all of the above dimensions are re-evaluated under the assumption, that the corrective measure is applied. This re-evaluation comes to the result, that the accident becomes less

common and the *occurrence* rating lowers to 2. This leads to a new *LCI* value of 2.9. Combined with the costs of this measure, the *risk reduction per costs ratio* is determined (30).

The corrective measures are then classified according to their feasibility values: the *acceptability* (4) is seen as relatively high. The *simplicity* (1) is rated as very low, since the measure needs a lot of interaction. However, the *compatibility* (4) and the *versatility* (4) are both judged to be high, since the measure improved the situation for other hazards as well. Overall, this leads to a *feasibility* value of 0.62.

This procedure is repeated for all the corrective measures derived from risks falling in the ALARP region. The collected corrective measures are illustrated in the allocation matrix (Figure 3.3). The regions of the matrix give an indication, which measures are more favorable than others. The actual choice of corrective measures is discussed with the safety delegate and if necessary with the research group head.

3.1.2 LARA Web Interface

One goal of the LARA project is to provide a user friendly and intuitive software for risk management in the research and teaching environment. A second version of this browser-based software was developed in the framework of this PhD project. This software allows performing the procedure described in the previous chapter in a simple and intuitive environment. The users are guided through the evaluations and can suggest hazards, corrective measures and worsening factors to the database. After an evaluation of the administrators, these entries are added to the database. Once an evaluation is finished, the information flow is provided with automatically created reports, which are sent to all the roles defined in Chapter 2.2.

The following screenshots of this web-based software give an overview of some functions. A more detailed explanation can be found in the Appendix B.

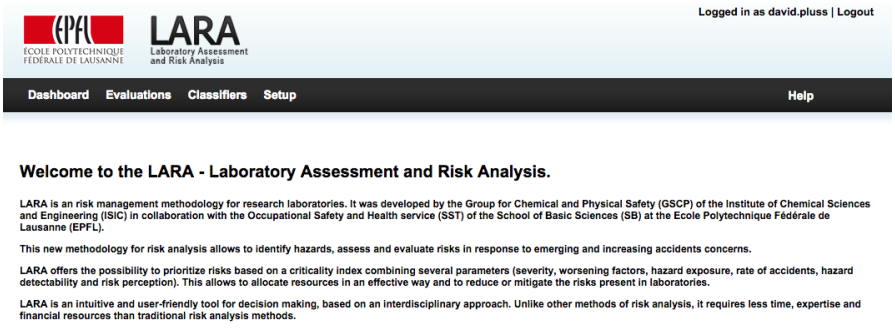


Figure 3.4 – The dashboard screen of LARA.

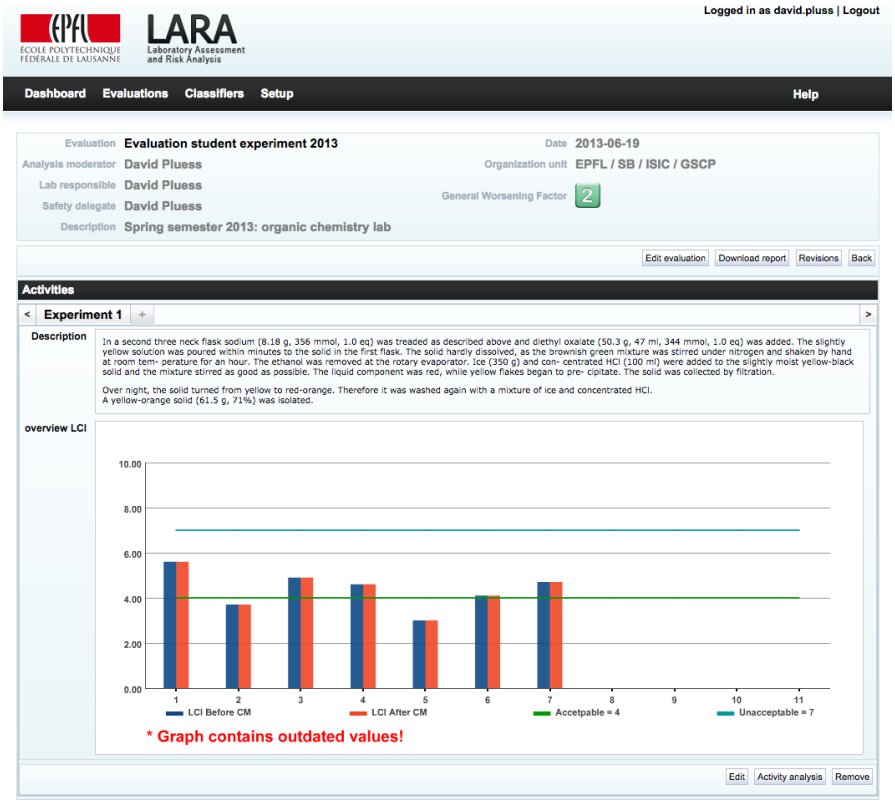


Figure 3.5 – In the evaluation overview, the user is able to add and consult all information related to a evaluation.

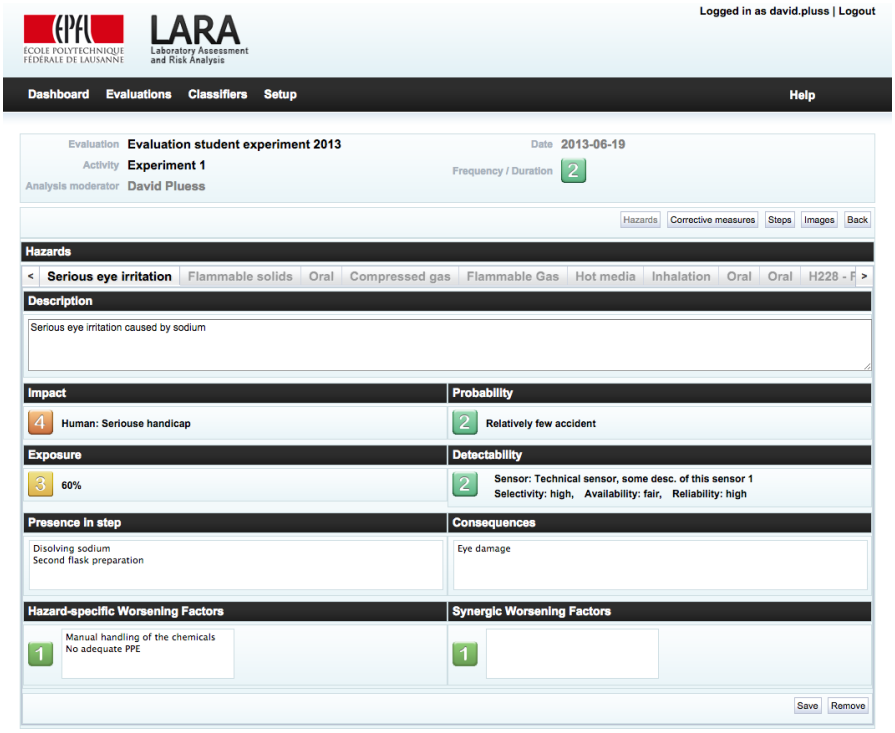


Figure 3.6 – The hazard overview allows to enter all the hazard-related information and provides the generation of the hazard data sheet.

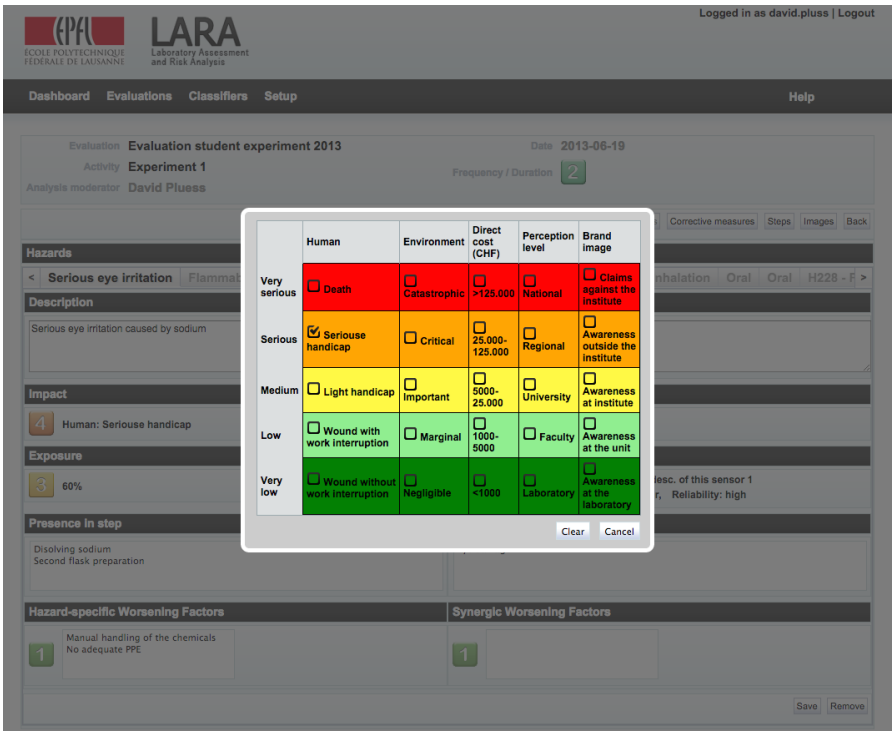


Figure 3.7 – The user can enter the specific risk dimension rating in pop-up windows (*severity* in this screenshot).

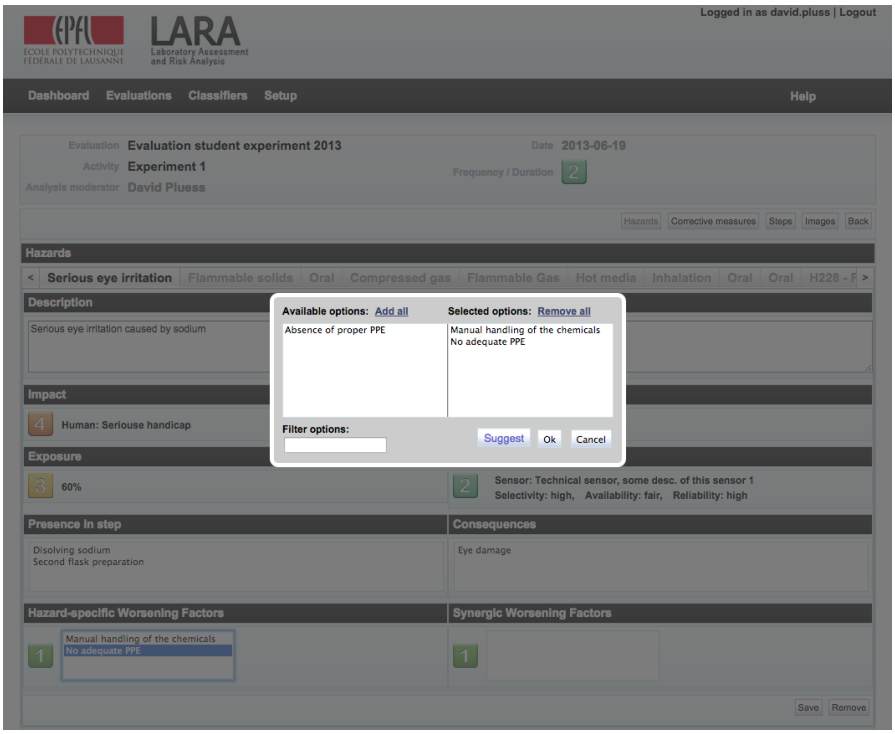


Figure 3.8 – Entering database specific values is possible trough a specific interface, which allows suggestions.

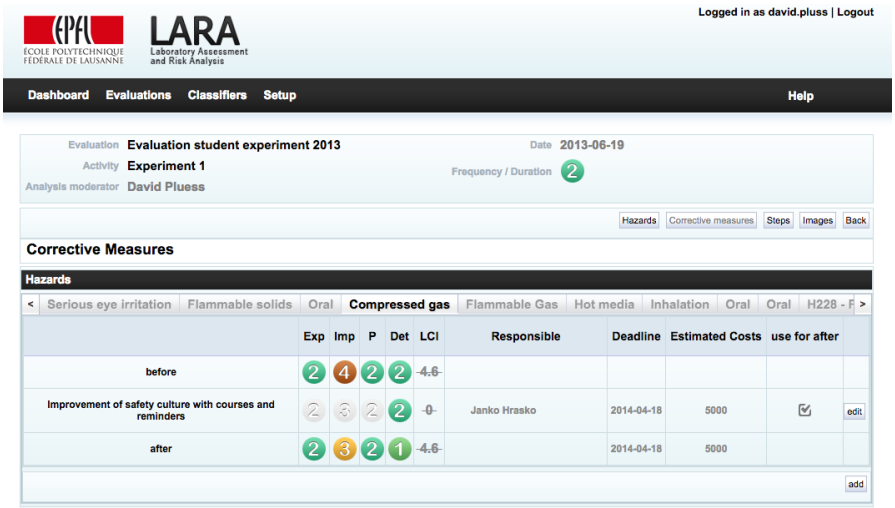


Figure 3.9 – Corrective measures are directly added to hazards to ensure optimal overview and integration of organizational factors.

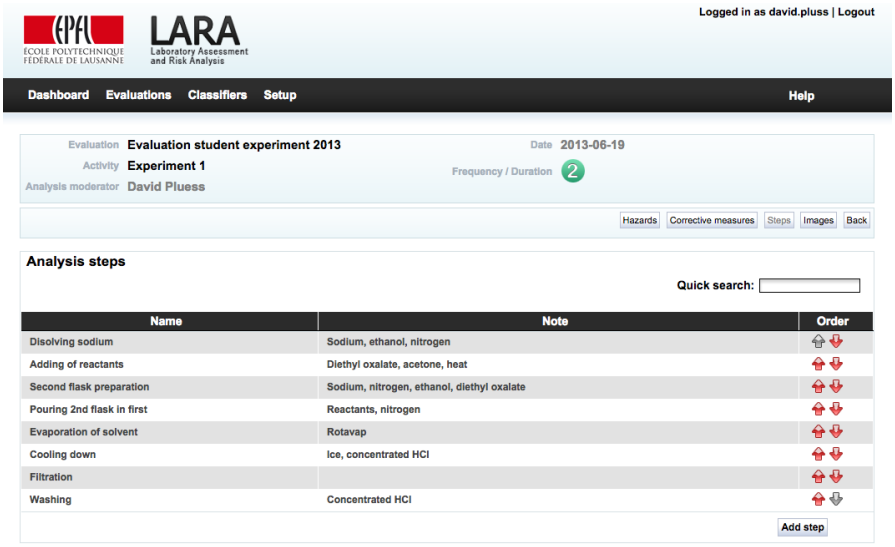


Figure 3.10 – Activity details, such as the related process steps can be entered easily using the interface.

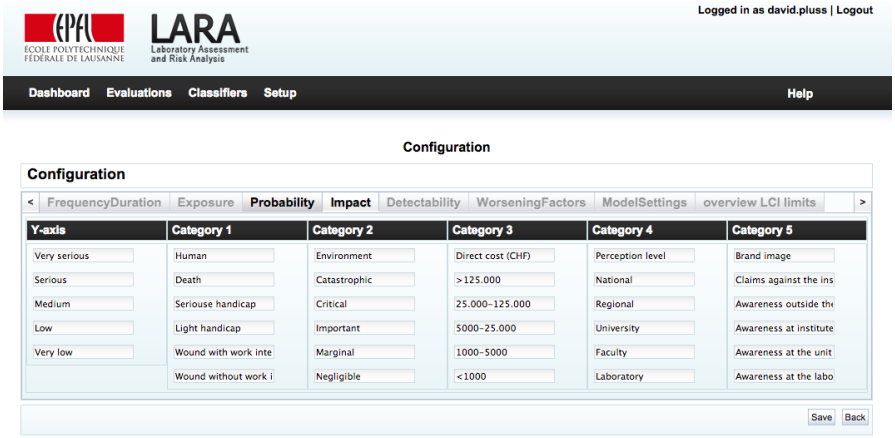


Figure 3.11 – The software is aimed at optimal user interference and allows modifications of all setting details.

3.2 EPFL

The Ecole Polytechnique Fédérale de Lausanne (EPFL) was founded as a part of the University of Lausanne, but was split off into an independent organization in 1969 under the control of the Swiss Confederation. It is part of the Swiss Federal Institutes of Technology (ETH) domain, which includes the following institutions: the Swiss Federal Institute of Technology in Zurich (ETHZ), Ecole Polytechnique Fédérale de Lausanne (EPFL), the Paul Scherrer Institute (PSI), the Swiss Federal Institute of Aquatic Science and Technology (EAWAG), the Swiss Federal Laboratories for Materials Science and Technology (EMPA), and the Swiss Federal Institute for Forest, Snow and Landscape Research (WSL). In numbers, EPFL presents itself as follows [EPFL, 2014]:

- 5 schools, 2 colleges, 1 transdisciplinary entity, 27 institutes, 340 laboratories
- 9'868 students (Bachelor, Master, PhD post-docs) of over 125 nationalities
- 5'534 staff (scientific, administrative, and technical, including PhD students)
- 859.4 million CHF annual expenses

The evaluations at EPFL are conducted at the Faculty of Basic Sciences (FSB). This faculty consists of chemistry, mathematics and physics institutes. The Occupational Safety and Health Service of the School of Basic Sciences (SB-SST) group is in charge of the safety for the faculty and provides *a support aimed at protection on the workplace for researchers and students of the School of Basic Sciences (SB) as well as for the hosts in its building* [SST, 2014].

3.2.1 Laboratory of Inorganic Synthesis and Catalysis

The first application example of LARA was performed at the Laboratory of Inorganic Synthesis and Catalysis (LSCI) at EPFL. The main research area of this group is to *develop catalysts that are made of earth-abundant elements for chemical transformations that are related to synthesis, energy, and sustainability* [LSCI, 2014]. The characteristics of this research group are:

- Professor Xile Hu, head of the research group
- Gerald Bauer (PhD student), safety delegate
- 4 postdoctoral scholars and 9 PhD students
- 1 apprentice and 1 administrative collaborator
- 10 different nationalities
- 5 laboratories

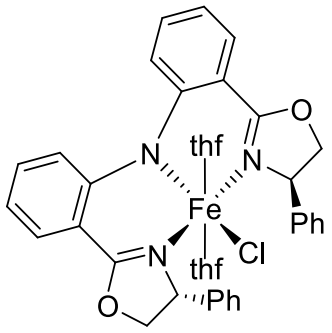


Figure 3.12 – The synthesis of [Fe(BoPa)Cl(THF)$_2$] is evaluated as a first example with the LARA method.

The objective of the evaluation is the multi-step synthesis of [Fe(BoPa)Cl(THF)$_2$] (Figure 3.12). This synthesis was performed according to the supplementary information from the article by Bauer et al. [2014]. The process was chosen to be evaluated in LARA due to the typical characteristics of an average inorganic synthesis. The procedure was developed based on similar syntheses and was performed several times, but no SOP was established. According to the responsible scientist (Gerald Bauer, who is also the safety delegate of LSCI), no noteworthy accident ever happened in the research group for this or for a similar synthesis. The main hazardous element in the process is assumed to be the use of n-Butyllithium, due to the high reactivity of this substance.

Due to the extent of a full risk assessment, the data shown in this section are condensed results of this evaluation. The full results of the risk assessment are given in Appendix C.1.

LARA Results

Process The first step of the process is the hydration of o-nitrobenzoic acid to anthranilic acid. As a second step, anthranilic acid is coupled with 2-chlorobenzoic acid to form 2,2'-iminodibenzoic acid, which is chlorinated in a third step to 2,2'-iminodibenzoyl chloride and coupled again with R-(-)-phenylglycinol to get the desired ligand 7C oxaz-NNN-Ph. This ligand is used to form the iron complex [Fe(Bopa-Ph)Cl(THF)$_2$], which is used for further investigations, but not as part of this evaluation.

The multi-step synthesis of [Fe(BoPa)Cl(THF)$_2$] involves six necessary steps to reach the desired product. Table 3.6 gives an overview of the mentioned steps, which are considered as activities in LARA and analyzed accordingly. Activity Nr. 5 includes operations with n-Butyllithium and has the highest average LCI of all activities (4.6). The highest number of identified hazard is 31 hazards in activity Nr. 4, having an average LCI of 4.1. The detailed procedures, hazard sources and identified risks can be found in C.1.

Table 3.6 – Involved activities in the synthesis of [Fe(BoPa)Cl(THF)$_2$].

Nr.	Activity	Hazard sources	Risks	Average LCI
1	Synthesis of anthranilic acid	5	13	4.0
2	Synthesis of 2,2'-Iminodibenzoic acid	6	14	4.0
3	Synthesis of 2,2'-Iminodibenzoyl chloride	4	17	4.2
4	Synthesis of 7C-Oxaz-NNN-Ph	7	31	4.1
5	Synthesis of (Bopa-Ph)Li	3	19	4.6
6	Synthesis of [Fe(Bopa-Ph)Cl(THF)$_2$]	4	15	4.3

Risks Most risks in this evaluation originate from the use of chemicals. In total, 109 risks were identified and assessed according to the LARA procedure. The average LCI value (4.2) for all risks is relatively low (on a scale from 1 to 10). The most unimportant risk is related to the heat source used in different synthesis steps (LCI 2.0), whereas the most important risks are related to the toxic and reactive properties of n-BuLi (highest LCI: 5.6). Table 3.7 gives an overview of the most important risks of the evaluation; the same risks are also presented in Figure 3.13. For simplification reasons, multiply occurring risks from different sources are left out. A complete list of all evaluated risks can be found in attachment C.1 Most risks in this evaluation originate from the use of chemicals. In total, 109 risks were identified and assessed according to the LARA procedure. The average LCI value for all risks is relatively low with 4.2 (on a scale from 1 to 10). The most unimportant risk is related to the heat source used in different synthesis steps (LCI 2.0), whereas the most important risks are related to the toxic and reactive properties of n-BuLi (highest LCI: 5.6). Table 3.7 gives an overview of the most important risks of the evaluation and Figure 3.13 shows the LCI values before corrective measures were applied. For simplification reasons, multiply occurring risks from different sources are reduced to the one with the highest risk score. A complete list of all evaluated risks and the detailed values for each risk factor can be found in Appendix C.1.

Table 3.7 – The most important risks in the synthesis of [Fe(BoPa)Cl(THF)$_2$].

Nr.	Risk	Origin	LCI
1	H250 Catches fire spontaneously if exposed to air	n-BuLi	5.3
2	H261 In contact with water releases flammable gas	n-BuLi	5.5
3	H300 Fatal if swallowed	CH_3SO_2Cl	5.2
4	H304 May be fatal if swallowed and enters airways	n-BuLi	5.6
5	H310 Fatal in contact with skin	CH_3SO_2Cl	5.4
6	H319 Causes serious eye irritation	THF	5.0
7	H330 Fatal if inhaled	CH_3SO_2Cl	5.4
8	H351Suspected of causing cancer	THF	5.0
9	H360 May damage fertility or the unborn child	DMF	5.2
10	H361 Suspected of damaging fertility or the unborn child	Toluene	5.2

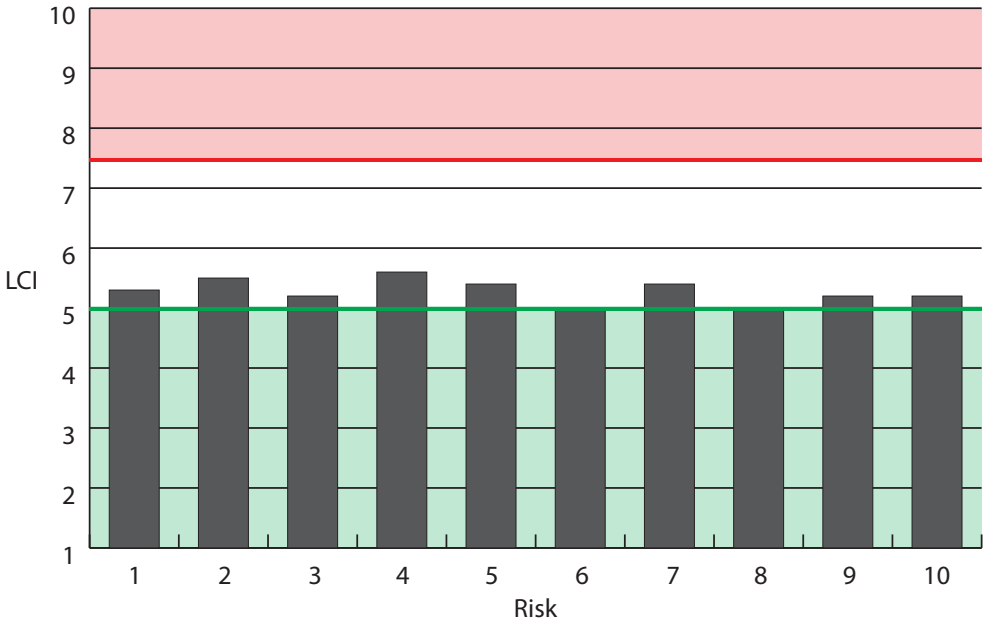


Figure 3.13 – LSCI: the most important risk in context of the ALARP region. All values above 7.5 are considered as unacceptable, whereas the values below 5.0 are considered as acceptable (as in Scenario b) from Figure 2.26).

Risk treatment For this evaluation, the limits of acceptability are set to 5.0 for acceptable risks and 7.5 for unacceptable risks (as in Figure 2.26b), the ALARP region is defined between those two values (Figure 3.13). No risk falls in the category *unacceptable*, therefore a treatment regardless of the costs is not necessary. The risks shown in Table 3.7 correspond to the ALARP region, therefore the risk allocation matrix is used to decide between possible corrective measures. Table 3.8 gives an overview of the options for the risk treatment. As for the risks, the corrective measures are reduced for simplification reasons: if a corrective measure affects more than one risk, the one with the highest risk reduction potential is taken into the comparison. A complete list of the corrective measures determined for the risk in the ALARP region can be found in Appendix C.1.

According to the results of the resource allocation matrix, most measures in this comparison are favorable both financially and non-financially (see Figure 3.14). The most favorable option is to raise safety awareness for the use of carcinogenic or teratogenic substances (Nr. 4), such as toluene or n-Butyllithium. The measure aims specifically at female scientist to avoid exposition of possibly pregnant women, since the teratogenic properties are suspected to cause the highest risks in this process. Other measures do not provide an ideal performance in financial and non-financial terms. On one hand, biological monitoring (Nr. 2) might show possibly dangerous expositions and lower the risk significantly, but the feasibility of such a measure is not given in this context. On the other hand, the improvement of the ventilation

Table 3.8 – Suggested corrective measures for the risks in the ALARP region.

Nr.	Corrective measure	Affects risk Nr.	Priority
1	Additional PPE	5	1
2	Biological monitoring	10	2
3	Improvement of ventilation	7	2
4	Information to raise awareness	9	1
5	Intensified safety training for critical substances	1	1
6	Training to avoid misuse of existing measures	2	1
7	Training to raise safety awareness	3	1

(Nr. 3) has a high feasibility, but lacks an ideal *risk reduction per costs potential*. However, the risk level in the process in not unacceptably high, therefore the decision remains with the research group head, which measures are actually advisable.

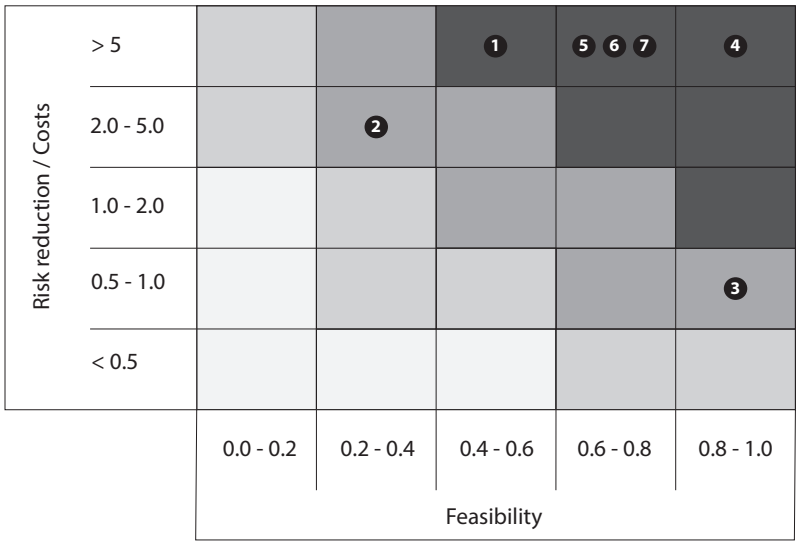


Figure 3.14 – LSCI: resource allocation matrix of the different corrective measures.

Outcome of the application The results of the evaluation reveal on one side the most important risks of the project. Even if they remain untreated in terms of corrective measures, awareness is raised and the involved scientists might be more careful when performing certain activities. On the other side, possible corrective measures were determined and their effectiveness both financially and non-financially were estimated. The options of risk treatment are not mandatory and will be discussed with the safety delegate of the research group. For this evaluation, the suggestion according to LARA is to lower the risk *H360: may damage fertility or the unborn child* with the corrective measure *information to raise awareness* (Figure 3.15). This measure allows to achieve an optimal impact with low resources. The general risk level is

rather low, thus leaving the other risks untreated seems acceptable.

In order to get the corrective measures applied in a reasonable amount of time, an action plan is established. In the further procedure of LARA, the risk evaluation results, the recommendation for corrective measures, and the action plan for the implementation of the corrective measures is distributed to all the roles in the LARA framework (see Chapter 2.2).

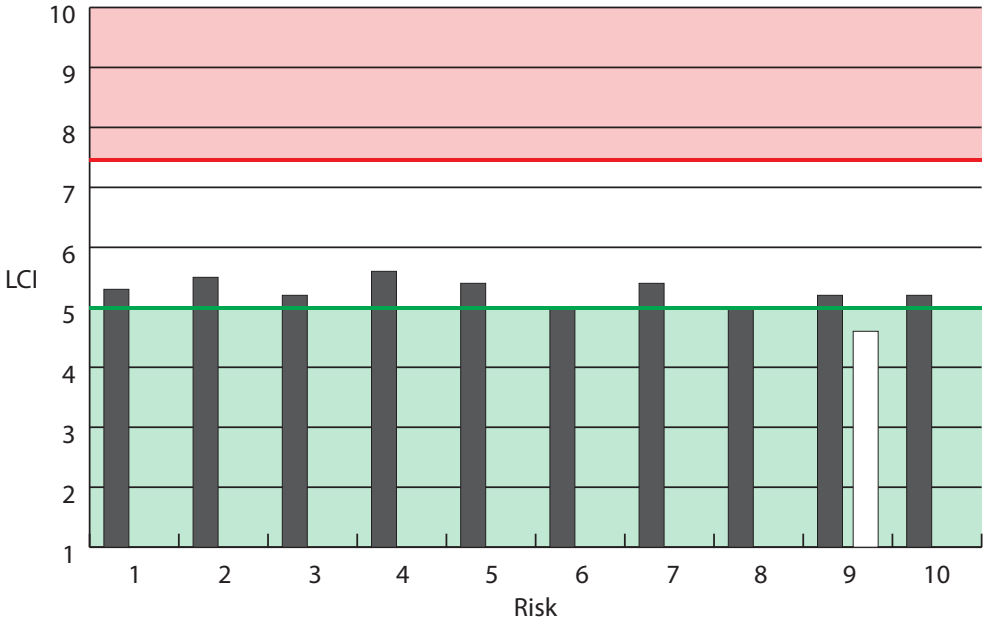


Figure 3.15 – LSCI: only the risk Nr. 9 is suggested to be treated according to the LARA results.

