This is part of a series of guidance documents produced by the VetBioNet infrastructure project. There are various international and national standards in place for undertaking infectious work in animals with pathogens that require high containment facilities. These VetBioNet guidance documents are intended to be used as examples of how to achieve best practice in the managerial interpretation of these standards.

ANNEX 2, Deliverable D3.6

Technical Report

Process guidelines for designing and upgrading BSL3/3+ facilities for farmed animal species

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CONTENTS

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1. INTRODUCTION

This document deals with the design, commissioning and upgrading of high containment farmed animal facilities (HCFAFs) as part of the VetBioNet WP “Best practices for biosafety, biosecurity and quality management in HCFAFs” (WP3).
HCFAFs are extremely complex and expensive to construct with costs running into tens of millions of euros, if not hundreds of millions, depending on the size of the facility/units. They need to be designed to have a working life span of several decades. During this period, it is expected that there will be a requirement to refurbish and upgrade the facility (or individual units) to overcome the wear and tear of use. Technical equipment may not only wear out but also become obsolete and not maintainable for ensuring biosafety and animal welfare.

In the construction of HCFAFs there are two basic types of faults leading to failure of a building to deliver what the operators of the building expected or required. These are:

1) The specification for the building was incorrect or it was not sufficiently detailed to control what was delivered.
2) The building was not constructed and delivered to specification.

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Both of these types of faults can lead to new buildings being unfit for purpose with associated delays in their ability to be used, huge expense to sort the issues out and in the worst case, the inability to use them for all or part of their original function.
When undertaking upgrading of an HCFAF, a third type of fault has also to be addressed:

3) The facility to be upgraded has major design or construction issues that are incompatible with the proposed upgrade.

Additional processes are required to prevent this type of fault from occurring, which will be addressed later in this report.

2. METHODOLOGY

In the design and construction of complex buildings such as HCFAFs, the main focus is on how the delivered facility meets the operational requirements, including any legal standards (e.g. biosafety, animal welfare and quality). To prove that this is the case, the building should undergo a commissioning process against what the operator has specified.

To minimise the risk of the two types of errors described above, building commissioning (Cx) is now considered an all-inclusive systematic quality assurance process to ensure that building systems are designed, installed, tested, and capable of being operated and maintained to function interactively according to the design intent and the owner's operational needs. The U.S. General Services Administration (GSA) defines commissioning as: "A systematic process of assuring by verification and documentation from the design phase to a minimum of one year after construction that all facility systems perform interactively in accordance with the design documentation and intent, and in accordance with the owner's operational needs, including preparation of operation personnel." For new constructions, the process ideally begins at a project's inception (i.e., the beginning of the design process) and continues through construction, start-up, inspection, testing, balancing, acceptance, training and an agreed warranty period (i.e., occupancy and operations).

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Building commissioning (Cx) therefore encompasses all the necessary planning, delivery, verification, and managing risks to critical functions performed in, or by, facilities. Cx also accomplishes higher biosafety and animal welfare by making sure that the building components are working correctly and that the operators' specifications (user requirements) have been implemented. It confirms that the building and its systems are effective, that there is documentation to show this and that the operators (including facility maintenance personnel) are appropriately trained to run and maintain it.

The process to undertake this follows the design safety qualification process illustrated below.

The process starts at the business case stage, where, to ensure an accurate estimate of costs for the proposed HCFAF, ample input by the design, engineering and quantity surveying staff is needed to assist the operator/owner in producing this.

2.1 USER BRIEF

The user brief (also known as the statement of client need) outlines the client's requirements, and gives the basis for appointing the project team that is going to

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deliver the HCFAF. The brief describes the requirements in design principles and overall terms. This includes the nature of usage, animal species, biosafety levels, bedding requirements, post-mortem and laboratory support that need to be accommodated.

As HCFAFs have an expected life-span of 40 to 50-years, the user brief should attempt to be future-proof. Predicting potential usage over decades is an impossible task. To address this, as a general rule, things should be as flexible as possible. Designing of an HCFAF for a particular disease or a particular animal model will lead to issues and future costs, as experience has shown that the life-span of the HCFAF will exceed the need/funding for such activities.

