International Workshop on "Vaccine Quality Management Systems"

July 10 - 11th 2013 – Hosted by Birmex, Mexico D.F.
1. Who We Are
Be a global supplier for fast track, high quality life science and process facilities
Telstar originated as a family owned company with its own brand and technology.

Telstar has a workforce of > 1000 people.

Telstar has a global scope and is established in 16 countries.

Telstar distributes its own products and services to more than 100 countries.

Total Turnover 130 M€; > 90 % generated outside Spain

Japanese Automation Firm Azbil acquires 80% Stake, Group turnover >€2 B
Telstar Group. Modular history.

- **Emtunga AB Modular Construction 1946**
- **Pharmadule AB founded 1986**
- **Pharmadule move production to Estonia, and Pharmadule OÜ founded 2005**
- **KeyPlants AB founded 2010**
- **Pharmadule AB liquidated 2011**
- **KeyPlants AB and Telstar SA partners Q1 2011**
- **Pharmadule OÜ management buy out and Telstar acquires substantial stake in 2011**
The Group in the World

Telstar Group

USA
Spain
Portugal
Mexico
Brazil
Argentina
France
Belgium
UK
Holland
Ireland
China
India
Estonia
Sweden
Italy
Locations around the Globe
Telstar Group

Telstar Worldwide facilities 25,000 m² (270,000 ft²)
Facilities
Telstar Group

Telstar Group HQ (Spain)

Telstar Technologies (Spain)

Life Sciences Solutions (Spain)

Telstar Life Sciences (UK)
LIFE SCIENCE CAPABILITIES:

We deliver one stop shop solutions for the Life Sciences Industry - from initial Site selections and Feasibility studies, to Concept/ Basic/ Detail Design moving into Construction and Commissioning/ IQ/ OQ as well as Validation - in short the whole project Life cycle.
Modular Offerings

- Project Types
  - Green field/Brown field
  - Upgrades, expansions and renovations

- Complete Range of Modular Solutions
  - Building Modules (Out-door/In-door)
  - Box in box solutions
  - Process Modules/Skids
  - Complete Standardized Facilities

- Project Delivery Options
  - From feasibility study to Turn-Key delivery
  - (Out-door/In-door/Hybrid)
  - Off-site construction for any Project
Engineering
Design Philosophy

- Design simplicity and efficiency will be a prime consideration.
- Design for constructability
- Design to budget & optimise cost
- Design for local conditions
- Design for available materials and suppliers
- Design with known quality products
- Design to avoid risk
- Design for maintenance efficiency
Process Layout Development

1. Visualisation of process flows by block-flow-diagrams

2. Process model

3. Adjacency / bubble diagrams (functional relations of separate neighbourhood units)

4. Areas and surfaces

5. Functional layout with zoning, material and personal flows
Design Option “3D Plant Engineering for Complex Plants and Areas“

Advantages:

- Space Management and inter-discipline design coordination
- Generation of isometric drawings
- Automatic material take-off for purchase orders
- Customer-specific piping classes
Front End Design and Delivery in 5 Steps

A Proven Approach

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- **Technology Transfer**
  - Existing Data Transfer from Client

- **Concept Design**
  - Architectural BOD:
    - Adjacency diagrams
    - Layout sketches
  - Mechanical BOD:
    - Classification drawings
    - Zoning drawings
  - Electrical BOD:
    - Single line diagram
  - Site and Structural BOD:
    - Initial layouts
    - Structural grid plan
  - Conceptual Cost & Schedule

- **Design Alt. Team Meeting**
  - OOM Estimate
  - Level 1 Schedule
  - Design Review

- **Concept Optimization**
  - Concept Design Data Finalized
  - “What if’s” Completed
  - OOM Estimate
  - Schedule
  - Comments on Draft Design Report

- **Study Report**
  - Issue Concept Design Report
Step 1 – Technology Transfer

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Step 1 – Alignment

- Step 1 is to achieve alignment with the goals and expectations of the customer’s stakeholders. Key project goal-setting criteria involve the following.

**Challenges**
- Scope definition
- Site limitations, multiple sites,
- Define existing systems
- Clear vision
- Interface with client
- Integration of lab/vivarium operations
- Implementation of corporate standards
- Budget
- Time frame
- Understanding animals/personnel segregation
- Expansion capabilities

**Goal:** Define present and future challenges, set objectives and project goals
Process and Operational Requirements & Facility Optimization

**Process Requirements:**
- Nature of research being conducted
- Strict control of physical environment
- Introduction Quarantine/ disease prevention
- Type and size of animals
- Number of different species
- Isolation of species and control groups
- Proper disposal of waste/ Incineration
- Barriers to prevent cross contamination

**Facility Design:**
- Circulation/flows
- Animal Quarantine
- Animals and Equipment access
- Expansion requirements
- Finishes/materials of construction
- Animal Wash Down system
- NIH Compliance
- Animal Watering System
- Redundant 100% outside air systems
Master Planning Approach – Program Definition