Remarks on the Application

The application of LARA for this example was possible without limitations. The scope of LARA matched the application for a chemical synthesis and the method gave enough possibilities to describe the activities, the hazard sources, and the hazards. The identification of chemical risks in LARA is beneficially influenced by the strict and very detailed hazard classification of the GHS system. The description of the hazards matched the requirements of a method for the research environment: the semi-quantitative approach allowed untrained scientist to describe and assess the risks. The LCI results of the risks assessment mostly fit the appraisement of the scientists performing the process. As in LARA, he sees the properties of n-BuLi as the most important risk to take care of, but not as an unacceptably high risk. The corrective measures are not assumed to be necessary, since the risks are not unacceptably high; a circumstance that is also demonstrated in LARA. This matches the real situation, where the process is conducted without any change and the risks are considered acceptable.

3.2.2 Group of Catalytic Reaction Engineering

The second application example of LARA was performed at the Group of Catalytic Reaction Engineering (GGRC) at EPFL. The research focus of this group is the*development of novel compact (micro)-reactors based on structured catalysts in the form of grids, gauzes and sintered metal fibers* [GGRC, 2014]. The characteristics of this research group are:

- Professor Lioubov Kiwi, head of the research group
- Tatiana Iouranova (senior scientist), safety delegate
- 3 postdoctoral scholars
- 4 PhD students
- 2 apprentice and 1 administrative collaborator
- 4 laboratories

The objective of this evaluation is a selective hydrogenation of 2-butyne-1,4-diol in a batch reactor (see Figure 3.16). The purpose of this experiment is to train students in the use of these devices and to demonstrate certain effects by changing the conditions of the reaction. The alterations studied in this evaluation consider the use of different solvents (ethanol, isopropanol and toluene). The experiments were performed according to the SOP in Appendix C.2. The process was chosen to be evaluated in LARA due to the typical characteristics of an instructional experiment for undergraduate students. According to the responsible scientist (Tatiana Iouranova, who was also the safety delegate of the research group), no noteworthy accident ever happened in relation to this experiment. The main hazardous element in the process is assumed to be the poisonous properties of the reactant 2-butyne-1,4-diol.

Due to the extent of a full risk assessment, the data shown in this section are condensed results of this evaluation. The full results of the risk assessment are given in Appendix C.2.

LARA Results

Process For this experiment, the substrate is placed into a stainless steel reactor (150 cm^3 autoclave, Büchi AG, Uster, Switzerland) equipped with a pressure controlled H_2 supply system. The hydrogen consumption in the reservoir is monitored with a press gas flow controller (BCP-6002, Büchi, Switzerland). A stainless steel 6 -blade disk turbine impeller provides agitation at 1900 - 2000 rpm. A bath circulator (HAAKE B-N3) is used to control the reaction temperature to within ± 1 K using water as a thermal medium. When the reactor is assembled, the apparatus is tested with various procedures. Afterwards, the system is purged with nitrogen, heated to reaction temperature and purged with hydrogen for starting the reaction. Sampling is done via

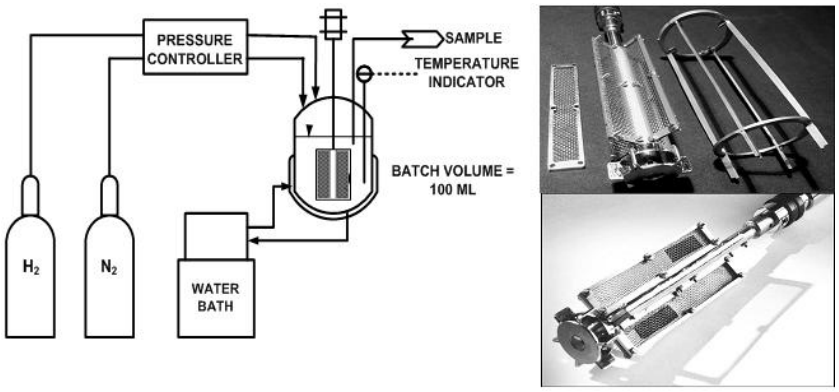


Figure 3.16 – Experimental setup of the studied process.

a valve of the reactor and transferred to the GC vial. After the reaction is finished, the system is cleaned with ethanol in an ultrasonic bath and dried in the oven.

The hydrogenation of 2-butyne-1,4-diol is considered as a single activity for the evaluation in LARA. Since the experiment is carried out with three different solvents, there are three mainly identical activities to be analyzed in LARA. Table 3.9 gives an overview of these three activities. Even though the procedures use different solvents, the average LCI value of the three activities is the same (4.2). Regardless of the solvent used for the process, ethanol is used in every activity for cleaning and preparation purposes, which leads to different amounts of hazard sources in the activities. The process carried out with toluene as solvent involves the most risks, whereas the one with ethanol is connected with the fewest risks. The detailed procedures, related hazard source and identified risks can be found in Appendix C.2.

Table 3.9 – Involved activities in the hydrogenation experiment series.

Nr.	Activity	Hazard sources	Risks	Average LCI
1	Selective hydrogenation (ethanol)	6	11	4.2
2	Selective hydrogenation (isopropanol)	7	14	4.2
3	Selective hydrogenation (toluene)	7	17	4.2

Risks As in the first example of the application of LARA, the most risks in this evaluation originate from the use of chemicals (33). 42 hazards were identified in total for all three activities with an average LCI value of 4.2 (on a scale from 1 to 10). The lowest LCI value was assigned to the risk of ejection of reaction mixture during the sampling for gas chromatography-mass spectrometry (3.5). The highest identified risk is assigned to flammable properties of the solvents with an LCI value of 5.2. Table 3.10 gives an overview of the most important risks of the evaluation and Figure 3.17 shows the LCI values before corrective measures were applied. For simplification reasons, multiply occurring risks from different sources are reduced to the one with the highest risk score. A complete list of all evaluated risks and the detailed values for

Table 3.10 – The most important risks in the hydrogenation experiment series.

Nr.	Risk	Origin	LCI
1	Hot medium	Heating	4.1
2	H301 Toxic if swallowed	2-butyne-1,4-diol	4.2
3	H331 Toxic if inhaled	2-butyne-1,4-diol	4.2
4	H319 Causes serious eye irritation	Isopropanol	4.8
5	H314 Causes severe skin burns and eye damage	2-butyne-1,4-diol	4.8
6	H304 May be fatal if swallowed and enters airways	Toluene	5.2
7	H220 Extremely flammable gas	H_2	5.3
8	H361 Suspected of damaging fertility or the unborn child	Toluene	5.3
9	H225 Highly Flammable liquid and vapor	Ethanol	5.3

each risk factor can be found in Appendix C.2.

Risk treatment When applying the same acceptability limits for this evaluation as for the first example, all risks would be acceptable. However, to illustrate the application of the resource allocation approach, the limits for this example are defined as follows: risks below an LCI value of 5.0 are considered as acceptable and risks with an LCI value higher than 7.5 are considered as unacceptable; however, such risks are not present in this example. Therefore the resource allocation focuses on the region of risks with an LCI value between 5.0 and 7.5, which should be reduced to ALARP. Table 3.11 gives an overview of the possible corrective measures. As for the risks, the presented corrective measures are reduced for simplification reasons: if a corrective measure affects more than one risk, the one with the highest risk reduction potential is taken into the comparison. A complete list of the corrective measures determined for the ALARP risks can be found in C.2.

Table 3.11 – Suggested corrective measures for the risks in the ALARP region.

Nr.	Corrective measure	Affects risk Nr.	Priority
1	Strict regulations concerning labeling	7	1
2	Information to raise awareness	8	1
3	Improve ventilation	9	2

According to the results of the resource allocation matrix, two of three measures in this comparison are favorable both financially and non-financially (see Figure 3.19). As for the first evaluation example, intensified efforts to raise awareness for specific risks are the most favorable option. Improvements in the ventilation system might be feasible to lower certain risks, but the *low risk reduction per costs ratio* makes this option not favorable for application in this context. A compulsive application of a corrective measure to lower the risks is however not necessary, since the overall risk level for these three activities is rather low.

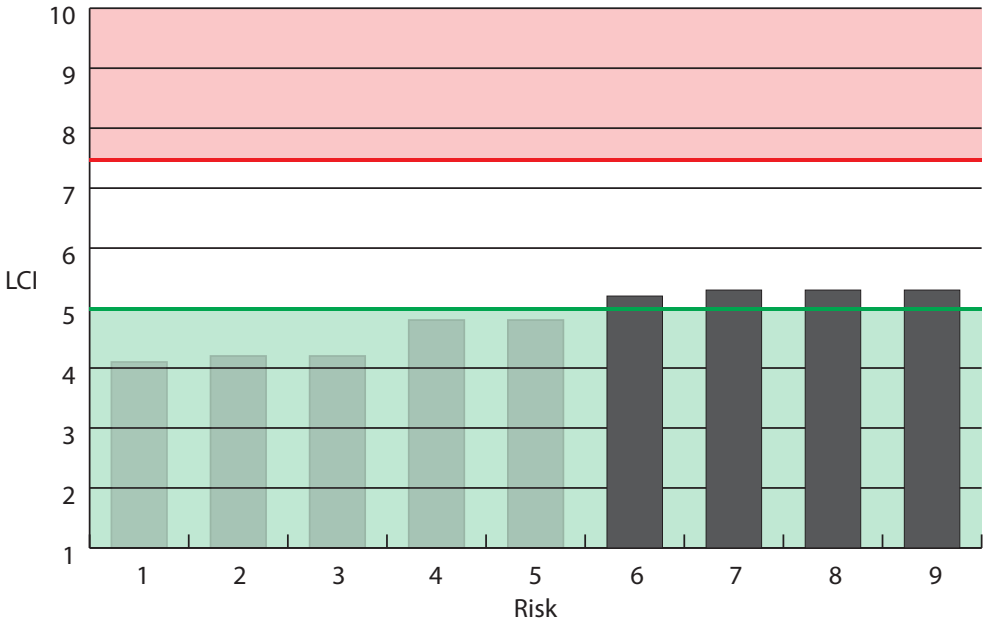


Figure 3.17 – GGRC: the most important risk in context of the ALARP region. All values above 7.5 are considered as unacceptable, whereas the values below 5.0 (greyed out in the Figure) are considered as acceptable (as in Scenario b) from Figure 2.26).

Outcome of the application The evaluation identified and evaluated the most important risks in this procedure, even though the risk level in general is rather low for all the involved activities; only 4 risks out of 43 are not considered as acceptable. Although two of three possible corrective measures are feasible in financial an non-financial terms, the suggestion based on the LARA evaluation is to accept the risks in the ALARP zone. The gain from a measure is still disproportional to the actual benefits, especially since the risk level is relatively low. Nevertheless, the risk evaluation results are reported to the roles in the LARA framework (see Chapter 2.2).

Remarks on the Application

The application of LARA for this example was possible with few limitations. The flexible focus of LARA allowed the description of the three similar activities and the involved risks. The majority of the risks are chemical risks and were easily determinable due to the GHS classification system; the remaining risks were identified using the other categories provided by LARA. As for the first application example, the LCI results of the risks assessment mostly fit the appraisement of the scientists performing the process and seem to fit the real risk situation. However, the corrective measures are not beyond controversy; a reduction in this region does not get a lot of acceptability by the scientists working in this environment. Since the activities

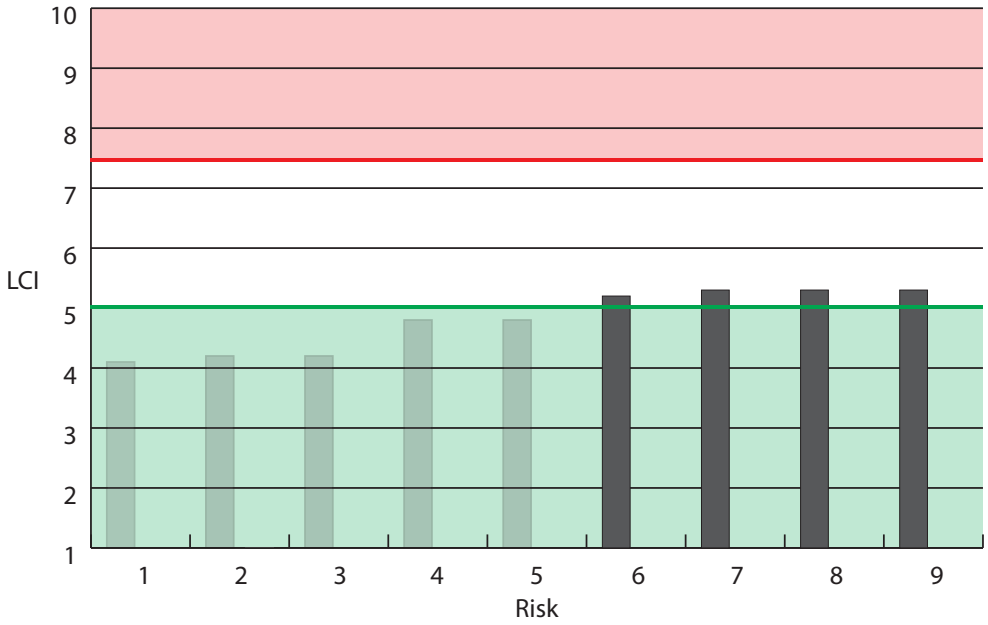


Figure 3.18 – GGRC: the risks in the ALARP region of this project remain untreated.

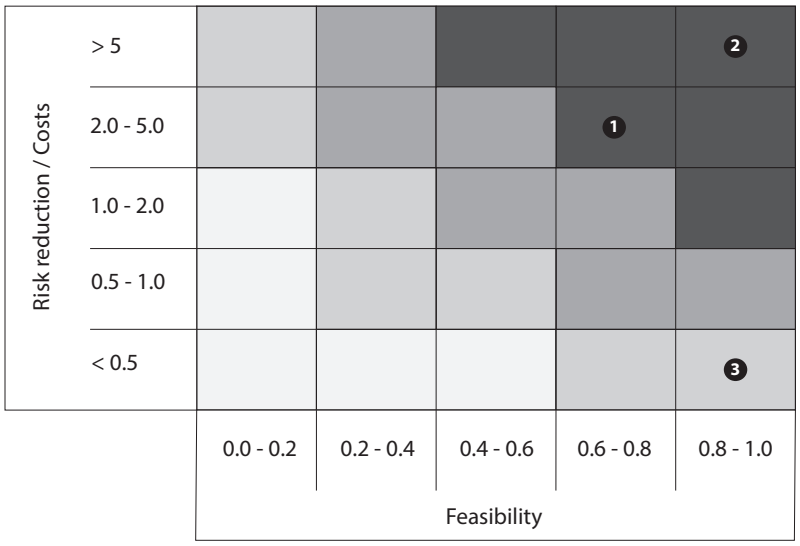


Figure 3.19 – GGRC: resource allocation matrix of the different corrective measures.

are not interdependent as in the first example and performed for educational purposes only, the legitimation of each experiment needs to be scrutinized in general. For this example, the use of toluene might be abandoned, since the solvent involves a high amount of risks.

3.3 University of Basel

The University of Basel was founded in 1460 and is a self-controlled university under the supervision of the cantons Basel-Stadt and Basel-Landschaft. In numbers, the institution presents itself as follows [University of Basel, 2014]:

- 7 faculties
- 11'000 students (Bachelor, Master), around 20% foreigners
- 2'000 PhD students
- 538.9 million CHF annual expenses

The occupational safety is organized by a centralized OSH service, even though the broad spectrum of the university reaches from social sciences to natural sciences. The evaluations of LARA were performed at the faculty of basic sciences, which includes the departments for biology, chemistry, mathematics and information sciences, pharmaceutical sciences, physics, and environmental sciences. The research group chosen for the evaluation is part of the chemistry department. This department is self-organized in terms of safety, featuring an own OSH service.

3.3.1 Chemistry Departement: Constable Group

The third application example of LARA in this thesis was performed at the Constable group at the chemistry department of the University of Basel. One of the focuses of this research group is aimed at *light harvesting using inorganic coordination complexes as dyes in dye-sensitized solar cells* [Constable group, 2014]. The characteristics of this research group are:

- Professor Edwin Constable, head of the research group
- No specific safety delegate
- 8 postdoctoral scholars
- 14 PhD students
- 9 different nationalities
- 5 laboratories

The objective of this evaluation is the preparation and the testing of the dye-sensitized solar cells. This is a repetitional task, which is performed each time a complex (see Figure 3.20) is tested for its feasibility for the use in these solar cells. The preparation was performed

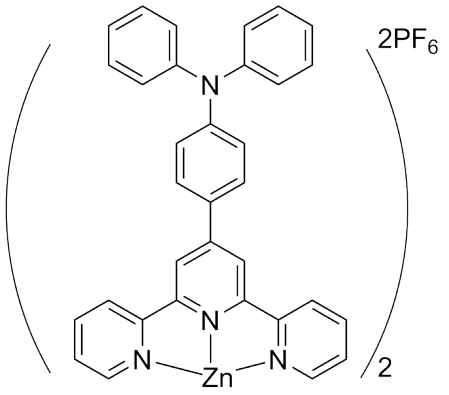


Figure 3.20 – Example of a dye used for the performed tests of the solar cells.

according to the supplementary information in the article by Bozic-Weber et al. [2012]. The process was chosen to be evaluated in LARA due to the typical characteristics of a repetitional task related to other processes. The process to prepare the solar cells changes constantly and is adjusted on a regular basis to fit the newest testing standards. Only negligible accidents happened in the research group when preparing the solar cells, for example burns when touching a hot surface. The main hazardous element in the process is therefore considered to be the heating of the solar cells during the preparation.

Due to the extent of a full risk assessment, the data shown in this section are condensed results for this process. The full results of the risk assessment are given in Appendix C.3.

LARA Results

Process A first part of the process is the preparation of the electrode of the solar cell. Therefore, a glass (FTO glass, Solaronix TCO22-7, 2.2 mm thickness, sheet resistance ≈ 7 Ω square $^{-1}$) is washed, cleaned and coated with a TiO_2 layer, by doctor blading a TiO_2 onto the conducting glass slide. Afterward, the electrode is dried with various temperatures; then a ligand and $ZnCl_2$ is applied. After an immersion in another solved ligand for 64 h the electrode is finished. For the preparation of the counter electrode, a hole is drilled into a similar piece of FTO glass, cleaned and an a Pt catalyst (H_2PtCl_6) is applied. The two electrodes are assembled using a thermoplast hot-melt sealing foil (Solaronix, Meltonix, 1170-25 Series, 25 microns thick) by heating while pressing them together. The electrolyte (a mixture of LiI, I_2, 1-mehtylbenimidazole and 1-butyl-3-methylimidazolinium iodide in MeCN) is applied via vacuum backfilling. The hole in the counter electrode is finally sealed using the hot-melt sealing foil and a cover glass. The testing of the cells is done by irradiating from behind using a light source SolarSim 150 (100 mW cm^{-}2 = 1 sun). The power of the stimulated light is calibrated using a reference Si photodiode.

The process to produce the solar cells was subdivided into three different activities shown in Table 3.12. The detailed procedures, the related hazard sources, and the identified hazards

can be found in Appendix C.3.

Table 3.12 – Involved activities in the preparation of solar cell for testing purposes.

Nr.	Activity	Hazard sources	Risks	Average LCI
1	Preparation of the electrode	8	22	4.8
2	Preparation of the counter electrode	5	10	4.6
3	Assembling of the solar cell	7	23	4.5

Risks Chemical risks are the main risks involved in this activity (50), even though the process does not involve a chemical reaction. The source of these chemical risks is the use of solvents for cleaning and application purposes. Not only chemicals are causing risks, physical risks are present in the form of hot media or UV radiation. The most unimportant risk in the evaluation is the risk of harmful effects caused by swallowing of zinc chloride (LCI of 3.6). On the other side of the LCI spectrum is the same substance due to its very toxic properties to the aquatic environment with long lasting effects (LCI of 6.0). Table 3.13 gives an overview of the most important risks of the evaluation and Figure 3.21 shows the LCI values before corrective measures were applied. For simplification reasons, multiply occurring risks from different sources are reduced to the one with the highest risk score. A complete list of all evaluated risks and the detailed values for each risk factor can be found in Appendix C.3. In general, the risk level is higher than in the other examples. A reason for this is a higher level of general worsening factors: untrained personnel, unclear and constantly changing procedures, and other particularities are present for this process. However, also the fact that the process is carried out relatively often increases the LCI level.

Table 3.13 – The most important risks in the preparation of the solar cells.

Nr.	Risk	Origin	LCI
1	UV Radiation	Light source	5.0
2	H225 Highly Flammable liquid and vapour	EtOH	5.2
3	Hot media	Heating	5.2
4	H318 Causes serious eye damage	1-methylbenzimidazole	5.4
5	H319 Causes serious eye irritation	MeCN	5.4
6	H330 Fatal if inhaled	UV-O_3 (Ozone)	5.5
7	H314 Causes severe skin burns and eye damage	H_2PtCl_6	5.6
8	H410 Very toxic to aquatic life with long lasting effects	$ZnCl_2$	6.0

Risk treatment In order to allocate resources for corrective measures, the ALARP region for this example is set between the LCI values 5.0 to 7.5 (as in Figure 2.26b). As in the first two examples, no risk needs to be treated regardless of the related effort. However, several risks need further investigation about possible corrective measures. Table 3.14 gives an overview

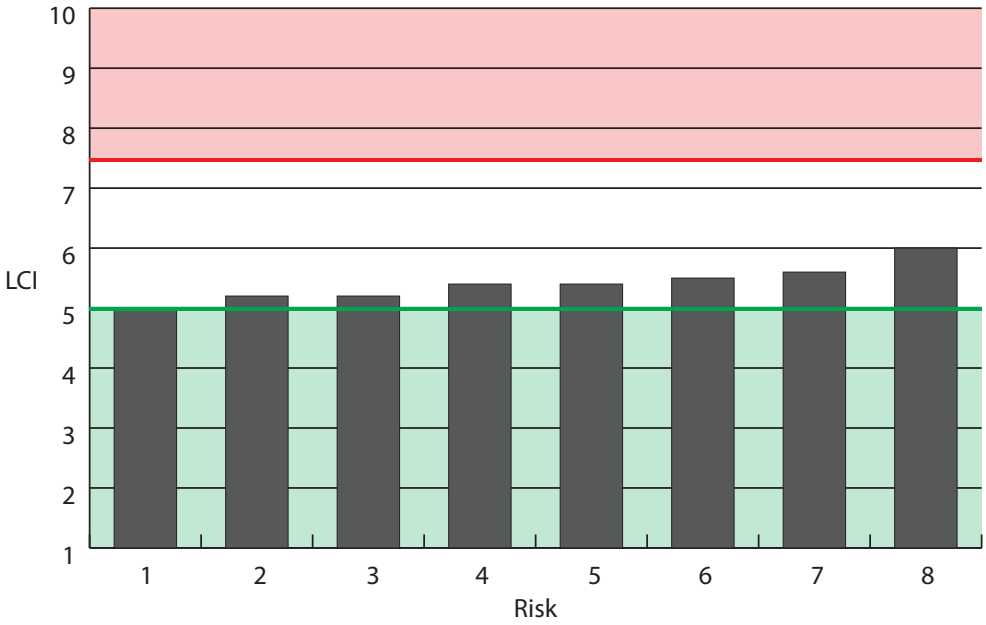


Figure 3.21 – Constable group: the most important risk in context of the ALARP region. All values above 7.5 are considered as unacceptable, whereas the values below 5.0 are considered as acceptable (as in Scenario b) of Figure 2.26).

of the possible corrective measures. As for the risks, the corrective measures are reduced for simplification reasons: if a corrective measure affects more than one risk, the one with the highest risk reduction potential is taken into the comparison. A complete list of the corrective measures determined for the ALARP risks can be found in Appendix C.3.

A large number of corrective measures are possible both financially and non-financially to treat the identified risks (see Figure 3.22). The most important risk with a serious environmental impact can be lowered with an improved waste management. The bandwidth of options includes specific options, such as the use of an ozone detector, but also less specific measures, for example intensified safety training.

Outcome of the application As for the other applications, the evaluation provides an extensive overview of the risks related to the process. For the whole process, eight risks fall in the ALARP region and should be reduced to as low as reasonably practicably. For these risks, a broad spectrum of possible corrective measures was found. The suggestion of the LARA procedure is to treat the risks as follows: the risk *hot media* with the corrective measure *warning signs*, the risk *H319 Causes serious eye irritation* with the corrective measure *improvement of safety training* and the risk *H410 Very toxic to aquatic life with long lasting effects* with the measure *improved waste management including controls* (see Figure 3.23). These measures

Table 3.14 – Suggested corrective measures for the risks in the ALARP region.

Nr.	Corrective measure	Affects risk Nr.	Priority
1	Disciplinary regulations to enforce PPE use	5	1
2	Improved waste management including controls	8	1
3	Improvement of safety training	5	2
4	Improvement of shielding	1	1
5	O_3-Detector	6	1
6	Reduction of storage quantities	2	2
7	Temperature indication	3	1
8	Warning signs	3	1

all provide a high effectiveness in financial and non-financial terms. Especially the improved training should be implemented, since a lack of organized training is a worsening factor for the entire laboratory and research group.

In order to get the corrective measures applied in a reasonable amount of time, an action plan is established. In the further procedure of LARA, the risk evaluation results, the recommendation for corrective measures and the action plan for the implementation of these corrective measures is distributed to all the roles in the LARA framework (see Chapter 2.2).

Remarks on the Application

Since the evaluation involves a high number of chemical risks, the scope of the LARA method allows a proper analysis of the involved risks. The estimated risks match the estimations of the persons involved in the process, even though the general risk level was estimated lower. A cause for this different estimation is the inclusion of worsening factors in the process, which increase the risk level for all risks involved. The corrective measures for the process are feasible, even though the risk level does not force a change of the procedure. However, the distinction between the regions of the allocation matrix is not ideal, since the corrective measures are relatively close. The corrective measure database does not include all possibilities of context change in a procedure; other aspects can allow such change as well: since the dye-sensitized solar cells became a widely researched topic, blank solar cells for testing became commercially available. Therefore, the process will be abandoned in the near future in this research group, lowering the overall risk level, even though this fact was not the main driving force.

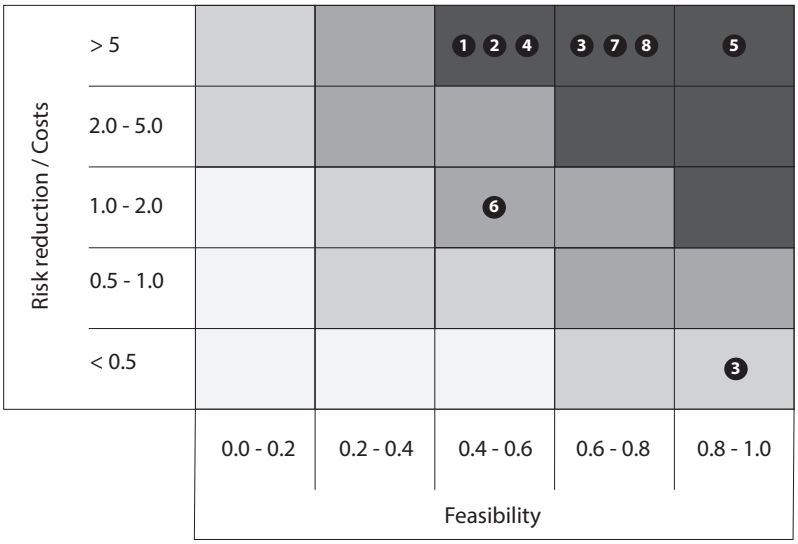


Figure 3.22 – Constable group: resource allocation matrix of the different corrective measures.

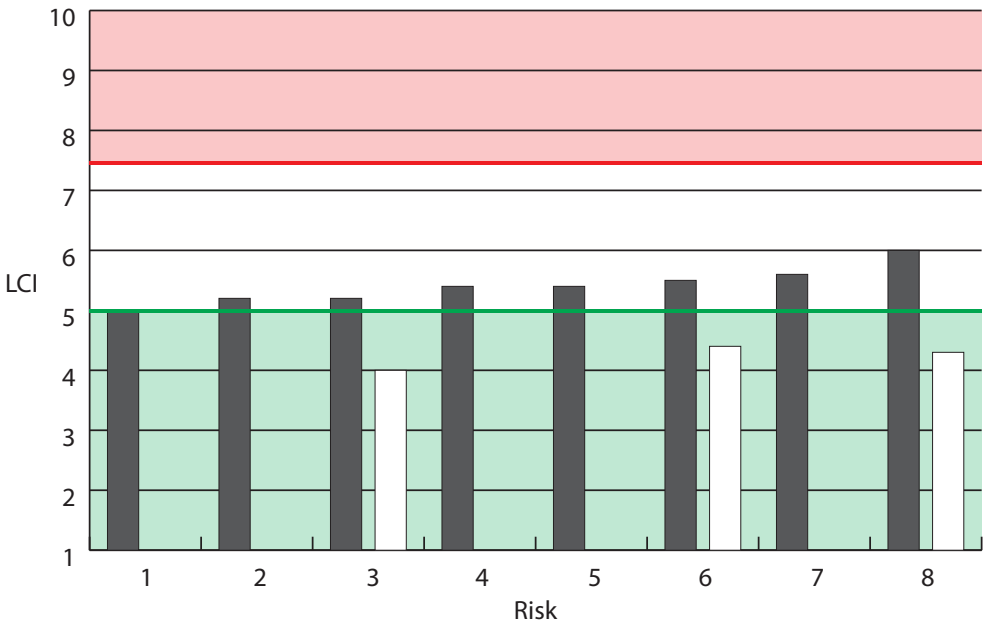


Figure 3.23 – Constable group: the risks Nr. 3, 6 and 8 are suggested to be treated according to the LARA results.

3.4 ETHZ

The Eidgenössische Technische Hochschule Zürich (ETHZ) was founded in 1855 as a national technical university under the control of the Swiss Confederation. As the EPFL, the ETHZ is part of the Swiss Federal Institutes of Technology. In numbers, the institution presents itself as follows [ETHZ, 2014]:

- 16 departements
- 18'000 students (Bachelor, Master), 110 nationalities
- 3'900 PhD students
- 1'467 million CHF annual expenses

The occupational safety is organized by a centralized OSH service, which deals with all topics related to security, health and environment at the university [CABS, 2014]. The evaluation of LARA was performed at the department of biology, which includes five institutes for different fields of biological research. The institute chosen for the evaluation is the Institute of Molecular Systems Biology (IMSB).

