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ROADMAP

DESIGN PROCESS OVERVIEW

FOR CONTAINMENT BUILDING PROJECTS

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Contents

INTRODUCTION

For the purposes of this paper, a Biocontainment facility is a laboratory, production facility, or similar building that handles contagious biological materials in a safe and responsible manner. This specialized facility, also called a containment facility or a high containment facility reduces the potential for biological agents to be released into the environment, provides a safe work environment for the employees, and supports good laboratory practices.

The containment industry traditionally categorizes Biocontainment facilities in four tiers: biosafety levels (BSLs) 1, 2, 3, and 4. Although these four tiers provide a preliminary understanding of the types of risk group (RG) agents that are handled in these facilities, no facility can be designed and built until a thorough risk assessment has been made. The risk assessment characterizes the agents to be handled, as well as the planned procedures and mitigation measures. The risk assessment addresses both biosafety and biosecurity considerations. The likelihood and consequence of occurrence are determined for all scenarios, and the acceptable risk is defined for the facility. All these factors of the risk assessment become the design drivers for the project. Each Biocontainment facility has unique features and design choices based on regulations; the availability of materials, equipment, spare parts, and service technicians; power supply; financial and human resources; tradition, culture, and need.

A thorough risk analysis is always necessary for determining the risks associated with any facility. The risk assessment needs to evaluate the purpose of the facility; the number of people required to operate the facility; the agents to be contained; the procedures to be employed; the facility requirements for storage space, biosafety cabinets, adjacency, shared equipment, aerosol generation, and waste procedures, and many, many more similar characteristics. If the facility is not thoroughly characterized and all contributing factors to the design requirements have not been identified and clearly defined, the facility that will be built based on inadequate design requirements will be useless at best and dangerous at the worst for its intended purpose.

Facilities rely on a mixture of operational and engineering controls to achieve the necessary level of containment. The nature of this mixture depends on the regulatory requirements and other conditions that apply at the site. Where power supply is robust and reliable, engineering controls will typically dominate the design for achieving adequate containment measures. In more resource-restricted regions, where power supply and access to fuel for back-up generators might be less predictable, operational and management controls will typically be the dominant design strategy to achieve a safe work environment. The exact specifications and design strategy of a high-containment facility is unique to the work planned for that facility; a thorough and comprehensive risk assessment is necessary for choosing the right solutions for the facility to be designed and built.

Designing a high-containment facility is a very complex, expensive, and ambitious task. Several groups of people play key roles that ensure the completed facility meets the needs and expectations of the owner/client.

ROLES AND RESPONSIBILITIES

Key players typically include the following stakeholders:

- ✓ Owner/client, including
  - User groups - provides input to the Design task group
  - Design task group - evaluates user needs and makes recommendation to Steering committee
  - Steering committee - decides on final strategy solution according to recommendations from the Design task group
- ✓ Design architect and engineering company (A&E)
  - Project lead – manages the overall project
  - Architect/designer – responsible for layout and design
  - Laboratory planner – identifies design requirements for laboratory procedures to be use at the facility
  - Engineering – responsible for utilities, capacity, redundancy, equipment, etc.
  - Maintenance and project engineering (MPE) lead
  - User requirement specifications (URS) writer – works in collaboration with the users
  - Quality controller – ensures that procedures are followed and quality specifications are met
  - Other individuals and tasks as required
- ✓ Contractors
  - Many of the same roles as the A&E
- ✓ Commissioning team – write protocols and performs testing
- ✓ Equipment suppliers
- ✓ Independent advisor/client support – reviews, recommends and approves

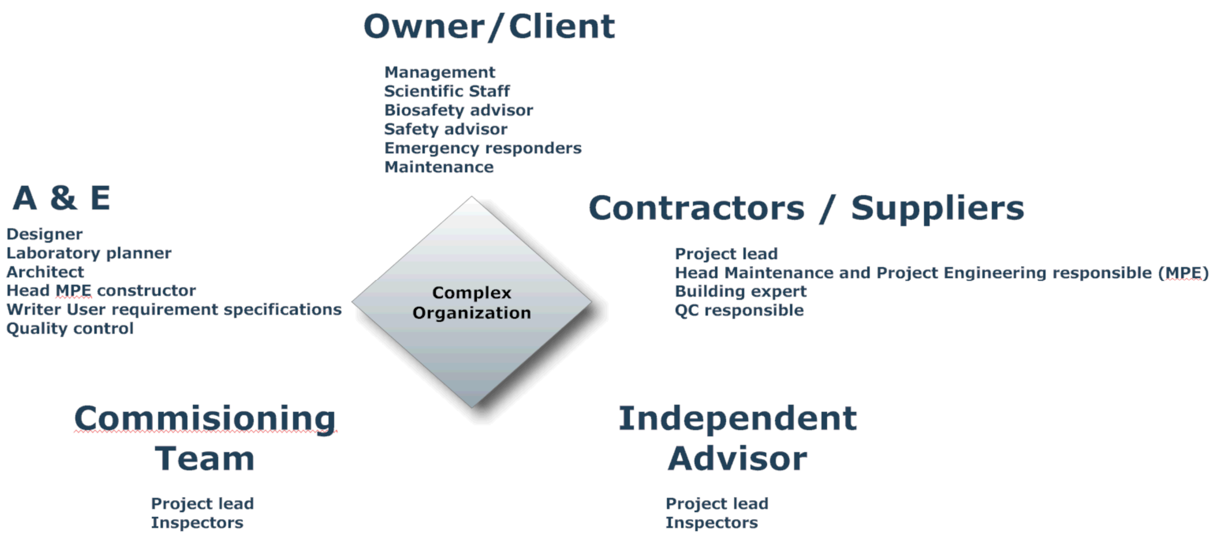


Figure 1

OWNER/CLIENT

The owner/client is responsible for:

- ✓ Understanding the technical requirements for the facility and balancing these with budgets and other constraints
- ✓ Ensuring that concerns and expectations from the general public and requirements from the regulatory authorities are met
- ✓ Providing the vision, mission, and needs of the facility to the A&E
- ✓ Ensuring that relevant guidelines and regulations as well as the biorisk management strategy of the facility have been conveyed to the A&E design team
- ✓ Ensuring total buy-in to the project from top to bottom in the owner organization
- ✓ Ensuring that all relevant stakeholders have been included, heard, and their input considered

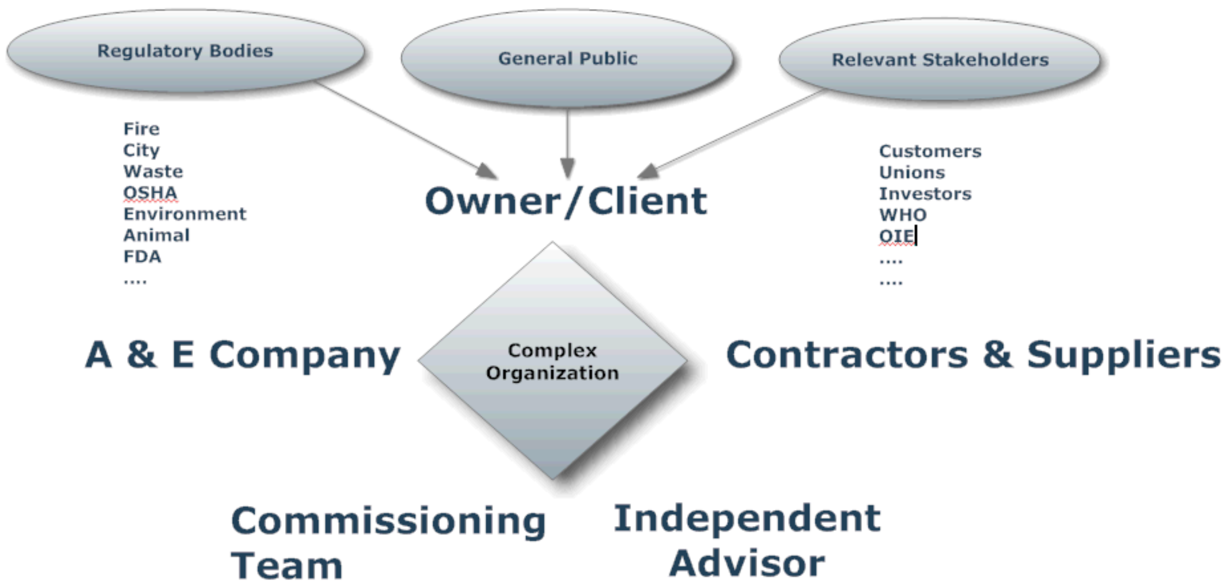


Figure 2

The owner/client wants the best facility for the least amount of money, as well as a robust, easily maintained state-of-the-art facility that will serve its purpose for many years into the future. Few owners/clients will acquire a high level of professionalism in this role, as most will not build repeatedly. (Many owners/clients are very glad to do this just once!) Thus the owner/client requires a professional, responsible, reliable, and experienced team of architects, engineers, and contractors on the project, as they will be the experts who advise and guide the owner/client through the complex and challenging design process from early planning through commissioning and handover of the facility.

