Welcome to our October Newsletter. In this issue we would like to give you a brief overview of BioPharma and outline our growth since 2006. We would also like to give you an overview of our High Containment Expertise, Design Solutions and recent projects delivered in this area. For more information on our current projects and to sign up to our email newsletter, please go onto our website www.bpe.ie or contact us directly on info@biopharma.ie. We do hope you enjoy this newsletter and thank you for your continued support. Any feedback or comments you may have would be highly appreciated.

BRIEF BPE OVERVIEW

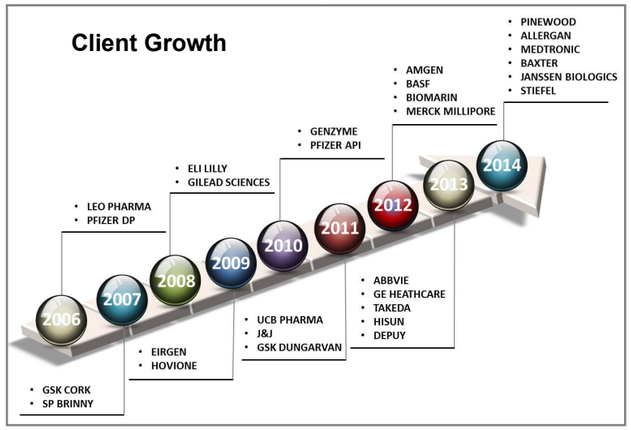
BioPharma Engineering was founded in 2006 with a team of six people led by John O'Reilly & Richard Holohan to service the Pharmaceutical and Life Science Industries, with the specific aim of concentrating on delivering mid range capital value projects. We believed that there was a real opportunity for a new engineering consultancy to provide a high level of service using experienced people to deliver value on these projects. In 2006 our first clients were GSK, Leo Pharma and Pfizer, all of whom we continue to work with today.

Over the last 8 years BioPharma has steadily expanded our client base to 24 active clients. Our success is built upon integrity, professional excellence and an uncompromising commitment to building long term relationships with our clients. Over the years, BioPharma has earned a world class reputation within the Pharmaceutical and Life Science Sector for delivering Quality, Innovative, and Right First Time Design within budget.

BioPharma has actively built a very strong and experienced design team with the ability to listen and to understand our customer needs and requirements and translate this understanding into successful design solutions which meet our client's objectives. Currently we have almost 40 design office personnel covering all of the key disciplines such as Project Management and Controls, Process Engineering, Electrical / Instrumentation and Automation, Mechanical/Piping, HVAC/Building services, Document Control, Construction Management and Safety coordination to provide the level of support required by our clients to deliver their projects seamlessly from concept to completion.

Both John and Richard are actively involved in all of our projects and ensure director level responsibility for each project being safely and successfully managed, regardless of size and complexity. Our approach guarantees a single point of responsibility for each client and a personal commitment to deliver each project to the agreed client needs and requirements.

We believe this approach is part of what separates us from our competitors and helps us to continue to grow and thrive in a very competitive market.



HIGH CONTAINMENT DESIGN

When faced with a challenge to design for a Highly Potent Product in either a new or existing facility, Biopharma adopt a systematic proven approach to containment design. With experience across both Bulk API and Secondary Manufacturing, BioPharma can provide a multifunction design team to deliver the required containment solution that encompasses all aspects of your process. For more information on this article please contact Mary Collins on mcollins@biopharma.ie

1) Introduction

Biopharma have delivered Process Designs for a number of clients for new and upgraded containment facilities to meet revised Occupational Exposure Requirements with the development of more potent pharmacological compounds, the Tech Transfer across sites and New Product Introductions (NPI), the requirement for high containment design is increasing.

By law, employers in the EU must protect their workers from being harmed by dangerous substances in the workplace. European legislation establishes a hierarchy of measures that employers need to adopt to control the risk to workers from dangerous substances. Refer to "Practical guidelines of a non-binding nature on the protection of the health and safety of workers from the risks related to chemical agents at work (Articles 3, 4, 5 and 6, and Annex II, section 1 of Directive 98/24/EC)".

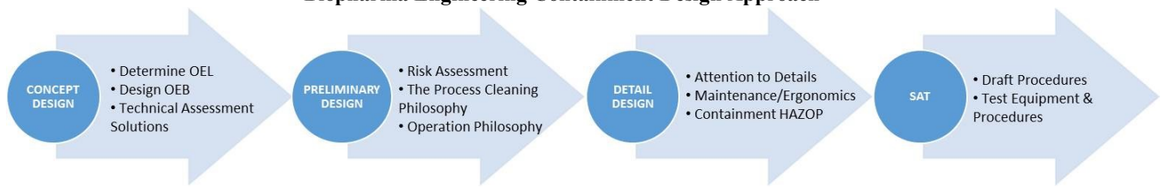
2) Containment Design

Biopharma have an established design philosophy for containment depending on the key client functional requirements (compound properties, scale of material handling and material handling activities).