3.4.1 Institute of Molecular Systems Biology: Aebersold Group

The fourth application example of LARA in this thesis was performed at the Abersold group at the Institute of Molecular System Biology of the ETHZ. *The Aebersold group is interested in developing and applying novel methods in quantitative mass spectrometry to accurately measure protein analytes in complex samples.* [Institute of Molecular Systems Biology, 2014]. The characteristics of this research group are:

- Professor Ruedi Aebersold, head of the research group
- 1 administrational collaborator
- 2 senior scientist
- 15 postdoctoral scholars
- 8 PhD students
- 10 different nationalities
- 1 laboratories with biosafety level 2

The subject of evaluation in this example is the proteolytic digestion of protein samples, which is part of a data acquisition workflow shown in Figure 3.24. This can either be done with a

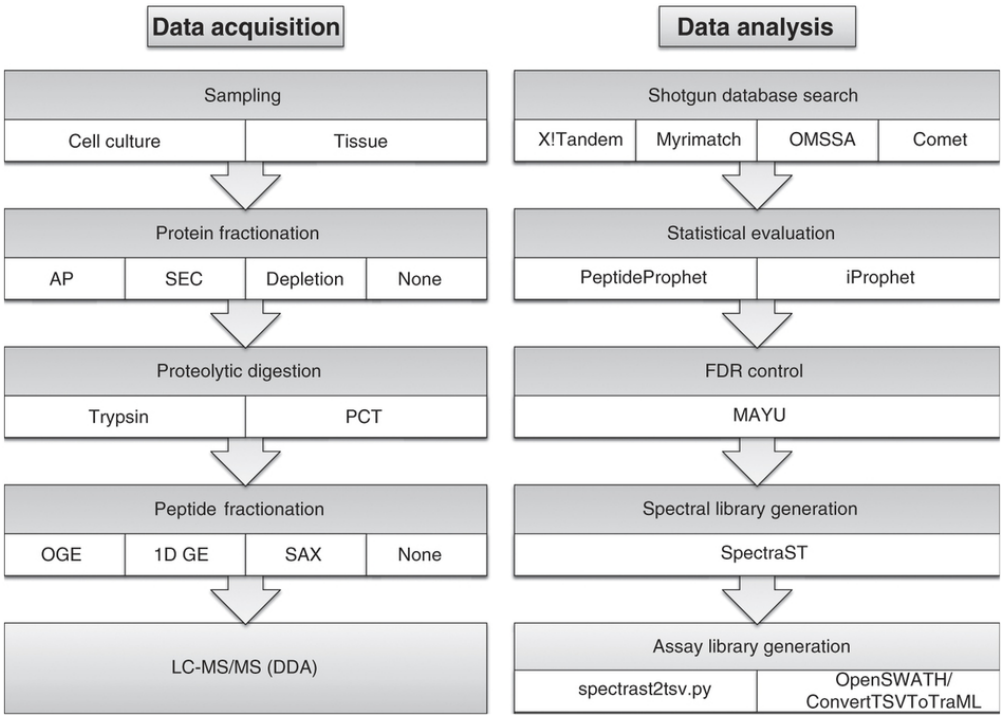


Figure 3.24 – The complete experimental workflow presented in Rosenberger et al. [2014].

trypsinization or via a pressure cycling technology (PCT) assisted lysis and digestion. The whole workflow and the associated results can be found in the article of Rosenberger et al. [2014]. The interest in this process to evaluate it in LARA is due to the field of application (biological chemistry) and the kind of process, which can be described as a routine task. According to a scientist familiar with the process, it is harmless and accidents to occur can only remotely be imagined.

Due to the extent of a full risk assessment, the data shown in this section are condensed results for the process. The full results of the risk assessment are given in Appendix C.4.

LARA Results

Process The proteolic digestion can be done via two routes: trypsinization or PCT-assisted lysis and digestion. The following procedures are shortened experimental instruction of the article Rosenberger et al. [2014]:

The protein samples were reduced with 5 mM TCEP, and alkylated with 10 mM iodoacetamide before overnight trypsinization. Protein from SEC fractions was denatured by incubation at 69°C for 10 min, reduced, alkylated and digested in the presence of 1% (v/v) Sodium-deoxycholate overnight. Trypsin was inactivated by lowering the pH to 2 and the peptides were immobilized onto C18 columns. After multiple washes, the peptides were eluted (50% acetonitrile/0.1% formic acid) and solvents were evaporated in a SpeedVac centrifuge. After

re-suspension, the samples were briefly sonicated before MS analysis.

pressure cycling technology (PCT) applies cycles of hydrostatic pressure between ambient and ultra-high levels to induce cell lysis and to enable precise thermodynamic control of biomolecular interactions. All PCT-processed samples were handled using Barocycler NEP2320 (PressureBioSciences, Inc, South Easton, MA). In brief, tissue or cell line samples were lysed in buffer containing 8M urea, 100mM ammonium bicarbonate supplemented with Complete protease and phosphatase inhibitor cocktail under Barocycler program (tissue samples: 60 cycles of 50 s 45 kpsi and 10 s 14.7 psi; cell line samples: 120 cycles of 20 s 45 kpsi and 10 s 14.7 psi) at 35 °C. Whole cell/ tissue lysates were then sonicated for 25 s with 1 min interval on ice for 4 times. After removing tissue debris or unbroken cells, if any, by centrifugation, protein lysates were reduced and alkylated prior to proteolytic digestion. Lys-C (enzyme to substrate ratio: 1:50) and trypsin (1:30) were sequentially added to digest the proteins. Digestion was accelerated under a PCT scheme of 50s 25kpsi and 10s 14.7psi (cell line samples: 25 s 25 kpsi, 10 s 14.7 psi for 45 mins), under which both Lys-C and trypsin remain active. Lys-C digestion was performed in 6 M urea for 45 cycles, whereas trypsin digestion was performed in further diluted urea (1.6 M) for 90 cycles (cell line samples: 24 s 25 kpsi, 10 s 14.7 psi for 90 min). Subsequently, trifluoroacetic acid (TFA) was added to a final pH of around 2 before C18 desalting using SEP-PAK C18 cartridges (Waters Corp., Milford, MA, USA).

These two procedures are treated as separate activities shown in Table 3.15. The detailed procedures, the related hazard sources and the identified hazards can be found in Appendix C.4.

Table 3.15 – Involved activities in the proteolytic digestion step of the data acquisition workflow.

Nr.	Activity	Hazard sources	Risks	Average LCI
1	Proteolic digestion (Trypsin)	5	16	2.4
2	PCT-assisted lysis and digestion	4	10	2.3

Risks Most risks in this evaluation are not related to biological hazard sources but to chemical compounds (24). In total, 26 risks were identified in these two activities, having a relatively low average LCI of 2.4. The most unimportant risk in the evaluation is the ultrasonic vibrations used for the sonication of the samples (LCI of 1.7). The most important risk does not indicate a significant risk either: the environmental effect of trifluoroacetic acid has a LCI value of 3.5. Table 3.16 gives an overview of the most important risks of the evaluation and Figure 3.25 shows the LCI values before corrective measures were applied. For simplification reasons, multiply occurring risks from different sources are reduced to the one with the highest risk score. A complete list of all evaluated risks and the detailed values for each risk factor can be found in Appendix C.4.

Table 3.16 – The most important risks in the proteolytic digestion step of the data acquisition workflow.

Nr.	Risk	Origin	LCI
1	H335: May cause respiratory irritation	Lys-C	2.1
2	H225: Highly flammable liquid and vapor	Acetonitrile	2.6
3	H226: Flammable liquid and vapor	Formic acid	2.6
4	H413: May cause long lasting harmful effects to aq. life	Iodoacetamid	2.6
5	H412: Harmful to aquatic life with long lasting effects	Trifluoroacetic acid	2.8
6	H319: Causes serious eye irritation	Acetonitrile	3.3
7	H314: Causes severe skin burns and eye damage	Trifluoroacetic acid	3.5
8	H412: Harmful to aquatic life with long lasting effects	Trifluoroacetic acid	3.5

Risk treatment In order to allocate resources for corrective measures, the ALARP region for this example is set similarly as for the other examples between the LCI values 3.6 to 6.3 (as in Figure 2.27). However, no risk is considered as unacceptable and none should be reduced to ALARP. Since all risks are acceptable for this example, corrective measures are neither determined nor evaluated.

Outcome of the application As for the other applications, the evaluation provides an extensive overview of the risks related to this process. It matches the assumptions done in advance of the evaluation: the risk level is very low. In the further procedure of LARA, the risk evaluation results are distributed to all the roles in the LARA framework (see Chapter 2.2).

Remarks on the Application

This evaluation was a challenging example for the LARA method, since risks related to this procedure do practically not exist. Even though chemicals are related to the activities, the compounds are present in a highly diluted form, which makes a hazardous event only remotely imaginable. The preparation of these solutions could be hazardous, but this is not considered as a part of this procedure. Therefore, most risk dimensions used in LARA remained on a very hypothetical level and the estimation of these factors was redundant. Nevertheless, it is part of the LARA procedure to evaluate the identified hazards, even if the risks are considered to be negligible. The risk evaluation was challenging and the results do not show major risks, but the evaluation results match the assumptions done before the evaluation.

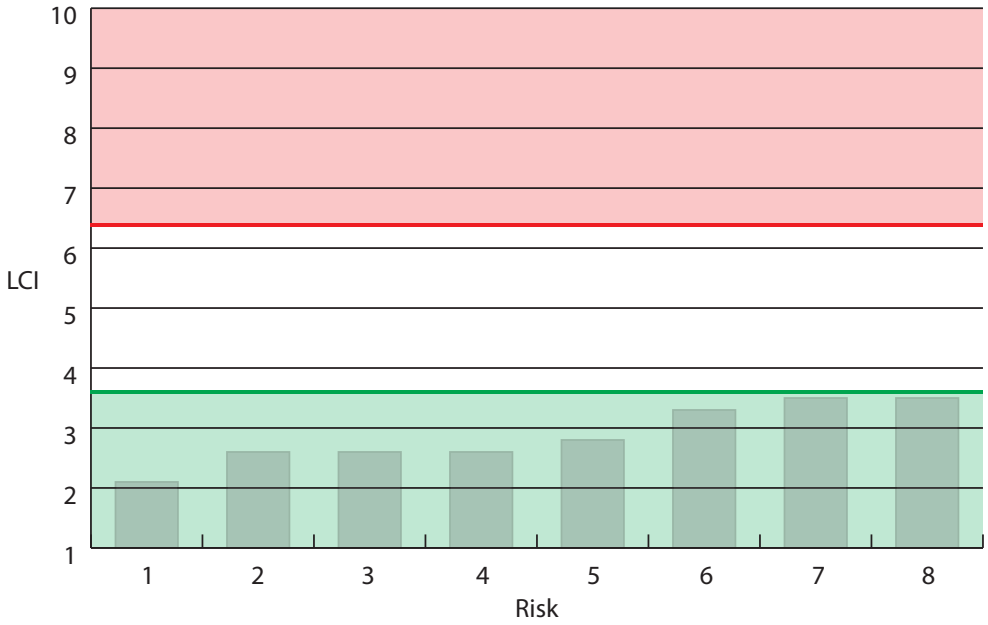


Figure 3.25 – Aebersold group: the most important risk in context of the ALARP region (as in the scenario of Figure 2.27). All values above 6.3 are considered as unacceptable, whereas the values below 3.6 are considered as acceptable (greyed out).

3.5 Comparison with Other Techniques

(Parts of this subsection are taken from the article: *Joint applicability test of software for laboratory assessment and risk analysis* [Pluess et al., 2014b].)

In order to compare the results of LARA with well-established risk management methods, two examples were selected: one from the University of Pardubice and one from EPFL. To have a variety of laboratory tasks, both chemical experiments and routine tasks were considered in the comparison. The first example was analyzed using the LARA method and a HAZOP procedure, whereas the second example was analyzed using the LARA method and the FMECA procedure. Both of these risk analysis procedures are widely accepted tools to identify and manage risks [Bluvband et al., 2004].

The joint tests described in this article are performed under conditions that simulate the environment for which the method is intended. The risk evaluations were performed and guided by a group of scientists, being familiar with the methods and having experience in performing FMECA and HAZOP procedures. For the LARA method, those scientists had a short introduction, but no information about the principles of the method. This was intended, since non-experts are the designated users of the LARA method. The scientists involved in the experiments provided the analysts with all information necessary, including details about the laboratory environment.

The test results highlight the different aspects of this new method to assess laboratory risks. The results do not only focus on the successfully evaluated risks, but also on the other factors of the evaluation, such as prerequisites and effort to perform the analysis. The tests provides us with answers for questions whether if the LARA method is easily performed, how quick it can be completed and if it is capable to uncover all risks connected with an experiment. In this article we focus on identification and evaluation of the risks; we omit the aspect of applying corrective measures, which is important part of risk analyses, but is not as relevant for this comparison.

3.5.1 Example 1: Synthesis of methyl nitrate

Description of process There is an intention to produce methyl nitrate for testing reasons at the Institute of Energetic Materials of the University of Pardubice. This uncommon, sensitive liquid explosive should be produced regularly in amounts of several kilograms. The synthesis and the product properties are well described in literature [Black, 1943]. Although the process itself does exhibit difficulties, it requires a certain level of experience. The laboratory intended for the preparation of this explosive does not differ much from standard laboratories equipped for organic synthesis. A couple of tests have been already performed in smaller amounts.

The synthesis is carried out in a beaker. A mixture of nitric and sulfuric acid is poured into a beaker. Methanol is then added dropwise while the reaction mixture is stirred well and cooled

in an ice bath. The temperature of the reaction mixture must be kept between 15-20°C. When the whole amount of methanol is added, the reaction mixture is left for five minutes at room temperature. Methyl nitrate is separated from the acid residue, washed with cold water and sodium carbonate solution.

An accident occurred during one of the test synthesis; a sudden decomposition of the product occurred. Later it was discovered that this was caused by the presence of ricin oil in methanol, which was used as a key precursor for methyl nitrate. It is highly probable that if the decomposition would have occurred in larger amounts, it would have caused an explosion.

Safety aspects of the synthesis were discussed with the leader of the project. According to his statement the most important risk is connected with sensitivity of methyl nitrate – even a small friction in a part of the equipment used for the synthesis could lead to an explosion. The accident mentioned above emphasizes that only pure chemicals (p.a.) should be used for this synthesis. The acids and toxic materials present during this synthesis may lead to increased risks as well, but can be reduced to minimum by appropriate safety measures.

Table 3.17 – Most important hazards according to HAZOP.

Nr.	Keyword	Element	Deviation	Consequences
1	More	Methanol	Faster dropping	Exoth. reaction, explosion
2	Other	Methanol	Impure methanol	Exoth. reaction, explosion
3	Other	Separation	Valve grease washout	Exoth. reaction, explosion
4	No	Stirring	No stirring	Local overheating, explosion
5	Other	Pouring	Reaction mixture poured	Irritation and intoxication
6	No	Separation	Valve grease not applied	Explosion caused by friction

HAZOP results The HAZOP analysis was performed according to BS IEC 61882:2001 by the team consisting of organic chemists, explosives and safety engineering experts. The synthesis was divided into six nodes: methanol nitration, stirring, cooling, pouring into separation funnel, separation and washing. Overall eighty-eight deviations were considered. Table 3.17 shows the six most serious hazards of the methyl nitrate synthesis. However HAZOP does not provide the quantitative risks evaluation and prioritization, therefore the relative importance of risks were chosen according to the experts' opinions. The analysis is well performable on a laboratory scale, although is designed mainly for industrial environment. HAZOP gives appropriate results and reflects the experience and predictions of experts. Despite the applicability and realistic results, the procedure is relatively complicated, time and resources consuming and not suited to be performed by non-expert.

LARA results LARA analysis performed by the same scientists revealed that all 15 identified risks arise from hazardous properties of the involved substances. The relevance of the analysis results is given by risk prioritization, which corresponds to the particular laboratory practice. The procedure determined that methyl nitrate explosives properties have the highest risk priority. Among the risks with highest importance belongs methyl nitrate toxicity, corrosive effects of nitric acid and methanol flammability. All these risks are mentioned in laboratory rules and personnel is periodically familiarized with them during safety training. The most important risks according to this analysis are presented in Table 3.18.

Comparison Table 3.17 and Table 3.18 reveals the most important hazards of this activity based on the results of both analyses. Almost all deviations identified by HAZOP lead to exothermic reaction and/or explosion of methyl nitrate. According to LARA, explosive properties of methyl nitrate have the highest priority. However these results do not reflect the experiences of the experts who performed HAZOP analysis, thus it is not so clear in which particular situation methyl nitrate explosive properties could exert. Remaining risks determined by LARA procedure are connected with the effect of involved substances on the personnel. This is in agreement with the deviation pointing out leakage of the reaction mixture identified by HAZOP.

In Chapter 1.4, the input and the output of each method is described. HAZOP as used in this example mainly matches the theoretical description of the input: a high level of expertise and resources (time) is required to perform the analysis. However, the data requirement is not different as the one from LARA, since the example itself is the limiting factor. The output remains qualitative and relies on the subjective expert judgement, whereas LARA offers a prioritization of the risks. The level of detail differs not significantly for both methods, due to the limitations of the input for the example.

Table 3.18 – Most important risks according to LARA.

Nr.	Risk
1	Explosion caused by methyl nitrate
2	Intoxication (inhalation) caused by methyl nitrate
3	Intoxication (skin) caused by methyl nitrate
4	Irritation (skin) caused by methyl nitrate
5	Intoxication (oral) caused by methyl nitrate

3.5.2 Example 2: Medium scale purification of solvents

Description of process The second example, which was chosen to test the LARA method, is the purification of larger quantities of solvents. This process is realized at the laboratory

of asymmetric catalysis and synthesis (LCSA) at EPFL. Large amounts of solvents, mainly ethyl acetate and pentane, are used in this laboratory for chromatographic purposes. Since the commonly available solvents are not sufficiently pure enough, a further purification is performed directly in the lab. The task is realized according to a planning, which obligates each member of the group to perform this process periodically. Even thought the task is planned and recurring, there is no SOP available.

For the purification, a Heidolph LABOROTA 20 medium scale rotary evaporator was used. The purification is realized several times per week with a quantity between 5L and 10L of solvent each time. For the ethyl acetate, the device is heated to 50°C and the pressure was set to 25 kPa. For the purification of pentane, the device was heated to 50°C and the pressure was set to 95 kPa. Until now, no accidents have occurred. According to the responsible scientist, the main risk in this process is related to the flammability of the solvents. Other hazards related to the chemical properties of the solvents, such as the hazards for the environment or toxicity, are estimated to be negligible.

FMECA results A team of scientists performed a systematical risk analysis of the most important components using the FMECA method. In total, 29 potential failures were identified and their relative priorities for applying measures were determined. Seven of these failure modes are only influencing the operability itself and are not relevant form a safety point of view. From the remaining 22 failure modes, 6 are related to mechanical operations and the remaining 16 are indirectly related to the hazardous properties of the solvents. Since those properties are not directly evaluated by the procedure, the relative importance and magnitude of the effects remain unclear after the FMECA analysis.

LARA results The same team of scientists used the LARA method to perform a risk analysis on this activity. This analysis revealed nine different hazards originating from different sources (chemicals and devices). All of those hazards are relevant from an occupational safety point of view. Four of the hazards are directly related to the hazardous properties of the solvents. The other five hazards present according to the LARA analysis are related to mechanical or physical risk.

Table 3.19 – Comparison of the risk priorities in Example 2 using LARA and FMECA method.

Hazard	Risk	LARA	FMECA
Blast shield	Injuries due to unintended closing	2	1
Lowering mechanism	Injuries due to pinching	2	5
Toxic substance (solvent)	Intoxication by inhalation	1	2/3/4
Irritating substance (solvent)	Eye irritation	3	2/3/4
Flammable substance (solvent)	Fire	5	2/3/4

Comparison Table 3.19 shows the most important hazards of this activity based on the results of both analyses. The most important hazard determined by the LARA method is the toxic properties (aspiration toxicity) of both solvents. In the FMECA analysis, the toxicity is indirectly related to the failure modes with the relative priority 2, 3 and 4 (all those failure modes are leading to leakage of solvent). Based on the FMECA method, the blast shield of the apparatus is the most hazardous element of this process, which is ranked second in the LARA method. The mechanical hazards do have the same importance according to the LARA method, since both do have similar occurrences and exposures. The FMECA analysis however ranked the similar hazards in a different order, even though the hazards are comparable. The FMECA analysis fails to differentiate between the different hazards originating from the chemical properties of the solvent.

As for the first example, the comparison is judged according to the criteria defined in Chapter 1.4. Since the input is limited again by the example itself, the data requirement can not be taken into account. However, the other requirements show the same tendencies as described in the theoretical section. FMECA requires more resources than LARA, which allows a non-trained user to perform a basic risk assessment. On the output side, FMECA shows less level of detail when it comes to prioritization of the risks; on the other side, LARA is able to generate a more meaningful output with the limited resources.

3.5.3 Evaluation of the results

The results of this study suggest, that the LARA can be used as a holistic risk analysis method in the academic laboratory environment. Even though only two examples were examined, the joint test at two universities showed the advantages compared to established risk analysis techniques.

One of the most important features of a risk management method is the capability to identify risks. Since no method is able to identify all the possible risks, an appropriate method should be capable of discovering the most important risks of a process. On the contrary, the more risks a method can identify, the higher is the probability to identify scenarios, which are either highly improbable or of no importance for occupational safety. In the first example, the HAZOP procedure identifies several scenarios, which are influencing the performance of the process, but are not important to the safety of the involved scientists. Such irrelevant scenarios (in terms of safety) can detract from the safety-related relevant scenarios; additionally, they are extending the analysis itself in terms of complexity. The LARA method is capable of identifying the same relevant scenarios as the HAZOP method. Additionally, the method is able of identifying relations, which the HAZOP procedure is not capable of. The same results were shown in the second example, comparing the results from LARA with the ones of the FMECA procedure.

The effort needed to perform a risk analysis is another important aspect, which influences the feasibility of a method. An ideal risk analysis method for academic research laboratories

should not require too demanding resources, since both qualified personnel in safety and time is a rare commodity in this environment. The systematic approach of the HAZOP procedure is not complex itself; however, in order to perform the analysis, an experienced user (the HAZOP moderator) needs to participate to find most of the scenarios. In contrast, the examined example showed that the LARA method is more intuitive when performing the risk analysis. Both methods anyhow need expertise about the process, but LARA needs less experience about the risk management method itself.

However, the comparison has shown some limitations of the LARA method as well. The method relies on a database, and is therefore as accurate as the database is. This drawback can be overcome by systematic use of the software at universities in order to fill the databases with possible hazards and risks.

3.6 Discussion

3.6.1 Application of LARA

The application of LARA for these examples had the intention to analyze the workflow and to evaluate its feasibility according to the goals of this method. For most parts, the LARA method provides a functioning risk management approach for research and teaching laboratories, regardless of the site of application. The advantages and limitations of the individual steps are described below.

Definition of the context As discussed in Chapter 2.2, the context defines the setting and the main mechanisms of the LARA risk management approach. The broader context had only limited implications on the use of LARA, depending on the different settings where it was applied. Different personal interpretations and differences in the safety cultures of the universities were shown in some peculiar questions, mostly in the judgment of certain parameters. An example for this is the general worsening factor definition of an evaluation: in environments that are perceived to be stricter concerning their regulations, analysts applied more self-criticism when choosing the factors present. However, a clear and consistent guidance in the LARA procedure can help to avoid such irregularities.

The organizational context defines the roles and responsibilities of the involved persons and groups. These differ significantly at the studied universities and could influence the risk documentation and the risk communication. Since the LARA application remained on a hypothetical level, the results had no implications on the safety framework at these universities. If LARA is actually implemented as a risk management approach in an existing safety framework, it will need to be adjusted to fit the organizational structures of an institution.

The technical context shapes how LARA identifies hazards and evaluates risks. As a first part, it is important to define the studied object correctly. The evaluation system of LARA should allow grouping of the different projects and subdividing them according to the activities and processes involved. For the examples evaluated in LARA, this was possible without any limitations.

Hazard identification The hazard identification is a central element of a risk assessment technique. LARA faces the challenging situation that a multitude of different types of hazards converge. To master this situation, a flexible focus was implemented in LARA by using an adaptable hazard database. For some kinds of hazards, this works as intended; especially the chemical hazard category is well described and allows the identification of all the hazards involved. Due to the GHS classification system of chemicals, the hazard originating from this category can be identified almost completely. In all evaluations discussed in this chapter, the chemical hazards were by far the most common hazards. On one side, this can be explained with the average number of hazard statements related to chemicals in the GHS system. On the

other hand, chemicals are involved in most processes in research laboratories, even if they are only used for secondary operations. When compared to other hazard classes, the number of hazards identified for chemicals might lead to misconceptions. However, other hazards were still identifiable by the LARA database approach, albeit not as numerous. Altogether, the database is a highly feasible approach to identify most hazards related to a project. This is also shown by the fact that there is agreement on the identified hazards by the involved scientists and no further hazards which went missing in LARA could be imagined.

Risk analysis A high number of risks were found for each single evaluation. Therefore it is important for the risk management to prioritize the risks correctly and to separate the less important from the more important ones. In LARA this is done with the use of four risk dimensions and the calculation of the LCI value. A general problem of risk dimensions, regardless of the method used, is the setting of the scale. The broader the covered field of hazards is, the less specific the scales need to be. Not all scales matched every specific situation; however, this is a drawback that comes with the comparability of different kinds of risks. Even though the dimensions were not feasible in every situation to describe a risk, they helped to identify the important factors contributing to the LCI value of each risk. Knowing this is of high importance for the risk mitigation, since the corrective measure should aim at the important elements in order to reach an optimal reduction potential.

The overall impression of the risk estimation method indicates that LARA is capable of prioritizing the risks correctly. Challenging issues for the risk analysis are those risks, which are rather insignificant. This was shown in the example performed at ETHZ, where the chemicals were highly diluted and the related risk dimensions were difficult to judge. However, the resulting risk scores for these risks matched the assumptions and proved their insignificance, which is a sign of feasibility for the prioritization approach.

Risk evaluation The risk evaluation process has the goal to indicate which risks are acceptable, which are unacceptable, and which ones should be reduced to ALARP. The classification of the acceptable risks matches the perception of the involved persons in all cases. Also the risks falling under the ALARP category match the conception intended in LARA: other than the acceptable risks, these risks cannot be readily classified as acceptable, but are perceived too low to be treated regardless of the costs. Even though an upper limit of acceptability is implemented in LARA, not a single risk was considered as unacceptably high. This is not surprising however, since it would indicate a major defect in the safety framework of one of these universities.

Risk treatment The resource allocation approach used in LARA has the intention to integrate a non-financial aspect in the choice of corrective measures for all risks in the ALARP region. A well-balanced choice of corrective measures helps to find a feasible solution how to treat

the risks. The choices of corrective measures for each evaluation are considered to be highly feasible in this context, since the acceptability plays an important role.

Risk control, risk documentation, and risk communication A crucial element of LARA as a risk management approach for universities is the embedment into an existing safety framework. This allows effective risk documentation and risk communication. One of the main goals of risk management is to be aware of risks and to apply corrective measure if necessary. However, these applications need to be determined exactly and realized in a reasonable amount of time, otherwise the risk management is done in vain. This is done preferably with an action plan including the responsibilities and detailed reports about the risks present.

For the application examples of LARA, this aspects was only examined on a hypothetical level, therefore no judgment about the feasibility can be made. However, the technical aspects in the software allow a timely and adequate distribution of the information gathered with the risk evaluation process.

3.6.2 Evaluation of the LARA Method

The intention of the LARA project is to provide a tool for risk management at universities. The ideal specifications of such a method were postulated as a result of the methodological discussion of Chapter 2.4. The results from the application suggest, that LARA fits these specifications in most parts. The intuitive approach allows non-experts in risk management techniques to perform a straightforward evaluation of the risks related to their processes. The required expertise is not related to the technique itself but to the experiment, and this knowledge is usually available. The time requirement is an improvement compared to the well-established risk management techniques, but a further improvement would be preferable. The deliverables match the expectations for such a technique; especially the semi-quantitative character makes an easier access to risk management possible and allows meaningful results. The variable focus of the risk identification however causes some slight limitations: the focus on characteristics might overlook some specific hazards and is not capable of identify completely unknown hazards. Yet, this is a demanding requirement for a risk management technique.

The results of the previously described applications suggest, that the LARA project reaches the goal of providing a risk management technique for the research and teaching environment. Especially the reduced requirement of resources compared to the other techniques make LARA an ideal choice for analyzing risks in this environment. The software application makes the approach a highly favorable choice for universities, since it makes the problem more accessible than other approaches. It considers the particular setting by the implementation of worsening factors, the novel semi-quantitative calculation method, and a resource allocation approach, that allows to consider non-financial aspects in the choice of corrective measures.

Conclusion

The evaluation of risk management at universities performed in the framework of this dissertation pointed out the most important aspects of this topic. A detailed methodological study of a selection of widely used risk management techniques showed, that they are not feasible for the academic environment without numerous limitations. Other approaches developed for this environment cover a specific field, but cannot be used as a holistic risk management approach for this setting.

To fill this gap, the LARA method was developed and applied at different Swiss universities. The results of these tests suggest, that this method overcomes the known limitations and is able to serve as a holistic risk management technique for research and teaching laboratories. Compared to the other presented methods, the LARA approach requires fewer resources, which is crucial for the academic setting, since neither manpower nor financial resources for risk management are abundantly available. This is achieved by various elements, such as the flexible focus during risk identification and a comprehensive risk description. Besides the regular risk dimensions used in other approaches, LARA integrates the peculiarities of the research environment with the use of worsening factors. These allow to model interdependencies, which help to lower the risk level significantly. Another important element that makes the method accessible is the use of a user-friendly and intuitive software. This software allows executing the workflow, generating risk evaluation reports, and directly communicating the results to the roles and responsibilities of an organization.

However, during the application of LARA some limitations were revealed. On one side, there are risks so low, that they are negligible in terms of safety. The application showed, that it is difficult to judge the magnitude of these risks on the scales of risk dimensions in LARA. An example for this is a toxic compound which is used in a highly diluted form. The hazard is present and the impact is defined by the properties of the compound, but the dilution makes the risks insignificant. However, this is not limited to the LARA approach only; most risk management techniques generate insignificant results due to their systematics. On the other side, there are some limitations which originate from the broad spectrum that LARA has to cover. This is a conflict of interest which arises from the comparability and is not a unique limitation of LARA; other methods deal with these topics as well. Besides these smaller flaws in the mechanism, LARA achieves the goals defined for this project in the main points.

Even though the impacts are unlikely to reach as disastrous extents as in the industry, major accidents could happen at universities as well. Besides the direct impact, such an accident could lead to other consequences: financial claims, reputation loss, limitation of resources for research, and others. It is in the interest of every institution to do everything reasonably practicable to avoid such accidents. A tool that helps to achieve this is the LARA risk management method. By making this approach more accessible than traditional methods, LARA allows risk management in a field, where such techniques are not widely applied yet. A comprehensive use of this method could help to be aware of the risks people face in their experiments and to allocate resources in an optimal way to avoid accidents from happening. Even though the method has its limitations and improvements should be tackled in the further studies, this method is capable of contributing to an important development in the research and teaching environment.

Perspectives and Recommendations

The LARA method presented in this dissertation is a feasible method for risk management at universities. However, like all other methods, it has not only benefits but also limitations. In order to improve the approach, the following developments are suggested to allow an even more elaborated risk evaluation at universities.

