PRESENT SCENARIO:
The globalization and open market policies have proved to be a boon for the industries, but also have generated the need for globally acceptable manufacturing facilities.

There are many flourishing manufacturing facilities, but not all are in compliance with the various regulatory standards.

NEED FOR A FACILITY:
Rapid change in manufacturing technology & various regulatory compliances to upgrade for better solution in line with cGMP.

With globalization, the need for a compliant facility has become a statutory necessity.
If you have decided to build a new factory ..... or to revamp an existing one .... ...be aware that planning is not easy and that it is not a smooth way...

PARTICIPANTS TO THE PLANNING PROCESS

- Forecasts for x years
- Objectives
- Budget
- Company internal approvals
- Technology
- Logistics
- Building services
- Building technology
- Approvals (pharmaceutical)
- Approvals (non-pharmaceutical)
- Planning
- Execution
- Internal
- Planner
- Authorities
PLANNING TEAM(S)

Represented works for a pharmaceutical plant:
- up to 80 different works
- more than 15 engineering specialties
- client representatives

Site / building prep + structure
Roof + facade
Building services
Interior + finishing works
Process related systems, Logistics + Warehousing
Pharmacists, Architects, Engineers, Specialists
Client representatives

SCHEDULE EXAMPLE
NORMS, REGULATIONS AND REQUIREMENTS

General laws + regulations

Pharmaceutical regulations, EU, FDA, PIC/S, WHO, requirements of pharmacy inspectors, product registration...

Labour and environmental requirements...

Norms
ISO, ATEX, etc...

Specific guidelines, (Biosafety, Fed Std, OSHA)
for conception, planning, operation...

Company standards, planning conditions (quantities, technologies, products, deadlines, budget...)

PLANNING STEPS

Process / Equipment
GMP and Hygiene Zoning
Quantitative data
Layout

Feasibility
Concept

Basic Design

Detail Design

Execution

Complete detailing for all disciplines
Layouts 1:20, 1:50
Tendering

Refining of elements
Calculations
Functional tendering
Layouts 1:100
According to the German Fee Schedule for Architects and Engineers HOAI 51 there are nine phases of work. The following work will be provided, either based on the HOAI or freely, during completion of your projects (excerpt of work):

**Identification of Basic Requirements and Draft Planning (HOAI LP 1-3)**
- Production of requirements profile/specification
- Concept: Audio / video / signage / controls / event technology
- Layout design
- Operational overview with alternatives
- Definition of interfaces to other contractors and trades
- Cost calculations

**Execution and Specification Planning (HOAI LP 5-7)**
- Erection and installation plans
- Cable planning
- Block diagrams
- Scheduling
- Detailed cost proposal
- Production of specification documents / bill of quantities
- Production of qualified tender list
- Receipt and evaluation of quotations
- Tender negotiations
- Assessment and recommendation of tenderers / price list

**Site Supervision (HOAI LP 8-9)**
- Site training
- Preliminary trade work (supervision and execution thereof)
- Supervision of commissioning
- Coordination and supervision of installation work
- Checking for compliance with the bill of quantities
- Technical analysis of documents
- Specialist technical partial and final handover

**PLANNING MODELS**

**CONVENTIONAL MODEL**

- Feasibility Concept
- Basic Design
- Detail Design
- Execution

**IMPROVED MODEL**

- Conceptual design
- Basic Design
- Detail Design
- Execution
FEASIBILITY VERSUS CONCEPTUAL STUDY

Feasibility

- Static
- Dominated by Economical Criteria
- No Project Alternatives:
- Yes / No only
- No Influence on Schedule of Subsequent Phases

Conceptual Study

- Includes the Feasibility Study
- Dynamic / prospective
- Dominated by Technical Criteria
- Project Alternatives are generated
- User oriented
- Choices possible
  - Costs
  - Technology
  - Organisation
- Reduces Time spent on subsequent Phases, while increasing their Precision

PLANNING MODELS

Strong Conceptual design → Basic Design → Detail Design → Execution

It pays to invest into a strong conceptual design

- Low initial costs
- Early clarification of main issues
- Powerful decision tool
- Possibility to develop alternatives
- “Freewheeling”
PLANNING SEQUENCE AND ITERATION PROBLEMS

RELATIVE COSTS OF THE DIFFERENT PHASES

The cheapest and most promising Phase is the Conceptual Phase!
POSSIBILITIES OF COST MINIMISATION

The best and cheapest chance to minimise cost of investment and operation is in Phase 1!