Furthermore the owner/client steps into the process with the background and knowledge from the existing laboratory or facility. The way it has worked for the last many years. The owner/client therefore brings important information to the table, namely what works, and what does not work. However, the owner/client might not have insight in the newest trends and developments in designing laboratories. The last 20 years diagnostic bio technology have changed from being agent characteristic focused to be more technology relying, using DNA/RNA as the main source of information. This means that the original small laboratories with only a few agents present today are changing to bigger open laboratories that share equipment and technology as long as cross contamination issues are addressed adequately.

DESIGN ARCHITECT AND ENGINEERING COMPANY

Experienced architect and engineering companies with many projects in their portfolio will with this experience add to the design discussions with the owner/client. The architects can challenge old perceptions and suggest solutions from similar projects, however, it is the owner/client that in the end will decide whether the specific work being done in this facility will benefit from some of the new trends in lab design, or whether the new facility should be a modern copy of the old one.

The A&E plays a key role in any building project, by translating the visions and needs communicated by the owner/client into a building that fits both the budget and the purpose. The building must be sustainable for an anticipated lifespan that fits with the purpose and mission of the facility. The design should include the latest technical developments. The A&E must also help the owner/client understand what is possible and available based on new technologies, techniques, and new developments, as the owner/client's only reference most often is an old laboratory or facility that needs to be replaced.

Close cooperation is required between the owner/client and the A&E to create a smooth and seamless work relationship in which both parties take full responsibility for efficient communication. The biggest challenges for the A&E involve communication with other key stakeholders. Scientists may think that the A&E instantly understands all underlying implications of any description of a procedure or requirement, and that the procedure or requirement can be incorporated into the building design safely, securely, and effectively without further elaboration on the technical explanation. The A&E needs to understand that blueprints and drawings might not be self-explanatory to a layperson. Clear and effective communication is extremely important, especially in the early phases of the project.

It has been demonstrated in numerous projects that face-to-face time and workshop meetings between all the stakeholders provides tremendous value and is a keystone for a successful project outcome. The time and resources invested early in the project will be repaid multiple times through savings in the later project phases.

Later in the project, timely inclusion of relevant authorities (e.g., the Occupational Safety & Health Administration, the Environmental Protection Agency) is also important, because rejections or delays of approvals can be detrimental to the project timeline and budget.

Choosing the right A&E to oversee the entire project is of outmost importance for the owner/client. The selected A&E should have a successful track record with similar projects that were completed on time and on budget. Both the owner/client and the A&E should clearly understand that building a Biocontainment facility is among the most difficult tasks in the building industry. Each facility has a different scope and purpose. The cookie-cutter approach cannot be applied, because each Biocontainment facility has a unique set of design requirements. For the same reason, stitching together a facility in a patchwork quilt from other projects from other segments of the industry with some similar requirements, such as pharmaceutical (clean rooms), oil-rigs (tightness to reduce explosion danger), and hospitals (disinfection and waste requirements) is not a feasible way to achieve the end goal, a safe facility for the workers, the community, and environment. Each Biocontainment facility is a unique design and building project.

CONTRACTORS

Bringing in contractors for the final design and building phase adds another layer of complexity to the process. Effective engagement of contractors requires clear communication and minimal midstream design changes. The A&E team oversees the performance of the contractors and is in daily close discussion with them. After the contractor budget is set, changes due to poor communication and/or midstream design changes will likely result in added costs assessed by the contractor to adapt the plan to accommodate the change or clarification. Contractors are driven by their own business model and will bill accordingly. Added contractor costs can accumulate very quickly, leading to projects that either excessively surpass allocated budgets or are compromised with regard to quality, maintenance, and/or flexibility. A cost-cutting process will be initiated, often referred to as "value engineering". At this point contact with the owner/client is often scarce, and original insight in why requirements were listed as they were might be lost or forgotten. It is critical for the successful outcome that value engineering addresses the details that *can* be finalized at a reduced cost, and do not touch the design requirements that are directly related to safety for the workers or protection of the environment and the community.

The contractor must be able to demonstrate extensive experience in the building methods and materials that will be used for the facility. Containment projects are not projects suitable for "on-the-job training" or the "learning by doing" attitude of an engaged and enthusiastic contractor or subcontractor. This is serious business that relies on skills and experience in all links in the chain. And understanding that each and every detail is equally important is mandatory. ("The devil lies in the details.")

COMMISSIONING TEAM

The commissioning team should be a third-party company independent from the A&E design company. The commissioning team's task is to reconcile the capabilities and motivation of the A&E with the needs of the owner/client. The commissioning team verifies that the design A&E team is providing a product that meets the specifications and expectations determined by the owner/client. Successful projects often bring the commissioning team aboard very early in the project, preferably during the last part of the design phase.

EQUIPMENT SUPPLIERS

In addition to the usual building-related equipment, a containment facility also requires a tremendous amount of specialized equipment. Each piece of equipment requires very close attention to technical support for specification and installation, as well as for the final verification that the equipment and the facility perform according to the initial written user requirement specifications and expectations.

As with the contractors, equipment suppliers are driven by their own business models. They will bill as required to stay in the market and maintain a healthy business. The owner/client is dependent on skilled and responsible suppliers who know the business, the consequences of the unsuitable equipment, and behave accordingly. If specialized Biocontainment equipment fails, people who rely on it could be in danger. Failure means not only a lost batch and lost money, but also exposure, contamination, and possibly death.

INDEPENDENT ADVISOR

The owner/client is often the weak link in these collaborations, because the core competency of the owner/client is far removed from managing building projects in a timely and professional manner. The core competencies of most owners/clients are to manage a laboratory or other biological facility (e.g., Central Public Health laboratory, a production facility, an environmental surveillance laboratory, or a research institution), provide papers for publication, provide fast and reliable diagnostic results for hospital treatment of sick people, control outbreaks, and ensure fast and efficient response to an unforeseen incident.

Some owners/clients therefore find value in strengthening the professional capabilities inside the institution by engaging an experienced entity who can help manage the project by leading relevant initiatives inside the owner/client's organization in a timely manner and creating the clarity and insight required to communicate the owner/client's perspective in a clear and concise manner to the A&E design team.

PREPARATION FOR THE PROJECT

Any building project can be divided into components that will be executed in a consecutive manner. Depending on the complexity of the project, the deadline for the finished project, and local authorities' approval processes and timelines, these different parts of the project may overlap. The more ambitious the project timeline and deadline, the more likely it becomes that a project fails to meet quality, monetary, and/or time constraints. It is rarely possible to acquire "good, cheap, and fast" simultaneously.