2.2 USER REQUIREMENT SPECIFICATION (URS)

The user requirement(s) specification (URS) is a document developed by the project team that specifies what the user expects from the HCFAF. It is considerably more detailed than the user brief and covers aspects such as:

- Legislative requirements it should meet
- Animal species, ages and groups it should house
- Operational requirements (e.g. HCFAFs are 24-hour buildings that should be able to run at least 6 months between shutdowns)

These elements form the basis of what the building will finally be commissioned against.

PRACTICAL TIP

For large and complex buildings, it is worth drafting a reference scheme, i.e. to do a basic design based on information to see what needs to be done:

if the sizing and adjacencies work;

if anything is missing or unclear in the URS;

to obtain a more accurate costing.

2.3 FUNCTIONAL DESIGN (FD) and FUNCTIONAL DESIGN QUALIFICATION (FDQ)

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The FD translates the URS into facility performance criteria based on functional and operational assumptions. The different functional design aspects that support the overall user and operational facility requirements (engineering requirements, safety, biosafety, security, environmental safety, animal welfare, regulatory) are later tested during the operational qualification (OQ) e.g. for:

- No single points of failure
- Maintenance strategies
- Access for personnel and animals
- What bedding/ animal comfort system and environmental enrichment is to be used
- Directional air flow strategy
- Gaseous decontamination strategy (type, ability to do rooms/suites separately)
- Sterilisation of waste strategy (effluent treatment, digester, incinerator (what is in and out of the negative pressure envelope) autoclave size and cycles necessary)

The FDQ checks that the FD concepts fulfil the URS and provide enough information for the Detailed Design.

2.4 DETAILED DESIGN (DD) and DETAILED DESIGN QUALIFICATION (DDQ)

The DD is the design and specification of the various subsystems in the building. These include the Effluent Treatment Plant (ETP), the Heating, Ventilation and Air conditioning (HVAC) system (includes HEPA filters), gaseous fumigation system and autoclaves.

The DDQ reviews the implementation of URS and FD requirements in the DD. Dependent on the complexity of the (sub)system, this review may consist of one or more different analysis formats to ensure the operational and biosafety risks have been identified, assessed and managed. This is normally done by quantitative risk assessment.

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At this point, the focus is often on the technical performance of the building, but it is also very important to consider ergonomics, material flow and animal movement. The handling of cattle and large pigs is particularly important because of their size and the physical health and safety implications for operators (see Appendix 1).

PRACTICAL TIP

If there are significant changes proposed to the ergonomic way of working across multiple areas, it is essential these are trialled in mock ups.

Do a Mock-up or Risk a Cock-up

2.5 QUANTITATIVE RISK ASSESSMENT (QRA)

A QRA is a formal, systematic risk analysis approach to quantifying the risks associated with operating the engineering process in HCFAF. A QRA is an essential tool to support the understanding of exposure to employees, the environment, owner/operator assets and its reputation. A QRA also helps to make cost-effective decisions and manage risks throughout the asset lifecycle.

The overall objective of the QRA is:

1) To identify the hazards associated with a facility
2) To determine the potential frequencies and consequences of the identified hazards
3) To determine the availability of the protective systems
4) To quantify the risks associated with a facility.

This is done in a structured way, by carrying out the following set of analyses:

- A HAZOP (Hazard and operability) study to identify a series of hazardous scenarios that could lead to significant adverse consequences (Appendix 2).
- A Determination of safety integrity study, typically done using the Layers of Protection Analysis (LOPA) method (Appendix 2).

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- A Fault Tree Analysis (FTA) to determine the event frequencies associated with the hazardous scenarios from the HAZOP and LOPA studies.
- A consequence analysis to determine the consequences of the hazardous release from a facility (including infectious, flammable, explosion and toxic)
- An impact analysis to determine the frequency of a specific hazardous impact using Event Tree Analysis (ETA). ETAs are “bottom up” analytical tree diagrams that determine the overall likelihood of a particular impact following a hazardous release (Appendix 3).
- Risk Reduction Measures to identify the options to reduce or mitigate the risks.