Systematic Hazard Identification

Hazard identification is a central element of every risk assessment workflow. In LARA, the hazard identification is done with a checklist-like database approach. This works ideally for a majority of the hazards present in scientific research laboratories, especially the chemical hazards; this is due to the GHS classification system of chemicals, which is part of the legislation for the use of chemicals. This system allows a detailed classification of hazards and provides hazard information for chemicals. For other hazards however, the classification is not as advanced and the hazards cannot be described and distinguished as detailed. An optimal improvement of the LARA method therefore aims at these classifications. Since the aim of LARA covers a broad field of hazards, different hazard identification strategies used simultaneously could help to identify more hazards.

Safety Framework Integration

LARA is intended as a method used in an existing safety framework. The interaction between those systems mainly concerns the roles and responsibilities which are used in LARA for the risk communication and risk documentation. A more intensive integration of LARA in this framework could improve the safety level of an institution. An important aspect are clear guidelines, when a risk management with LARA is mandatory and needs to performed prior to a process. For processes in the design stage, such an obligation could lower the risk level

significantly, since risks can actively be avoided before even occurring by changing details of the process; doing this with corrective measures in existing processes is related to higher costs and does not always lead to satisfying results. Another example of the integration into existing structures is the use of LARA for student experiments performed in laboratory courses. An integration of LARA could not only identify and evaluate unknown risks, but could also be used for educational purposes to raise awareness for occupational safety. However, these aspects are related to the organizational structures and need to be adapted to the situation present at an institution. A general plan, how such an adaption needs to be done and what LARA can achieve, could be part of further studies related to this project.

Calculation Improvement

The calculation method used in LARA is based on Bayesian networks. This approach allows absorbing the effect of uncertainties in semi-quantitative judgments and provides a linear relationship between the different risk scores. The uncertainties related to these judgments are not always caused by the same reasons and might even be different for the risk dimensions used in LARA. Once LARA is used in laboratories at various institutions, statistical relevant data about the risks and the risk judgments will be available. This data could be used for various purposes. A further investigation could identify patterns in the behavior of the users. Since the Bayesian calculation method uses probability distributions, these distributions could be improved according to these studies. Another benefit of the Bayesian calculation method is, that an adaptive element can be integrated. This could be used to remove biases of users and to display the risk situation found in a laboratory more precisely, independently of who is doing the analysis.

Database Connectivity

The database of LARA is the backbone of the method and provides flexibility and the possibility to expand and adapt the method constantly. Most laboratories already work with numerous databases, for example chemical structure databases, which also contain safety information for most common compounds. Some of these databases can be linked with electronic laboratory notebook tools, allowing a simple integration of information. A similar approach could be an optimal extension of the LARA software, since it would make the hazard identification easier and more accessible. A later version of LARA could allow a direct integration of electronic laboratory notebook data and automatically gather the information provided by the chemical databases. This would be an important extension of the method, since the hazard identification allows automation on certain levels and would help to minimize the required time to perform an analysis.

Corrective Measures

The ideal choice of corrective measures is as important for a risk management technique as an optimal hazard identification. In LARA the choice between the options is facilitated by the use of an allocation matrix, which allows the integration of financial and non-financial factors in the selection process. However, the identification of corrective measures is not an integrated part of the LARA workflow; the corrective measures are mainly based on experience. An approach to systematically identify corrective measures could improve the choice and the feasibility of measures, before an actual selection takes place. Some approaches to systematize the discovery of possible corrective measures (e.g. STOP as described in Chapter 1.1) already exist. A development of such a method could improve the resource allocation even further and help to increase the safety level at universities.

A LARA Databases

A.1 Hazards

Table A.1 – Chemical hazards used in LARA.

Hazard group	Hazard
Explosives	H200: Unstable explosive
Explosives	H201: Explosive; mass explosion hazard
Explosives	H202: Explosive; severe projection hazard
Explosives	H203: Explosive; fire, blast or projection hazard
Explosives	H204: Fire or projection hazard
Explosives	H205: May mass explode in fire
Explosives	EUH001: Explosive when dry
Explosives	EUH006: Explosive with or without contact with air
Flammability	H220: Extremely flammable gas
Flammability	H221: Flammable gas
Flammability	H222: Extremely flammable aerosol
Flammability	H223: Flammable aerosol
Flammability	H224: Extremely flammable liquid and vapour
Flammability	H225: Highly flammable liquid and vapour
Flammability	H226: Flammable liquid and vapour
Flammability	H227: Combustible liquid
Flammability	H228: Flammable solid
Reactivity	H230: May react explosively even in the absence of air
Reactivity	H231: May react explosively even in the absence of air at elevated pressure and/or temperature
Reactivity	H240: Heating may cause an explosion
Reactivity	H241: Heating may cause a fire or explosion
Reactivity	H242: Heating may cause a fire

Continued on next page

Table A.1 – continued from previous page

Hazard group	Hazard
Reactivity	EUH014: Reacts violently with water
Reactivity	EUH019: May form explosive peroxides
Reactivity	EUH044: Risk of explosion if heated under confinement
Instability	H250: Catches fire spontaneously if exposed to air
Instability	H251: Self-heating; may catch fire
Instability	H252: Self-heating in large quantities; may catch fire
Instability	H260: In contact with water releases flammable gases which may ignite spontaneously
Instability	H261: In contact with water releases flammable gas
Oxidizer	H270: May cause or intensify fire; oxidizer
Oxidizer	H271: May cause fire or explosion; strong oxidizer
Oxidizer	H272: May intensify fire; oxidizer
Gas under pressure	H280: Contains gas under pressure; may explode if heated
Gas under pressure	H281: Contains refrigerated gas; may cause cryogenic burns or injury
Corrosion	H290: May be corrosive to metals
Oral hazards	H300: Fatal if swallowed
Oral hazards	H301: Toxic if swallowed
Oral hazards	H302: Harmful if swallowed
Oral hazards	H303: May be harmful if swallowed
Oral hazards	H304: May be fatal if swallowed and enters airways
Oral hazards	H305: May be harmful if swallowed and enters airways
Skin hazards	H310: Fatal in contact with skin
Skin hazards	H311: Toxic in contact with skin
Skin hazards	H312: Harmful in contact with skin
Skin hazards	H313: May be harmful in contact with skin
Skin hazards	H314: Causes severe skin burns and eye damage
Skin hazards	H315: Causes skin irritation
Skin hazards	H316: Causes mild skin irritation
Skin hazards	H317: May cause an allergic skin reaction
Eye hazards	H318: Causes serious eye damage
Eye hazards	H319: Causes serious eye irritation
Eye hazards	H320: Causes eye irritation
Eye hazards	EUH070: Toxic by eye contact
Inhalation hazards	EUH071: Corrosive to the respiratory tract
Inhalation hazards	EUH029: Contact with water liberates toxic gas
Inhalation hazards	EUH031: Contact with acids liberates toxic gas
Inhalation hazards	EUH032: Contact with acids liberates very toxic gas
Inhalation hazards	H330: Fatal if inhaled

Continued on next page

Table A.1 – continued from previous page

Hazard group	Hazard
Inhalation hazards	H331: Toxic if inhaled
Inhalation hazards	H332: Harmful if inhaled
Inhalation hazards	H333: May be harmful if inhaled
Inhalation hazards	H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled
Inhalation hazards	H335: May cause respiratory irritation
Inhalation hazards	H336: May cause drowsiness or dizziness
Germ cell mutagenicity	H340: May cause genetic defects
Germ cell mutagenicity	H341: Suspected of causing genetic defects
Carcinogenicity	H350: May cause cancer
Carcinogenicity	H351: Suspected of causing cancer
Reproduction toxicity	H360: May damage fertility or the unborn child
Reproduction toxicity	H361: Suspected of damaging fertility or the unborn child
Reproduction toxicity	H361d: Suspected of damaging the unborn child
Reproduction toxicity	H362: May cause harm to breast-fed children
Specific target organ toxicity	H370: Causes damage to organs
Specific target organ toxicity	H371: May cause damage to organs
Specific target organ toxicity	H372: Causes damage to organs through prolonged or repeated exposure
Specific target organ toxicity	H373: May cause damage to organs through prolonged or repeated exposure
Environmental hazards	H400: Very toxic to aquatic life
Environmental hazards	H401: Toxic to aquatic life
Environmental hazards	H402: Harmful to aquatic life
Environmental hazards	H410: Very toxic to aquatic life with long lasting effects
Environmental hazards	H411: Toxic to aquatic life with long lasting effects
Environmental hazards	H412: Harmful to aquatic life with long lasting effects
Environmental hazards	H413: May cause long lasting harmful effects to aquatic life
Environmental hazards	H420: Harms public health and the environment by destroying ozone in the upper atmosphere
Nanoparticles	Dry nanofibers
Nanoparticles	Nanoparticles in suspension
Nanoparticles	Nanoparticles in a matrix
Nanoparticles	Nanoparticles in powder form

Table A.2 – Physical hazards used in LARA.

Hazard group	Hazard
Noise	Noise emitted continuously (8H Lex >85 dB per day)
Noise	Occasional impulsive noise (Peak >135 dB)
Ultrasonic & Infrasonic	Ultrasonic & Infrasonic
Vibrations	Vibrations on hands (Acceleration a <5 m/s2)
Vibrations	Whole body vibrations (Acceleration a <0.8 m/s2)
Hypobaric or hyperbaric environment	Hypobaric environment
Hypobaric or hyperbaric environment	Hyperbaric environment
Electricity	Accessible energized objects
Electricity	Power outage
Electricity	Arc flash
Electricity	Short circuit
Thermic Hazards	Hot media
Thermic Hazards	Cold Media
Thermic Hazards	Exposition to elevated temperatures ($T > 33°C$)
Thermic Hazards	Exposition to cold temperatures ($T < 15°C$)
Thermic Hazards	Frequent variations of temperature
Pressure hazards	High pressure devices
Pressure hazards	Vacuum

Table A.3 – Electromagnetic fields and waves hazards used in LARA.

Hazard group	Hazard
Laser	Pulsed laser
Laser	Continuous light laser
Laser	IR laser
Laser	Visible
Laser	UV laser
Laser	Tunable laser
Laser	Class 2M
Laser	Class 3R
Laser	Class 3B
Laser	Class 4
Radiofrequency-microwaves	Source of radiofrequency radiation with frequency <= 100 kHz
Radiofrequency-microwaves	Source of radiofrequency radiation with frequency F: 100 kHz <F <=110 MHz
Radiofrequency-microwaves	Source of radiofrequency radiation with frequency F: 110 MHz <F <= 10 GHz
Radiofrequency-microwaves	Source of microwave radiation with frequency F: 10 GHz <F <= 300 GHz
Radiofrequency-microwaves	Completely shielded radiofrequency-microwave source
Radiofrequency-microwaves	Partially shielded or unshielded radiofrequency microwave source
Static Magnetic Field	Magnetic field with 0.5 mT line at distance >50 cm from the equipment's edge
Static Magnetic Field	Magnetic field with 0.5 mT line at distance <= 50 cm from the equipment's edge
UV-IR non-coherent radiation	Unshielded UV-C (190 nm - 290 nm) source
UV-IR non-coherent radiation	Unshielded UV-B (290 nm - 320 nm) source
UV-IR non-coherent radiation	Unshielded UV-A (320 nm - 400 nm) source
UV-IR non-coherent radiation	Unshielded IR source
Ionizing rays	Alpha particles
Ionizing rays	Beta particles
Ionizing rays	Gamma rays
Ionizing rays	X-rays

Table A.4 – Biological hazards used in LARA.

Hazard group	Hazard
Danger of infection by MO or viruses	Biosafety level 1
Danger of infection by MO or viruses	Biosafety level 2
Danger of infection by MO or viruses	Biosafety level 3
Danger of infection by MO or viruses	Biosafety level 4
Genetically modified organisms	Biosafety level 1
Genetically modified organisms	Biosafety level 2
Genetically modified organisms	Biosafety level 3
Genetically modified organisms	Biosafety level 4
Allergen or toxic substances of MOs	Biosafety level 1
Allergen or toxic substances of MOs	Biosafety level 2
Allergen or toxic substances of MOs	Biosafety level 3
Allergen or toxic substances of MOs	Biosafety level 4
Contact with animals	Bites
Plants	Allergens or toxic substances

Table A.5 – Mechanical hazards used in LARA.

Hazard group	Hazard
Noise	Noise emitted continuously (8H Lex>= 85 dB day)
Noise	Occasional impulsive noise (Peak>= 135 dB)
Ultrasonic & Infrasonic	Ultrasonic & Infrasonic
Vibrations	Vibrations on hands (Acceleration a <= 5 m/s2)
Vibrations	Whole body vibrations (Acceleration a <= 0.8 m/s2)
Hypobaric or hyperbaric environment	Hypobaric or hyperbaric environment
Electricity	Accessible energized objects
Electricity	Power outage
Electricity	Arc flash
Electricity	Short circuit
Thermic Hazards	Hot media
Thermic Hazards	Cold Media
Thermic Hazards	Exposition to elevated temperatures (T>33°C)
Thermic Hazards	Exposition to cold temperatures (T<15°C)
Thermic Hazards	Frequent variations of temperature
Pressure hazards	High pressure devices
Pressure hazards	Vacuum

A.2 Worsening Factors

Table A.6 – **General worsening factors used in LARA**.

Worsening factor group	Worsening factor
Climate	Too hot/cold
Climate	Odors
Climate	Noise
Climate	Humide climate
Electrical	Outdated electrical systems/equipment
Electrical	Overloaded sockets
Ergonomics	Heavy weights
Ergonomics	Respiratory protecting device
Ergonomics	Cramped benches
Ergonomics	Cramped fumehoods
Ergonomics	Cramped passages
Lighting	Inadequate lighting
Lighting	No daylight
Lighting	Reflections
Lighting	Inadequate distribution
Lighting	Inadequate colors
Safety	Warning signs not visible
Safety	Missing safety training
Safety	Missing waste management
Safety	Misplaced safety equipment
Safety	Stage of chemicals not ideal (e.g. labelling)
Safety	Blocked emergency exits
Safety	Missing safety equipment
Safety	Warnings not hearable
Safety	Excess of information
Social conditions	Too many or too few people in room
Social conditions	Different spoken languages
Social conditions	Group composition not ideal
Social conditions	Leader not ideal
Social conditions	Discrimination or mobbing
Social conditions	Awarneness
Work organisation	Lack of procedures
Work organisation	Unclear workflow
Work organisation	Responsabilities unclear
Work organisation	Responsability overload
Work organisation	Lack of training

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Table A.6 – continued from previous page

Worsening factor group	Worsening factor
Work organisation	Pressure of time
Work organisation	Distortions
Work organisation	Lack of breaks
Work organisation	Stress
Work organisation	Missing advanced training
Work organisation	Missing fitness for duty
Work organisation	Rule overload
Work organisation	Missing supervision
Work organisation	Lack of communication
Work organisation	Complex procedures
Work organisation	Night work
Work organisation	Overtime
Work organisation	Too many working hours
Work related	Narrow space
Work related	Uncomfortable position
Work related	Uncomfortable postures
Work related	Repetitional tasks
Work related	Qualitative underchallenged personal
Work related	Quantitative underchallenged personal
Work related	Qualitative overchallenged personal
Work related	Quantitative overchallenged personal
Work related	Permanent attention
Work related	Isolation

Table A.7 – **Hazard-specific worsening factors used in LARA**.

Hazard-specific worsening factor
Absence of access limits
Absence of automatic extinguishing system
Absence of beam stops
Absence of fire extinguisher
Absence of protective equipment
Absence of signalisation of the EM field
Bad labelling conditioning and sorting
Contact without PPE
Control unit in unprotected zone
Excessive quantity stored
Expired products
Ferromagnetic objects near strong static fields
Ignition source
Inaccessible places
Incompatibles wastes mixing
Lack of banisters
Lack of carefullness
Lack of caution
Lack of lab access control
Lack of oxygen
Lack of protective equipment
Lack of ventillation system
Leakage of the ventilation system
Loose-fitting clothes
Low perception of the effects (low dose effect)
Metallics prosthesis wearer
MSDS not available
Noise
Pacemaker wearer
Person had cataract operation
Presence of reflecting surfaces
Short circuiting
Simultanous use of the hood for working and storage
Sparks
Substances in gas or pulverulent forms
Temperature elevation
Tools that can be started without protection
Unknown wastes

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Table A.7 – continued from previous page

Hazard-specific worsening factor
UV photosensitised person (naturally or due to medication)
Wastes in need of subsequent treatment
Work requiring oral communication

B LARA Manual

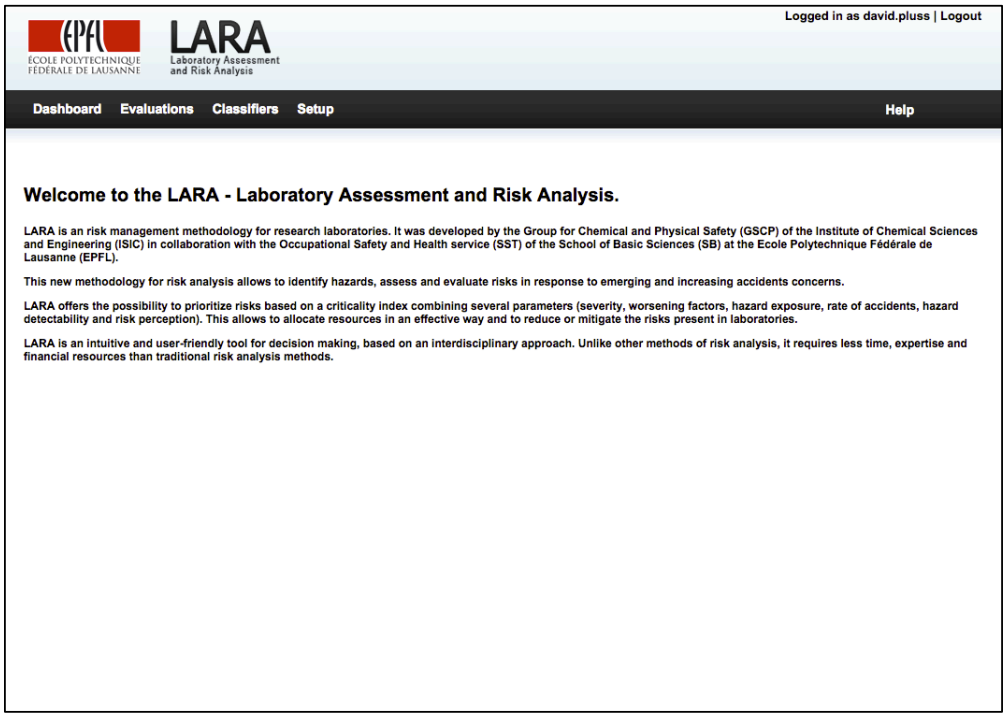
LARA MANUAL

INTRODUCTION

LARA is an integrated risk management methodology developed for research laboratories by the Group of Chemical and Physical Safety (ISIC-GSCP) of the Institute of Chemical Sciences and Engineering; and the Occupational Safety and Health (SB-SST) of the School of Basic Sciences at the Ecole Polytechnique Fédérale de Lausanne.

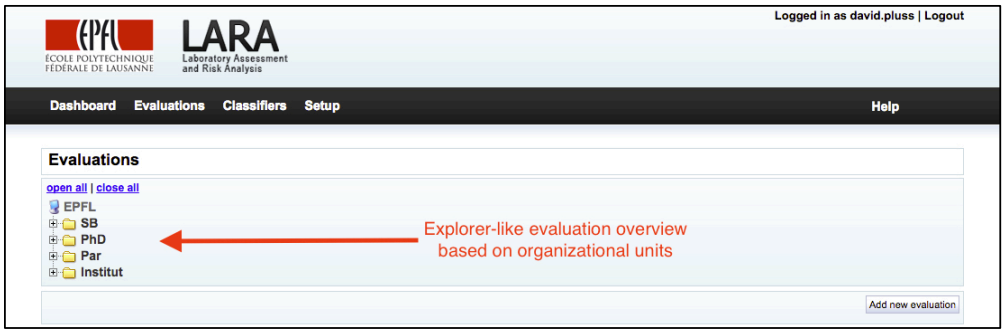
This new methodology for complex risk analysis exhibits multi-functionality allowing identifying hazards, assessing and evaluating risks in response to emerging and increasing accidents concerns. LARA offers the possibility to prioritize risks based on a criticality index combining several parameters allowing implementing and quantifying corrective measures to reduce or mitigate the risk.

LARA is an intuitive and friendly user tool for decision-making, based on an interdisciplinary approach. Unlike other methods of risk analysis, it mobilizes less time, human and financial resources.



EVALUATION MANAGEMENT

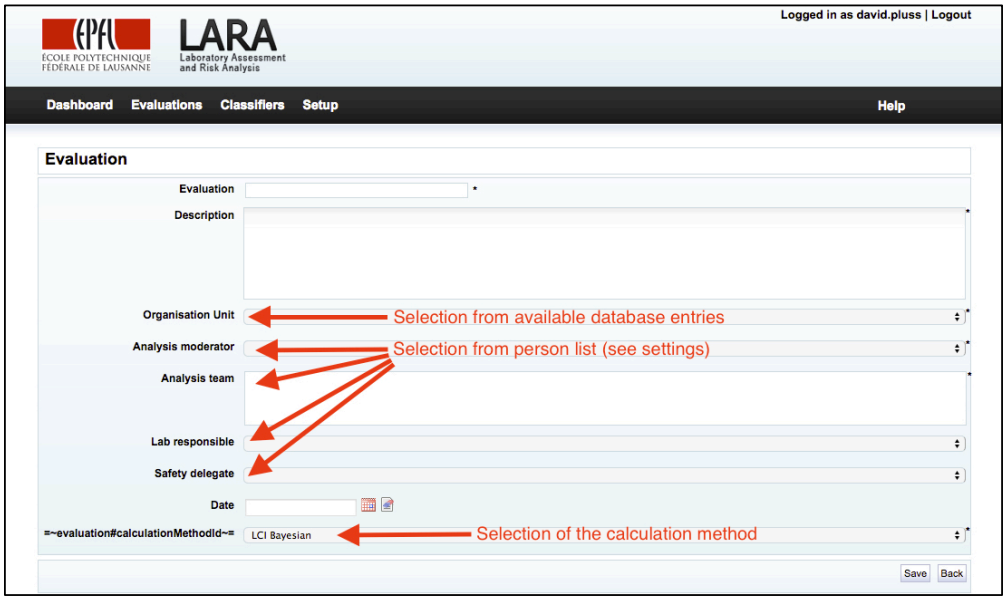
The first part of the LARA software is the evaluation part, which is the main part for basic users. An evaluation is assigned to a project and the involved activities are part of this evaluation. In LARA, the user adds an evaluation to a specific research group (the organization units are editable by the administrators, which also define the rights for the specific users for each single organization unit).



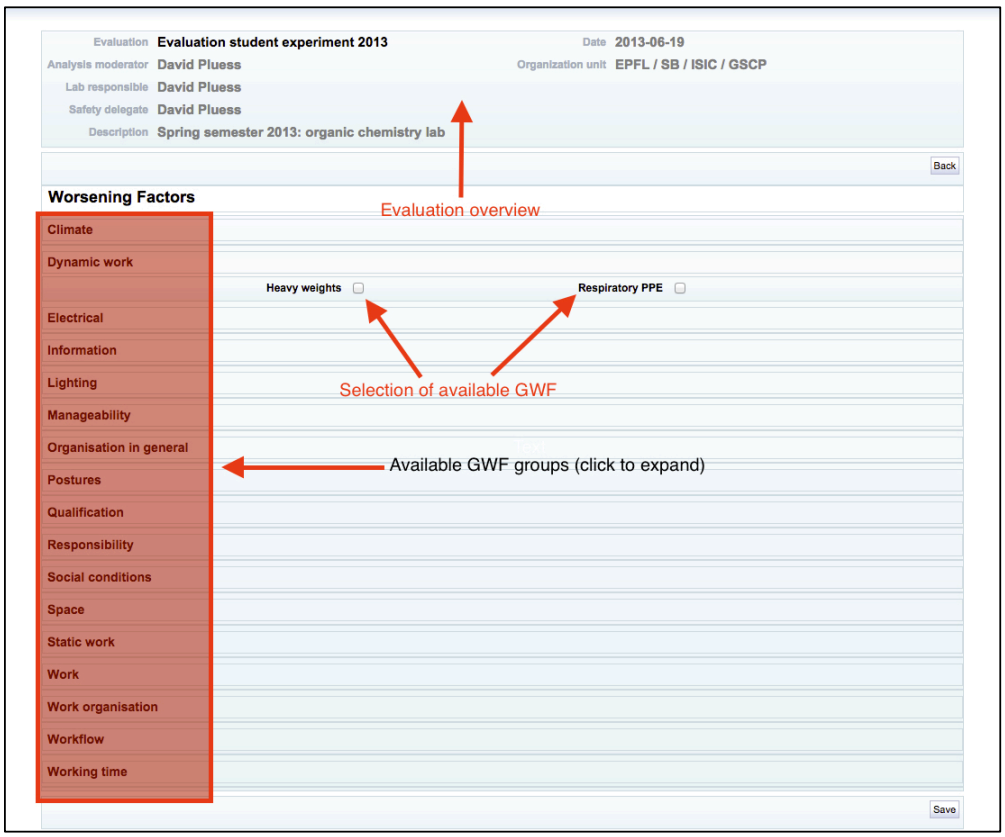
The interface to generate an evaluation lets the user add following information when generating an evaluation:

- Description of the project
- Organization unit
- Analysis moderator
- Analysis team
- Laboratory responsible
- Safety delegate
- Date

Person related selections are limited to the person list defined by the administrators in the setup. Since LARA gives the possibility to store multiple calculation files, the desired one is selected for an evaluation in the evaluation interface.

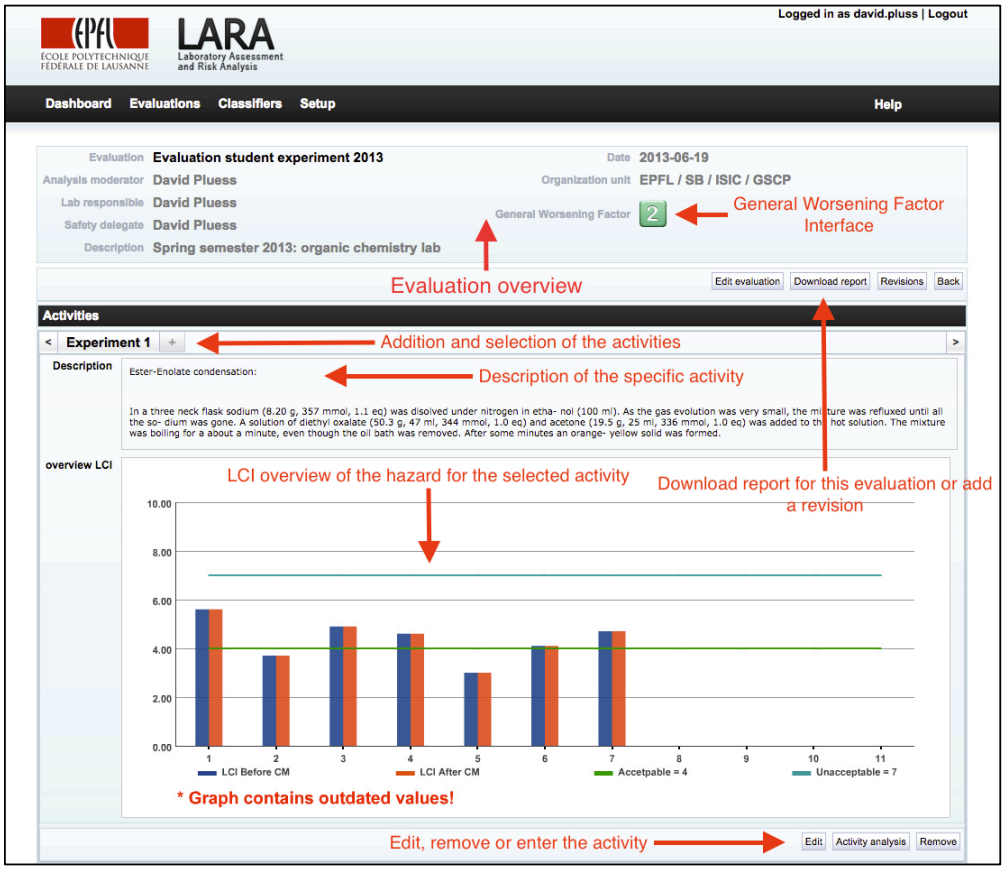


After a creation of an evaluation, the user gives the information about the general worsening factors by choosing from the ones stored in the LARA database. According to the groups in the database, the user can select if a factor is present.



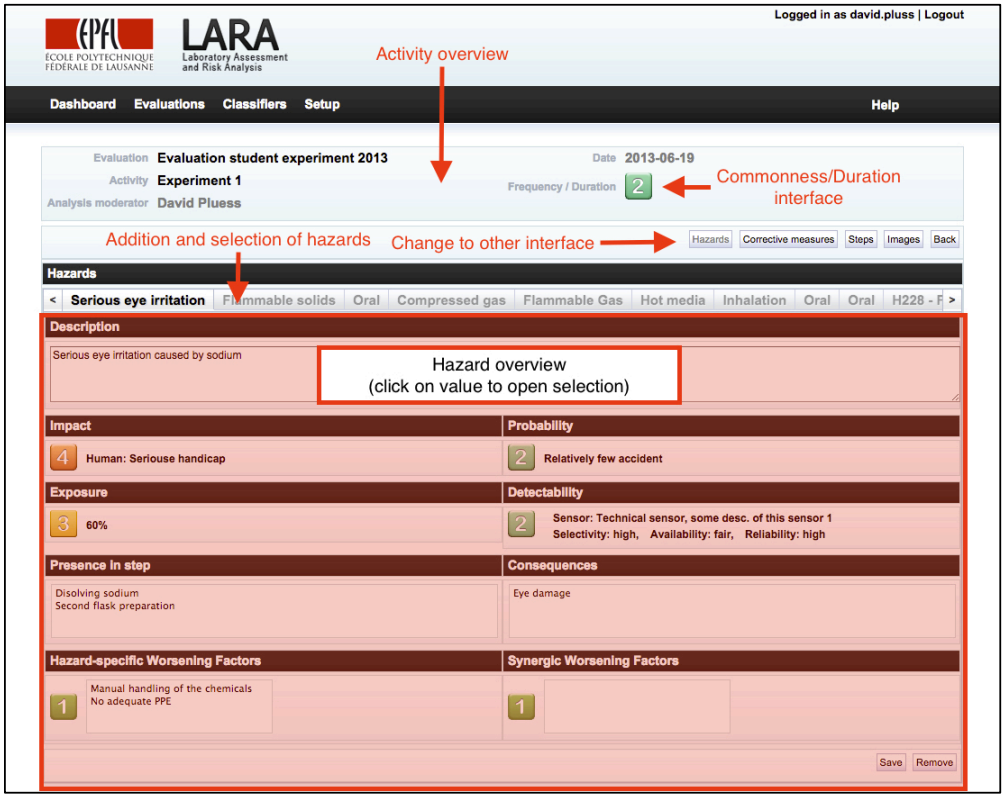
The evaluation overview gives an overview of the entered information and displays the value for the GWF according to the choice of the user. In the lower part of interface, the user can add activities to the evaluation or switch between existing ones. When a new activity is added to the evaluation it can be described accordingly. Once the evaluation is finished, the LCI values of all hazards are displayed in in a bar chart. If the calculation file is updated, the values are not changed for existing evaluation; however, they are marked as outdated values.