For any facility, the stages of the building project include:

- ✓ Planning and programming (Basis of Design)
- ✓ Conceptual design
- ✓ Basic design
- ✓ Detailed design
- ✓ Construction
- ✓ Commissioning
- ✓ Handover

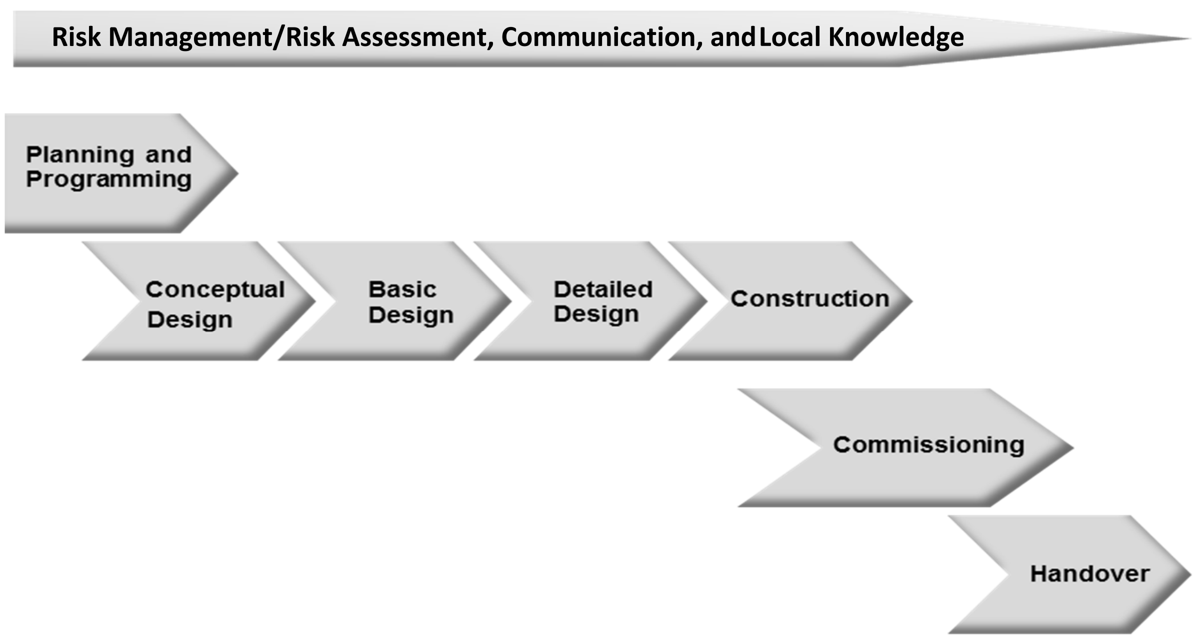


Figure 3

Each of these stages will be discussed in further detail below. While these stages may overlap, there are three activities that are ongoing throughout the life of the building project: Risk Management/Risk Assessment, Communication, and Local Knowledge. These three activities are discussed next.

RISK MANAGEMENT/RISK ASSESSMENT

Any action, decision, or choice throughout the entire project will likely have impacts on either the budget, the quality/functionality of the facility, or the timeline A thorough risk management strategy and mitigation process must be ongoing for the entirety of the project. The critical path throughout the project must always be visible and considered, and any threats to the process must be analyzed and mitigated. Risk assessments must be documented, reviewed, and revised, and risk management decisions for mitigating the risks must be clearly communicated to everyone involved. It is important to keep in mind that risk assessment is an ongoing process during the project.

COMMUNICATION

Most building processes suffer from lack of clear, efficient, and timely communication. All design changes, decisions, adjustments, and revisions of drawings must be communicated in writing in a timely manner to all relevant stakeholders. Communication may be the biggest challenge, particularly in such complex building projects as high-containment projects. It will quickly become evident whether the A&E has the experience and skills necessary or if they are new to this type of project. This is where an experienced entity on the owner/client's team (client support) can help to foster an effective working relationship between the owner/client and the A&E team from the beginning. This working relationship is critical to help set the standard for these ambitious projects.

LOCAL KNOWLEDGE

Local knowledge of and insight into building tradition, materials, experience, and workers' skills are very important. The optimal building team is a partnership between those who have the expertise and experience provided by a successful track record of building containment facilities and others who have local knowledge of construction methods and materials as well as professional relations and networks in the region.

When projects are undertaken in resource-limited regions, additional factors may prove challenging.

Factors to consider include, but are not limited to:

- ✓ Design that will minimize future operational costs
- ✓ Adequate finances for duration of project
- ✓ Availability of resources
- ✓ Availability of previous experience and expertise in building similar facilities
- ✓ Staff training and experience in design

- ✓ Availability of quality materials and expertise for construction
- ✓

Some of the same challenges can also be seen in highly industrialized western countries that do not necessarily have an upfront monetary constraint, but still lack adequate knowledge and experience in the complex requirements and skills necessary for building high-containment facilities.

In some regions throughout the world, a safety and security factor must be added to the already-complex design equation. Such requirements might include:

- ✓ Securing the building site against theft or attacks
- ✓ Securing safe transport of deliveries of equipment and materials to the building site
- ✓ Allowing sufficient time for approvals of requests to border control authorities (import and export control issues)
- ✓ Providing safe accommodation and transport for foreign experts on site

STAKEHOLDERS

There are many different entities that have an interest in these kinds of projects. Most important is the users that will end up inside the facility and live with the design choices in the future.
Owners/clients should be involved and thoroughly engaged in the project from the earliest planning phase, even before establishing the program. In some projects this group is almost not present, and most often the quality and usability of the facility sadly reflects this fact.

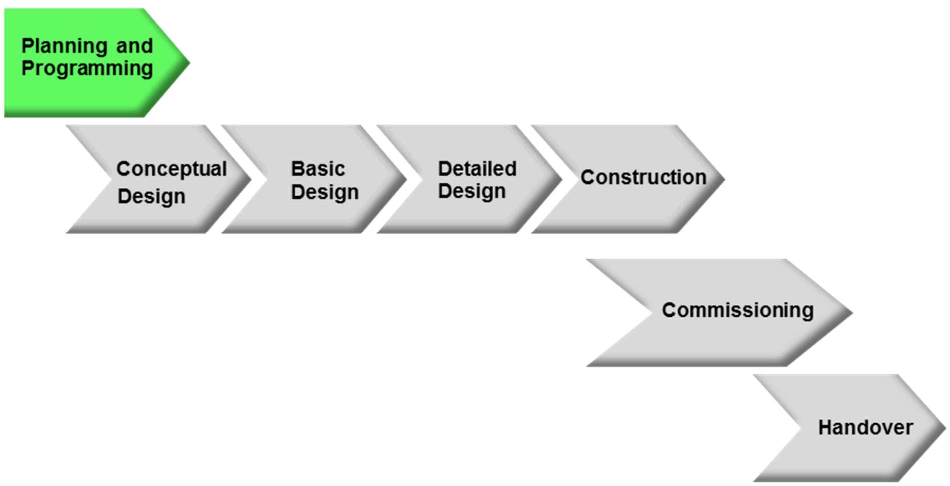
A ***user group*** should be formed consisting of all the stake holders, such as researchers, waste handling personnel, animal caretakers, technical maintenance staff, and management. The user group's specific and early input is necessary for the project to have a successful outcome, from an operational perspective.

A ***design task group*** should be authorized to make decisions about the project design, establish drafts for project-specific design drivers and design terms, resolve conflicts, and oversee that relevant user input is provided in a timely manner.
The owner/client can either participate as a member of the design task group or choose an experienced building consultant in the planning phase as his or her representative in the design task group. The consultant will support the owner/client and work in the owner/client's interests.

A ***steering committee*** resolves issues that cannot be otherwise resolved. The steering committee can also authorize project changes and commit funds.

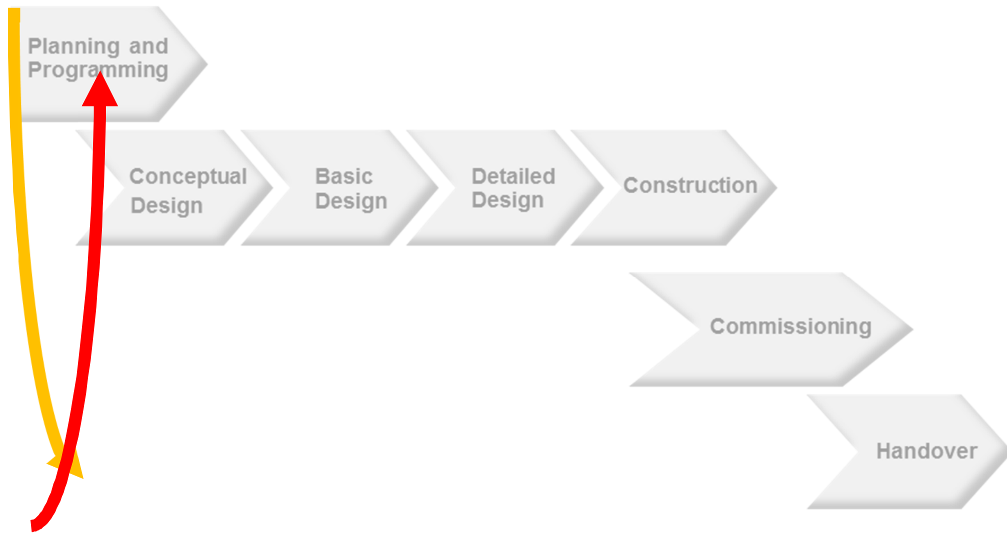
Selection of the A&E firm/consultants should occur during the planning phase. This selection should be based upon references, expertise, and other factors that assure the firm is competent to design the required containment facility.
The programming phase and the end result in form of a report "the Program", is the basis for the design phase. The project is defined and conceptual design strategies and decisions are documented.