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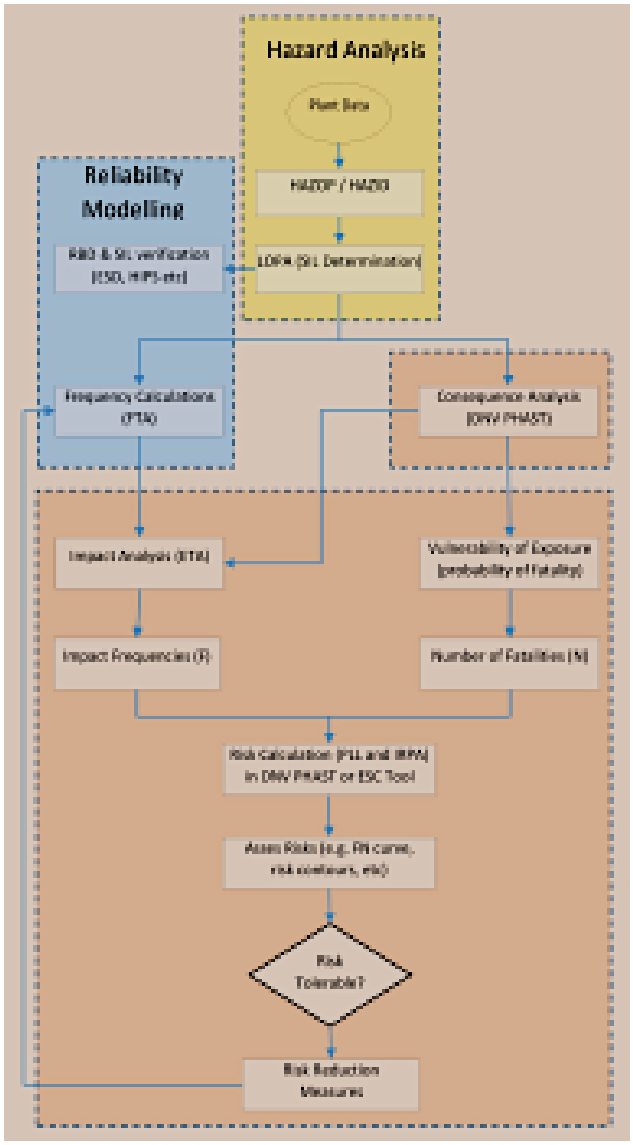

2.6 RISK MANAGEMENT

The key element when using any QRA, is the decision on what level of risk is considered tolerable or acceptable.

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When designing and specifying HCFAFs, it is important to have a mechanism in place to have a clear agreement on the level of risk acceptance. Otherwise, hypothetical biosafety risks will be considered in cases where the presence of an infectious agent is biologically insufficient to give an infectious dose (if present at all), leading to complex solutions and excessive engineering with the associated reduction in Reliability, Availability and Maintainability (Appendix 4).

This does put pressure on the users and scientists to provide suitable data at the risk assessment stage and may require experimental work and mathematical modelling to provide suitable data.

2.7 PROCUREMENT

Due to the high costs of HCFAFs and the fact that they are mainly run by national/government organisations, procurement will be a highly formalised process and in Europe covered by EU procurement rules.

It is necessary to ensure both the URS and DD address the procurement process and also the requirements for:

- Factory Acceptance testing, of appropriate subsystems
- Installation Qualification

Once a contractor has been appointed, the process moves into the Construction and Fabrication phase.

2.8 CONSTRUCTION AND FABRICATION PHASE

Delivering DD in the construction and manufacturing phase requires a new set of skills and processes. The construction of HCFAFs is highly complex and will involve a large number of personnel. The main contractor will generally appoint subcontractors, to undertake specialised tasks (e.g. wall and floor finish) and also the delivery of certain (sub) systems (e.g. autoclave, ETPs, elements of the HVAC).