Conceptual Design
- Factory size
- Factory organization
- Technology
- GMP

Basic Design
- Small teams
- Brainstorming
- Alternatives
- New ideas

Detail Engineering

Execution

DETERMINATION OF COSTS
in relation to the planning stage

The better the concept, the higher the precision

Cost estimation

Cost calculation

Tender documents
Offers

Final quotations

PRICE PAID
PRECISION OF COSTS
in relation to the planning stage

± 30%
Cost estimation

Feasibility
Conceptual design

± 20%
Cost calculation

Basic Design

± 10%
Tender documents
Offers

Detail Design

± 5%
Final Quotations

Execution
Supervision
Documentation

The better the concept,
the higher the precision

DETERMINATION OF COSTS
in relation to the planning system

Feasibility
Conceptual design

Basic design

Detail design

Execution
Supervision
Documentation

Turnkey price:
poor control

General planner:
good control
The Purpose of the Conceptual Design is to arrive to

- Layout
- General Factory Organisation Procedures
- Hygiene Concept
- Technology Concept
- Air Handling and Utilities Concepts

which can be successfully presented to Authorities for a Pre-Approval Design Review

and to get a high degree of safety about

- Investments
- Schedule

TARGETS OF PHARMACEUTICAL FACTORY PLANNING

- Planning of a production plant
  - future oriented
  - flexible
  - economical in investments and operating costs
  - GMP conform
  - conform to local / international regulations

- High motivation of staff by high quality of working place
- Efficient planning
- Adequate quality standard (value for money)
- Architecture compatible with local surroundings
**HOW TO REACH A GOOD CONCEPTUAL DESIGN RESULT?**

<table>
<thead>
<tr>
<th>Right team</th>
<th>Good method</th>
<th>Right team</th>
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</thead>
<tbody>
<tr>
<td>Good method</td>
<td>Discipline</td>
<td>Good method</td>
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<td>Discipline</td>
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**PEOPLE AND PLANNING**

**A Quote:**

“You do not really understand something unless you can explain it to your grandmother.”

*Albert Einstein*

The idea is to work intensively with a small group of people, possibly detached from their daily chores.

These people must have the necessary know-how (or back-ups) and the power of decision.
JUDGEMENT ERRORS

Role of participants: To plan AND to decide

Large Organisations
Individuals
Concept Team

Number of Participants

100%
90%
80%
70%
60%
50%
40%
30%
20%
10%

PLANNING METHODS

By Experimenting and Innovating
By Adding Individual Functions
By Cloning Existing Units
By Systematic Planning
By Turnkey Contracting

There are many design methods

Individuals

OPTIMAL PLANNING METHOD

- Masterplan
- General organisation factory
- Departments
- Functional groups
- Equipment, single units

PLANNING FROM INSIDE TO OUTSIDE

PLANNING FROM MACRO TO MICRO

PLANNING FROM IDEAL TO REAL

NEED FOR FOCUSING

- Economy of scale
- Efficiency / Best practice
- Flexibility
- Performance
- Organisation

Analysis of
- Product range
- Process
- Technologies
- Organisation

Conceptional design
- Make or buy
- Specialisation
- Capacity increase
- Technology
- Standardisation
- Regulatory aspects
- Results versus costs

- Requirements
- Vision of client
PLANNING METHOD
DEVELOPMENT OF IDEAL ORGANISATION

Information
- Analysis process
- Identification key problems
- Analysis Material / Information flow
- Identification necessary infrastructure

Strategy
- Plant strategy + Process architecture
- Evaluation + Selection
- Adaptation Process, machinery + equipment

Resulting Organisation
- Verification process flow, material flow
- Other requirements, constraints, etc.
- Definition Modules Functional units Vertical Horizontal
- Definition of constraints, etc.

Analysis organisation
- Analysis of products and production volumes
- Analysis machinery / equipment
- Analysis space situation

PLANNING METHOD
RATIONALISATION, INNOVATION AND OPTIMISATION

Morphological Analysis + Search for Solutions
- GMP-Concept
- Technological Alternatives
- Degree of Automation
- Investment / Budget
- Forecasts, Quantities, Product Mix
- Batch Sizes
- Galenical Properties

Capacity and Rationalisation Analysis
- GMP-Concept
- Degree of Automation
- Batch Sizes
- Foreseen Equipment
- Shifts ?
- Product Seasonality
- Campaign Sizes
- Cleaning + Change-over Times

Dimension Machines (Type/Quantity)
**PLANNING PROCEDURE: CONCEPTUAL DESIGN**

- **Development of the masterplan for the design on the green field**
- **Development of the integration of the layout into an existing building structure**

**PLANNING PROCEDURE: CONCEPTUAL DESIGN FORECASTS**

Product lists, quantities

Sorting by galenical forms

Sorting by types ("conventional", toxic, hormones, beta-lactames, etc.)