PLANNING AND PROGRAMMING



In meetings during the programming phase, the owner/client's specific goals, priorities, and uses for the building are discussed in detail. The design A&E company is added to the team. Drafting the design drivers and terms from the planning phase will be formulated as a common project basis, valid for all parties of interest in the project.

The goal of the programming phase is to uncover, evaluate and document all relevant information at the beginning of the project, thereby reducing the need for backtracking and redesign later. A thorough programming process is essential for maintaining an orderly and cost-effective design process later in the project. Many problems that owner/clients encounter with the design of their building could have been avoided or minimized by employing a thorough programming process. The later in the process corrections and new requirements are brought forward, the larger the impact on the overall costs of the project.



Cost of Change goes up during a project, while **Decision Impact** goes down.

Specific goals of the planning and programming phase include:

- ✓ Identification of the owner/client's specific goals, priorities, and uses for the building
  - Diagnostic laboratories
  - Research laboratories
  - Training laboratories for universities
  - Animal research (large or small, aerosol inhalation experiments, necropsy)
  - Large-scale vaccine production
- ✓ Identification of design drivers and terms used in the design phase
- ✓ Development of a common vocabulary for the project
- ✓ Development of draft URS
  - Level of quality
  - Identification of containment elements that require validation and testing
  - Preferences and requirements
- ✓ Review of owner/client needs by the A&E design company
- ✓ Refinement of user needs
- ✓ Development of a detailed written program as the outcome
- ✓ Communication of goals and objectives for the facility communicated to all groups

During programming a draft of the URS should be established. The URS describes requirements and level of quality and provides an early sense of which containment elements will require validation and testing. The URS will also be a part of the design phase. It is drafted by the design A&E company in very close collaboration with the owner/client and approved by the owner/client or his or her representative.

The A&E team should guide and encourage the owner/client to consider all important issues in the planning and programming phase, help the user group understand the ramifications of their decisions, and make recommendations based on past experience and professional knowledge. The URS becomes a document that can be used to verify that the actual requirements from the owner/client are met by the contractors and equipment suppliers. Therefore each specific requirement in the URS must be clearly stated, every requirement must be measurable, and the origin of the requirement must be identified.

The origin of the requirement should address such questions as:

- ✓ Is it from mandatory regulation or international guideline that if deviated from will jeopardize later approval from the regulating authorities?
- ✓ Is it from a risk assessment that analyzed the agents to be used and procedures to be applied and therefore will endanger the surrounding community, environment, or work conditions of the staff if omitted during a later value-engineering phase?
- ✓ Is it for convenience (“nice to have” or is it necessary for subsequent approval “need to have”)?

The knowledge to address such questions is available when the URS is written by the initial stakeholders, the owner/client and the A&E. The reasons behind each requirement should be traceable and documented. Only then can a later budget-cutting round or dialogue with a supplier be accomplished without jeopardizing the entire building project and approval by the authorities.

Some suppliers might offer a product or piece of equipment that almost meets the criteria. Late in the building phase, the people tasked with negotiating and selecting between the offered equipment might not be the same people who wrote the URS in the beginning of the project. Big mistakes and wrong decisions can be made at this point, because the knowledge was not transferred adequately. A little more effort to reference why a requirement was included can make a big difference later in the project

When users are confronted with equipment that has been modified due to value-engineering or accepted as “close enough,” they become very frustrated because the requirement specifications were not met. Users often are forgotten or left out in the middle project phases, as general project management and meeting structure does not easily include or easily interface with the users at this point. Users have a tendency to continue the iterative process of modifying the facility, which does not benefit either the timeline or the budget of the project. Science and technology move on, users become aware of new and better solutions, but at some point in any project it is important to close down the option for any new input to the project and prevent the users from adding on new requirements. Thus, the better and clearer the URS are written up front when the user has input to the requirements, the fewer wrong decisions are made later on.

IMPACT ASSESSMENT

The pharmaceutical industry historically uses Impact Assessment analysis to single out the critical equipment.

Critical equipment is defined as equipment that:

- ✓ Has direct product contact
- ✓ Supplies components of the product
- ✓ Maintains product condition
- ✓ Generates data that will be used to approve or reject a product
- ✓ Is used for cleaning
- ✓ Is managing or controlling processes with impact on product quality without independent control

The same type of analysis can be used for containment projects to consider systems or equipment that will contribute to containment, safety, or protecting the environment.

Such equipment will:

- ✓ Prevent exposure
- ✓ Protect the facility worker
- ✓ Protect the community
- ✓ Contribute to decontamination
- ✓ Provide access control
- ✓ Perform inventory control

These very important systems cannot undergo a value-engineering process without performing another complete risk assessment involving all the stakeholders, including the owner/client, as he or she is the only one able to foresee and understand the ultimate consequences of deviating from the original URS.

Some requirements can be shifted from an engineering control solution to a management and operation strategy, if the actual goal of the requirement can be managed by processes, written standard operating procedures (SOPs), and personnel training; other requirements cannot! Making this distinction is very important to the success of the project.

After the URS for equipment, supplies, utilities, etc. have been written and approved; the design A&E team thoroughly reviews all owner/client requirements so that appropriate design decisions can be made. The project requirements are finally collected in a clearly organized written program that will serve as a reference throughout the design process.
Items analyzed in the programming phase and included in the program or the URS should include:

- ✓ Mission and vision of the facility, future expansion estimates, scientific research programs and goals, whether vivariums are included and what building lot or area is available for the project etc.
- ✓ Other needs, limitations, expectations, wishes, local aspects, aesthetics, sustainability, anticipated life span of the facility, energy conservation, /Leadership in Energy and Environmental Design (LEED) certification
- ✓ Scope of work: size of the building; staffing, private/public segregation strategy, number of rooms; room uses (open, closed, clean labs); types of research, agents, animals, procedures, cross contamination etc.
- ✓ Handling agents for already eradicated, almost eradicated, or emerging diseases or handling agents that are endemic in the surrounding community
- ✓ Biorisk management strategy, safety, security, and accessibility requirements, including preliminary risk assessments for biosafety, biosecurity, cleanroom, containment, animal, chemical, and environmental aspects
- ✓ Structured review of national and international rules, regulations, and guidelines, and documented decisions on which design parameters to follow
- ✓ Codes and regulations: outline of planning and building department parameters
- ✓ Existing and anticipated utility locations and requirements, including local waste regulations
- ✓ Animal care and use requirements
- ✓ Accreditation requirements (laboratories, production facilities, animal facilities)
- ✓ Process equipment strategy (technology – single use equipment versus fixed equipment)
- ✓ Decontamination requirements (wash down/fumigation) and waste management strategy
- ✓ Initial analysis of community/neighbor relationships or anticipated obstacles, relationship and cooperation strategy with local authorities during emergencies, etc.
- ✓ Documented preventive maintenance strategy decisions and approved responses, including acceptable downtime for the facility, proactive preventive maintenance, and/or failure of system

- ✓ Site context: weather, noise, solar access, vehicle access, handicap accessibility, geological structure, mud, cliff, flooding, tornadoes, sand/dust storms, earthquake, and general campus/site analysis
- ✓ Future decommission strategy when the facility is closed, including decontamination of building structure and general waste-handling, recycling strategy
- ✓ Budget and priorities: Preliminary cost analysis for building phase and future operation, usually based on area and/or volume, to be refined later
- ✓ Project scheduling, timeline
- ✓ Risk assessments – economic, timeline, process, perception, workers, community, and environment

Many risks must be evaluated and mitigation measures selected in a timely manner. All above-listed items will be valuable input to the many risk assessments to be performed at this early stage.

