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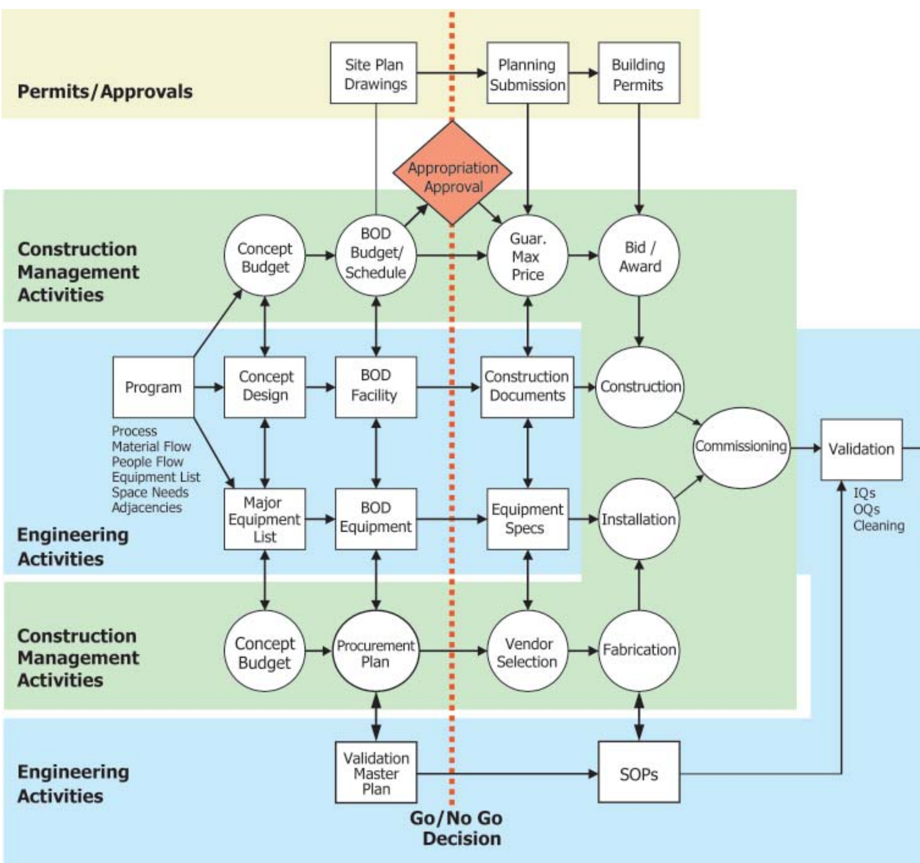
Make the Project Process Work for You — Steven DeRochi, AIA

How many times have the most obvious things caused you to scramble to meet your project goals? Following a clear project plan can be your best defense against these missteps. But every project has a whole series of sequential activities that are proceeding in parallel for various reasons.

There is no mystery as to how an ideal project process is organized. Most pharma companies follow some variation of the roadmap below. Understanding the dynamics of the diagram and orchestrating the work to satisfy it – that is the key.

Some strategies in playing the game:



Keep your wiggle room, i.e. contingency money in the estimate. Every project starts off with fuzzy information; at each succeeding stage the project gets more definitive. In the last stage, it is actually built. Make sure that you have a clear understanding of the assumptions you are starting with (like plant utilities are adequate), so that when they start to drift (200' to pick up plant steam) you have enough contingency to cover it. Or when it blows up (you need a new boiler), you have the basis to approach the user for more money.

Do your homework. The first step in any project is developing the program. The more you know about the project (and the user signs off on), the less fuzz there is. If you are dealing with a renovation, part of your initial data base is the existing building. Make sure your designers look into all the crannies. *(continued on page 3)*

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RVSA's Cogeneration Plant

PS&S is involved in the design, permitting and construction of a major expansion to the Rahway Valley Sewerage Authority (RVSA) wastewater treatment plant. The expansion plans for the 50 mgd plant, based on a feasibility study performed by PS&S, incorporate cogeneration to reduce energy and biosolids disposal costs, lower overall air emissions and improve electrical power reliability.