Strategy for marginal products (quantities, types, galenical forms):
  Make or buy
**ABC ANALYSIS**

Example

- Number of products: 50
- Total number of units: 100,000,000
- Average weight unit (g): 0.5

**SELECTION OF TECHNOLOGY AND EQUIPMENT**

**EXAMPLES OF SELECTION FACTORS**

- Vision of client
- Properties of products to be processed
- Output requirements
- Degree of automation, sophistication
- Supplier: price, service and serviceability
- Cleanability and maintenance needs
- Space constraints
- Previous experience, available equipment (standardization)
- GMP issues
- Safety of operator
SELECTION OF TECHNOLOGY AND EQUIPMENT

• Vision of client:
  size, degree of sophistication, automated guided vehicles, architecture, budget, future-oriented or not
• Properties of products to be processed
• Output requirements
• Degree of automation, sophistication
• Supplier: price, service and serviceability
• Cleanability and maintenance needs
• Space constraints
• Previous experience, available equipment (standardization)
• GMP issues
• Safety of operator

SELECTION OF TECHNOLOGY AND EQUIPMENT

• Vision of client
• Properties of products to be processed:
  eg granulation properties: is direct compression possible or dry granulation?
• Output requirements
• Degree of automation, sophistication
• Supplier: price, service and serviceability
• Cleanability and maintenance needs
• Space constraints
• Previous experience, available equipment (standardization)
• GMP issues
• Safety of operator
SELECTION OF TECHNOLOGY AND EQUIPMENT

• Vision of client
• Properties of products to be processed:
  type of granulation, aseptic processing or terminal sterilization, ampoules or syringes
• Output requirements
• Degree of automation, sophistication
• Supplier: price, service and serviceability
• Cleanability and maintenance needs
• Space constraints
• Previous experience, available equipment (standardization)
• GMP issues

• Vision of client
• Properties of products to be processed
• Output requirements
  High capacity / one shift, low capacity / 2 or 3 shifts
• Degree of automation, sophistication
• Supplier: price, service and serviceability
• Cleanability and maintenance needs
• Space constraints
• Previous experience, available equipment (standardization)
• GMP issues
• Safety of operator
SELECTION OF TECHNOLOGY AND EQUIPMENT

• Vision of client
• Properties of products to be processed
• Output requirements
• Degree of automation, sophistication
  fully automated preparation of solutions, with CIP/SIP, equipment for solids with CIP capability, cartoning, palettisation, etc.
• Supplier: price, service and serviceability
• Cleanability and maintenance needs
• Space constraints
• Previous experience, available equipment (standardization)
• GMP issues
• Safety of operator
SELECTION OF TECHNOLOGY AND EQUIPMENT

- Vision of client
- Properties of products to be processed
- Output requirements
- Degree of automation, sophistication
- Supplier: price, service and serviceability
- Cleanability and maintenance needs
- Space constraints
  Can influence the type or the supplier: eg difference in size between FBG and “one-pot” system
- Previous experience, available equipment (standardization)
- GMP issues
- Safety of operator
SELECTION OF TECHNOLOGY AND EQUIPMENT

- Vision of client
- Properties of products to be processed
- Output requirements
- Degree of automation, sophistication
- Supplier: price, service and serviceability
- Cleanability and maintenance needs
- Space constraints
- Previous experience, available equipment (standardization)
- GMP issues
  - Aseptic processing problems: automated loading of freeze-dryer, increased automation
- Safety of operator

In most cases, several factors will play a role simultaneously
SELECTION OF TECHNOLOGY AND EQUIPMENT
MORPHOLOGICAL ANALYSIS

PROCESS ALTERNATIVES

PLANNING METHOD
PROCESS AND ORGANIZATION FLOW CHARTS

Whereas a process flow chart reflects the process only, an organization flow chart includes the process, its organization as well as additional elements such as quantities, personnel needs, hygiene zoning, equipment and inter-relationships within the production or between production and related functions.

The process flowchart must be transformed into an organisational flow chart

Organization flow charts exist at different levels, micro- and macro:
   Micro: within a department
   Macro: within a production unit/plant
PLANNING METHOD
FLOWS PERSONNEL AND MATERIALS

Selection of alternative important, later changes practically impossible

LOGISTICS

Goods IN handling
- Cleaning
- Administration
- Sampling
- Palletisation
- Etc

Storage activities
- Main storage
- Special storages

Goods OUT handling
- Picking
- Commissioning
- Administration
- Etc

Production

Exterior
Clients
Logistic centre
LOGISTICS

Raw material
Primary packaging material
Secondary packaging material
Finished products

Receiving area
Preparation area for raw and primary packaging material
Shipping
Production area
Marshalling
Bulk store

Warehouse Pharma

Sampling Booth
Storage capacity:
pallet places

Sampling
Quarantine separation
Change of pallets to/from production
Procedures in material air locks

« GOOD GMP »

- Minimized risk of contamination / cross-contamination
- Clear material flows (uni-directional whenever possible)
- Clear personnel flows (uni-directional whenever possible)
- Unambiguous definition of GMP zones
- Separation clean – dirty (washing areas)

Overkill
Cost issues
Nice to have
GMP is not an attribute, no black and white attitudes
A good pharmaceutical factory is a factory that is:

- Pharmaceutically approved (qualification / validation)
- Economical to operate and maintain
- Flexible and adaptable quantity-wise and for new technologies

To design such an excellent pharmaceutical plant, an integrated, multi-disciplinary and experienced team is required. The objectives, the vision, the method and the involvement of each member of the team will achieve this goal, and not the principle “function follows adding up individual inputs”