The risk of the project not meeting budget and/or timeline due to equipment or building materials arriving late or unforeseen harsh weather conditions not considered in the timeline is one set of risk factors. The response time for reviews and approvals from the relevant authorities for building and environmental permits must also be considered, as this can cause significant delay or even halt a project. These considerations must be addressed very early in the project and timed accordingly.

The earlier these issues can be addressed, the more likely the project will be successful. However, if the permits and other required paperwork are submitted too early in the process, required detail may be missing. These risks are normally evaluated by the A&E, as they are the experts on building processes and will have vast experience and knowledge from former containment projects of what can go wrong and why.

The risks this facility will create for the workers, the surrounding community, or the environment depend on the mission, the scope, and the planned procedures for the facility. These risk factors must be addressed upfront, as these factors may need to be mitigated by the early design choices, the equipment, and the risk mitigation strategy for the facility and be approved by the regulatory authorities. These risks should be addressed in a close collaboration between the scientific experts - i.e., the owner/client and the A&E. The process should be driven and timed by the A&E, but cannot occur without input from the future users of the facility.

In the end of the planning and programming phase, the program should be reviewed against the project-specific design drivers and the available budget. All main and major needs should be identified and a final conclusion should enable the owner/client to determine whether the project is feasible with the existing scope, whether the scope of the project should be changed, or whether shut the project down at this stage.

Insufficient allocation of time for the planning and programming phase will likely prohibit the comprehensive determination and organization of the basic scope and underlying requirements of the project. In that case, the design phase will be initiated too early, resulting in subsequent time- and money-consuming corrections and adjustments.

DESIGN PHASES

The design phases are sequential and include several design steps in which the level of detail becomes more and more sophisticated. Terms associated with this phase of the building project include Basis of Design (BOD), Conceptual/Schematic Design (30%), Preliminary/Basic Design (60%), and Final/Detailed Design (90%), and concurrent Design Review on all three stages 30%, 60% and 90%. During these design steps the actual requirements and the more specific and detailed understanding of the project becomes clear, together with the following economic consequences and time perspective.

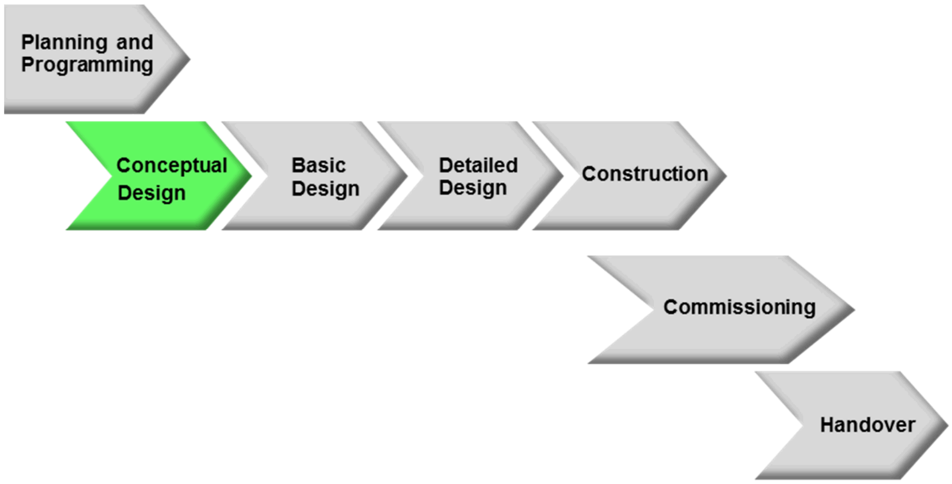
Through integrated design, the building project should result in a facility that satisfies functional demands, process, procedure and equipment layout requirements, while allowing adequate space for operability and maintenance (both routine and non-routine), as well as allowing necessary movement of product, materials, personnel, animals, components, waste, and raw material.

The initial risk analysis should determine whether to keep all utilities out of the facility in a service space or inside the facility and eventual containment area.

The materials and layout of the facility should provide a contained environment with surfaces and room finishes enhancing easy safety and visual communication between the rooms, easy cleaning, hygienic environment, biosafety, biosecurity, and general safety requirements.

Additionally, the facility should comply with national building regulations, including all valid work environment codes, fire codes and international best practices.

SCHEMATIC / CONCEPTUAL DESIGN



The conceptual design is sometimes called the schematic design. It comprises the building into a defined, feasible design concept. The design will be in the form of narrative sections describing the concept, schematic drawings, flowcharts, bubble diagrams, adjacency charts, and the like.

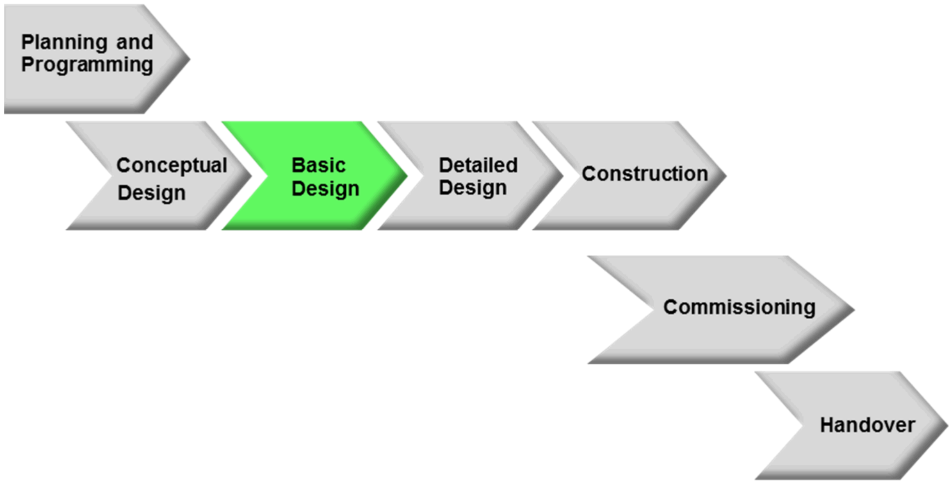
The conceptual design will address all significant areas of design and will be reviewed with the owner/client and in most cases also an assisting A&E firm before proceeding to the next design phase with even more detailed drawings. This review will uncover whether there are any critical process steps or design solutions that need to be addressed with special care. This is the last stage where the consequences of design changes are not detrimental to cost or progress.

A preliminary cost estimate can also within reasonable margins be provided at this stage. Work in this phase typically includes the following:

- ✓ Schematic site plans
- ✓ Preliminary building floor plans, sections, and elevations to determine space needs, dimensions, areas, and volumes
- ✓ Sketches showing relationships of spaces, containment borders, clean/dirty zones, circulation, directional airflows, logistics, capacity, uses, including process, material, personnel, waste, cleaning flows of the facility
- ✓ Complete (depending on size and complexity of the project) conceptual room layout of all special furniture, larger equipment, plumbing fixtures, etc.
- ✓ Impact assessment analyses documenting which construction details, materials, utilities, and equipment are critical for the correct performance of the facility and ensuring compliance with safety- or security-related requirements

- ✓ Preliminary material choices (including documentation of material suitability/compatibility)
- ✓ Preliminary selection on laboratory, laboratory support, and animal-holding equipment
- ✓ Fumigation/wash down decontamination strategy and requirements for chemical resistance of surfaces/equipment (plus demands for tightness of building/rooms)
- ✓ Preliminary mechanical, electrical, and plumbing issues addressed, including strategies for how to clean clogged waste lines
- ✓ Preliminary mechanical, electrical, plumbing, and structural engineering calculations
- ✓ Preliminary structural engineering questions answered
- ✓ Constructability/preliminary concept for building systems
- ✓ Code and regulation research and coordination with regulating agencies (licensing, building department, fire department, city planning department, etc.)
- ✓ Preliminary cost estimate (plus or minus 30%)
- ✓ Time schedule consolidated (including timeline and milestones for relevant approvals from authorities)
- ✓ Design presented to interested parties (including relevant authorities – such as fire brigade and environmental authorities for dialogue and eventual corrections to be implemented in the next stages of the project)
- ✓ Design revised subsequent to owner/client discussions
- ✓ Preliminary commissioning plan established (based on URS documents)

PRELIMINARY / BASIC DESIGN



When the conceptual design has been reviewed, the next phase, the basic design development is the process of refining the design by working out details, including the selection of materials and the engineering systems and including all the comments from the conceptual design. The aim is to finalize all design decisions before proceeding with construction documents, the very detailed and expensive documents that the contractor will need to complete the project. At this level any change will be extraordinary costly, as even a minor change will have impact on a whole series of drawings, plumbing, ductwork, equipment, electrical etc.
A more detailed cost estimate can also be provided during this phase.