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1 Week 2 3 Weeks 4 1 Week
Step 2 – General Process Room Criteria

- **Telstar integrated team approach**
  - Architecture – seamless floor, sizing, critical adjacencies
  - HVAC – Air supply and exhaust filtered to remove dust and hair, room at negative pressure related to corridor, sensors to monitor temperature and humidity
  - Structural – floor loading at 125 to 150 psf minimum
  - Electrical – equipment and systems requirements, distribution
  - Plumbing – 15 sm – diameter minimum floor drain with strainer, solids trap, disposal unit, and threaded cover, not required for rodent rooms

Imaging Suite  
Necropsy  
Procedure Suite 1
Room Data Sheet
Master Planning Approach – Team Workshop
Step 3 – Team Workshop

- Facility block diagrams
- Animal, personnel, equipment and waste flow
- Code research results
- Order of magnitude cost estimates
- Adjacency diagrams
- Initial programming of spaces
- Confirmation of design with Animal Care and Use Committee
Master Planning Approach - Stage 1 and 2

Legend

- Vivarium - Area 3 (Existing Areas)
- Vivarium - Area 3 (Renovated Areas)
- Vivarium - Area 6 (750K - Phase 1)
- Vivarium - Area 6 (1.2MM - Phase 2)

Stage 1 Construction
Master Planning Approach – Concept Development

1 Week

3 Weeks

1 Week

2 Weeks

1 Week
Comments on Draft Design Report

- Feedback comments from the client to be integrated into final concept realization model.

10 Aug. 2006 Decision Made:

- Vivarium users are generally satisfied with size of Phase One Expansion location and adjacencies.
- Isolated slab and sound insulation of the Vivarium area.
- Vivarium users are open to the issue of Wash Area in Expansion Phase 2 as a leading element.
- ROD should be provided by the water supply system.
- Keep BL2 connection for transfer of materials to the Labs.
- Machine Room space is going is going to be available to potential use for Necropsy. (2009)
- The Entry into Vivarium would be through the Locker Rooms Gowning Room.

Imaging Suite:

- 36" aisle size in the existing Housing Room is the guideline for the Housing Room Layout.
- Adjoining door requirement is for frequency of use, also the Housing Rooms are dedicated to Imaging Procedure Room.
- Intravital Microscopy System - requires a separate room. Prep., surgery, anesthesia and microscope work. (Bench - 3'-0" x 3'-0", 3'-0" x 4'-0", computer)
- Plethysmography Chambers - open space requirement, (2) 6'-0" tables and computer


1. The comment on RODI was made to be sure that the system is sized for the needs of the animal watering system.
2. The transfer of the machine shop space for use by the Vivarium will be made when the machine shop moves to Area 4 in the 1st Qtr of 2007. Thus the design for some needs to precede that by being done in 2006.
3. The microscope room may also have a requirement for darkening and so needs to be so constructed.
Step 4: Concept Optimization, Integration – Overall Master Plan
## Master Planning Approach – Concept Realization

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Step 5 – Final Report and 3-D Model

- Review/Example of Facility Concept Modeling
All process model input required for the various unit operations is identified on a single sheet.
The calculation results are summarized in a Block Flow Diagram.
Output from the process model is used to size media and buffer prep and hold equipment.
Utility estimates are based on the process model results and production schedule.
Process Flow Diagrams—capturing the integrated design of process, CIP and SIP operations
### Projected Equipment Utilization

Production Schedule for 2 x 5000 L Bioreactor Trains and 1 Purification/week

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Data presented in table to show which operation is running each day. May also be presented as Gantt chart.
Our Process for Delivering Projects

• CARE: our project delivery process that turns integrated E&C into capital project benefits
  • Control cost
  • Accelerate schedule and start-up
  • Reduce risk
  • Enhance value
Control Cost

- Make most of the construction and start-up decisions in the conceptual design phase, thus eliminating costly rework
- Collaborate with project team to attain optimal solutions for construction, start-up, and turnover
Control Cost

- Apply strict project controls
  - Strong project management
  - Open communication
  - Control of Key components and equipment within the Telstar Group
- Subject Mater Expert Equipment Input @ CD phase with ability to optimise Process Cycle times
- Global Procurement Capability

- Carefully schedule work activities
  - Reduce unscheduled overtime
  - Minimize craft interference
  - For Modular Construction ability to fabricate in controlled environment
Accelerate Schedule

- Integrate the activities of all disciplines, suppliers, and contractors
  - Ability to include detailed equipment layouts into CD phase for Fill Finish Equipment
  - Lean Validation utilising Engineering documents into Protocol Preparation and Execution
  - Modular Fabrication in our Estonia Workshop