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PRACTICAL TIP

As well as the commissioning engineers, it is important that the end user and facilities maintenance are properly resourced to remain part of the process, as there are often a large number of detail decisions to be made at short notice that impact on the practical operation of the buildings. Once made, these decisions will often last the life time of the building and therefore must be correct.

The Devil is in the Detail

2.9 FACTORY ACCEPTANCE TESTS (FAT)

Factory Acceptance Testing (FAT) should ensure that the (sub)systems are tested and dimensions verified as far as possible under factory conditions, so that only functional systems are installed, thus reducing changes during installation and commissioning. The FAT should be carried out against the detailed design criteria and legislation and relevant standards etc. This process and information need to cover the installation qualification below.

For the FAT, the correct personnel need to be involved and should include:

- someone from the commissioning team who can test the equipment against the DDQ and ensure compliance with legislation and standards;
- an end user who can test the equipment from a functional and practicality aspect (ergonomics etc).

2.10 INSTALLATION AND INSTALLATION QUALIFICATION

After installation, the system dimensions and features are verified against the detailed design drawings to generate as built drawings before the installed systems are tested under operational modes, failure modes and maintenance modes, e.g.:

- Pipes are connected to the correct services
- HEPA filters are installed with correct dampers, sampling ports, challenge ports, etc.
- All effluent pipes are connected as per containment strategy

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- Barrier penetrations achieve the tightness as required

At this stage, system maintenance teams should be increasingly involved.

PRACTICAL TIP

To ensure that equipment is fit for purpose, it is necessary to determine "how" to test/verify it, etc. A common issue is that the exact specifications/criteria by which the equipment is to be tested once installed are not clearly defined, or the method for testing is not specified. For example, it is stated that the equipment “needs to conform to Standard XY” but it is not indicated how to test that it does actually comply with that standard (e.g. issues with MSC’s that cannot be sealed for fumigation once operational).

It is important to avoid ambiguous terms such as “correct dampers”– without defining their specification.

2.11 COMMISIONING AND OPERATION QUALIFICATION

The functionality of mechanical and electrical systems is tested across their operating ranges, and under realistic failure modes to validate the functional design requirements, which the contractors are accountable for, e.g.:

- Stability of pressure cascades, effective air change rates
- Leak tightness of dampers and doors
- Temperature mapping of ETP and autoclave
- Directional airflow under failure modes
- Response to black building test

It is important that not only the maintenance staff are involved at this point but also the staff that will run the building and the biosafety professionals that will apply for the licencing of the building to work with pathogens. The application to the regulator will include some of commissioning and operation data and the regulator may wish to see other parts of it during the inspection/audit.

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It is also helpful to try the animal facilities out, movements of animals and associated products waste and food.

It is important that the operation manuals, commissioning data and operation qualification are complete and kept up to date if changes are made as a result of commissioning process. In the case of a complex building such as a HCFAF, it is likely there will be snags found during this process and how they are handled needs to be recorded.

2.12 OPERATION AND PERFORMANCE QUALIFICATION (INCLUDING HANDOVER)

The final step is the process where the building is validated against the users' requirement and there is a transition to the operational teams that will run the building and the maintenance staff.

There should be a defined handover process and training programme which will be based on the operation manuals. The day-to-day operating procedures should then be developed by the team that will operate the building. These operating procedures and risk assessments for the infectious agents worked on and procedures undertaken in the building, together with commissioning data, will be required to license the building.

This process will involve operating the building with clean animals to eliminate any operational issues when working with infectious materials (once licensed).

3 UPGRADING OF HIGH CONTAINMENT FARMED ANIMAL FACILITIES

HCFAFs are designed for a 40 to 50 years lifespan. During this period, it is likely that there will be changes in the use (different diseases, types of research etc.) and changes in standards due to technical/knowledge advances. During this lifetime, it will be necessary to replace the majority of the electro-mechanical components due to wear and tear and obsolescence/unavailability of components. Strategies for this are given in VetBioNet's "Best practice for facility management, including emergency response and planning" (Deliverable/D3.10).