Work in this phase typically includes the following:

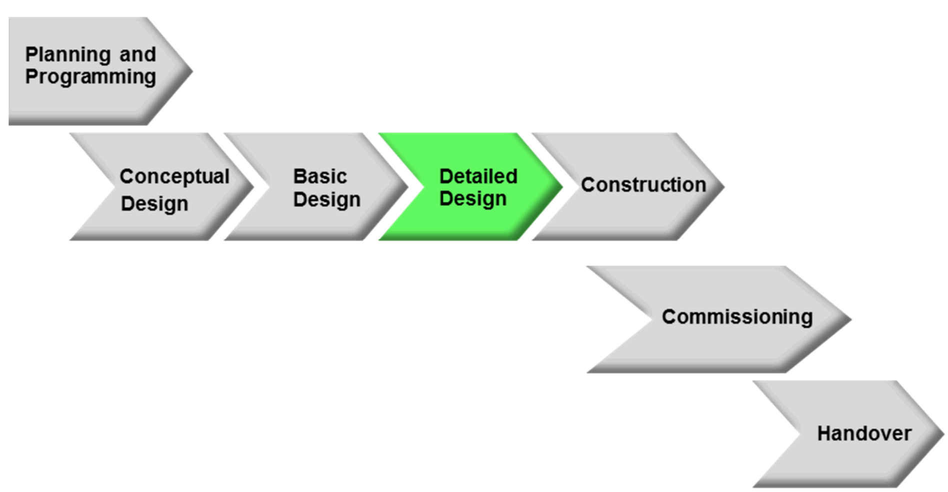
- ✓ Finalize (all) specific engineering drawings and specifications such as structural system, heating and cooling systems, security systems, lighting system, etc.
- ✓ Finalize construction techniques, selection of materials and decide which details that might benefit from physical testing, chemical exposure, mock up testing etc.
- ✓ Finalize heating, ventilation, and air conditioning (HVAC) equipment, duct, and piping requirements; dimensioning; and schematic HVAC layout
- ✓ Finalize mechanical, electrical, plumbing, and structural engineering calculations
- ✓ Finalize all design issues that affect the look of the building and the rooms, including windows, roof, interior finishes, interior/exterior colors, overhangs, roof pitch, etc.
- ✓ Finalize laboratory, laboratory support, and animal-holding equipment and identify any long lead items, export control regulations, import/export permits and develop a procurement plan for timely delivery; identify warranty and liability issues. Do the warranty start with delivery date or with installation and testing date.

- ✓ Finalize any code/regulation issues (Apply for authorities approval – it takes time and should be done soon enough to preserve the project time schedule.)
- ✓ Establish formal Biocontainment risk assessment for authorized approval (based on preliminary BSL risk assessment from planning phase)
- ✓ Establish preliminary procedures overview (list of SOPs)
- ✓ Complete outline specifications and compile a written list of criteria and requirements for materials and building methods
- ✓ Revise cost estimate (plus or minus 10%), considering probable labor and material requirements

The output of the basic design phase, the design development package, should be reviewed by the owner/client and if possible an assisting A&E firm before proceeding further with the project.

When considering complex projects, these would benefit from a third party (peer review) to verify general layout decisions, review the design drawings and capacity calculations, as well as the dimensions. Although the design team has been deeply involved, overall review by a third party may identify errors or issues in the design that could be very costly to correct once construction commences. Selection of a third party review team is extraordinary important, as these projects are special and unique. It must be a company that has a long and successful history in the field with similar projects. The cost of a third-party review is repaid many times over in saved construction change costs.

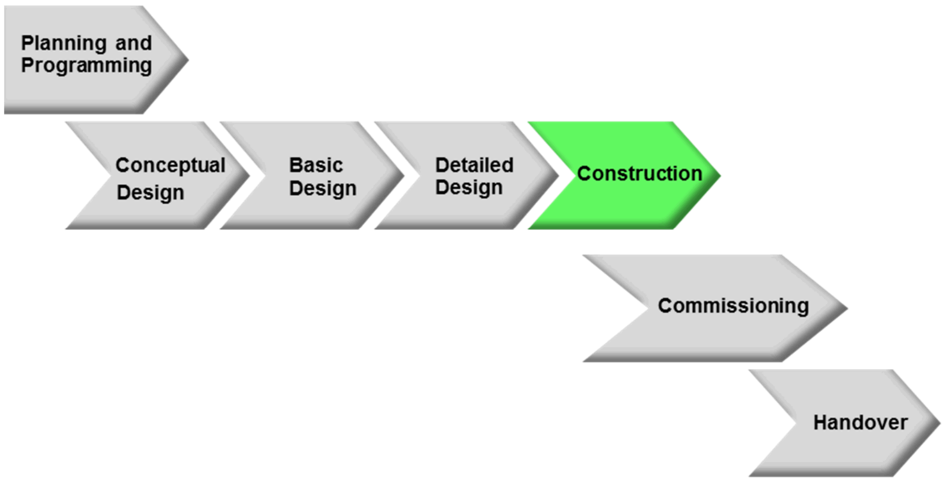
FINAL / DETAILED DESIGN



The detailed design phase consists of:

- ✓ Production of design documents
- ✓ Bidding process (tender phase)
- ✓ Contracting

CONSTRUCTION



The construction phase includes a number of different closely related and interdependent tasks:

- ✓ Construction/design documentation
- ✓ Bidding and negotiating
- ✓ Contracting
- ✓ Construction administration
  - Developing a schedule
  - Starting up
  - Managing changes
  - Reviewing processes
  - Testing, correcting, and obtaining final approval of completed work
  - Warranty verification

The construction and detailed design phases will partially overlap in most projects.
Based on approved design development documents, detailed construction drawings and written specifications are developed that describe in specific detail the construction work to be done. These are the documents upon which the construction contract will be based and which the contractor will use to build the facility.

If a building permit is required (which is almost always the case), at this stage all information is available for the application. However, as stated earlier, applying for approvals now might be too late for smooth and fast progress of the project. Earlier discussions or submissions of partially completed applications should have taken place between the stakeholders and the authorizing agencies.

Work in this phase typically includes the following:

- ✓ Prepare specific and detailed documents and construction drawings required to bid, apply for approval from fire, building and planning departments, build mockups and get the performance evaluation of these constructions approved and complete construction. The documents will include dimensioned floor plans; elevations; sections; details; engineering plans such as electrical, mechanical, structural, and/or civil engineering plans; landscape plans; energy use analysis; and written specifications that cover all materials, methods of construction, and construction contract requirements. Specifications should be closely coordinated with construction drawings. Highlight all impact assessments-identified topics and flag items that cannot or must not be changed or modified without a strict change procedure control and reapproval from the users and designers.
- ✓ Complete all coordination with consultants and contractors. Drawings and written specifications including quality control requirements and procedures are essential to avoid conflicts between the various trades during construction.
- ✓ Resolve any outstanding issues with regards to building, materials or codes/regulations. It is important to emphasize that issues should be minor at this point. Big changes at this point will have detrimental impacts on cost, schedule, and quality.

Before the bidding process is initiated, it is important to perform yet another thorough risk assessment of the whole project and decide on the best bidding process/strategy for this specific project.

This risk analysis should address the economic and timeline risks; weather impact on project progress, the minimum qualifications for acceptable contractors; size and business history of the contractors, availability of service and support organizations in the region, probability of quality failures according to compliance with codes, regulations, and guidelines applicable for the project; and work-related experience with local A&E companies/contractors. The owner/client should review this risk analysis and be involved in the final decision for the selected bidding process.

The economic model for the project must be communicated to the contractors before the bids are given. There are two basic strategies: “total cost of ownership” or “lowest cost during

building phase." The operation and maintenance costs play a big role in the future operation budget for such a facility and should be faced up front. An ideal bidding process will furthermore force potential contractors to specify what alternatives and technologies might be available for reducing costs and use this as yet a selection criteria for the project.
The project is put out in a tender, one or more contractor(s) are selected, and a construction contract is drawn up between the contractor(s) and the owner/client or the A&E, depending on the structure of the contract.