Organizational operations for the evaluation are available between the overview and the activity interface: download finished evaluation reports or add revisions for the evaluation.

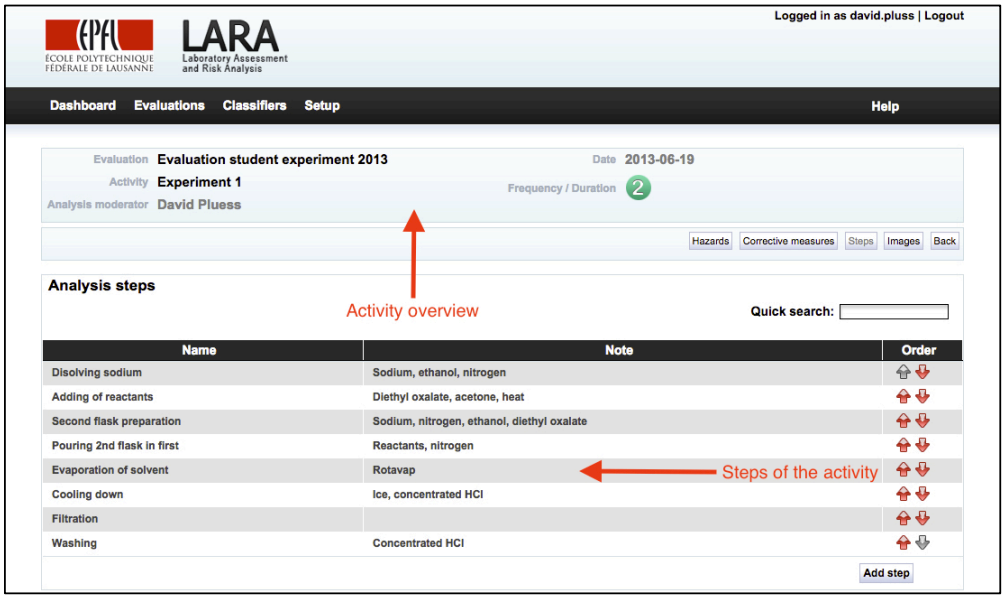


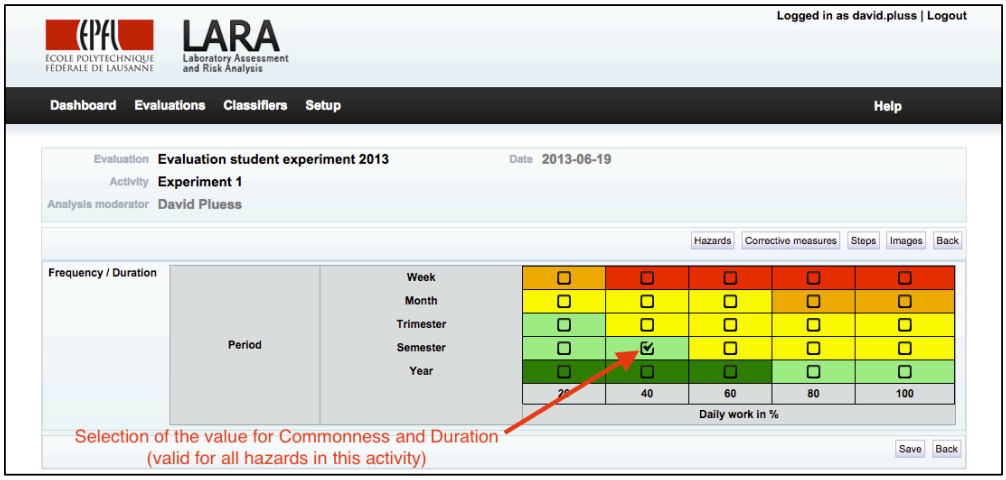
The “activity analysis” button opens the analysis management for the selected actvitiy.

ANALYSIS MANAGEMENT



When the user enters the activity analysis interface, the general parameters valid for all the hazards of this activity are defined: first, the steps are described including the hazardous components and then the commonness value is determined. An interface (5 x 5 square, colors indicating 5 different possible values (1-5)) allows assigning a value for the first calculation parameter. Both axis of the scale are adjustable for the main administrator of the software.



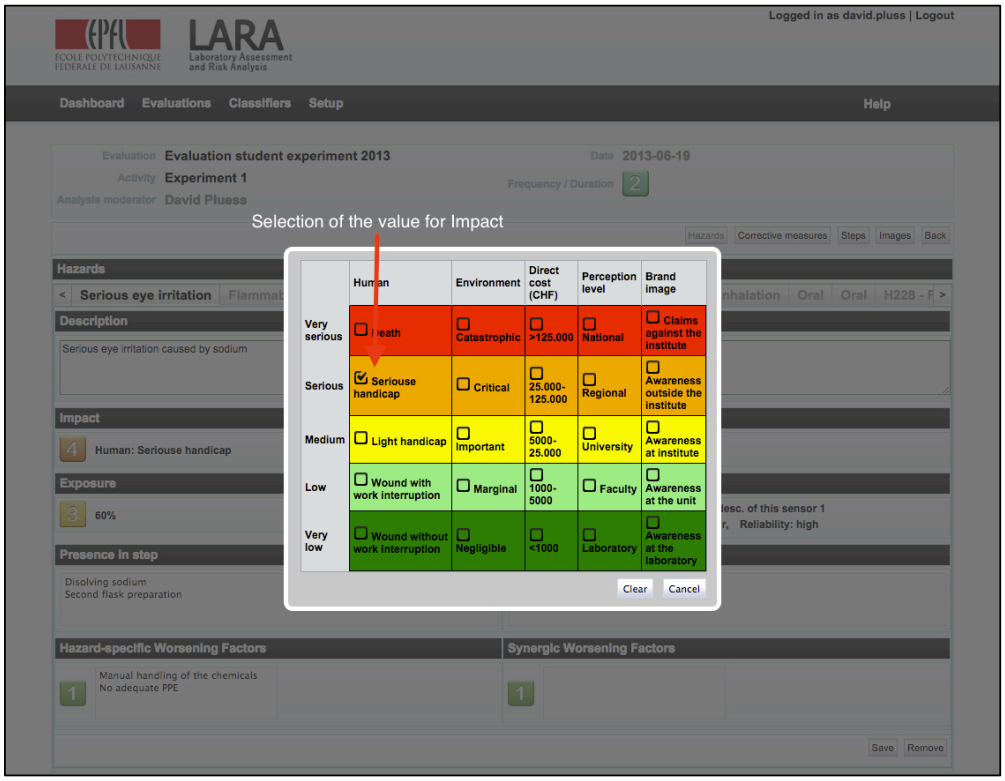


The hazard overview shows the parameters of this activity and lets the user add hazards from the database or switch between. For each hazards, the user can add a short description and choose a consequence: the selection of possible consequences is depending on the selected hazard. The consequences are part of the database and the user has the possibility to add suggestion. The suggestions will be added to the database after revision of an administrator.

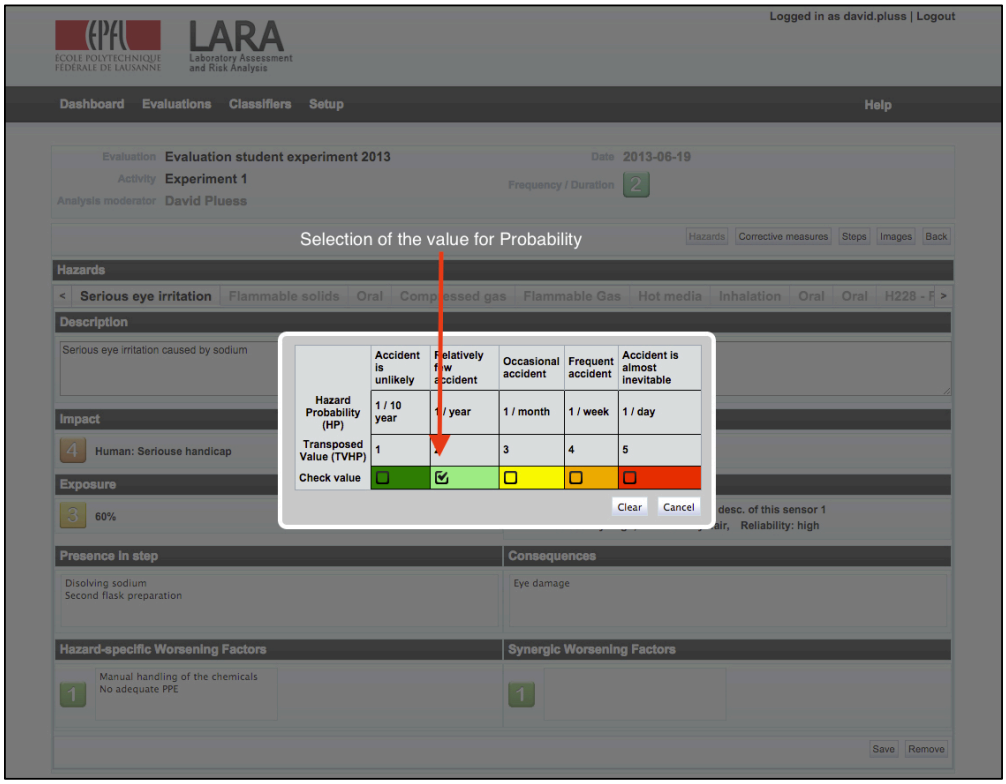
Then the user chooses the values for the risk dimensions:

The impact of a hazard is the first parameter for the calculation of the risk. The value is given by the vertical axis (1-5) for each of the possible field of impact. The scale (very serious, serious, etc.) and the choices (e.g. regional

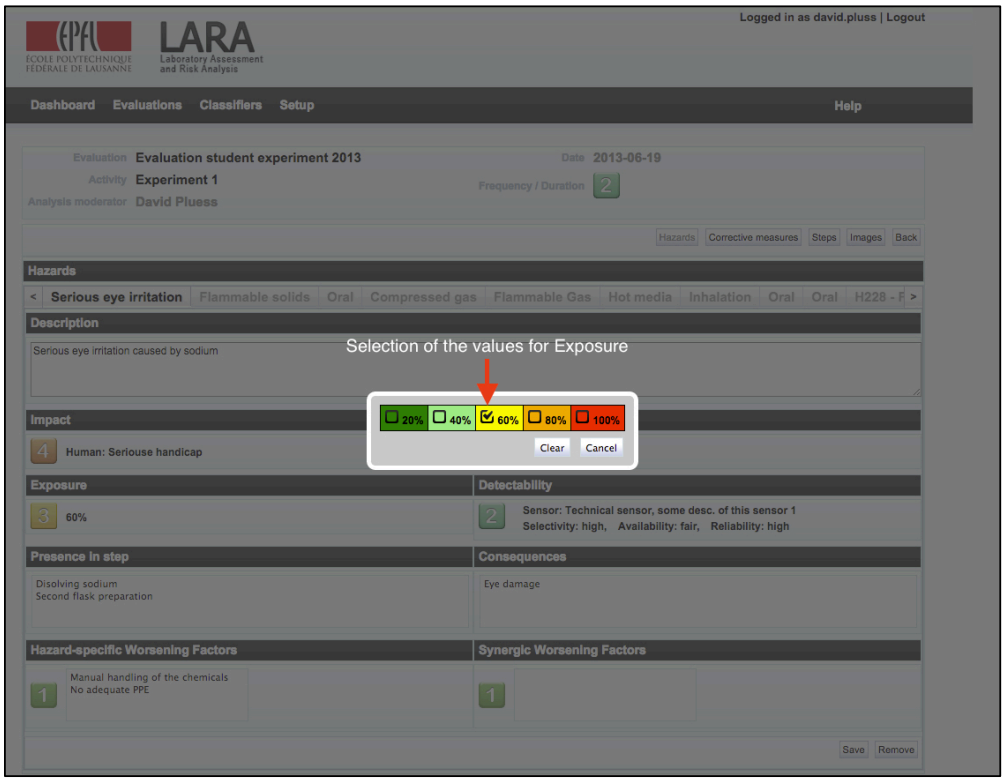
for the field of impact “perception level”) are adjustable by the main administrator of the software.

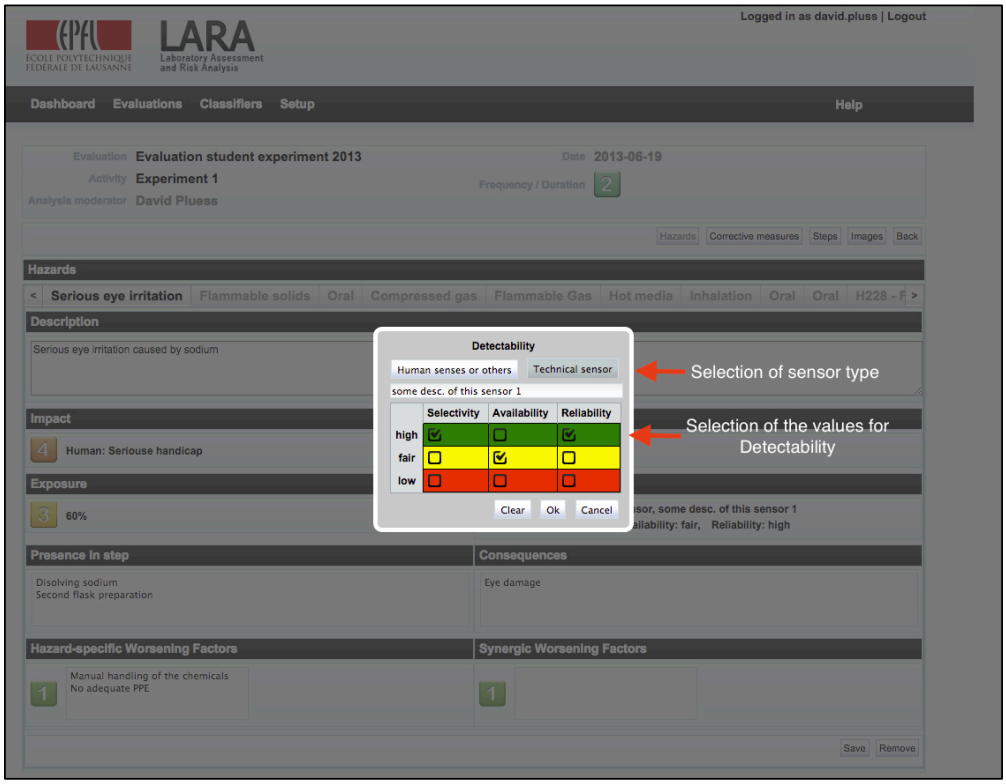


The probability is the second parameter for the calculation of the risk. The value is given by a choice of 5 different options (1-5). The qualitative description of a value (“Accident is unlikely”) as well as the quantitative (“0.01-0.03”) is adjustable by the main administrator of the software.

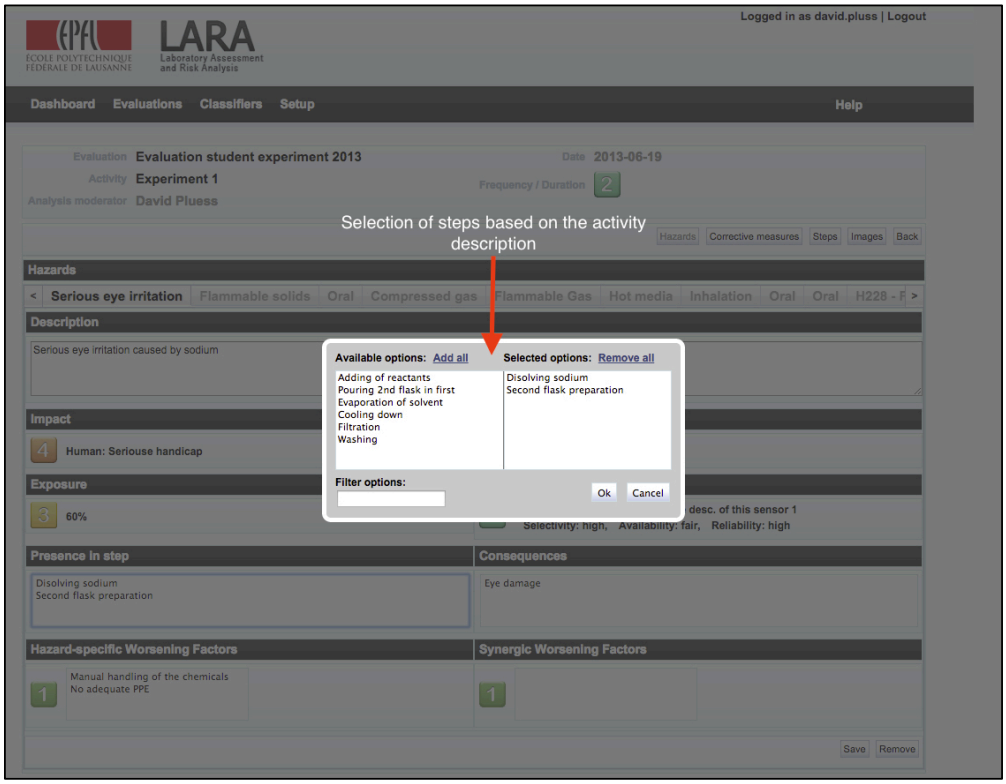


In a similar way, the other factors of the risk dimensions are determined.



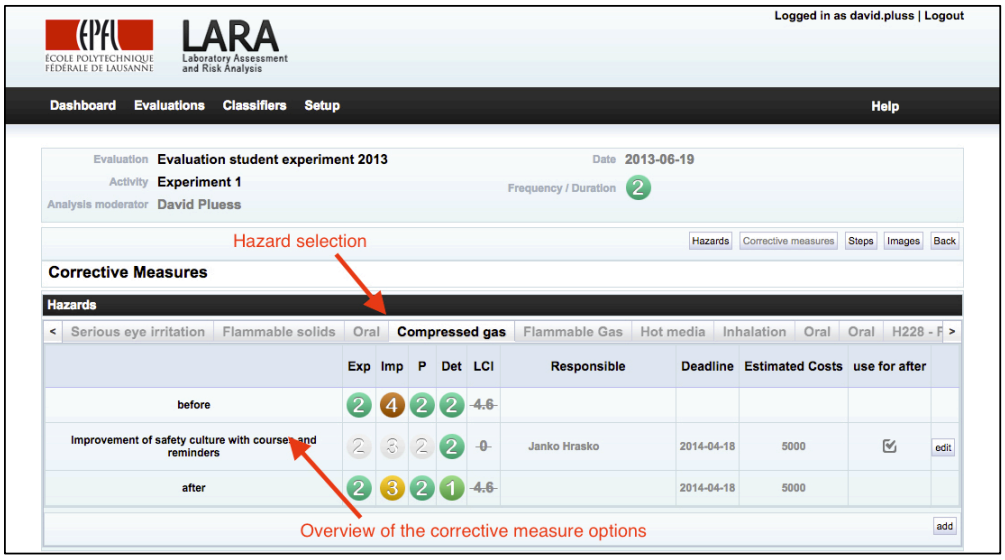


The rest of the interface is a database selection for each specific hazard. The different types of worsening factor are the other parameters used for the calculation of the risk. Each hazard has a specific list for each type of worsening factors (stored in the database). The user can chose from this list and add factors to the analysis for this hazard. Each single factor has an internal value in the database. The sum of these values (of the chosen factors) is compared with a fixed scale (settings) in order to give the final value for the worsening factor type, which is shown in the interface. Other than the specific worsening factors, the choice of synergetic worsening factors is related to the other hazards present in the analysis.

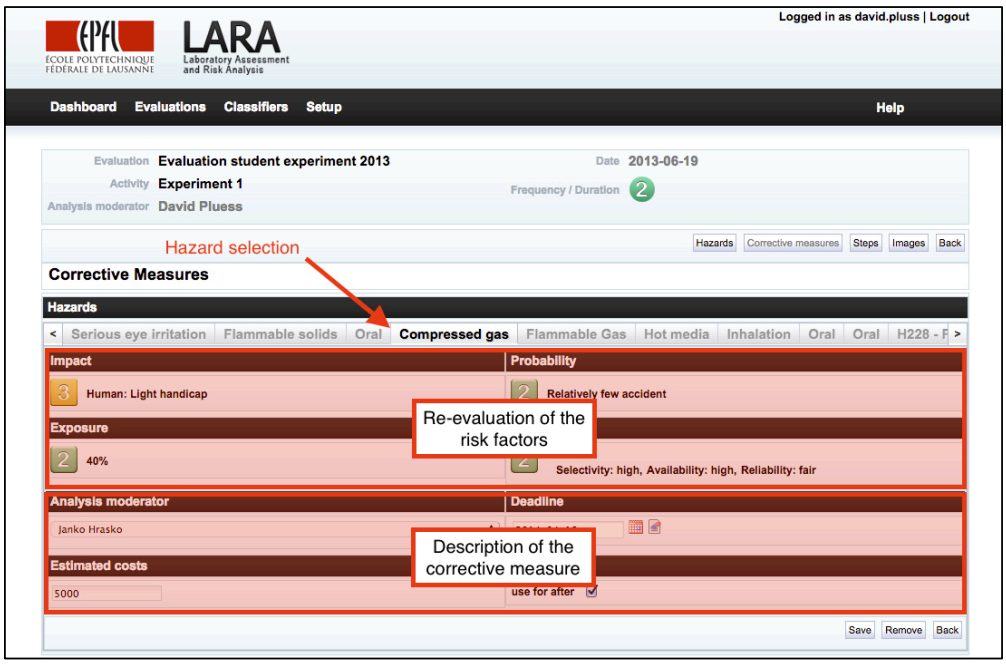


Once the hazards for an activity are described, the user can switch to the corrective measure interface below the activity overview. In this bar, the user can also access the step interface and add images to the activity, which are then stored in the evaluation report.

The corrective measure overview shows the LCI values before, after and when a specific corrective measure is applied.

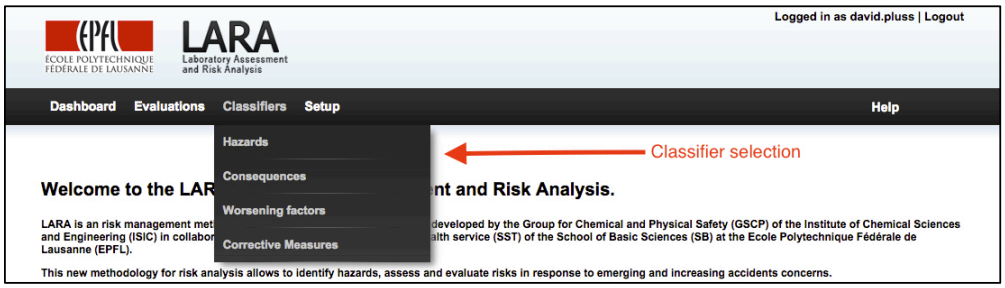


The corrective measures interface gives the user the possibility to add corrective measures related to each single hazard (options are stored in the database) and chose their effectiveness. The user changes the values of each corrective measure manually. As part of additional information, the user can assign responsible persons, deadlines and estimated costs to each corrective measure.



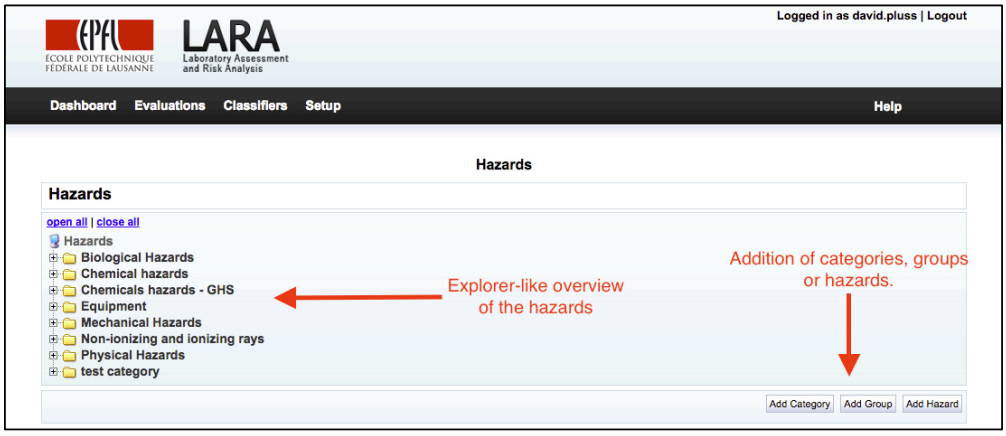
DATABASE MANAGEMENT

The second part of the LARA software is the management of the classifiers, i.e. everything that is part of the database. Normal users do not have the permissions to do so, but they have the possibility to suggest a database entry. After a validation by an administrator, the newly suggest item will be added to the database. Following classes are editable in LARA



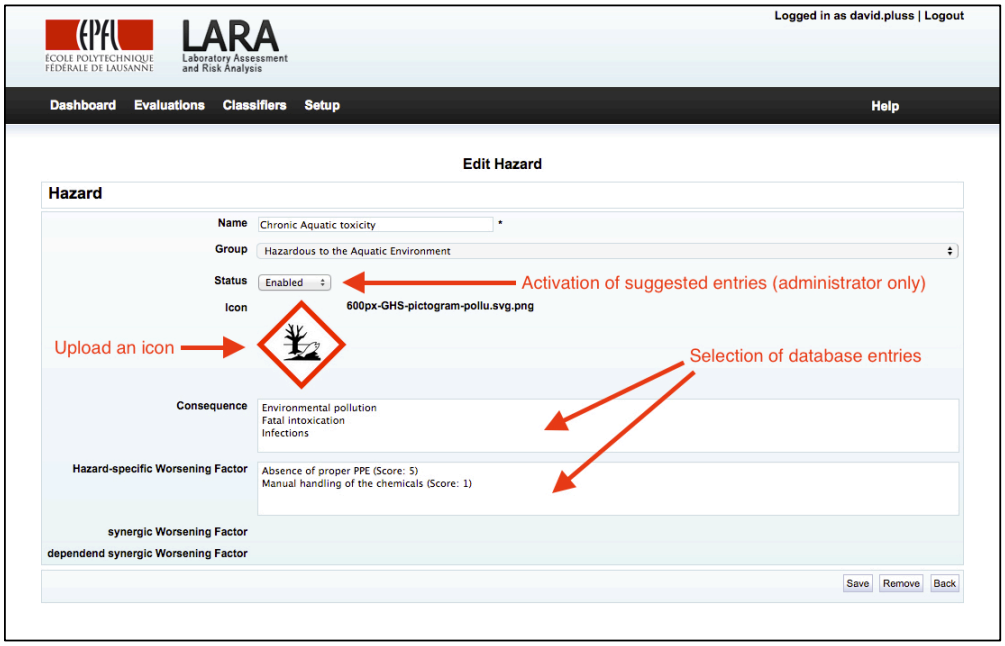
HAZARDS

The hazard overview shows the hazard categories, groups and hazards in a explorer-like hierarchy. Each type of hierarchy can be added through the overview interface.



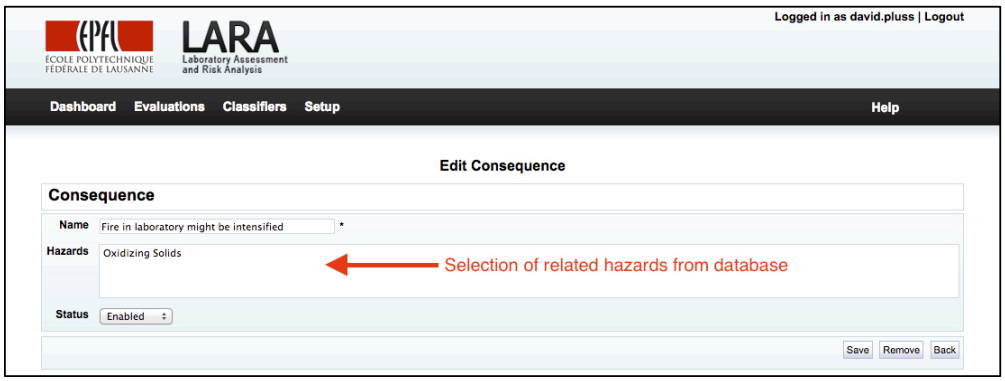
The hazard editing interface allows to add a new or to edit an existing hazard. Additional to the general information, a hazard symbol icon can be assigned form an existing choice or uploaded from the user. Each hazard has linked database entries: consequences, hazard-specific worsening factors, and synergetic worsening factors.

Every user can suggest new hazards; however, they are not implemented directly in the hazard database. Before it can be used in LARA, an administrator has to validate the hazard and enable it (only visible for administrators)



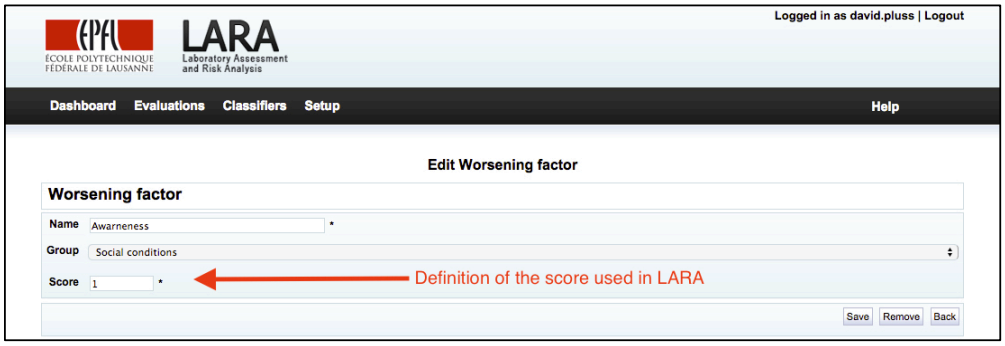
CONSEQUENCES

This interface lets the user add consequences and assign them to hazards from the database. As for the hazards, suggested consequences need to be validated first, before they can be used in LARA.



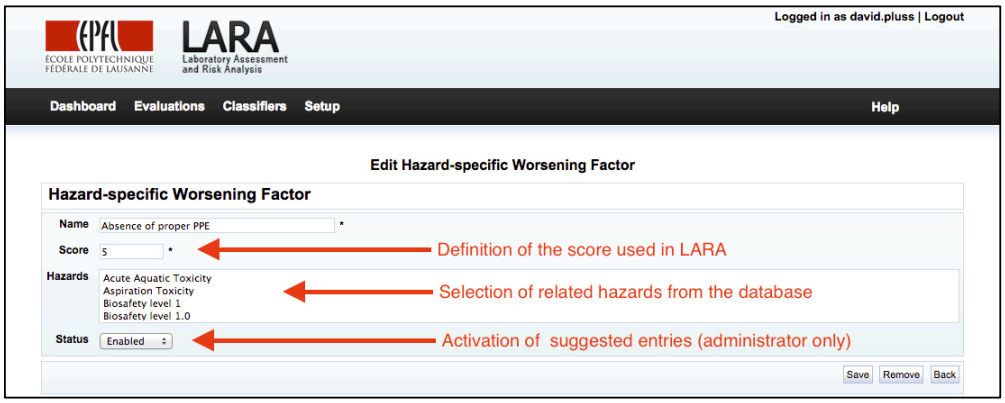
GENERAL WORSENING FACTORS

This interface lets the user add general worsening factors and assign them to a worsening factor group. Additionally, a value is assigned which is used for the calculation. A normal user cannot suggest this kind of worsening factors.