The cogeneration facility will be capable of producing 6.1 MW of prime power, meeting the full electric consumption needs of the proposed 105 mgd plant. Four 1.51 MW gas engine generators will operate on natural or digester gas, a biosolids processing by product. Electricity will be generated at 13.2 kV to tie directly to the existing switchgear at the main site substation.

Exhaust heat from the engines will be utilized to support drying of up to 116 tons of dewatered biosolids. Thermal energy from the engine jacket water will be utilized for plant and digester heating.

The new cogeneration plant will replace RVSA's high-emission fuel oil/gas diesel aeration blower-drives with motors to reduce maintenance and take credit for emission off-sets in facility air permitting. Annual savings of as much as $700K/year are projected.

Utilization of onsite generated digester gas minimizes dependence on utility natural gas. Self-generation of electric power and reduction in biosolids volume reduces cost of offsite disposal. The plant will be financed through tax-free, low interest municipal bonds.

MULTI-PURPOSE PILOT PLANT DESIGN — David Greene, PE

INTRODUCTION

Today's pilot plants need the flexibility to respond quickly to changing market opportunities while simultaneously achieving the quality needs of customers and regulatory agencies.

A multi-purpose plant should:

- operate over a range of rates / conditions
- handle a wide range of feeds and products
- provide for change in operational sequence
- be easy to clean
- include a good HVAC system
- comply with current and future cGMPs
- segregate operations to allow parallel processing
- include a flexible and reliable control system
- use flexible utility and environmental systems
- provide for a range of product activity
- have validatable systems and procedures

The pilot plant can be configured in two ways: systems dedicated to particular intermediates or decoupled with separate unit operations to allow individual reactor combinations to be fed to a range of centrifugation, filtration, crystallization and drying systems.

Key design requirements for a multipurpose pilot facility:

EQUIPMENT SELECTION

Reactor volume is the major variable as all associated equipment including separators, dryers, vacuum systems, and off gas treatment are sized based on the reactor volume and the range of operating conditions.

Glass-lined reactors are used to accommodate a range of corrosive materials but a mix of materials which includes stainless steel and/or hastelloy can be included to improve heat transfer. A range of reactor sizes is also useful to optimize equipment utilization and yield. Variable speed drives and split jackets will improve flexibility. Typical reactor parameters are capacities of 100-5000 liters, operating conditions of -80 to 200°C, 15 mm Hg to 100 psig, pH from 1.5-13.

As some reactor systems require special safety considerations, it may be appropriate to dedicate one or more reaction systems to a specific type of reaction such as hydrogenation or phosgenation.

A mix of stainless and hastelloy Nutsche filters provides general purpose separation. These filters can be provided with jackets and vacuum pumps for improved dewatering and initial cake drying. Similarly one or more centrifuges can be included with an appropriate dryer to provide an alternative recovery method.

Solvent recovery and disposal must address the requisite level of purity and the effect of recycle on the process particularly if a common solvent is used for multiple products. Typically, a batch distillation system is provided but advanced techniques may be appropriate for a multipurpose facility.

A CIP system should be provided to ensure reproducibility of cleaning and minimize downtime.

Definition of Modular Requirements

- maximum number and type of process inputs to each reactor
- number of feed systems
- space requirements
- inter-group connectivitiy requirements

MODULARITY

In order to use the modular concept, the controlling design scenario for each item and system must be identified.

The intent is to make each functionally similar system identical to minimize capital and operating costs and improve operational quality.

Advantages of Modular Design

- any unit can handle any process requirement
- standardized connectivity
- common automation and control operations
- minimum design variation
- layout

CONNECTIVITY

In dedicated plants, product changes often require extensive pipe routing changes as unit operation types or sequences are changed. Adding, removing, or rebuilding lines is costly and time-consuming. The preferred method is to provide a transfer system to minimize downtime when making changes.

SOLIDS HANDLING

Organic synthesis processes generally charge bulk solids to reactors and commonly produce dry solid intermediates or products.