Work in this phase typically includes the following:

- ✓ Prepare the formal documents for bidding such as the Invitation to Bid, Instructions to Bidders, Bid Form, etc.
- ✓ Advertise bids and solicit contractors to bid on the project
- ✓ Coordinate and provide bid documents to bidders
- ✓ Check bidders' qualifications (references, insurance, experience, years in the field, successful projects of similar character, personnel, contact previous clients etc.)
- ✓ Provide additional information (in the form of addenda to the construction documents) as needed to bidders
- ✓ Meet with contractors and material suppliers and clarify any outstanding questions
- ✓ Receive bids
- ✓ Assist owner/client in negotiation and preparation of Owner/Contractor Agreement and other necessary formal documents
- ✓ Evaluate incoming bids – the A&E usually collects, compare and list the information and validates that the bids are in compliance with the project demands and tender specifications

There are many different types and models of contracts for the actual building phase of such a project, depending on the continent or region of the site. Local issues can include but are not limited to:

- ✓ How legal and union issues are normally addressed in the specific region
- ✓ The general building tradition
- ✓ How complex or simple the project is anticipated to be
- ✓ How much responsibility the contractor is comfortable in taking
- ✓ How much right the initial design team has in influencing the actual choice of contractors due to tender processes

More or less freedom of decision can be given to the building contractors in the contract, depending on the local issues listed above. The local nature of the contract will reflect how the official communication will occur between the different parties of the building project.

High-containment projects are highly complex and among the most difficult and challenging projects to build at all. History has shown repeatedly that these projects can end in disastrous conditions if issues are not addressed in mutual collaboration. Nevertheless, in some cases there are heavy restrictions on how communication can and may go on, as well as different communication cultures and traditions, depending on company attitude, culture, and continent.

Containment building projects today range from projects in which the owner/client is eliminated from participation early in the process, after providing input to the user brief and without approving the URS, to projects with the design team and expelled from the project and site somewhere between the conceptual design and the detailed design. In such cases, the contractor takes over. In other projects, no third-party commissioning team is involved; in yet-other projects, no document will be issued during the entire process from the earliest stage to handover without the owner/client's signature and approval. In other projects, the initial designers and a third-party commissioning agent together with the owner/client will perform the actual commissioning and validation testing and bring the facility into service together. This shows the difficulty of outlining typical communication lines in a building project, because there are no rigid rules; communication lines depend on the culture, the companies, and the region, among other factors.

Other factors can include:

- ✓ The model of the contract
- ✓ The skills of the owner/client
- ✓ Whether there is an independent advisor to perform some of the tasks for the owner/client
- ✓ Whether it is the contractor or the owner/client who assumes responsibility for the equipment purchase and installation

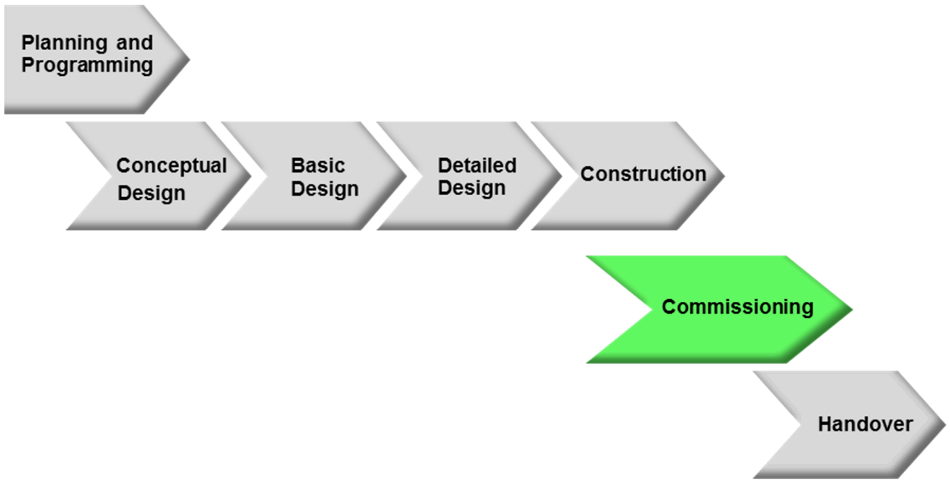
On-site (observation) supervision and thorough, as well as timely, submitting and processing of paperwork throughout construction is necessary to assure that communication flows smoothly, that high standards are maintained, and that the owner/client gets their construction money's worth.

Work in this phase typically includes the following:

- ✓ Establishing an overall supervision plan that specifies the level of supervision. This plan also describes the frequency of the supervision as well as specifying the critical elements that require the most attention. The plan should also describe how the supervision is documented (photo, reporting, video, physical testing/sampling, etc.) as well as the format for revisions, date/time stamping, initials, etc.

- ✓ Making periodic, announced and unannounced site visits (as defined in the supervision plan) while the project is under construction, observing construction for compliance of design intent, and engaging in dialogue with the contractors and subcontractors for clarifications of technical and non-technical questions
- ✓ Templates for Request for Information (RFI's), and average expected response time for clarification and answers
- ✓ Photographically documenting all issues of dispute
- ✓ Training the contractors and focusing on critical issues
- ✓ Conducting frequent, formal on-site meetings with contractors, suppliers, owner/client, etc.
- ✓ Distributing meeting notes describing decisions made, disputes resolved, and waste management, Environment, Health and Safety (EH&S) issues raised.
- ✓ Conducting quality inspections according to written plans for verification of the following:
  - Correct drawing revisions are present on site, and all previous revisions removed from site
  - Quality procedures are followed and sign off sheets are up to date
  - Building site is safe, tidy and clean
  - Equipment and installations are documented on a timely and ongoing basis
  - Other quality-related indicators
  - Accidents are tried prevented, PPE is worn according to regulations
- ✓ Administering changes with owner/client and contractor (there are *always* changes!)
- ✓ Clarifying drawings as required
- ✓ Completing additional drawings as required
- ✓ Verifying that actual installation is according to piping and instrument (PI) and/or other diagrams. If not, initiate corrective actions before other building/utility and equipment structures/installation will obstruct corrective actions.
- ✓ Verify that any construction detail that needs testing before being further embedded in the structure is quality tested according to the expectations and test plans
- ✓ Processing documents and paperwork for contractor's payment, changes, submittals from the contractor, change orders, etc. in a timely manner
- ✓ Participating in resolution should any disputes arise during construction or testing

TESTING / COMMISSIONING / VALIDATION / QUALIFICATION PHASE



While the commissioning and qualification/validation phase may be the most important phase, it is often neglected.

During the actual construction phase, it is imperative to initiate the commissioning and qualification/validation process as soon as feasible. Early attention to this process is intended to ensure that all equipment, installations, and construction meet the specifications and the performance intent at the end of the project.

For all installed equipment, the following should be determined:

- ✓ Which equipment should be tested before delivery to the site: factory acceptance test (FAT)?
- ✓ Which equipment should be tested or maybe even retested after actual installation: site acceptance test (SAT)?
- ✓ What overall performance tests are needed when all installations of equipment and utilities are finished?
- ✓ Which systems should go into simultaneous testing, to verify that all systems are able to function at the same time without interfering with performance of other equipment, data collection, etc.?

General emergency scenarios and power failure conditions identified in the risk assessments during the programming and detailed design phase must be simulated and tested thoroughly. All equipment and utility systems must be tested under worst conditions. For power failure, scenarios of long and short durations must be verified, as some equipment might react differently depending on the length of power failure.

Failure mode testing verifies that all equipment and utilities will be shut down in a controlled manner or kept running on emergency power/uninterruptible power supply (UPS). This kind of testing also determines whether equipment/utilities that *did* shut down during power failure will restart in a safe manner after power is re-established.