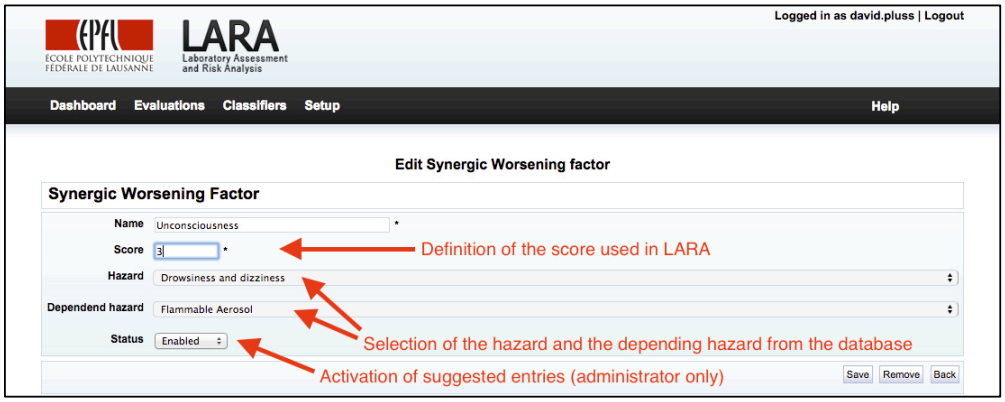
HAZARD-SPECIFIC WORSENING FACTOR

This interface lets the user add hazard-specific worsening factors and assign them to hazards from the database. Additionally, a value is assigned which is used for the calculation. As for the hazards, suggested hazard-specific worsening factors need to be validated first, before they can be used in LARA.



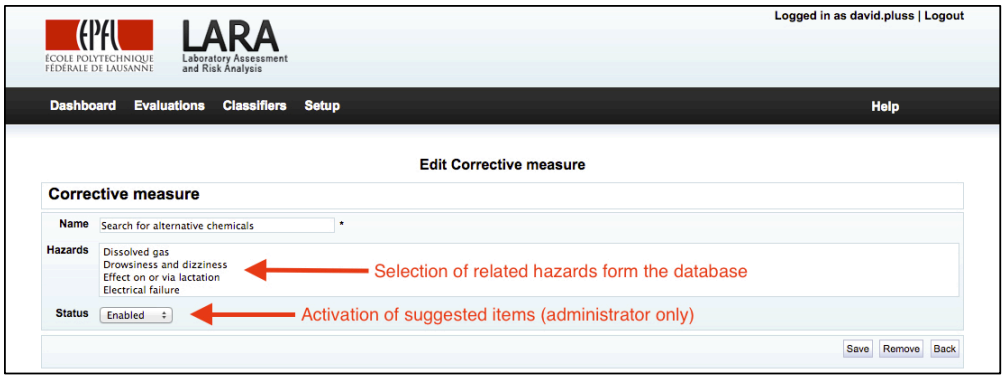
SYNERGETIC WORSENING FACTORS

This interface lets the user add hazard-specific worsening factors and assign them to hazards from the database. Additionally, a value is assigned which is used for the calculation. As for the hazards, suggested synergetic worsening factors need to be validated first, before they can be used in LARA.



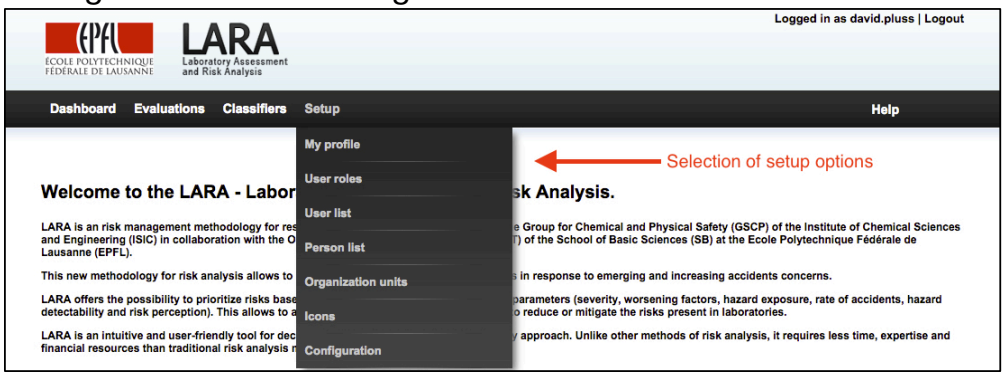
CORRECTIVE MEASURES

This interface lets the user add corrective and assign them to hazards from the database. As for the hazards, suggested corrective measures need to be validated first, before they can be used in LARA.

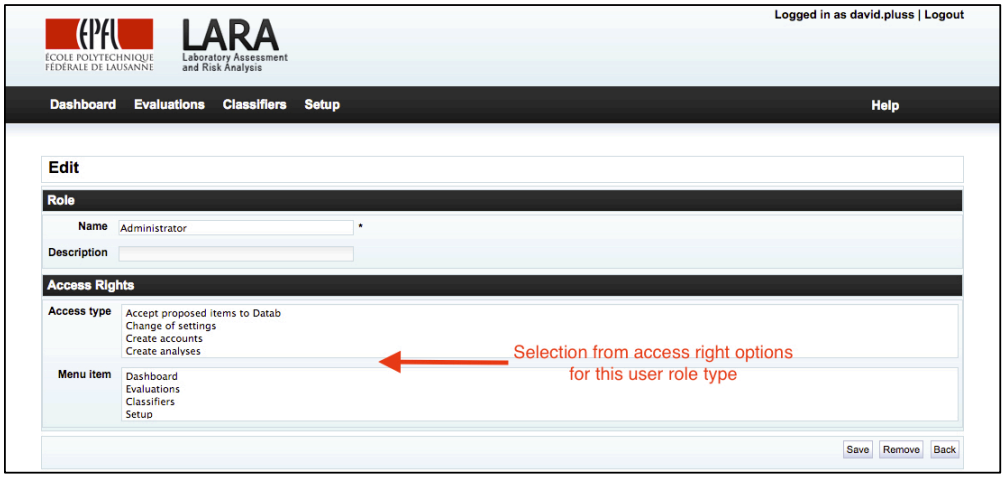


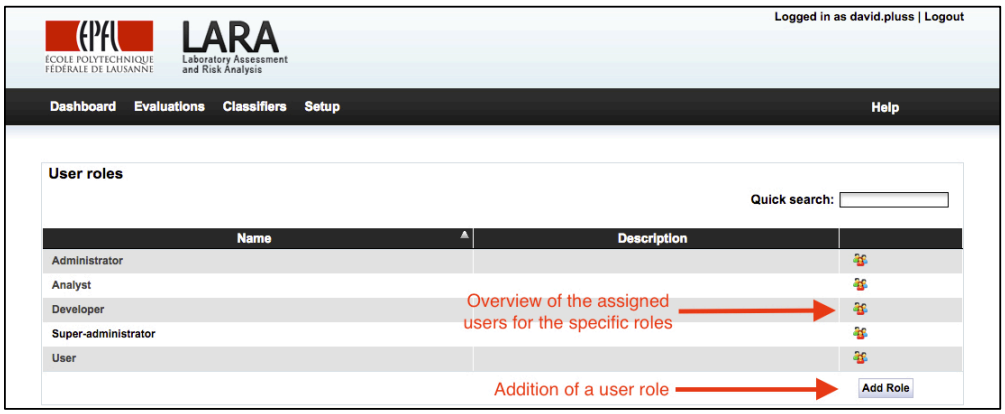
SETTINGS

In the setting part of LARA, the various variables for the risk management can be changed.



An important part is the user management:





In LARA, following user groups are defined:

USER is allowed to see analyses and evaluations for certain groups, institutes, faculties or institutions (as set by the administrator).

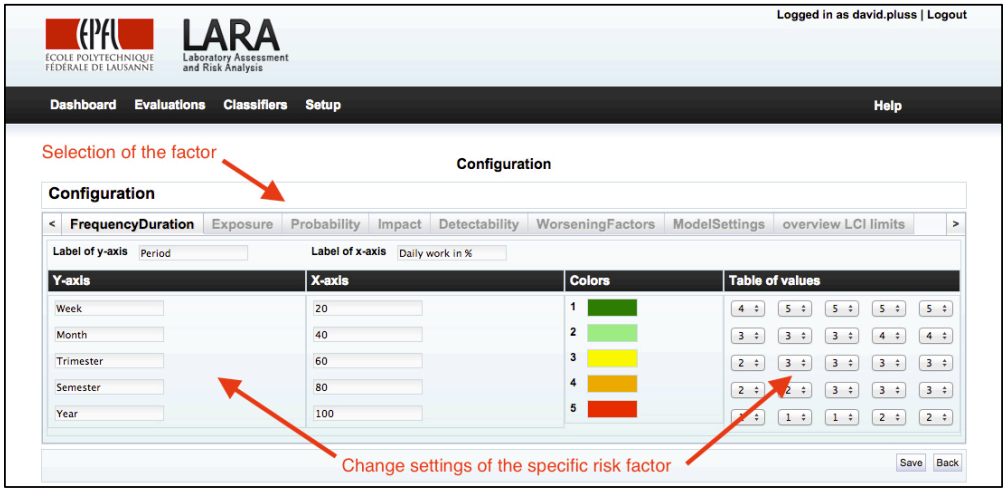
ANALYST is allowed to see, create and edit analyses and evaluations for certain groups, institutes, faculties or institutions (as set by the administrator). Has the right to propose new items to the database.

ADMINISTRATOR is allowed to see, create and edit analyses and evaluations for certain groups, institutes, faculties or institutions. Defines the access right of users and analysts. Has the right to propose new items to the database. Accepts propositions for the database and completes the information. Is able to edit the content of the database. Can create account and set them to either user or analyst. Can delete evaluations or analyses.

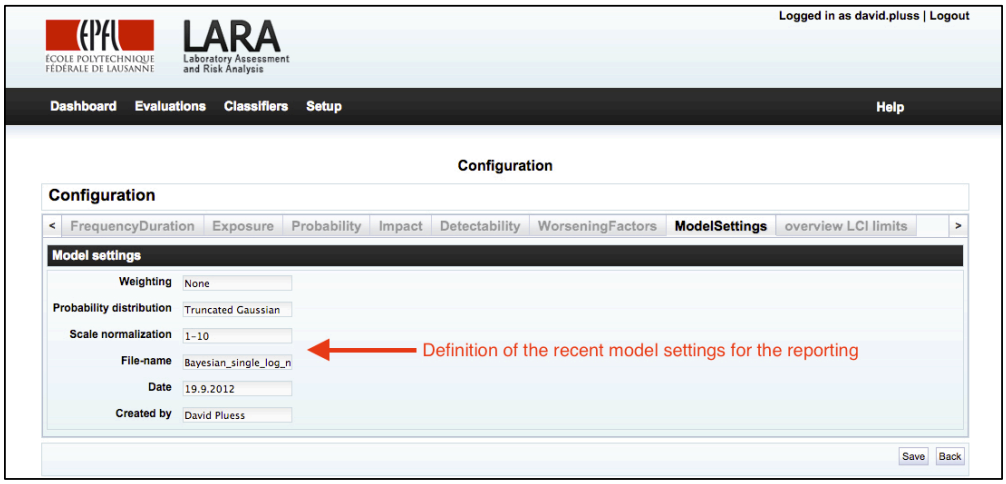
SUPER-ADMINISTRATOR is allowed to see, create and edit analyses and evaluations for certain groups, institutes, faculties or institutions. Defines the access right of users, administrators and analysts. Accepts propositions for the database and completes the information. Is able to edit the content of the database. Can create account and set them to user, analyst, administrator or super-administrator. Can delete evaluations or analyses. Is allowed to perform any changes in the settings.

	User	Analyst	Administrator	Super-Administrator
See analyses	X	X	X	X
Create analyses		X	X	X
Edit/delete analyses		X	X	X
Propose items to Database		X	X	X
Accept proposed items			X	X
Edit database			X	X
Create accounts			X	X
Change of settings				X

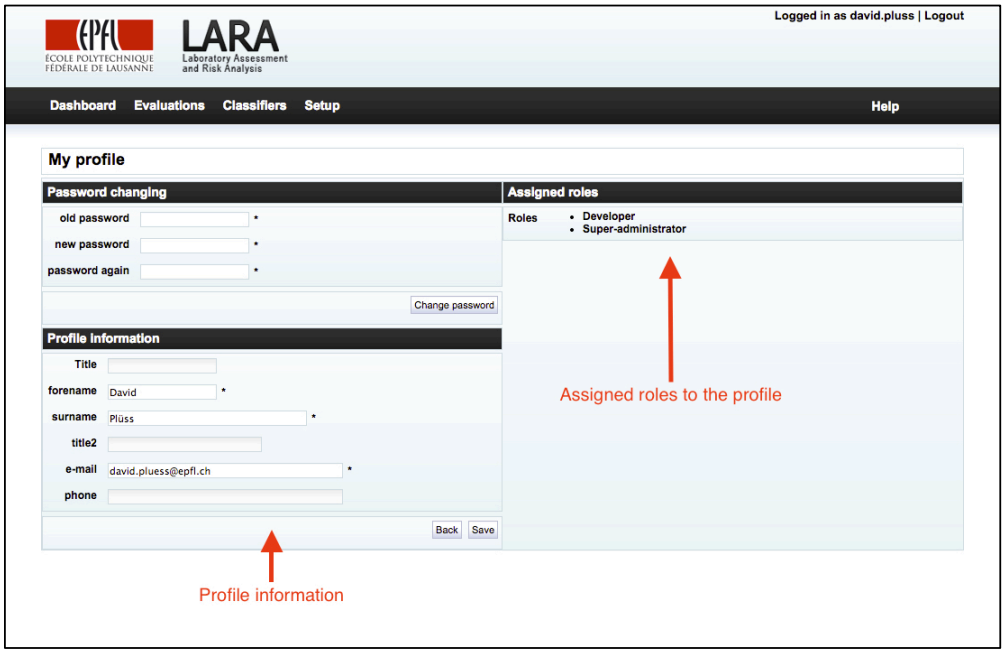
In LARA, all risk dimensions are changeable by the administrator of the system in order to provide the flexibility and to adapt the settings to the situation present.



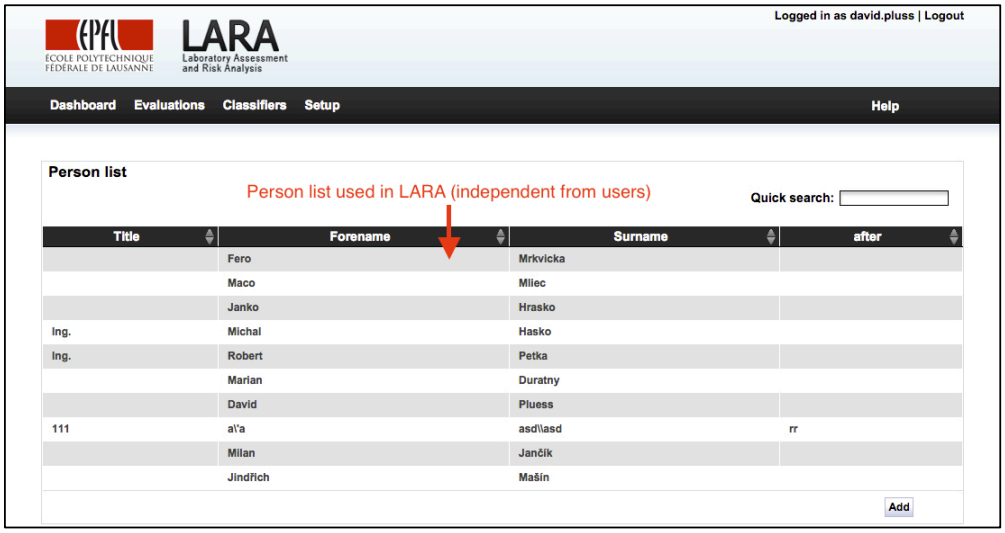
Also the calculation engine is changeable. The interface to change the calculation allows defining the exact parameters to ensure traceability.



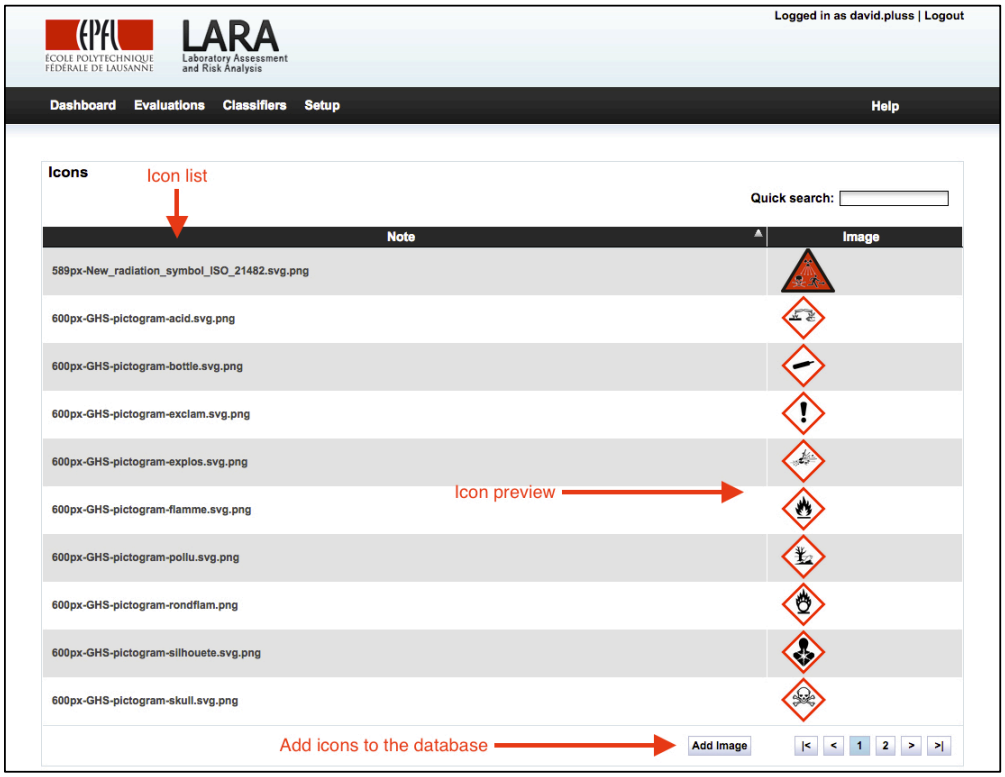
Additionally, the user is able to change his account settings:



Some items are not directly stored in the database, since they do not have a direct implication for hazard. The first kinds of these items are persons. In LARA, the persons related to an evaluation are not necessarily registered as users; therefore they can be added separately.



The second kinds of items are hazard symbols: they can also be stored in the setup by each administrator.



LARA CALCULATION FILE

LARA gives the possibility to add different kind of calculation files and to choose between the calculation methods for each single evaluation. The basic mechanism is as follows:

LARA hands over the values for variables (definition see below) to a server running Octave (a freeware clone of Matlab), which calculates the LCI values using the calculation file and hands them back to LARA. If Bayesian Network is used, Octave uses an API to calculate the values using Hugin.

The calculation file needs to be compiled as a .m-File (standard Matlab calculation file which works as well with Octave).

In order to work with the LARA interface, the parameters used in the calculation file need to be defined as followed:

- Severity: Severity_matlab_input
- Probability:
  - Commonness: Frequency_matlab_input
  - Occurrence; Rate_matlab_input

- Involvement: Exposure_matlab_input
- Detectability:
  - Availability: Availability_matlab_input
  - Reliability: Reliability_matlab_input
  - Selectivity: Selectivity_matlab_input
- Worsening factors:
  - HSWF: Hazard_specific_matlab_input
  - SWF: Interrelations_matlab_input
  - GWF: Special_conditions_matlab_input

Additional information for the use of Bayesian networks

Hugin uses following commands to calculate the values:

%The following two files are required for the calculation using Hugin and need to be stored on the server. The path needs to be renamed in order to work.

ghapi = NET.addAssembly ('C:\Program Files\Hugin Expert\Hugin Researcher 7.6 (x64)\HDE7.6CS\Lib\hugincs-7.6-2.0-x64.dll')

%The .net-File contains the Hugin information and needs to be compiled using the Hugin-Software.

d = HAPI.Domain ('C:\Program Files\Hugin Expert\Hugin Researcher 7.6 (x64)\Samples\Basic_Version_test2_truncated_3.net', HAPI.DefaultClassParseListener);

Severity_input = d.GetNodeByName ('Severity_input');

Severity_input.SelectState (Severity_matlab_input);

Rate_input = d.GetNodeByName ('Rate_input');

Rate_input.SelectState (Rate_matlab_input);

Exposure_input = d.GetNodeByName ('Exposure_input');

Exposure_input.SelectState (Exposure_matlab_input);

Frequency_input = d.GetNodeByName ('Frequency_input');

Frequency_input.SelectState (Frequency_matlab_input);

```
Availability_input = d.GetNodeByName ('Availability_input');
Availability_input.SelectState (Availability_matlab_input);

Reliability_input = d.GetNodeByName ('Reliability_input');
Reliability_input.SelectState (Reliability_matlab_input);

Selectivity_input = d.GetNodeByName ('Selectivity_input');
Selectivity_input.SelectState (Selectivity_matlab_input);

Hazard_specific_input = d.GetNodeByName ('Hazard_specific_input');
Hazard_specific_input.SelectState (Hazard_specific_matlab_input);

Interrelations_input = d.GetNodeByName ('Interrelations_input');
Interrelations_input.SelectState (Interrelations_matlab_input);

Special_conditions_input = d.GetNodeByName ('Special_conditions_input');
Special_conditions_input.SelectState (Special_conditions_matlab_input);

 d.Compile ();
d.Propagate(HAPI.Equilibrium.H_EQUILIBRIUM_SUM,HAPI.EvidenceMode.H_EVIDENCE_MODE_NORMAL);

LCI = d.GetNodeByName ('LCI_value');
LCI.GetExpectedUtility();
import(n,12) = ((((ans-4.51)*9)/(7.69-4.51))+1        %Normalization to 10
end
```

C LARA Application Examples: Details

C.1 Laboratory of Inorganic Synthesis and Catalysis

Evaluation LSCI	
Organization	EPFL
Research Group	Laboratory of Inorganic Synthesis and Catalysis (LSCI)
Laboratory	BCH 3201
Group head	Prof. Xile Hu
Safety delegate	Gerald Bauer
Responsible scientist	Gerald Bauer
Analysis moderator	David Nicolas Pluess
Date	05.08.14
Description of the evaluation	Evaluation of the synthesis to form [Fe(Bopa-Ph)Cl(THF)2]
General worsening factors present	Too hot/too cold (Climate) Respiratory protecting device (Dynamic work) Group composition not ideal (Social) Overloaded benches (Space) Overloaded fumehoods (Space) Too many working hours (Working hours)

Appendix C. LARA Application Examples: Details

Evaluation LSCI			
Responsible scientist:	Gerald Bauer	**Laboratory** BCH 3201	**Date** 05.08.14
Activity	Step-Nr.	Step	
2-Chlorobenzoic acid	1	Dissolution of nitro benzoic acid and addition of Pd/C	
	2	Stirring in H2 Atmosphere	
	3	Filtering off and evaporation of solvent	
2,2-Iminodibenzoic acid	1	Mixing of all reactants and addition of DMF	
	2	Heating to 140°C (24h)	
	3	Evaporation of solvent	
	4	Dissolution in water	
	5	Filtering of the solution	
	6	Acidification	
	7	Filtering and drying	
2,2-Iminodibenzoyl chloride	1	Suspension of reactants	
	2	Heating to reflux (overnight)	
	3	Filtering and washing	
	4	Quenching of the filtrate	
	5	Drying of the organic phase	
	6	Recrystallization	
7C Oxaz-NNN-Ph (GB13_043)	1	Dissolution of reactants and addition of tryethylamin	
	2	Cooling (0°C) and addition of 2,2-iminodibenzoyl chloride	
	3	Stirring for 1 h	
	4	Cooling (0°C) and addition of methanesulfonyl chloride	
	5	Warming to room temperature and stirring for 2h	
	6	Quenching of the mixture	
	7	Extraction of the organic phase	
	8	Column chromatography	
(Bopa-Ph)Li	1	Dissolution of the reactants in toluene	
	2	Addition of n-BuLi	
	3	Stirring for 2h	
	4	Addition of pentane	
	5	Filtration and drying	
[Fe(Bopa-Ph)Cl(THF)2]	1	Dissolution of the reactants in THF	
	2	Addition of FeCl2(THF)1.5	
	3	Stirring overnight	
	4	Evaporation of solvent	
	5	Redisollution in toluene	
	6	Filtration	
	7	Concentration and precipitation with pentane	
	8	Filtration	
	9	Recrystallization	

Evaluation LSCI													
Responsible scientist:	Gerald Bauer		**Laboratory**	BCH 3201				**Date**					05.08.14
Activity	Origin	Nr.	Hazard	Step 1	2	3	4	5	6	7			LCI
2-Chlorobenzoic acid	Nitrobenzoic Acid	1	H315 Causes skin irritation	•									3.7
		2	H319 Causes serious eye irritation	•									4.6
		3	H335 May cause respiratory irritation	•									4.2
	Methanol	4	H225 Highly Flammable liquid and vapour	•									4.0
		5	H301 Toxic if swalloed	•									3.2
		6	H311 Toxic in contact with skin	•									3.7
		7	H331 Toxic if inhaled	•									3.9
		8	H370 Causes damage to organs	•									4.3
	Pd/C	9	H315 Causes skin irritation	•									3.9
		10	H319 Causes serious eye irritation	•									5.0
		11	H335 May cause respiratory irritation	•									4.2
	H2	12	H220 Extremely flammable gas		•								4.7
	Evaporation	13	Hot medium			•							2.8
2,2-Iminodibenzoic acid	Anthranilic acid	14	H319 Causes serious eye irritation	•									4.4
	2-Chlorobenzoic acid	15	H319 Causes serious eye irritation	•									4.4
	Copper(I)oxide	16	H302 Harmful if swallowed	•									3.1
		17	H410 Very toxic to aquatic life with long lasting effects	•									4.8
	K2CO3	18	H302 Harmful if swallowed	•									3.1
		19	H315 Causes skin irritation	•									3.5
		20	H319 Causes serious eye irritation	•									4.4
		21	H335 May cause respiratory irritation	•									3.7
	Heating	22	Hot medium		•	•							3.0
	DMF	23	H226 Flammable liquid and vapour	•									4.5
		24	H312 Harmful in contact with skin	•									3.7
		25	H332 Harmful if inhaled	•									3.9
		26	H319 Causes serious eye irritation	•									4.4
		27	H360 May damage fertility or the unborn child	•									5.2
2,2-Iminodibenzoyl chloride	DCM	28	H315 Causes skin irritation	•		•		•					4.1
		29	H319 Causes serious eye irritation	•		•		•					4.9
		30	H335 May cause respiratory irritation	•		•		•					4.2
		31	H336 May cause drowsiness or dizziness	•		•		•					3.8
		32	H351 Suspected of causing cancer	•		•		•					4.5
		33	H373 Causes damage to organs through prolonged or repeated exposure	•		•		•					4.3
	Thionyl chloride	34	H302 Harmful if swallowed	•									3.3
		35	H314 Causes severe skin burns and eye damage	•									4.8
		36	H331 Toxic if inhaled	•									4.1
	Reflux	37	Hot medium		•			•					2.6
	Hexane	38	H225 Highly Flammable liquid and vapour					•					5.0
		39	H304 May be fatal if swallowed and enters airways					•					5.2
		40	H315 Causes skin irritation					•					3.4
		41	H336 May cause drowsiness or dizziness					•					3.7
		42	H361 Suspected of damaging fertility or the unborn child					•					5.2
		43	H373 Causes damage to organs through prolonged or repeated exposure					•					4.0
		44	H411 Toxic to aquatic life with long lasting effects					•					4.1
7C Oxaz-NNN-Ph (GB13_043)	Triethylamine	45	H225 Highly Flammable liquid and vapour	•									4.8
		46	H302 Harmful if swallowed	•									3.5
		47	H311 Toxic in contact with skin	•									3.7
		48	H331 Toxic if inhaled	•									3.6
		49	H314 Causes severe skin burns and eye damage	•									4.8
		50	H335 May cause respiratory irritation	•									4.0
	DCM	51	H315 Causes skin irritation	•									3.6
		52	H319 Causes serious eye irritation	•									4.4
		53	H335 May cause respiratory irritation	•									3.6
		54	H336 May cause drowsiness or dizziness	•									2.9
		55	H351 Suspected of causing cancer	•									4.0
		56	H373 Causes damage to organs through prolonged or repeated exposure	•									3.8
	KOH	57	H290 May be corrosive to metals	•									3.2
		58	H302 Harmful if swallowed	•									3.3
		59	H314 Causes severe skin burns and eye damage	•									4.6
	Cooling	60	Cool media		•								2.5
	Methanesulfonyl chloride	61	H300 Fatal if swallowed				•						5.2
		62	H310 Fatal in contact with skinH330 Fatal if inhaled				•						5.4
		63	H314 Causes severe skin burns and eye damage				•						4.6
		64	H330 Fatal if inhaled				•						5.4
		65	H335 May cause respiratory irritation				•						4.1
	Hexane	66	H225 Highly Flammable liquid and vapour							•			4.6
		67	H304 May be fatal if swallowed and enters airways							•			5.0
		68	H315 Causes skin irritation							•			3.4
		69	H336 May cause drowsiness or dizziness							•			3.0
		70	H361 Suspected of damaging fertility or the unborn child							•			5.0
		71	H373 Causes damage to organs through prolonged or repeated exposure							•			3.6
		72	H411 Toxic to aquatic life with long lasting effects							•			4.1
	Ethyl acetate	73	H225 Highly Flammable liquid and vapour							•			4.6
		74	H319 Causes serious eye irritation							•			4.8
		75	H336 May cause drowsiness or dizziness							•			3.3
(Bopa-Ph)Li	Toluene	76	H225 Highly Flammable liquid and vapour	•									4.9
		77	H304 May be fatal if swallowed and enters airways	•									5.0