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Upgrades present a particular challenge in that they have to work with elements of the existing structure and, depending on the extent of the upgrade, with existing sub-systems.

Once the user brief has been drawn up, the state of the existing HCFAF should be surveyed and the performance measured, and the results of this exercise compared to the user requirements. The key questions are what upgrades are necessary to deliver the user brief and whether this is feasible/financially viable. Upgrading an existing building is usually subject to physical constraints that must be considered. It is also important to get a complete picture of the state of the building. Upgrading systems over the years means a large amount of downtime, so unless the HCFAF was originally designed to allow areas of independent running, there will be a large amount of down time with the associated loss of science and income.

4 RECORD KEEPING AND CHANGE CONTROL

HCFAFs are complex buildings with a long-life span. Not only its operational and maintenance documents should be maintained, but also the documents related to its design and commissioning should be archived.

Any design or operational changes must be appropriately controlled (risk assessment, approval, re-commissioning if necessary and recording). This should be controlled by the HCFAF owner/operator, as staff running and maintaining the facility change over time, and if the facilities management is sub-contracted, subcontractors can change. A building passport showing the history of the building is often a good idea.
It is important that the records be archived for the life of the building, especially during mid-life refurbishments or upgrades, as information will be needed about the original design and how it was executed.

Appendix 1: Tips on Designing Cattle Handling systems

- Safety must be paramount – always consider how people can get out of the way safely and easily

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- Give consideration to each of the individual components of a cattle handling system – the holding areas and the crowd pen area, the race or passageway, the crush and the exit
- The entrance to the race or passage way should be set at a maximum angle of no more than 30-degrees with a straight side to the crowd pen
- Do not dead end the race or right angles in corridors as cows should be able to see and follow the animal in front. A study has shown 90 per cent of cattle will choose to turn to the left if confronted with a barrier or novel object, systems that turn cows left handed in a handling facility encourages movement.
- Cows like to go back to the place where they came in. Moving them in the direction of light, or back towards the pen or feeding area will encourage them to move forward.
- Make sure the crush is suitable for the cows which will be handled in it and the operations which it will be used for most frequently. Squeeze crushes are able to handle a wide range of cattle sizes and calm animals more due to their action.
- Ensure any barriers used are a minimum of 1.5 metres (5ft) high but ideally 1.6m-1.8m (5ft 2in-5ft 9in)

  Source : Designing a cow handling system, Miriam Parker

Appendix 2: Quantitative Risk Assessment Techniques

These are the more common types of risk assessment techniques. Some overlap and others are complementary. Essentially when designing an HCFAF, there is necessity to identify potential pitfalls, assessing what the impact of this might be and then putting in place appropriate control or mitigation measures. The timing of applying these techniques within the procurement and design stages is critical, otherwise there can be costly additions to the contract, both in time and money.

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PRACTICAL TIP

When doing risk assessments for HCFAFs, it is crucial to understand the building's primordial role to keep animal experiments running safely. Once started, experiments should not be stopped due to single points of failure in the design of the building and its systems risking biosafety. This can also help to avoid/reduced shutting down experiments during upgrading time.

ELIMINATE SINGLE POINTS OF FAILURE

Failure Modes and Effects Analysis (FMEA)

FMEA is a systematic method for analysing a product or process's potential for failure and the impact of that failure.

The analysis is also used to assess the potential risks that are associated with an identified failure. These are then used to prioritize the implementation of corrective measures. It is designed to identify and correct weaknesses in a product before it gets into the mass production phase. FMEA serves as a guide to the development of a product or system in order to reduce the associated risk. An effective FMEA will result in major improvements to the safety, quality, reliability, delivery, and cost of a product or system. The main goal of an FMEA is to improve the design of a product or system. An FMEA is carried out by a cross-functional team of subject experts early in the product development process (see FMEA - Safeopedia).