Solids Handling Considerations

- quarantine areas (raw materials and products)
- levels of protection: laminar flow booths, glove boxes, HEPA filtration, dedicated HVAC systems, barrier technology
- charging size and method
- finishing needs (milling/grinding)
- materials flow arrangement

Intermediate Bulk Containers (IBCs) are generally used to charge reactor systems to protect operators and the environment from toxic and active ingredients and products.

It's important to identify solids handling requirements early in the project since there may be a significant impact on the layout and space requirements. Although provision may be made for isolation and reprocessing of wet intermediates, it's better to select process equipment to avoid wet cake in IBCs.

IBC Advantages

- minimizes operator involvement
- minimizes area contamination
- active or toxic material can be weighed, blended, milled, etc. in a contained area
- direct addition of precise quantity of material at the appropriate time and rate
- quick charge of materials

IBC System Components

- dispensary equipment to fill the IBCs
- LFBs for small container charging
- dedicated gravity-fed reactor charge stations
- solids charge stations
- space for movement / storage of IBCs
- IBC cleaning
- IBC with sealable inlets and outlets
- packout equipment

CONTAINMENT

Closed systems are preferred to relying on SOPs or personnel protection equipment (PPE). Various levels of containment, generally referred to as Classes 1-4, are established based on the toxicity or pharmacology of the expected chemicals, generally referred to as Operator Exposure Level (OEL). A multipurpose plant must anticipate the future requirements as it is prohibitively expensive to retrofit for higher levels of containment.

Isolation is used to protect personnel and the environment from toxic and/or active chemicals while barriers are used to protect the process from the environment. As the former is best done with negative pressure and the latter with positive pressure, a combination of isolators and air locks may be used to contain potent chemicals.

Containment Techniques

- dedicated IBCs
- barrier/isolation
- laminar/downflow booths
- closed equipment
- special transfer devices
- pressure differential
- automated cleaning and sterilization

PROCESS CONTROL AND AUTOMATION

Ideally a multi-purpose facility would employ a fully integrated process control system based on structured, flexible software architecture with underlying systems for unit operation control, equipment identification and recipe information. The use of modular design and control provides identical instrumentation and control for similar systems to allow generic manufacture and transfer of intermediates and products.

GOOD MANUFACTURING PRACTICE

During the initial analysis of process requirements, it will be necessary to define the critical steps and parameters and make provision in the design for the appropriate controls to ensure a repeatable, validatable process. In a multipurpose facility, the critical parameters may be unique for each product and the design must provide the appropriate instrumentation and controls to allow for the requisite flexibility. The design effort must be based on knowledge of the initial and anticipated operation of the facility. While addressing personnel, material and process flows, the plan must also accommodate personnel safety, containment, and handling of raw materials, products and wastes and environmental requirements.

HEATING AND COOLING UNITS

The critical parameters for heating and cooling systems are the number of temperature levels required to satisfy the process requirements and the range of temperature needed. With a knowledge of the available fluids, the designer can select an appropriate fluid and heating/cooling system preferably using a single fluid.

The choice of system affects installed and operating costs and the degree of reaction control. Process design requirements for a multipurpose heating/cooling system include temperature range, control requirements, range of instantaneous heat transfer requirements.

From a process viewpoint, the single fluid system is desirable because it provides the best temperature control. Central systems are the least expensive but may not be suitable if many different levels of temperature are required.

ENVIRONMENTAL CONTROL

Multipurpose plants utilize the same techniques as dedicated plants for the removal of toxic components from vent streams and chemicals from liquid wastes. However since any chemical component could end up in any item, all items should have access to each disposal route.

The approach is to identify, early in the design, all waste categories and provide segregated manifold lines for each accessible by all potential users.

PLANT LAYOUT

A good plant layout is a compromise between operating needs and capital cost. The layout must consider containment, segregation, personnel, waste, process and material flow requirements along with the need for maintenance and operational accessibility.