Appendix C. LARA Application Examples: Details

Evaluation LSCI													
Responsible scientist:	Gerald Bauer		**Laboratory**	BCH 3201				**Date**			05.08.14		
Activity	Origin	Nr.	Hazard	Step 1	2	3	4	5	6	7			LCI
		78	H315 Causes skin irritation	•									3.4
		79	H336 May cause drowsiness or dizziness	•									3.5
		80	H361 Suspected of damaging fertility or the unborn child	•									5.2
		81	H373 Causes damage to organs through prolonged or repeated exposure	•									4.5
	n-BuLi	82	H225 Highly Flammable liquid and vapour		•								5.3
		83	H250 Catches fire spontaneously if exposed to air		•								5.3
		84	H261 In contact with water releases flammable gas		•								5.5
		85	H304 May be fatal if swallowed and enters airways		•								5.6
		86	H314 Causes severe skin burns and eye damage		•								4.6
		87	H336 May cause drowsiness or dizziness		•								3.5
		88	H361 Suspected of damaging fertility or the unborn child		•								5.2
		89	H373 Causes damage to organs through prolonged or repeated exposure		•								4.3
		90	H411 Toxic to aquatic life with long lasting effects		•								4.4
	Pentane	91	H225 Highly Flammable liquid and vapour			•							4.6
		92	H304 May be fatal if swallowed and enters airways			•							5.4
		93	H336 May cause drowsiness or dizziness			•							3.5
		94	H411 Toxic to aquatic life with long lasting effects			•							4.2
[Fe(Bopa-Ph)Cl(THF)2]	Toluene	95	H225 Highly Flammable liquid and vapour					•					4.6
		96	H304 May be fatal if swallowed and enters airways					•					4.8
		97	H315 Causes skin irritation					•					3.0
		98	H336 May cause drowsiness or dizziness					•					3.1
		99	H361 Suspected of damaging fertility or the unborn child					•					5.2
		100	H373 Causes damage to organs through prolonged or repeated exposure					•					3.8
	Pentane	101	H225 Highly Flammable liquid and vapour							•	•		4.8
		102	H304 May be fatal if swallowed and enters airways							•	•		5.4
		103	H336 May cause drowsiness or dizziness							•	•		3.7
		104	H411 Toxic to aquatic life with long lasting effects							•	•		4.2
	Evaporation	105	Hot medium				•						2.0
	THF	106	H225 Highly Flammable liquid and vapour	•							•		5.0
		107	H319 Causes serious eye irritation	•							•		5.0
		108	H335 May cause respiratory irritation	•							•		4.2
		109	H351 Suspected of causing cancer	•							•		5.0

Evaluation LSCI

Responsible scientist: Gerald Bauer **Laboratory** BCH 3201 **Date** 05.08.14

Nr	Hazard	Impact	Probability			Detectability			WF			LCI
			Exposure	Occurence	Involvement	Reliability	Selectivity	Availability	GWF	HSWF	SWF	
1	H315 Causes skin irritation	1	4	4	3	3	5	1	1	3	1	3.7
2	H319 Causes serious eye irritation	4	4	2	3	3	5	1	1	2	1	4.6
3	H335 May cause respiratory irritation	3	4	2	3	3	5	1	1	2	2	4.2
4	H225 Highly Flammable liquid and vapour	3	4	2	3	1	5	3	1	2	1	4.0
5	H301 Toxic if swalloed	3	4	1	3	1	5	1	1	1	1	3.2
6	H311 Toxic in contact with skin	3	4	1	3	3	5	1	1	2	1	3.7
7	H331 Toxic if inhaled	3	4	1	3	3	5	1	1	2	2	3.9
8	H370 Causes damage to organs	4	4	2	3	1	1	3	1	2	1	4.3
9	H315 Causes skin irritation	1	4	4	3	3	5	3	1	2	1	3.9
10	H319 Causes serious eye irritation	4	4	2	3	3	5	3	1	2	1	5.0
11	H335 May cause respiratory irritation	3	4	2	3	3	5	1	1	2	2	4.2
12	H220 Extremely flammable gas	4	4	2	3	1	1	3	1	2	3	4.7
13	Hot medium	1	4	4	3	1	1	1	1	1	2	2.8
14	H319 Causes serious eye irritation	4	4	2	2	3	5	1	1	2	1	4.4
15	H319 Causes serious eye irritation	4	4	2	2	3	5	1	1	2	1	4.4
16	H302 Harmful if swallowed	2	4	1	2	5	3	3	1	1	1	3.1
17	H410 Very toxic to aquatic life with long lasting effects	5	4	2	2	1	3	3	1	1	1	4.8
18	H302 Harmful if swallowed	2	4	1	2	5	5	3	1	1	1	3.1
19	H315 Causes skin irritation	1	4	4	2	3	5	3	1	1	1	3.5
20	H319 Causes serious eye irritation	4	4	2	2	3	5	1	1	2	1	4.4
21	H335 May cause respiratory irritation	3	4	2	2	3	5	1	1	1	2	3.7
22	Hot medium	1	4	4	4	1	1	1	1	1	2	3.0
23	H226 Flammable liquid and vapour	3	4	2	2	5	3	3	1	2	3	4.5
24	H312 Harmful in contact with skin	2	4	3	2	5	5	3	1	2	1	3.7
25	H332 Harmful if inhaled	2	4	3	2	5	3	3	1	2	2	3.9
26	H319 Causes serious eye irritation	4	4	2	2	5	5	1	1	2	1	4.4
27	H360 May damage fertility or the unborn child	4	4	2	2	3	3	3	1	3	2	5.2
28	H315 Causes skin irritation	1	4	4	4	3	5	3	1	2	1	4.1
29	H319 Causes serious eye irritation	4	4	2	4	3	5	1	1	2	1	4.9
30	H335 May cause respiratory irritation	3	4	2	4	3	1	3	1	1	2	4.2
31	H336 May cause drowsiness or dizziness	2	4	3	4	3	1	1	1	2	3	3.8
32	H351 Suspected of causing cancer	4	4	2	4	3	1	1	1	2	1	4.5
33	H373 Causes damage to organs through prolonged or repeated exposure	4	4	1	4	1	1	3	1	2	1	4.3
34	H302 Harmful if swallowed	2	4	2	2	3	5	3	1	1	1	3.3
35	H314 Causes severe skin burns and eye damage	4	4	2	2	3	5	3	1	2	1	4.8
36	H331 Toxic if inhaled	3	4	2	2	3	3	3	1	1	2	4.1
37	Hot medium	1	4	4	2	1	1	1	1	1	2	2.6
38	H225 Highly Flammable liquid and vapour	4	4	2	2	3	5	3	1	1	3	5.0
39	H304 May be fatal if swallowed and enters airways	5	4	2	2	3	5	1	1	2	2	5.2
40	H315 Causes skin irritation	1	4	3	2	3	5	3	1	2	1	3.4
41	H336 May cause drowsiness or dizziness	2	4	3	2	3	1	3	1	2	3	3.7
42	H361 Suspected of damaging fertility or the unborn child	4	4	2	2	3	5	3	1	3	2	5.2
43	H373 Causes damage to organs through prolonged or repeated exposure	4	4	2	2	1	1	3	1	1	2	4.0
44	H411 Toxic to aquatic life with long lasting effects	3	4	2	2	3	3	3	1	2	1	4.1
45	H225 Highly Flammable liquid and vapour	4	4	2	2	3	5	3	1	2	1	4.8
46	H302 Harmful if swallowed	2	4	2	2	3	5	3	1	2	1	3.5
47	H311 Toxic in contact with skin	3	4	2	2	3	5	1	1	2	1	3.7
48	H331 Toxic if inhaled	3	4	2	2	3	3	1	1	1	1	3.6
49	H314 Causes severe skin burns and eye damage	4	4	2	2	3	5	3	1	2	1	4.8
50	H335 May cause respiratory irritation	3	4	2	2	3	3	3	1	1	1	4.0
51	H315 Causes skin irritation	1	4	4	2	3	5	3	1	2	1	3.6
52	H319 Causes serious eye irritation	4	4	2	2	3	5	1	1	2	1	4.4
53	H335 May cause respiratory irritation	3	4	2	2	3	1	3	1	1	1	3.6
54	H336 May cause drowsiness or dizziness	2	4	3	2	3	1	1	1	2	1	2.9
55	H351 Suspected of causing cancer	4	4	2	2	3	1	1	1	2	1	4.0
56	H373 Causes damage to organs through prolonged or repeated exposure	4	4	1	2	1	1	3	1	2	1	3.8
57	H290 May be corrosive to metals	1	4	3	2	5	5	5	1	1	1	3.2
58	H302 Harmful if swallowed	2	4	2	2	5	5	3	1	1	1	3.3
59	H314 Causes severe skin burns and eye damage	4	4	2	2	3	5	3	1	1	1	4.6
60	Cool media	1	4	3	2	3	1	1	1	1	1	2.5
61	H300 Fatal if swallowed	5	4	2	2	3	5	3	1	1	1	5.2
62	H310 Fatal in contact with skinH330 Fatal if inhaled	5	4	2	2	3	5	3	1	2	1	5.4
63	H314 Causes severe skin burns and eye damage	4	4	2	2	3	5	3	1	1	1	4.6
64	H330 Fatal if inhaled	5	4	2	2	3	5	3	1	2	1	5.4
65	H335 May cause respiratory irritation	3	4	2	2	3	3	5	1	2	1	4.1
66	H225 Highly Flammable liquid and vapour	4	4	2	2	3	5	3	1	1	1	4.6
67	H304 May be fatal if swallowed and enters airways	5	4	2	2	3	5	1	1	2	1	5.0
68	H315 Causes skin irritation	1	4	3	2	3	5	3	1	2	1	3.4
69	H336 May cause drowsiness or dizziness	1	4	3	2	3	1	3	1	2	1	3.0
70	H361 Suspected of damaging fertility or the unborn child	4	4	2	2	3	5	3	1	3	1	5.0
71	H373 Causes damage to organs through prolonged or repeated exposure	4	4	1	2	1	1	3	1	1	1	3.6
72	H411 Toxic to aquatic life with long lasting effects	3	4	2	2	3	3	3	1	2	1	4.1
73	H225 Highly Flammable liquid and vapour	4	4	2	2	3	3	3	1	1	1	4.6
74	H319 Causes serious eye irritation	4	4	2	2	3	5	3	1	2	1	4.8
75	H336 May cause drowsiness or dizziness	2	4	3	2	3	1	3	1	2	1	3.3
76	H225 Highly Flammable liquid and vapour	4	4	2	3	3	5	5	1	1	1	4.9
77	H304 May be fatal if swallowed and enters airways	4	4	2	3	5	5	3	1	2	1	5.0
78	H315 Causes skin irritation	1	4	2	3	5	5	3	1	2	1	3.4
79	H336 May cause drowsiness or dizziness	2	4	3	3	3	1	3	1	2	1	3.5
80	H361 Suspected of damaging fertility or the unborn child	4	4	2	3	3	3	3	1	3	1	5.2
81	H373 Causes damage to organs through prolonged or repeated exposure	4	4	2	3	1	1	3	1	2	2	4.5
82	H225 Highly Flammable liquid and vapour	4	4	3	3	5	5	3	1	2	1	5.3
83	H250 Catches fire spontaneously if exposed to air	4	4	3	3	3	5	3	1	2	1	5.3
84	H261 In contact with water releases flammable gas	4	4	3	3	3	3	3	1	3	1	5.5
85	H304 May be fatal if swallowed and enters airways	5	4	2	3	5	5	3	1	2	1	5.6
86	H314 Causes severe skin burns and eye damage	4	4	2	3	3	5	1	1	1	2	4.6
87	H336 May cause drowsiness or dizziness	2	4	3	3	5	3	1	1	2	1	3.5
88	H361 Suspected of damaging fertility or the unborn child	4	4	2	3	3	5	3	1	3	1	5.2
89	H373 Causes damage to organs through prolonged or repeated exposure	4	4	2	3	1	1	3	1	2	1	4.3
90	H411 Toxic to aquatic life with long lasting effects	3	4	2	3	3	3	3	1	2	1	4.4
91	H225 Highly Flammable liquid and vapour	4	4	2	3	3	5	1	1	2	1	4.6
92	H304 May be fatal if swallowed and enters airways	5	4	2	3	3	5	3	1	1	1	5.4
93	H336 May cause drowsiness or dizziness	2	4	3	3	3	1	3	1	2	1	3.5
94	H411 Toxic to aquatic life with long lasting effects	3	4	2	3	5	3	3	1	1	1	4.2
95	H225 Highly Flammable liquid and vapour	4	4	2	1	3	5	5	1	1	2	4.6
96	H304 May be fatal if swallowed and enters airways	4	4	2	1	5	5	3	1	2	2	4.8
97	H315 Causes skin irritation	1	4	2	1	5	5	3	1	2	1	3.0
98	H336 May cause drowsiness or dizziness	2	4	3	1	3	1	3	1	2	1	3.1

Evaluation LSCI												
Responsible scientist:	Gerald Bauer		**Laboratory**	BCH 3201						**Date**	05.08.14	
Nr	Hazard	Impact	Probability			Detectability			WF			LCI
			Exposure	Occurence	Involvement	Reliability	Selectivity	Availability	GWF	HSWF	SWF	
99	H361 Suspected of damaging fertility or the unborn child	4	4	2	1	3	3	3	1	3	3	5.2
100	H373 Causes damage to organs through prolonged or repeated exposure	4	4	2	1	1	1	3	1	2	1	3.8
101	H225 Highly Flammable liquid and vapour	4	4	2	3	3	5	1	1	2	2	4.8
102	H304 May be fatal if swallowed and enters airways	5	4	2	3	3	5	3	1	1	1	5.4
103	H336 May cause drowsiness or dizziness	2	4	3	3	3	1	3	1	2	2	3.7
104	H411 Toxic to aquatic life with long lasting effects	3	4	2	3	5	3	3	1	1	1	4.2
105	Hot medium	1	4	3	1	1	1	1	1	1	1	2.0
106	H225 Highly Flammable liquid and vapour	4	4	2	3	5	5	5	1	1	2	5.0
107	H319 Causes serious eye irritation	4	4	2	3	5	5	5	1	2	1	5.0
108	H335 May cause respiratory irritation	3	4	2	3	3	1	3	1	2	2	4.2
109	H351 Suspected of causing cancer	4	4	2	3	3	3	3	1	2	1	5.0

Evaluation LSCI

Responsible scientist: Gerald Bauer **Laboratory** BCH 3201 **Date** 05.08.14

Refering Hazard	Corrective Measure	LCI before	LCI after	ΔLCI	Financial aspect		Feasibility				
					Costs [CHF]	**Reduction/costs**	A	S	C	V	**F**
107	Training to raise safety awareness	5	4.6	0.4	10'000	3.7	5	5	4	5	0.98
109	Biomonitoring	5	4.1	0.9	40'000	2.2	2	2	3	1	0.39
61	Training to raise safety awareness	5.2	4.6	0.6	10'000	5.7	3	3	5	4	0.67
27	Biomonitoring	5.2	5.0	0.2	40'000	0.6	2	2	3	1	0.39
27	Information to raise awareness	5.2	4.6	0.6	5'000	12.6	5	4	5	5	0.94
88	Biomonitoring	5.2	4.0	1.2	40'000	3.1	2	2	3	1	0.39
88	Information to raise awareness	5.2	4.6	0.6	5'000	11.5	5	4	5	5	0.94
82	Intensified safety training for critical substances	5.3	4.4	0.9	10'000	9.4	3	3	5	4	0.67
83	Intensified safety training for critical substances	5.3	4.4	0.9	10'000	9.4	3	3	5	4	0.67
62	Additional PPE	5.4	4.6	0.8	5'000	16.6	1	5	3	4	0.58
64	Improvement of ventilation	5.4	4.6	0.8	80'000	1.0	5	5	4	5	0.98
64	Training to avoid misuse of existing measures	5.4	4.6	0.8	10'000	7.7	3	3	5	4	0.67
85	Training to raise safety awareness	5.6	5.4	0.2	10'000	2.3	3	3	5	4	0.67

C.2 Group of Catalytic Reaction Engineering

Evaluation GGRC	
Organization	EPFL
Research Group	Group of Catalytic Reaction Engineering
Laboratory	CH H3 554
Group head	Prof. Lioubov Kiwi
Safety delegate	Tatjana Iouranova
Responsible scientist	Tatjana Iouranova
Analysis moderator	David Nicolas Pluess
Date	05.08.14
Description of the evaluation	Selective hydrogenation in a batch reactor
General worsening factors present	Excess of information (Safety) Missing safety training (Safety) Different spoken languages (Social) Too many/few people in lab (Social) Permanent attention (Work) Too many working hours (Working hours)

Evaluation GGRC				
Responsible scientist:	Tatjana Iouranova		**Laboratory** CH H3 554	**Date** 05.08.14
Activity	Step-Nr.	Step		
Selective hydrogenation	1	Filling of the reaction with the subtrate dissolved in the solvent		
	2	Placing of the catalyst on the stirrer		
	3	Asembling of the reactor		
	4	Purging of the system using N2 (3 times)		
	5	Depressurize the reactor		
	6	Heat up the reactor 337K		
	7	Purge the system with H2 (8 bar)		
	8	Sample via GC		
	9	Stop stirring		
	10	Release the pressure		
	11	Set the temperature to 298K		
	12	Let the reactor cool down under stirring		
	13	Cleaning of the reactor		

Appendix C. LARA Application Examples: Details

Responsible scientist:	Tatjana Iouranova		**Evaluation GGRC Laboratory**	CH H3 554												**Date**	05.08.14
Activity	Origin	Nr.	Hazard	Step 1	2	3	4	5	6	7	8	9	10	11	12	13	LCI
Selective hydrogenation with ethanol as solvent	2-butyne-1,4-diol	1	H301 Toxic if swalloed	•													4.2
		2	H312 Harmful in contact with skin	•													3.5
		3	H314 Causes severe skin burns and eye damage	•													4.8
		4	H317 May cause an allergic skin reaction	•													3.9
		5	H331 Toxic if inhaled	•													4.2
		6	H373 Causes damage to organs through prolonged or repeated exposure	•													3.6
	Ethanol	7	H225 Highly Flammable liquid and vapour	•												•	5.3
	H2	8	H220 Extremely flammable gas							•	•	•					5.3
	Pressure	9	Overpressure				•	•	•	•	•	•					3.9
	Heating	10	Hot medium						•	•	•	•	•				3.9
	Sampling (GC)	11	Ejection of reaction mixture								•						3.5
Selective hydrogenation with isopropanol as solvent	2-butyne-1,4-diol	12	H301 Toxic if swalloed	•													4.0
		13	H312 Harmful in contact with skin	•													3.7
		14	H314 Causes severe skin burns and eye damage	•													4.6
		15	H317 May cause an allergic skin reaction	•													3.9
		16	H331 Toxic if inhaled	•													4.0
		17	H373 Causes damage to organs through prolonged or repeated exposure	•													3.6
	Ethanol	18	H225 Highly Flammable liquid and vapour													•	5.3
	H2	19	H220 Extremely flammable gas							•	•	•					5.3
	Pressure	20	Overpressure				•	•	•	•	•	•					3.7
	Heating	21	Hot medium						•	•	•	•	•				4.1
	Sampling (GC)	22	Ejection of reaction mixture								•						3.5
	Isopropanol	23	H225 Highly Flammable liquid and vapour	•													4.2
		24	H319 Causes serious eye irritation	•													4.8
		25	H336 May cause drowsiness or dizziness	•													3.7
Selective hydrogenation with toluene as solvent	2-butyne-1,4-diol	26	H301 Toxic if swalloed	•													4.2
		27	H312 Harmful in contact with skin	•													3.5
		28	H314 Causes severe skin burns and eye damage	•													4.8
		29	H317 May cause an allergic skin reaction	•													3.7
		30	H331 Toxic if inhaled	•													4.2
		31	H373 Causes damage to organs through prolonged or repeated exposure	•													3.6
	Ethanol	32	H225 Highly Flammable liquid and vapour													•	5.3
	H2	33	H220 Extremely flammable gas							•	•	•					5.1
	Pressure	34	Overpressure				•	•	•	•	•	•					3.7
	Heating	35	Hot medium						•	•	•	•	•				4.1
	Sampling (GC)	36	Ejection of reaction mixture								•						3.5
	Toluene	37	H225 Highly Flammable liquid and vapour	•													4.2
		38	H304 May be fatal if swallowed and enters airways	•													5.2
		39	H315 Causes skin irritation	•													3.2
		40	H336 May cause drowsiness or dizziness	•													3.7
		41	H361 Suspected of damaging fertility or the unborn child	•													5.3
		42	H373 Causes damage to organs through prolonged or repeated exposure	•													3.9

Evaluation GGRC												
Responsible scientist:	Tatjana Iouranova		**Laboratory**		CH H3 554					**Date**	05.08.14	
Nr	Hazard	Impact	Probability			Detectability			WF			LCI
			Exposure	Occurence	Involvement	Reliability	Selectivity	Availability	GWF	HSWF	SWF	
1	H301 Toxic if swalloed	3	2	2	1	5	5	3	2	1	1	4.2
2	H312 Harmful in contact with skin	2	2	3	1	3	5	3	2	1	1	3.5
3	H314 Causes severe skin burns and eye damage	4	2	2	1	5	5	5	2	1	1	4.8
4	H317 May cause an allergic skin reaction	2	2	3	1	5	5	3	2	2	2	3.9
5	H331 Toxic if inhaled	3	2	2	1	3	3	5	2	1	1	4.2
6	H373 Causes damage to organs through prolonged or repeated exposure	4	2	2	1	1	1	1	2	1	1	3.6
7	H225 Highly Flammable liquid and vapour	4	2	2	4	5	3	3	2	2	1	5.3
8	H220 Extremely flammable gas	4	2	2	3	3	3	3	2	1	1	5.3
9	Overpressure	3	2	2	4	1	1	1	2	2	2	3.9
10	Hot medium	1	2	3	3	5	3	3	2	2	2	3.9
11	Ejection of reaction mixture	2	2	2	1	3	5	5	2	1	2	3.5
12	H301 Toxic if swalloed	3	2	2	1	5	5	3	2	1	1	4.0
13	H312 Harmful in contact with skin	2	2	3	1	3	5	3	2	2	1	3.7
14	H314 Causes severe skin burns and eye damage	4	2	2	1	5	5	5	2	1	1	4.6
15	H317 May cause an allergic skin reaction	2	2	3	1	5	5	3	2	2	2	3.9
16	H331 Toxic if inhaled	3	2	2	1	3	3	5	2	1	1	4.0
17	H373 Causes damage to organs through prolonged or repeated exposure	4	2	2	1	1	1	1	2	1	1	3.6
18	H225 Highly Flammable liquid and vapour	4	2	2	4	5	3	3	2	1	1	5.3
19	H220 Extremely flammable gas	4	2	2	3	3	3	3	2	2	1	5.3
20	Overpressure	3	2	2	4	1	1	1	2	1	2	3.7
21	Hot medium	1	2	3	3	5	3	3	2	2	2	4.1
22	Ejection of reaction mixture	2	2	2	1	3	5	5	2	1	2	3.5
23	H225 Highly Flammable liquid and vapour	3	2	2	1	3	3	5	2	2	1	4.2
24	H319 Causes serious eye irritation	4	2	2	1	5	5	5	2	1	2	4.8
25	H336 May cause drowsiness or dizziness	2	2	3	1	3	3	3	2	2	1	3.7
26	H301 Toxic if swalloed	3	2	2	1	5	5	3	2	2	1	4.2
27	H312 Harmful in contact with skin	2	2	3	1	3	5	3	2	2	1	3.5
28	H314 Causes severe skin burns and eye damage	4	2	2	1	5	5	5	2	2	1	4.8
29	H317 May cause an allergic skin reaction	2	2	3	1	5	5	3	2	2	2	3.7
30	H331 Toxic if inhaled	3	2	2	1	3	3	5	2	1	1	4.2
31	H373 Causes damage to organs through prolonged or repeated exposure	4	2	2	1	1	1	1	2	2	1	3.6
32	H225 Highly Flammable liquid and vapour	4	2	2	4	5	3	3	2	2	1	5.3
33	H220 Extremely flammable gas	4	2	2	3	3	3	3	2	1	1	5.1
34	Overpressure	3	2	2	4	1	1	1	2	1	2	3.7
35	Hot medium	1	2	3	3	5	3	3	2	2	2	4.1
36	Ejection of reaction mixture	2	2	2	1	3	5	5	2	2	2	3.5
37	H225 Highly Flammable liquid and vapour	3	2	2	1	3	3	5	2	2	1	4.2
38	H304 May be fatal if swallowed and enters airways	5	2	1	1	3	3	3	2	2	1	5.2
39	H315 Causes skin irritation	1	2	3	1	5	3	6	2	1	1	3.2
40	H336 May cause drowsiness or dizziness	2	2	3	1	3	3	3	2	2	1	3.7
41	H361 Suspected of damaging fertility or the unborn child	4	2	2	1	3	3	3	2	3	2	5.3
42	H373 Causes damage to organs through prolonged or repeated exposure	4	2	2	1	1	1	1	2	2	2	3.9

Appendix C. LARA Application Examples: Details

Evaluation GGRC												
Responsible scientist:		Tatjana Iouranova		**Laboratory**		CH H3 554				**Date**	05.08.14	
Refering Hazard	Corrective Measure	LCI before	LCI after	ΔLCI	Financial aspect Costs [CHF]	**Reduction/costs**	Feasibility A	S	C	V	**F**
38	Strict regulations concerning labeling	5.2	4.8	0.4	15'000	2.4	3	3	3	4	0.63
41	Information to raise awareness	5.3	4.6	0.6	5'000	12.3	5	4	4	5	0.92
19	Improve ventilation	5.3	5.1	0.2	80'000	0.3	5	5	4	5	0.98

Three Phase Reaction in a Semi-Batch Reactor over Structured Catalyst (II)

Practical Chemical Reaction Engineering

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TP6

2013

The proposed project deals with the development of noble metal (Pd, Pt)-based catalysts for liquid-phase hydrogenation of acetylenic alcohols. You will investigate the effect of various parameters (e.g. catalyst/reaction modifiers, catalyst supports, solvents) on selectivity and activity. The reaction kinetics study and modeling are implicit as well.

MAIN TARGETS

- Get acquainted with a semi-batch reactor operation carrying out three-phase catalytic reactions.
- Study the kinetics of selective 3-phase catalytic hydrogenation of 2-butyne-1,4-diol (B_3D) over noble metal (Pd, Pt) based catalysts.
- Investigate the effect of reaction conditions and catalyst modifiers on the reaction kinetics.

TABLE OF CONTENTS

1. INTRODUCTION

Heterogeneously catalyzed liquid-phase hydrogenations are a class of reactions that are valuable in fine chemical industry and selective hydrogenation of carbon-carbon triple bond is among them. The process is commonly carried out in batch or semi-batch reactors where to one reactant initially contained in a stirred tank reactor the second reactant continuously added to the reactor, with no flow out of the reactor.

1.1. Gas/liquid reactions on solid catalysts

During a heterogeneous catalytic process which involves liquid and gaseous (e.g., hydrogen) reagents and solid porous catalyst, the following steps take place (Fig. 1): (1) mass transfer of hydrogen from gas to bulk liquid phase; (2) mass transfer of the liquid reactant and dissolved hydrogen from the bulk phase to the external surface of solid catalyst; (3) mass transfer of the liquid reactant and dissolved hydrogen inside the pores of solid catalyst; (4) adsorption of the reactants on the catalyst surface; (5)chemical reaction; (6) desorption of the products from the catalyst surface; (7) mass transfer of the products inside the pores of solid catalyst to its outer surface; (8) mass transfer of the products from the catalyst outer surface to the bulk phase.

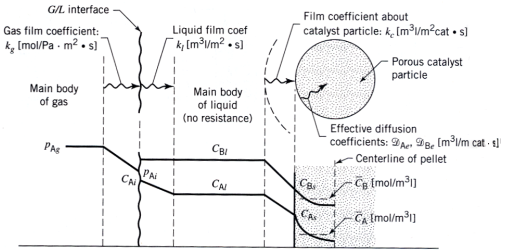

Figure 1. Sketch showing the resistances involved in the G/L reaction on a catalyst surface

The slowest step is the rate-limiting one. If it is the external mass transport (steps 1, 2, 8), then the external mass transfer limitations exist and govern the course of the whole heterogeneous process. If it is the internal mass transport (steps 3, 7), then the course of the process

is governed by internal mass transfer limitations. If step 5, i.e., the reaction, is the slowest (adsorption and desorption are usually fast and reversible), then the process proceeds in the kinetic regime. Only in this regime the reaction kinetics can be measured and the reaction mechanism can be studied.

A critical step in obtaining reliable quantitative kinetics is to ensure the absence of all transport limitations including external and internal heat and mass transfer effects as well as the rate of hydrogen transfer from the gas phase to the liquid phase.

1.1. Catalyst optimization

Metallic Pd is known to be the most selective catalyst for -C≡C- hydrogenations. The peculiar behavior of Pd is attributed to the strong adsorption of alkynes compared to that of alkenes which yields to high selectivity to a semi-hydrogenated product [1]. However, its catalytic performance can be strongly influenced by the dispersion, nature of support and the use of Pd promoters and additives to the reaction mixture. The optimization of these parameters is of crucial importance for achieving the highest activity-selectivity-stability.

1.1.1. Effect of the catalyst support

The role of the support is one of the main factors affecting heterogeneously catalyzed processes. The support not only influences the distribution, structure, dispersion and morphology of metal particles, but also contributes to catalysis (e.g., strong metal-support interaction). Besides, surface area and pore distribution of the support control the internal diffusion limitations. As supports, metal oxides, carbonates and carbon are often used for the preparation of hydrogenation catalysts.

1.2. Intrinsic reaction kinetics

The intrinsic reaction kinetics consists of the three elementary steps of the catalytic cycle that take place on the catalytic surface: the adsorption of the reactants, the surface reactions and the desorption of the products.

Kinetic models make the assumption that the overall reaction kinetic is the sum of elementary steps of adsorption/desorption and surface reactions. In most cases, the adsorption/desorption steps are assumed to be reversible and at equilibrium while the surface reaction steps are often assumed irreversible and considered the rate determining step.

--C≡C- hydrogenation is commonly described by Langmuir-Hinshelwood mechanism.

1.3. Model reaction

Catalytic hydrogenation of 2-butyne-1,4-diol (B_3D) to 2-butene-1,4-diol (B_2D) is taken as a model reaction since B_2D is an important product in the production of Vitamin B6 (pyridoxol) and an intermediate of furan nudeus pharmaceuticals. The scheme of reaction is shown in Figure 3. The target product is formed through *path a*. Due to over-hydrogenation of B_3D (*path b*) and consecutive hydrogenation of B_2D (*path c*), B_1D is formed. Moreover, crotyl alcohol, n-butyraldehyde and butanol can be formed from B_2D through *paths d*, *e* and *f* consequently. Both high selectivity towards B_2D and maximum B_2D yield are desirable.

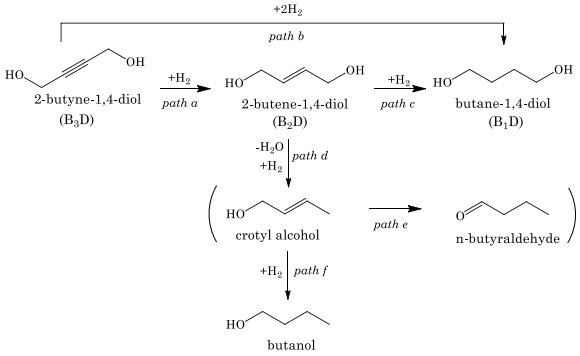

Figure 2. Reaction network of B_3D hydrogenation

2. Objectives

- *Get acquainted with a semi-batch reactor operation carrying out three-phase catalytic reactions.* You will learn how to charge and operate an autoclave, perform the tests to determine the presence/absence of mass transfer limitations, chose the reaction conditions under the kinetic regime.
- *Study the kinetics of selective 3-phase catalytic hydrogenation of 2-butyne-1,4-diol (B_3D) over Pd(Pt)-based catalysts.* Determine kinetic parameters, such as activation energy, reaction orders, kinetic and adsorption constants. Develop reaction mechanism and use Berkeley Madonna software to test its consistency with the real experimental results.
- *Investigate the effect of reaction conditions and catalyst modifiers on the reaction kinetics.* The effect of various parameters (such as catalyst support, solvent, etc.) on catalyst activity/selectivity will be studied. The basic knowledge will be apply in order to explain these effects.