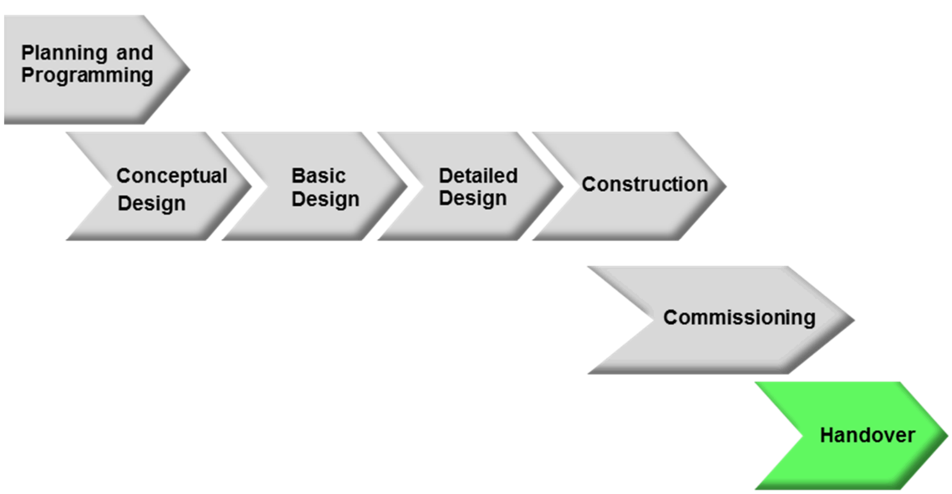
This phase validates the risk management strategies developed from the risk assessments conducted in previous phases and determines whether detailed design decisions are meeting the actual intended goal. If any inadequacies are identified, engineering controls may need to be redesigned or addressed by other means (e.g., extra SOPs and extended training of the staff).

This phase also provides valuable data for the system performance for t=0, the start-up of the facility. Whenever preventive maintenance and subsequent testing will be performed in the future, comparison to these initial test values will give the owner/client valuable insight in how the condition of the facility compares to the initial condition.

Involving the users in this phase is often valuable, as testing all the equipment and provoking failure modes will provide users with valuable insight into the systems and training in both shutdown and startup procedures. In addition, technicians will surely find more creative ways to run the systems and introduce errors than even the most inventive design engineers would ever envision.

Including the staff and technical department in testing provides a shortcut to the handover, in addition to training and insight. Such involvement often results in a more extensive testing program that will be closely aligned with how the facility will actually be run when taken into service.

HANDOVER



Before handover of the facility, a full documentation package describing all details for the project must be delivered to the owner/client.

This package will consist of:

- ✓ Drawings, floor plans, and other building-related documentation
- ✓ PI diagrams with TAG (identity) -numbered critical components and descriptions
- ✓ Electrical diagrams
- ✓ Installation drawings and descriptions
- ✓ PID values for relevant equipment (proportional, integral and derivative)
- ✓ Calibration reports
- ✓ Risk assessments (biosafety and biosecurity) and the following design rationales that needs to be formally written and kept for future reference
- ✓ Technical specifications including documentation for eventual approvals from authorities
- ✓ Functional descriptions, user manuals
- ✓ Signed and approved test reports from design qualification (DQ), FAT ,SAT, and concluding performance (PQ) testing
- ✓ Software documentation, backup of programs, and explanation
- ✓ List of alarms
- ✓ Lists and description of spare parts, recommended frequency of replacement, with identification number and supplier
- ✓ CE marking if applicable (Conformité Européne Directive 93/68/EEC)
- ✓ Procedures for planned and emergency shutdown and startup
- ✓ Maintenance schedules and procedures
- ✓ Documentation of training of the staff

Training must be scheduled with the owner/client and ideally would be timed to occur just before the staff puts the equipment and the facility into use. If training occurs too early, important details from the training will have been forgotten before the skills can be practiced. If it is scheduled too late, the staff might already have put equipment and systems into use and handled the equipment in an inappropriate way due to lack of knowledge. Training should be performed on site by the contractor or equipment supplier and should be in a language with which the staff is comfortable. The language of the written documentation of the systems and equipment must be negotiated with the owner/client early in the project phase.
When all testing, calibration, adjustments, and training have been completed, the owner/client will be responsible for the facility. Handover activities include a walk-through of the facility, to be performed by the A&E, the commissioning team, and the owner/client. At this time, any

errors or missing parts should be identified and a plan defined for how and when these issues will be addressed and completed.

Even after a thorough walk-through and error identification and resolution, new issues are likely to arise in the first couple of years. Such issues should be covered under a guarantee or warranty provided by the contractors and suppliers, which may need to be defined in the initial contract with suppliers and contractors. The owner/client must collect evidence of the issues and, if urgent, contact the contractor immediately. If the issues are not urgent, the owner/client will present the collected information and evidence to the contractor at a formal meeting one year after handover before the warranty runs out. The contractor and the owner/client will cooperatively identify issues that should be fixed at the contractors expense and agree on a workable timeline. The contract can be extended to specify annual meetings to address facility issues for five years; for some projects even longer period of time may be specified. Timely and adequate training of the staff is mandatory; equipment broken by mistreatment or misuse will not be covered under the warranty.

Containment projects are complex and very challenging, but they are also extremely rewarding and fun to build. Containment projects require every one of the stakeholders to push his or her capabilities to the limit; full confidence, openness, and constructive collaboration, effort, and intense work are also required of all stakeholders. These projects are taxing, but when a containment facility building project is successful, it is also one of the most fulfilling projects for participants. It can even at times be considered to be fun!

OPERATION AND PERSONNEL MANAGEMENT ASPECTS

When the whole design, building and commissioning process is over, and the facility is taken into use – then the next challenge arises.

That is the human aspect and the management challenges of bringing the staff into the new facility.

Those managers that assumed the hard part was getting it right from a design and building perspective will often at this point fully understand what “change management” really means and what a challenge it actually is to bring people out of old settings and into new ones.

If the staff has had nothing to say during the whole programming and design process, it is most often a big step for these people to suddenly create a feeling of ownership and enthusiasm. The closer the day for moving into the new settings, the more complaints and concerns will normally surface.

On the other hand, if some of the staff or a couple of key persons that are considered the leaders and opinion makers amongst the personnel has been engaged during the design and commissioning phase of the facility, the easier it will be to bring the staff in a successful way into the new building.

Most modern facilities today will end up being more complex and advanced than the old laboratory. Almost all equipment today comes with associated software and is more electronically based than previous models. In the old days a decent mechanical skillset could get most equipment up running again, today it is not so easy. It is not any different than the same development that has happened with cars. Today it takes a mechanic with a computer to diagnose and troubleshoot an engine that will not start, in the old days much more could be fixed by the owner.

This means that a close relationship and mutual respect between the users of the facility and the engineering department or offsite service technicians needs to develop. Modern containment facilities cannot run safely without a preventive maintenance program, keeping all equipment in shape and in a safe condition. Top management often oversee their own role in facilitating the transfer of the staff into new settings, and forget their part in developing new work relationships between departments, that earlier did not have to depend so much on collaboration and planning around each other's schedules.

If these types of matter are not addressed adequately in a timely manner, the staff will not likely be willing to give it that extra effort and energy it needs to move the tasks successfully from the old facility to the new one.

FUTURE OPERATION AND EQUIPMENT MAINTENANCE

Depending on how the end deliverables in the contract with the contractor has been set up, the maintenance of the facility will either be a well defined task or - for the first couple of years - a scary experience

In these types of facilities the documentation of the equipment and systems is more important than many first time build owners/clients ever envision.

If the equipment and utility systems have been delivered with documentation consisting of as-built drawings, lists of spare parts, exchange frequency, part numbers, suppliers contact details, procurement lead times, service contracts etc, it will be a fairly well defined task for the maintenance and engineering department at the facility to plan and perform the yearly maintenance and replace of parts that will get worn out.

However, many projects are left hanging with a thin documentation package, and most teams are so exhausted at the end of the project, that few have the energy and stamina to continue to review and request the documentation that is missing from the contractor. Experienced contractors that have built these types of facilities before will know what is expected, and request the information and assemble the file. Contractors new to the containment field will get a surprise, and seldom have allocated resources and time enough for this part.

Again it cannot be emphasized enough. An owner/client that has not been engaged in these types of projects before, are dependent on architects and engineering companies, contractors, suppliers and consultants that have been in the field for a number of years, and been successful, who understands the tasks, the requirements and the consequences if not fulfilled. There is so much that is “not said, not written but taken for granted it is understood” in the high containment facility field. Your project should not be a part of the learning curve of an eager contractor that thinks it would be great to do this as well.
If local expertise is not available in the region, at least an international sister company that do have this expertise should be added to the team and have decide on the final recommendations and oversight.