A typical multipurpose plant includes one or two reactor levels. When there is no overriding process reason for gravity transfer between reactor systems, a single reactor level improves modularity, piping design, solids handling and batch distillation. Typically 3-4 levels are used for recovery and isolation. The top level might be used for crystallization; intermediate floor for filtration or centrifugation and a lower floor for drying. The drying floor might also accommodate packout or a separate level could be employed for that purpose.

IBC storage, dispensing, and movement can significantly affect the layout. The dispensing systems could be located on the upper level proximate to the charge systems; alternatively, the dispensing could be located on the ground floor and an elevator(s) used to move IBCs between the dispensing areas, charge systems, storage, and cleaning areas.

cGMP Design Considerations

- dedicated solids charge station for each reactor located above the reactor
- linear equipment arrangements adjacent to pipe manifold headers
- maximum use of gravity transfer
- clean room and corridor requirements
- space for anticipated future requirements
- milling/grinding philosophy
- height limitations
- material, personnel, waste and process flow patterns
- utility requirements
- segregaed dispensing, charging, milling, and packout of solids
- integration or separation of reaction and recovery and systems ?
- manifold locations for changeover conveniently located
- access for operations, maintenance and cleaning
- space for portable process equipment
- identical arrangements of similar modules

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MAKE THE PROJECT PROCESS WORK FOR YOU *-from page 1*

Maintain your balance. At the program stage, make sure that you have a budget and a schedule that work (or at least a plausible strategy to make them work). In every succeeding stage, make sure that your design satisfies the program, the budget and the schedule. The program gets more detail, the schedule gets more tasks, the budget more line items. Make sure that each element keeps up and reflects the others. Or proceed at your peril.

Always, always have a fall-back plan. Murphy's Law is immutable and everlasting. But there is always a way out. When making a decision, understand your options if it doesn't pan out. Some options provide much better exit doors than others.

Allow plenty of time for the things that you can't control. Like the Town. Like your validation team. Like your management team. Give them lots of warning for when you need things. Make them your friends – ask them what they need to do their part. Don't surprise them! Get the Validation Master Plan started as soon as you have enough for them to think about. Build the time into the schedule for the appropriation request to work its way through the system.

Expedite! You are the only one on the team with the whole picture. Communicate. Make sure you understand who needs what, if they are getting it, what needs to be done to shake it loose if they aren't. Most people actually want to do the right thing; help them help you.

Congratulations! You have just completed Project Management 101. ■

Point of View

While home recently nursing a case of the flu, I began to reflect on some of the predictions I had heard as a kid growing up in the late 1950s. It was believed that in 50 years, right about now, coincidentally, science would have found a way to eradicate all diseases, robots would do most of our work, commercial space travel would be a reality, and all we humans would have to worry about was how to fill up all the leisure time we would have. I remember wondering what I would do with all that free time, how many books I could read and movies I could watch and soccer games I could play before getting bored. Well, now that those 50 years have passed, I have discovered that I needn't have been concerned. In fact, I now have the opposite problem, as most of you do, of not having enough time to get everything done plus get eight hours of sleep.

As far as disease eradication, from the biotech and vaccines facilities we are designing, engineering, and validating, I can see that there is no shortage of "bugs", both viral and bacterial, still keeping our scientists busy looking for cures. In the past five years, PS&S has designed and validated traditional vaccine facilities such as small pox vaccine for the US government's anti-terrorism program and hi-tech therapeutic cancer vaccines. We are currently engaged in designing recombinant BCG vaccine facilities to fight the resurgence of tuberculosis. We have also done feasibility studies and created a blueprint for a gobal AIDS vaccine manufacturing faciltiy that awaits the development of the target vaccine.

The "World Health Organization" estimates that TB kills two million people each year, and I was glad to hear that pharmaceutical companies are now entering that fight. We know that AIDS kills many more people, especially in the Third World, and each day scientists are racing to develop new vaccines, which gets us closer to new hopes.

Thinking back to the predictions, I find that things didn't work out so badly after all. Too much leisure time is not good for the soul, and what is life without a sense of purpose, anyway? Besides, I think a Caribbean vacation still beats space travel; in fact, I am almost sure of it.

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