Structured What If Technique (SWIFT)

SWIFT is a brainstorming method used in safety-critical industries and facilities such as HCFAFs, radioactive waste management, offshore installations and control of major accident hazards plants. It uses a structured approach (using guide words) to generate "What if?" questions to assess the safety of a method or process. It can be applied to proposed or existing scenarios, and gives more reassurance that all the right questions have been asked than the method often used in risk assessments, where the questions asked rely solely on the competence of the person carrying out the assessment (see SWIFT - IOSH Magazine).

Hazard and operability (HAZOP) study

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This is a systematic brain storming process of assessing the existence of hazards in equipment and vulnerability of its operation. It is a risk assessment tool that provides information to the management who can make decisions to improve safety and conduct safe operations. Hazard and operability (HAZOP) studies concentrate on recognizing hazards and operability problems in an orderly approach, where hazard identification and operability are the main attentions. Hazard and Operability Study (HAZOP): see the document produced under NADIR on the IVBW site (http://ivbw.camp9.org/page-1434634).

In HCFAF terms, a hazard is any object or operation that could possibly cause an accident or accidental release of infectious agents or chemicals that are toxic, flammable or explosive and may injure humans or animals or cause a loss of properties. Operability is the functionality that could possibly otherwise lead to a violation of environmental, biosafety regulations or negatively impact profitability/reputation if something went wrong.

Safety and reliability are ensured during the design and development of machinery or designing process, considering codes of practices and standards. The production of machinery requires knowledge of engineering, biosafety safety and experience of individual experts and the industry.

Sometimes teams are under pressure to keep the project on time, which may lead to errors and mistakes causing accidents. It is therefore important that time is planned in early. The HAZOP study is therefore essential to anticipate/correct these safety faults and hazards before an accident takes place (see HAZOP - Safeopedia).

Layer of Protection Analysis (LOPA)

LOPA is a risk assessment and hazard evaluation method, which provides a simplified balance between qualitative process hazard analysis (PHA) and detailed and costly quantitative risk analysis.

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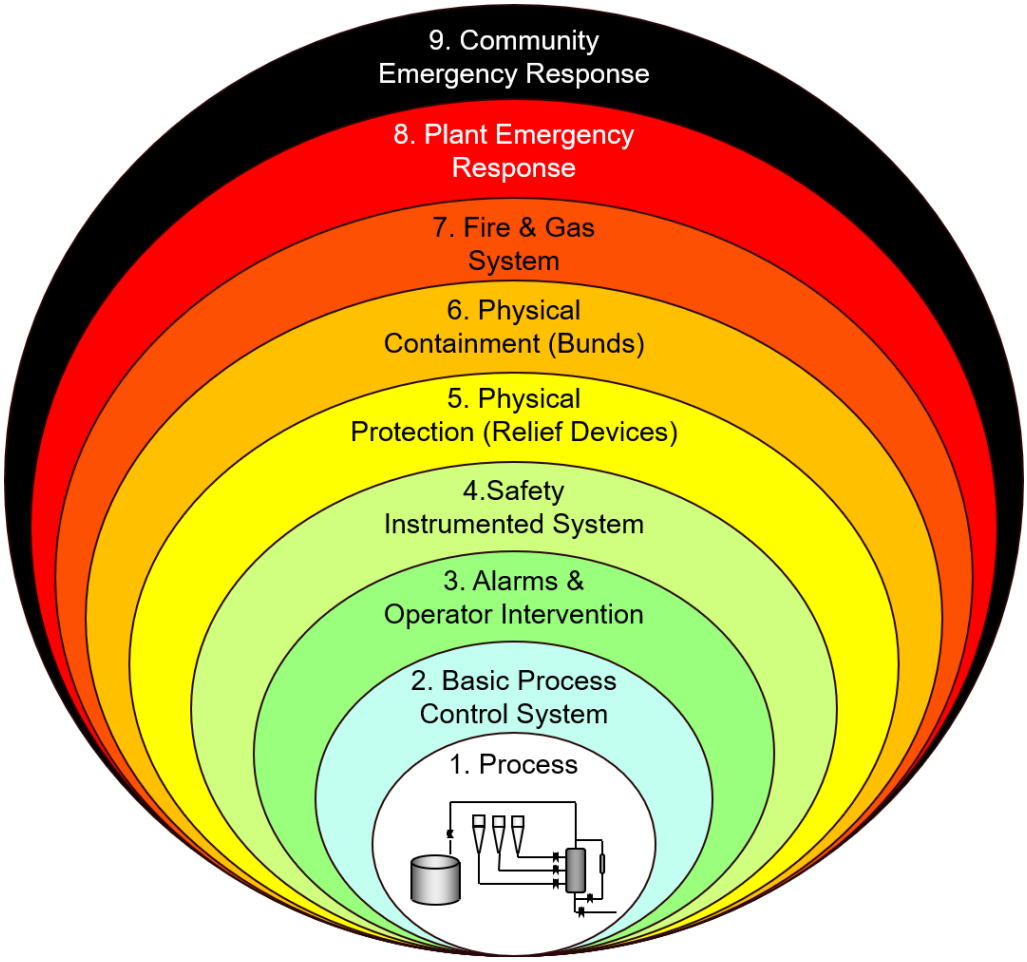