3. Experimental

3.1. Catalyst preparation

Pd(Pt)-based catalysts were prepared by deposition of metal nanoparticles on a structured support. Sintered metal fibers (SMF) filters are used as a structured support for the active metal phase. The SMF sheets have high permeability, good mechanical strength, and high thermal conductivity, making them advantageous for exothermic hydrogenation. They can be easily shaped and placed to various types of reactors. The SMF are coated with a layer of different oxides (e.g. ZnO, Al_2O_3, MgO, etc) on which Pd(Pt) nanoparticles are deposited.

3.2. Experimental setup

The commercial semi-batch stirred stainless steel reactor (150 cm^3 autoclave, Büchi AG, Uster, Switzerland) equipped with a pressure controlled H_2 supply system is schematically represented in Figure 4.

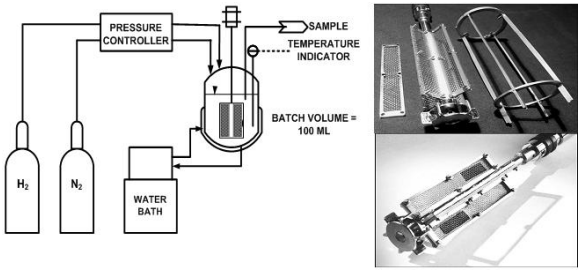

Figure 3. Experimental setup for study of a three-phase reaction in a semi-batch reactor

Hydrogen consumption in the reservoir is monitored on-line with a press gas flow controller (BPC-6002, Büchi, Switzerland). A stainless steel 6-blade disk turbine impeller (equipped with a self-gassing hollow shaft) provides effective agitation at 1900-2000 rpm. A bath circulator (HAAKE B-N3) is used to control the reaction temperature to within ±1 K using water as the thermal medium.

3.3. Experimental procedure

The conditions of a typical experiment are: P_{H_2}= 8 bar, T = 337 K, 2000 rpm, m_{B_3D} = 8 g, $m_{solvent}$ = 75 g, $m_{catalyst}$ ~ 0.5 g.

Fill the reactor with the substrate dissolved in the solvent.

The structured catalyst is cut in rectangular pieces and placed between two metal gauzes fixed on the self-gassing hollow shaft stirrer. Make sure the entire catalyst surface is freely accessible and not blocked by the metal frame. Weight the catalyst before placing it to the grid.

Open the program in the computer (Desktop bls 2.1) and create a new file (File New Reaction Name/Number Save).

Place the rubber O-ring into the reactor. Place the agitator with the catalyst in the reactor lid. Push up until it snaps into place. Make sure that all lines to and from the reactor are closed. Assemble the reactor.

To test scratching noises switch on the stirring. Be sure that the agitator does not scratch the reactor walls at low stirring rate. If it does, readjust the reactor and lid. When you finish, make sure that the stirrer is switched off.

Purge the system of oxygen by inert (N_2) Use the program. (1) click "bcp"; (2) click "inert"; (3) let N_2 to fill the reactor; (4) stir for 30 seconds; (5) open the valve to release the pressure. Repeat the procedure 2 more times. Then depressurize the reactor and switch on the stirring.

Heat up the reactor. Make sure that the tank of water is full (to cover all the coils) and the valve for thermostat cooling is open. Set the reaction temperature: (1) switch on the bath; (2) press "set"; (3) adjust the temperature by turning the black knob; (4) Once the temperature is set, push the "set" button; (5) Turn the black knob clockwise and then counterclockwise to switch the control on. Once the reaction is finished repeat the same procedure but set the temperature at 298 K. To cool down efficiently keep the stirring on.

Once the reaction temperature is reached purge the system with hydrogen (this part should be done as fast as possible): (1) stop the stirring; (2) set the reaction pressure using the bls 2.1 program; (3) push "bcp" button of the program menu; (4) press the "active" button; (5) release the pressure by opening the valve. Repeat the steps (2)-(5) two times.

To start reaction, press "Charge" button in the program menu. Once the reaction pressure is reached the H_2 consumption has to be reset to zero: (1) press "stop" button in the program panel; (2) press "reset" button; (3) press "run" and "ok". To start recording the data press the green "play" button and the "time start" button. Start stirring immediately.

Take a sample (about 0.3 ml) from the autoclave via the valve on the top of the reactor and transfer it to the GC vial. Before taking a sample, clean a sampling tube. A small depressurization of the reactor is normal. The time intervals between samples depend on the reaction rate. Take 7-9 samples during the reaction (~4 at maximum conversion).

Once the reaction is finished press: (1) "bcp"; (2) "stop" button of the "bpc" menu (to stop the H_2 supply); (3) "stop" button of the main program screen (to stop the recording); (4) stop stirring; (5) release the pressure; (6) set the bath temperature at 298 K; (7) switch on stirring and keep it until the reactor is cooled down to room temperature. When the reactor is cooled down stop the stirrer and the thermostat. Close the H_2 supply-line and depressurize the reactor. Remove the reactor from the lid.

Clean the reactor with ethanol (remember to open the sampling tube), agitator and lid. Remember to remove the O-ring before. Dry the reactor with air.

Clean the vials with ethanol in ultrasonic bath and dry them in the oven.

3.4. Data treatment.

The samples taken during the reactions are analyzed by gas chromatography (GC). For this, small samples of the reaction mixtures are periodically withdrawn from the reactor via a sampling tube and analyzed by gas chromatography (GC). The GC analysis is performed using Auto System XL (Perkin Elmer) equipped with a 30 m Stabilwax (Crossbond Carbowax-PEG, Restek, USA) 0.32 mm capillary column with a 0.25 mm coating. The carrier gas (He) pressure is 101 kPa. Injector and FID temperatures are 473 K and 523 K, respectively. The oven temperature is hold for 4 min at 323 K, then increased to 473 K at a ramp of 30 K/min. All the reaction mixture components have the same GC-response factors, i.e., the peak area percentage corresponds to the weight percentage of a component.

4. DETAILED PLAN OF EXPERIMENTS

The "concentration versus time" profiles should be presented for each reaction component.

As a measure of activity, the initial reaction rate should be calculated (per amount of catalyst and/or active phase, e.g. $mol_{B_3D}/(mol_{Pd} \cdot s)$).

Selectivity (integral selectivity), yield and conversion should be calculated. These results could be presented as plots of "Selectivity to B_2D vs. B_3D conversion" and "B_2D yield vs. B_3D conversion".

The following plan of experiments is proposed:

A. Preliminary tests.

In a series of blank tests you will carry out the reaction in the absence of the catalyst. The support without the active metal phase should be tested as well.

B. Diffusion limitations with the structured catalyst.

Structured Pd(Pt)-based catalyst should be tested under reaction conditions in terms of external and/or internal diffusion limitations. Once the kinetic regime of the process is found, the reaction kinetics can be studied.

C. Determination of kinetic parameters.

The apparent activation energies under kinetic regime have to be determined by varying the reaction temperature between 313 K and 368 K.

The reaction rate should be studied at different hydrogen pressures and the order toward hydrogen can be found.

D. Influence of the solvents on the catalytic results.

The influence of the solvents on the catalysis could be studied. Ethanol, iso-propanol and toluene could be used. In addition the reaction is to be carried out in a solvent-free system.

E. Effect of the support on the catalyst properties.

The effect of different supports (e.g. ZnO, Al_2O_3, etc.) on the catalyst activity/selectivity will be studied.

F. Stability of the catalyst.

The optimized catalyst will be subjected to several reuse runs in order to evaluate its stability.

G. Kinetic modeling.

The kinetic modeling using a Langmuir-Hinshelwood model and Madonna Berkley software is to be carried out. A set of reaction rate expressions will be proposed by applying Langmuir-Hinshelwood model and then runs under kinetic regime will be modeled by Berkley Madonna software.

5. References

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[2] Manual on catalyst characterization. Recommendations of IUPAC 1991, prepared by J. Haber. Pure and Applied Chemistry, Vol. 63, No. 9, p. 1227-1246, 1991.

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Appendix I – List of chemicals and safety considerations

Name	Chemical formula	Form	Danger
2-butyne-1,4-diol (B_3D)	$C_4H_6O_2$	Solid	
Ethanol	C_2H_6O	Liquid	
Isopropanol	C_3H_8O	Liquid	
Toluene	C_7H_8	Liquid	
Hydrogen	H_2	Gas	

For all manipulations, you need to wear safety equipment composed of safety glasses, nitrile gloves and lab coat.

C.3 Constable Group

Evaluation Constable Group	
Organization	University of Basel
Research Group	Group of Catalytic Reaction Engineering
Laboratory	215
Group head	Prof. Edwin Constable
Safety delegate	Nik Hostettler
Responsible scientist	Nik Hostettler
Analysis moderator	David Nicolas Pluess
Date	22.08.14
Description of the evaluation	Solar cell preparation
General worsening factors present	Too hot/too cold (Climate) Outdated electrical systems/equipment (Electrical) Warnings not hearable (Safety) Repetitional tasks (Work) Distortions (Work organization) Pressure of time (Work organization)

Evaluation Constable Group						
Responsible scientist:	Nik Hostettler		**Laboratory**	215	**Date**	22.08.14
Activity	Step-Nr.	Step				
Preparation of electrode 1	1	Cleaning of the glass with ultrasonic				
	2	Treatment with UV-O3 system				
	3	Immersion in TiCl4 solution (70°C)				
	4	Washing with water and ethanol				
	5	Doctorblading with TiO2 paste				
	6	Heating under air flow (various temperatures upt to 500°C)				
	7	Treatment with TiCl4 solution				
	8	Rinsing with water and ethanol				
	9	Sintering for 30 min at 500°C				
	10	Cooling down to 80°C				
	11	Imersion in ligand (dilluted in DMSO)				
	12	Washing with DMSO and ethanol				
	13	Immersion in ZnCl2 EtOH solution				
	14	Washing with EtOH				
	15	Immersion in ligand solution (CH2Cl2)				
Preparation of counterelectrode	1	Drilling a hole in the glass				
	2	Heating to 450°C				
	3	Washing with water and ethanol				
	4	Deposit H2PtCl6 in propan-2-ol				
	5	Heating to 400°C				
Assembling of the solar cell	1	Heating and sealing the electrodes with sealing foil				
	2	Application of electrolyte (LiI, I2, 1-methylbenzimidazole and 1-butyl-3-methylimidazolinium, MeCN)				
	3	Sealing if the hole with sealing foil				
	4	Irridiation with SolarSim 150 light source (100 mW cm-2)				

Appendix C. LARA Application Examples: Details

Responsible scientist:	Nik Hostettler		**Evaluation Constable group Laboratory**	215														**Date**	22.08.14
Activity	Origin	Nr.	Hazard	Step															LCI
				1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	
Preparation of electrode 1	Acetone	1	H225 Highly Flammable liquid and vapour	•															4.5
		2	H319 Causes serious eye irritation	•															5.2
		3	H336 May cause drowsiness or dizziness	•															4.3
	EtOH	4	H225 Highly Flammable liquid and vapour	•			•				•				•	•	•		5.2
	Hellmanex surfactant	5	H315 Causes skin irritation	•															3.8
		6	H318 Causes serious eye damage	•															5.4
	UV-O3 (Ozone)	7	H270 May cause or intensify fire; oxidizer		•														4.3
		8	H330 Fatal if inhaled		•														5.5
		9	H319 Causes serious eye irritation		•														5.2
		10	H370 Causes damage to organs		•														4.4
		11	H372 Causes damage to organs through prolonged or repeated exposure		•														4.4
	TiCl4	12	H314 Causes severe skin burns and eye damage			•				•									4.7
	Heating	13	Hot media						•			•							5.0
	ZnCl2	14	H302 Harmful if swallowed													•			3.6
		15	H314 Causes severe skin burns and eye damage													•			5.2
		16	H410 Very toxic to aquatic life with long lasting effects													•			6.0
	DCM	17	H315 Causes skin irritation															•	4.1
		18	H319 Causes serious eye irritation															•	5.4
		19	H335 May cause respiratory irritation															•	4.7
		20	H336 May cause drowsiness or dizziness															•	4.1
		21	H351 Suspected of causing cancer															•	4.7
		22	H372 Causes damage to organs through prolonged or repeated exposure															•	4.7
Preparation of counterelectrode	Heating	23	Hot media		•			•											5.2
	Drilling	24	Pinch points	•															4.3
	EtOH	25	H225 Highly Flammable liquid and vapour			•													4.5
	H2PtCl6	26	H302 Harmful if swallowed				•												3.9
		27	H314 Causes severe skin burns and eye damage				•												5.6
		28	H317 May cause an allergic skin reaction				•												4.3
		29	H334 May cause allergy or asthma symptoms or breathing difficulties				•												4.1
	Propan-2-ol	30	H225 Highly Flammable liquid and vapour				•												4.5
		31	H319 Causes serious eye irritation				•												5.4
		32	H336 May cause drowsiness or dizziness				•												4.3
Assembling of the solar cell	Heating	33	Hot media	•															4.7
	LiI	34	H315 Causes skin irritation		•														4.3
		35	H319 Causes serious eye irritation		•														5.2
	Iodine	36	H312 Harmful in contact with skin		•														3.9
		37	H332 Harmful if inhaled		•														3.9
		38	H315 Causes skin irritation		•														4.3
		39	H319 Causes serious eye irritation		•														5.4
		40	H335 May cause respiratory irritation		•														3.9
		41	H372 Causes damage to organs through prolonged or repeated exposure		•														4.9
		42	H400 Very toxic to aquatic life		•														4.5
	1-methylbenzimidazole	43	H302 Harmful if swallowed		•														4.1
		44	H315 Causes skin irritation		•														4.1
		45	H318 Causes serious eye damage		•														5.4
		46	H335 May cause respiratory irritation		•														4.1
	1-butyl-3-methylimidazoli	47	H315 Causes skin irritation		•														3.9
		48	H319 Causes serious eye irritation		•														5.4
		49	H335 May cause respiratory irritation		•														4.1
	MeCN	50	H225 Highly Flammable liquid and vapour		•														4.7
		51	H302 Harmful if swallowed		•														3.9
		52	H312 Harmful in contact with skin		•														4.1
		53	H332 Harmful if inhaled		•														4.1
		54	H319 Causes serious eye irritation		•														5.4
	Light source	55	UV-IR Radiation				•												5.0

Evaluation Constable group												
Responsible scientist:	Nik Hostettler	**Laboratory**			215					**Date**	22.08.14	
Nr	Hazard	Impact	Probability			Detectability			WF			LCI
			Exposure	Occurence	Involvement	Reliability	Selectivity	Availability	GWF	HSWF	SWF	
1	H225 Highly Flammable liquid and vapour	3	5	2	1	3	3	3	3	1	2	4.5
2	H319 Causes serious eye irritation	4	5	2	1	5	5	5	3	2	1	5.2
3	H336 May cause drowsiness or dizziness	2	5	3	1	3	3	5	3	2	2	4.3
4	H225 Highly Flammable liquid and vapour	3	5	2	5	3	3	5	3	1	1	5.2
5	H315 Causes skin irritation	1	5	3	1	3	5	5	3	2	1	3.8
6	H318 Causes serious eye damage	4	5	3	1	5	5	5	3	2	1	5.4
7	H270 May cause or intensify fire; oxidizer	3	5	2	1	3	3	5	3	1	1	4.3
8	H330 Fatal if inhaled	5	5	1	1	5	3	5	3	1	2	5.5
9	H319 Causes serious eye irritation	4	5	2	1	5	5	3	3	2	1	5.2
10	H370 Causes damage to organs	4	5	2	1	1	1	3	3	2	1	4.4
11	H372 Causes damage to organs through prolonged or repeated exposure	4	5	2	1	3	1	1	3	2	1	4.4
12	H314 Causes severe skin burns and eye damage	3	5	2	2	5	5	5	3	2	1	4.7
13	Hot media	2	5	3	3	5	3	5	3	3	2	5.0
14	H302 Harmful if swallowed	2	5	1	2	5	5	3	3	1	1	3.6
15	H314 Causes severe skin burns and eye damage	4	5	2	2	3	5	5	3	1	1	5.2
16	H410 Very toxic to aquatic life with long lasting effects	5	5	2	2	3	3	3	3	2	1	6.0
17	H315 Causes skin irritation	2	5	3	2	5	5	3	3	1	1	4.1
18	H319 Causes serious eye irritation	4	5	2	2	3	5	3	3	2	1	5.4
19	H335 May cause respiratory irritation	3	5	2	2	3	3	5	3	1	2	4.7
20	H336 May cause drowsiness or dizziness	2	5	3	2	5	3	3	3	1	1	4.1
21	H351 Suspected of causing cancer	4	5	2	2	1	1	3	3	2	1	4.7
22	H372 Causes damage to organs through prolonged or repeated exposure	4	5	2	2	3	1	1	3	2	1	4.7
23	Hot media	2	5	3	4	3	3	5	3	3	2	5.2
24	Pinch points	2	5	3	2	5	3	5	3	2	1	4.3
25	H225 Highly Flammable liquid and vapour	3	5	2	2	5	3	3	3	1	1	4.5
26	H302 Harmful if swallowed	2	5	2	2	5	5	5	3	1	1	3.9
27	H314 Causes severe skin burns and eye damage	4	5	2	2	3	5	5	3	2	2	5.6
28	H317 May cause an allergic skin reaction	2	5	3	2	3	3	5	3	2	1	4.3
29	H334 May cause allergy or asthma symptoms or breathing difficulties	2	5	2	2	3	3	3	3	2	1	4.1
30	H225 Highly Flammable liquid and vapour	3	5	2	2	5	3	3	3	1	1	4.5
31	H319 Causes serious eye irritation	4	5	2	2	3	5	5	3	2	1	5.4
32	H336 May cause drowsiness or dizziness	2	5	3	2	5	3	5	3	2	1	4.3
33	Hot media	2	5	3	2	5	3	3	3	3	2	4.7
34	H315 Causes skin irritation	2	5	3	2	3	5	5	3	2	1	4.3
35	H319 Causes serious eye irritation	4	5	2	2	5	5	3	3	1	1	5.2
36	H312 Harmful in contact with skin	2	5	2	2	3	3	3	3	1	1	3.9
37	H332 Harmful if inhaled	2	5	2	2	3	5	3	3	1	1	3.9
38	H315 Causes skin irritation	2	5	3	2	3	5	5	3	1	2	4.3
39	H319 Causes serious eye irritation	4	5	2	2	3	5	3	3	2	1	5.4
40	H335 May cause respiratory irritation	2	5	2	2	5	5	5	3	1	1	3.9
41	H372 Causes damage to organs through prolonged or repeated exposure	4	5	2	2	3	1	1	3	2	2	4.9
42	H400 Very toxic to aquatic life	3	5	2	2	3	3	3	3	1	1	4.5
43	H302 Harmful if swallowed	2	5	2	2	3	3	3	3	1	2	4.1
44	H315 Causes skin irritation	2	5	3	2	3	5	3	3	1	1	4.1
45	H318 Causes serious eye damage	4	5	2	2	3	5	5	3	2	1	5.4
46	H335 May cause respiratory irritation	2	5	2	2	5	3	3	3	2	1	4.1
47	H315 Causes skin irritation	2	5	2	2	5	3	5	3	1	1	3.9
48	H319 Causes serious eye irritation	4	5	2	2	3	5	3	3	2	1	5.4
49	H335 May cause respiratory irritation	2	5	2	2	5	3	5	3	1	2	4.1
50	H225 Highly Flammable liquid and vapour	3	5	2	2	3	3	3	3	2	1	4.7
51	H302 Harmful if swallowed	2	5	2	2	5	3	3	3	1	1	3.9
52	H312 Harmful in contact with skin	2	5	3	2	3	5	3	3	1	1	4.1
53	H332 Harmful if inhaled	2	5	2	2	3	3	5	3	2	1	4.1
54	H319 Causes serious eye irritation	4	5	2	2	5	5	3	3	2	1	5.4
55	UV-IR Radiation	2	5	3	2	5	3	3	3	3	3	5.0

Appendix C. LARA Application Examples: Details

Evaluation Constable group													
Responsible scientist:		Nik Hostettler		**Laboratory**		215						**Date**	22.08.14
Refering Hazard	Corrective Measure	LCI before	LCI after	ΔLCI	Financial aspect		Feasibility						
					Costs [CHF]	**Reduction/costs**	A	S	C	V	**F**		
55	Improvement of shielding	5.0	4.3	0.7	2'000	35.6	3	3	3	2	0.57		
23	Warning signs	5.2	4.0	1.2	150	803.3	5	3	3	2	0.74		
23	Temperature indication	5.2	3.9	1.3	3'000	44.1	5	4	2	1	0.74		
4	Reduction of storage quantitites	5.2	5.0	0.2	10'000	2.0	2	2	3	4	0.49		
45	Discilpinary regulations to enforce PPE use	5.4	3.6	1.8	5'000	35.2	1	2	3	5	0.44		
45	Improvement of safety training	5.4	3.6	1.8	15'000	11.7	3	2	3	5	0.61		
54	Discilpinary regulations to enforce PPE use	5.4	3.6	1.8	5'000	35.2	1	2	3	5	0.44		
54	Improvement of safety training	5.4	3.6	1.8	15'000	11.7	3	2	3	5	0.61		
8	O3-Dector	5.5	4.4	1.1	2'000	53.6	5	5	3	1	0.82		
27	Improvement of safety training	5.6	3.8	1.8	15'000	11.7	3	2	3	5	0.61		
27	Discilpinary regulations to enforce PPE use	5.6	3.8	1.8	5'000	35.1	1	2	3	5	0.44		
16	Improved waste management including controls	6.0	4.3	1.7	20'000	8.4	3	2	2	3	0.52		

C.4 IMSB: Aebersold Group

Evaluation IMSB	
Organization	ETHZ
Research Group	Institute of Molecular Systems Biology (IMSB)
Laboratory	HPT E 56
Group head	Prof. Ruedi Aebersold
Safety delegate	
Responsible scientist	George Rosenberger
Analysis moderator	David Nicolas Pluess
Date	17.09.14
Description of the evaluation	Proteolic digestion
General worsening factors present	Pressure of time (Work organization) Repetitional tasks (Static work) Different spoken languages (Work organization)

Evaluation IMSB						
Responsible scientist:	George Rosenberger		**Laboratory**	HPT E 56	**Date**	17.09.14
Activity	Step-Nr.	Step				
Proteolic digestion (Trypsin)	1	Reduction of the protein samples with TCEP				
	2	Alkylation with iodoacetamide				
	3	Overnight trypsinization				
	4	Lowering of the pH to 2				
	5	Immobilization with C18 column chromatography				
	6	Multiple washings				
	7	Elution of the peptides				
	8	Evaporation of the solvents				
	9	Resuspension and sonication				
PCT-assisted lysis and digestion	1	Proteins are lysed in the buffer				
	2	Barocycler programm at 35°C				
	3	Sonication of samples				
	4	Centrifugation				
	5	Protein digestion with Lys-C and trypsin				
	6	Acceleration under different PCT schemes				
	7	Lowering of the pH to 2				
	8	C18 desalting				

Responsible scientist:	George Rosenberger		Evaluation IMSB Laboratory	HPT E 56	Date	17.09.14
Activity	Origin	Nr.	Hazard	Step 1 2 3 4 5 6 7 8 9		LCI
Proteolic digestion (Trypsin)	Iodoacetamid	1	H301: Toxic if swallowed	•		2.0
		2	H317: May cause an allergic skin reaction	•		2.0
		3	H301: Toxic if swallowed	•		2.0
		4	H334: May cause allergy or asthma symptoms or breathing difficulties	•		2.0
		5	H413: May cause long lasting harmful effects to aquatic life	•		2.6
	Acetonitrile	6	H225: Highly flammable liquid and vapour	•		2.6
		7	H332: Harmful if inhaled	•		2.0
		8	H302: Harmful if swallowed	•		2.0
		9	H312: Harmful in contact with skin	•		2.0
		10	H319: Causes serious eye irritation	•		3.3
	Formic acid	11	H226: Flammable liquid and vapour	•		2.6
		12	H314: Causes severe skin burns and eye damage	•		3.3
	Trifluoroacetic acid	13	H314: Causes severe skin burns and eye damage	•		3.5
		14	H332: Harmful if inhaled	•		2.1
		15	H412: Harmful to aquatic life with long lasting effects	•		3.5
	Sonication	16	Ultrasonic vibrations			1.7
PCT-assisted lysis and digestion	Ammonium bicarbonate	17	H302: Harmful if swallowed	•		2.0
	Sonication	18	Ultrasonic vibrations	•		1.7
	Lys-C	19	H315: Causes skin irritation	•		2.1
		20	H317: May cause an allergic skin reaction	•		2.1
		21	H319: Causes serious eye irritation	•		2.1
		22	H334: May cause allergy or asthma symptoms or breathing difficulties	•		2.1
		23	H335: May cause respiratory irritation	•		2.1
	Trifluoroacetic acid	24	H314: Causes severe skin burns and eye damage	•		3.5
		25	H332: Harmful if inhaled	•		2.1
		26	H412: Harmful to aquatic life with long lasting effects	•		2.8

Appendix C. LARA Application Examples: Details

Evaluation ISMB												
Responsible scientist:	George Rosenberger		**Laboratory**		HPT E 56					**Date**	17.09.14	
Nr	Hazard	Impact	Probability			Detectability			WF			LCI
			Exposure	Occurence	Involvement	Reliability	Selectivity	Availability	GWF	HSWF	SWF	
1	H301: Toxic if swallowed	2	2	1	1	3	3	3	1	1	1	2.0
2	H317: May cause an allergic skin reaction	2	2	1	1	3	3	3	1	1	1	2.0
3	H301: Toxic if swallowed	2	2	1	1	3	3	3	1	1	1	2.0
4	H334: May cause allergy or asthma symptoms or breathing difficulties	2	2	1	1	3	3	3	1	1	1	2.0
5	H413: May cause long lasting harmful effects to aquatic life	3	2	1	1	3	3	3	1	1	1	2.6
6	H225: Highly flammable liquid and vapour	3	2	1	1	3	3	3	1	1	1	2.6
7	H332: Harmful if inhaled	2	2	1	1	3	3	3	1	1	1	2.0
8	H302: Harmful if swallowed	2	2	1	1	3	3	3	1	1	1	2.0
9	H312: Harmful in contact with skin	2	2	1	1	3	3	3	1	1	1	2.0
10	H319: Causes serious eye irritation	4	2	1	1	3	3	3	1	1	1	3.3
11	H226: Flammable liquid and vapour	3	2	1	1	3	3	3	1	1	1	2.6
12	H314: Causes severe skin burns and eye damage	4	2	1	1	3	3	3	1	1	1	3.3
13	H314: Causes severe skin burns and eye damage	4	2	2	1	3	3	3	1	1	1	3.5
14	H332: Harmful if inhaled	2	2	2	1	3	3	3	1	1	1	2.1
15	H412: Harmful to aquatic life with long lasting effects	4	2	2	1	3	3	3	1	1	1	3.5
16	Ultrasonic vibrations	1	2	1	1	3	3	3	1	1	1	1.7
17	H302: Harmful if swallowed	2	2	1	1	3	3	3	1	1	1	2.0
18	Ultrasonic vibrations	1	2	1	1	3	3	3	1	1	1	1.7
19	H315: Causes skin irritation	2	2	2	1	3	3	3	1	1	1	2.1
20	H317: May cause an allergic skin reaction	2	2	2	1	3	3	3	1	1	1	2.1
21	H319: Causes serious eye irritation	2	2	2	1	3	3	3	1	1	1	2.1
22	H334: May cause allergy or asthma symptoms or breathing difficulties	2	2	2	1	3	3	3	1	1	1	2.1
23	H335: May cause respiratory irritation	2	2	2	1	3	3	3	1	1	1	2.1
24	H314: Causes severe skin burns and eye damage	4	2	2	1	3	3	3	1	1	1	3.5
25	H332: Harmful if inhaled	2	2	2	1	3	3	3	1	1	1	2.1
26	H412: Harmful to aquatic life with long lasting effects	3	2	2	1	3	3	3	1	1	1	2.8

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Acronyms

ACS American Chemical Society. 38, 39, 49

AHP Analytic Hierarchy Process. 75

ALARP as low as reasonably practicable. 15, 71, 73, 93, 94, 102, 107, 108, 113, 119, 123

CHR Chemical Hazard Review. 37, 38

CSB Chemical Safety Board. 38

EAWAG Swiss Federal Institute of Aquatic Science and Technology. 99

EMPA Swiss Federal Laboratories for Materials Science and Technology. 99

EPFL Ecole Polytechnique Fédérale de Lausanne. 87, 99, 105, 117

ETA Event Tree Analysis. 25–28, 31–34, 49

ETHZ Swiss Federal Institute of Technology in Zurich. 99, 117, 123

FMEA Failure Modes and Effects Analysis. 21

FMECA Failure Modes, Effects and Criticality Analysis. 21–23, 31–34, 65

FSB Faculty of Basic Sciences. 99

FTA Fault Tree Analysis. 23–28, 31–34, 49

GGRC Group of Catalytic Reaction Engineering. 105

GHS Globally Harmonized System of Classification, Labeling and Packaging of Chemicals. 50, 51, 104, 108, 122

GSCP Group of Chemical and Physical Safety. 4

GWF General Worsening Factors. 62, 63

HAZOP Hazard and Operability analysis. 4, 18–21, 23, 31–34, 38, 48

HSWF Hazard-Specific Worsening Factors. 62, 63

ICI Institute of Chemical Industry. 18

ICPR International Commission for the Protection of the Rhine. 2

IMSB Institute of Molecular Systems Biology. 117

JSA Job Safety Analysis. 28, 29, 31–34, 48, 49

Lab-HIRA Laboratory Hazard Identification and Risk Analysis. 37, 38

LCI Laboratory Criticality Index. 56, 66–68, 71, 76, 84, 88, 100, 101, 104, 106–108, 113, 119, 123

LSCI Laboratory of Inorganic Synthesis and Catalysis. 99

MSDS Material Safety Data Sheets. 50

NASA National Aeronautics and Space Administration. 21

OSH Occupational Safety and Health. 36, 46, 53, 81, 111, 117

OSHA Occupational Safety and Health Act. 36

PCT pressure cycling technology. 119

PPE Personal Protection Equipment. 78

PSI Paul Scherrer Institute. 99

RPN Risk Priority Number. 22, 65

SB-SST Occupational Safety and Health Service of the School of Basic Sciences. 99

SOP Standard Operating Procedure. 29, 31, 100, 105

SSUV Statistical Service of Swiss Insurance Companies. 59

STEL Short-Term Exposure Limit. 76

STOP Strategical, Technical, Organizational and Personal. 15, 72, 77, 128

SUVA Swiss National Accident Insurance Fund. 59

SWF Synergetic Worsening Factors. 62, 63

TWA Time-Weighted Average Exposure. 76

WSL Swiss Federal Institute for Forest, Snow and Landscape Research. 99

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