- Benefit from real-time schedule management
  - Concurrent design and construction
  - “Just-in-time” equipment supply
  - Increased workflow efficiency
  - Controlled environment for craft labour in our Estonia workshop
Reduce Risk

- Conduct a thorough risk evaluation during each project step
- CM engaged during project planning
- Continued in alignment sessions throughout the project phases
- Drive down the risk profile with Risk Mitigation Strategy
- Move activities up in the project timeline
- Optimal balance with craft loading and schedule float
Risk Management

**STEP 1**
Risk Management Planning

**STEP 2**
Risk Identification

**STEP 3**
Risk Assessment and Prioritisation

**STEP 4**
Quantitative Risk Analysis

**STEP 5**
Risk Response Planning

**STEP 6**
Risk Tracking and Control
Enhance value

- Direct control of the site safety program
- Modular or Hybrid Solutions for Fast Track Projects and areas of low skilled local labour
- Direct control of the engineering, procurement, and construction planning and scheduling requirements
- Direct control of the subcontractor/vendor quality control and assurance management
- Understanding the Client’s Process
- Early Targeting of Commissioning/Start-up, integrated with Lean Validation and Regulatory compliance
- Clear Communication
- A drive for continuous improvement of the effectiveness of resources, methods, relationships, and best practices
**Modular Hybrid Project Execution**

A predictable way for execution with risk mitigation

**1-5 months**

CD/BE

**5—10 months depending on scope**

Detailed Design

**Fabircation**

**2-4 weeks**

Transport

**Assembly**

**Commissioning**

**2-5 months depending on scope**

Delivery

**Activities at Site**

Site Construction

**Taking Over**

Defining the project against the business drivers

**Key to project success!!**
Modular Project Execution

Design and Engineering

Fabrication

Site Erection & Completion

Delivery
ISO Certified Fabrication

World Class Clean Pipe Weld Workshop
5. A Solution to Today’s Challenges
The Issues

Pharmaceutical companies are demanding projects that are more cost effective, have shorter schedule and higher quality.

Therefore the Design and Construction Industry Productivity Trends MUST continue Towards a Positive & Improving Trend through investment and innovation.
There is a continuous increasing demand for:

- Lower cost
- Shorter Schedule
- Predictably and higher quality
- Flexibility
How Can We Improve?

• **The Options**
  There are a Variety of Options and Alternatives utilized to improve project delivery and productivity

• **We have tried different Project Execution Approaches:**
  o Design, Bid, Build
  o Engineering, Procurement & Construction Mgt. (EPCM)
  o Integrated Project Delivery including Qualification
  o Shell buildings with panels, building modules
How Can We Improve?

Standardization with Innovative Modular Design and Off Site Fabrication
Outlook

- Most Processes and Process Facilities will be Hybrid Modular
- Standardization
- Modular Unit Operations
- Modular Execution is rapidly developing and cost has decreased substantially in the last five years – a trend that will continue
Modular Solutions Changing From.....
Process planning for a multi-purpose pharmaceutical OSD manufacturing plant

Integrated Solution

Process Solution

Modular Solution

....to Integrated Process Solutions...
... To Standardization...

- Standard Facilities (Biotech, OSD, Fill Finish)
- Functional Modules
A New Generation Modular Facilities
A New Generation Modular Facilities

Lower cost
Shorter schedule

Predictability and higher quality
Flexibility
Outlook Summary

- "Modular" has become a buzzword
- Fewer have the experience and resources to execute
- Modularization has proven to be beneficial in many applications
- The Modular Concept is rapidly developing and advancing
  - Modules and Skids for unit operations
  - Standardized Solutions
  - Lower cost
- Modularization is a broad concept – Make sure to Understand What It Means to fit your application
1. Develop a Pre-engineered Modular Aseptic Facility for SVP, aimed at emerging markets, either internal or traditional modules.

2. Facility designed for either Lyophilised Powder or Solutions.

3. Facility to handle either Vials or Syringes; range from 2 to 20ml.

4. Facility to be a single storey design with formulation on ground floor, second line to be easily added without interruption to existing operations.

5. Line speed to be from 200 to 600 vials (2ml) per minute, with either manual or automatic loading of the Lyo.

6. The Facility to be designed for either closed RABs or BI Technology and a Grade C background.

7. Facility battery Limit is the Capper.
MAS – next development step
1. Manufacture Modules, initially 100% in Estonia. If Business grows consider manufacture in China and Southth America (Brazil or Argentina)

2. Use Telstar Equipment in modules
   1. Lyo’s.
   2. Autoclaves.
   3. cRABS or Isolators.
   4. WFI & Clean Steam Generation and distribution systems.
   5. Telstar Modular Clean Room Systems).
   6. Azbil EMS

3. Partner for Filling Line (Bosch; Marchesini).

4. Formulation vessels to be manufactured, in Estonia.

5. If Demand exists Fabrication to move to South America and China
5. References
Thank you for your attention