The LOPA technique can be put into place by companies who are striving to achieve a specific risk target or to lower risk as low as reasonably practicable (ALARP). By using the LOPA method, the user is able to ascertain the level of risk that is associated with hazardous events in the workplace. It bases its analysis on the severity of the event and the likelihood of it taking place.

When the level of risk has been determined, then the organization can work out the total amount of risk reduction that is required and the levels of protection that need to be put in place (see LOPA - Safeopedia).

Appendix 3: Fault Tree Analysis (FTA) and Event Tree Analysis (ETA)

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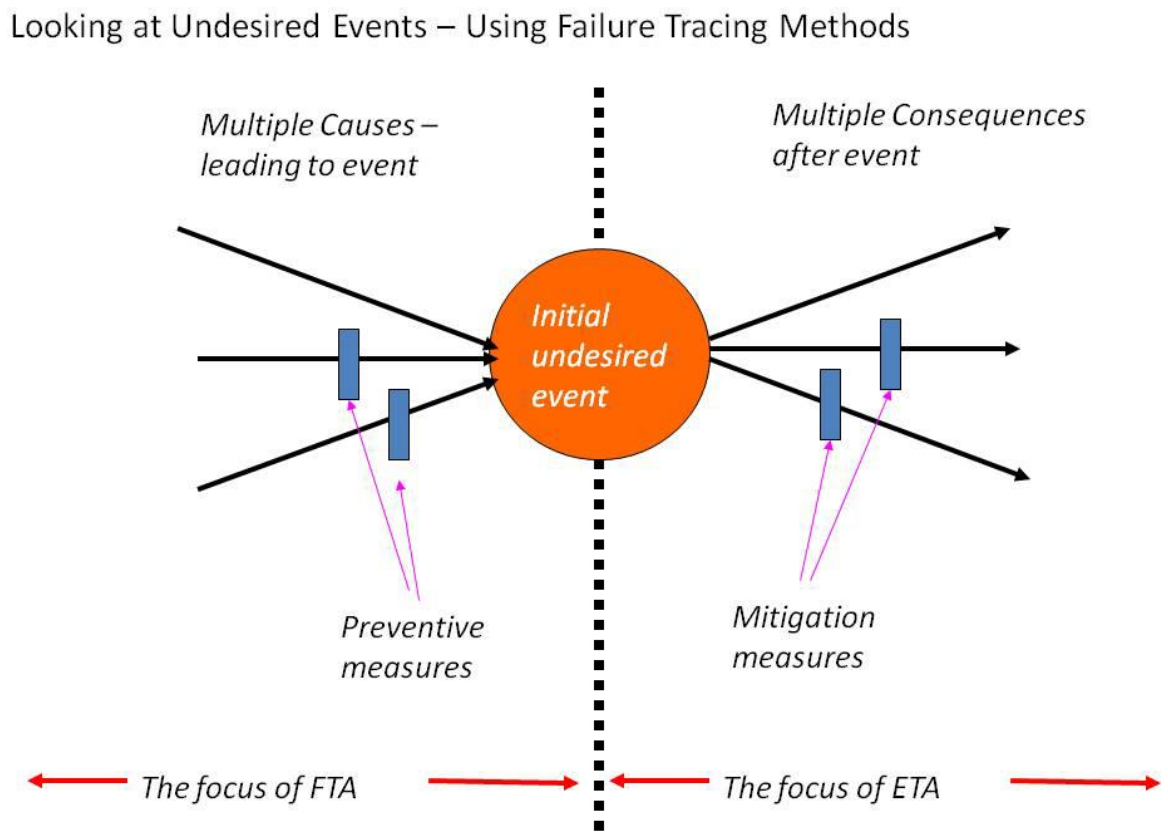
It is easy to get confused between these two techniques. The two are in fact complimentary (and are often used together) but focus on opposite sides of an undesired event. The diagram below shows how they fit together:



This model is sometimes called a “bow-tie” model (because it looks like one) and when complimentary FTAs and ETAs are used, it is called the bow-tie technique. The diagram only shows a single “undesired event”; in reality, multiple causes can lead to many different events initially, each then escalating with multiple consequences. One can analyse each event with FTA and ETA. In summary, FTA is concerned with analysing faults which might lead to an event, whereas ETA is interested in stopping it escalating (see NEBOSH).

Bowtie risk assessment was used in Deliverable 3.7 (“Best Practice in Post-Mortem Rooms”). Its strength lies in its visual representation of risk, although FTA and ETA can be used for quantitative data, if available (see Introduction to bowtie | UK Civil Aviation Authority).

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Appendix 4: Reliability, Availability and Maintainability (RAM) studies

RAM studies are used as a way of assessing the capabilities of a system, both in design phase and in operational phase. As facilities and plants such as HCFAFs are run for a longer period of time, a RAM study can provide an assessment of the facilities' life time capabilities and allow operators to maximize their utilisation.

A RAM study centres around three separate areas:

- Reliability Services – Predicting the probability in which a system will not experience an unplanned outage;
- Availability Services – Predicting the probability in which the system is working in a functioning state when required, including both planned and unplanned outages;
- Maintainability Services – Predicting the probability in which a product / system can be repaired following a failure within a specific time frame.

Reliability	Maintainability	Availability
Constant	Decreases	Decreases
Constant	Increases	Increases
Increases	Constant	Increases
Decreases	Constant	Decreases

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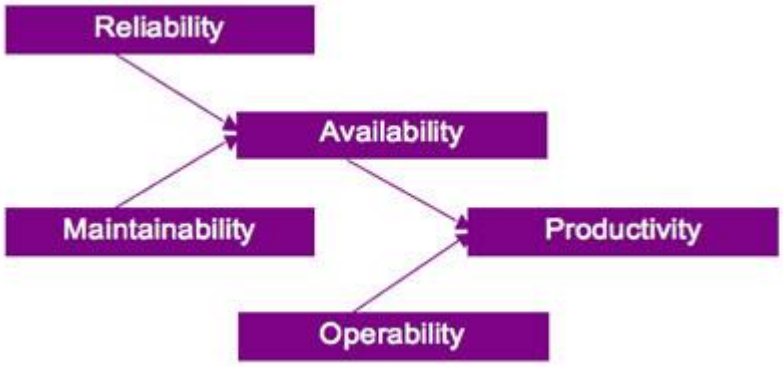
With the combination of these three services into a single study, ESC is able to offer a RAM study that models the predicted production capabilities of a facility.
The benefits of undertaking a RAM study include:

- A reduction in the maintenance and sparing costs, while maintaining and/or increasing usage levels;
- A decrease in the duration of any unplanned and planned outages;
- Optimisation of capital improvement options at the plant and enterprise levels, when improve budgets are constrained;
- Accurate forecasts of equipment lifecycle costs that reflect the equipment age, duty cycle and maintenance effectiveness;
- Alignment of maintenance resources based on the criticality of equipment to production revenue.



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