For API manufacturing, areas of highest risk include isolation of dry bulk intermediate and final active ingredients due to the material properties, quantity and duration of operator exposure. However sampling, maintenance and equipment cleaning must also be considered at the design stage to ensure exposure protection measures are not compromised.

For secondary manufacturing, initial handling of API is also deemed to be the greatest potential risk, but consideration is required for particle size of the API as it may preferentially leak even when blended with excipients. Here, sampling, cleaning and maintenance strategies are required to ensure a complete contained solution.

Biopharma Engineering Containment Design Approach



a) Design Process

I. Determine Occupational Exposure Band for the Compound (API or Granulate).

This is typically based on the assessment of the material occupational Exposure Limit (µg/m3 TWA 8hours) and other material toxicological effects such as skin sensitizer, mutagenicity and others. Refer to Table 1. For New Products this may not be available but a general band or Occupational Exposure Band is assumed for the design. Companies generally use either 4 or 5 bands, projects referenced here refer to the 5 bands as per Table 1.

II. **Define Operational, Cleaning & Maintenance Tasks for Process Activity**.

The entire facility, the laboratory and the waste handling facilities also need to be assessed to ensure the correct handling of material in all these areas are included. Solutions include closure of floor drains and the use of absorbent material for spills, contained filtering of waste streams to ensure API does not enter the general waste systems.

Table 1.

GENERAL CONTAINMENT STRATEGY	OEB	OEL	POTENCY	TOXICITY
Totally contained/ Secondary Containment / Robotic handling	5	<1 µg/m³	<0.5 mg/day	Highly Toxic
Closed handling within isolator	4	1-10 µg/m³	0.5-5 mg/day	Toxic
Open handling within isolator	3	10-100 µg/m³	5-50 mg/day	Less toxic
Local specific extract	2	100-1000 µg/m³	50-500 mg/day	Almost Non-toxic
General ventilation	1	1000-5000 µg/m³	>500mg/day	Non-toxic

III. **Technical Assessment of Suitable Containment Options (Scale & Activity)**

Based on the compound OEB, a suitable Containment Design Level must be agreed. Once the target has been agreed, a containment risk assessment of the suitable options is recommended to ensure that all the requirements are catered for i.e. Potential locations where the product can dry out and become airborne needs to be reviewed and the proposed solutions risk ranked. Attention is required to be given to simplifying the operations, ergonomics, cleanability factors like surface finish, drainability, Cleaning in Place and materials of construction. HVAC systems need to be reviewed in order to determine appropriate pressure profiles, filtration specifications, HVAC utility loads and the requirements for new licensed emission points.

IV. Functional Test:

The strategy for start-up needs to be agreed at the outset to ensure it is facilitated in the design. For example some companies will complete placebo site acceptance tests with materials like lactose or Paracetamol to support a non air suit start up while others will require the use of air suits on start up until environmental monitoring occupational hygiene tests are completed.

BIOPHARMA HIGH CONTAINMENT EXPERIENCE

Containment designs have improved significantly in the last 20 years and engineering solutions are readily available for OEB 1-4. The difficulty now is determining what containment solution provides the most cost effective result. A cost benefit analysis of the options is required as initial capital cost needs to be weighed against operator hours, maintenance costs and cycle time impacts. Flexible containment solutions can provide a good cost effective solution for a shorter campaign but are expensive if multiple turnarounds and products are involved.

Also when designing for Highly Potent OEB5 material, solutions are not as clear cut. Firstly a design target is needed and it needs to be specific i.e. for an OEB 5 multiproduct project we recently completed the agreed target was 0.3 µg/m^3. Occupational Health Professionals or the Design Team may decide to add a safety factor to allow for the fact that seals, deteriorate over time and therefore the equipment needs to pass a higher hurdle first day in order to ensure that a certain level is achievable in the long run. For a design < 0.5 µg/m^3 most equipment vendors will require a secondary containment device and for this flexible containment has provided a good solution .

BioPharma Recent Process Experience

Designs completed for up to and including OEB5:

- OEB5 Multiproduct Milling Suite (Isolator Containment)
- OEB5 High Containment Gram Lab (RTP, Isolator, Contained Slide Valve)
- OEB 4 API & Excipient Material Dispensary (LAF, Multiple Packaging)
- OEB4 Continuous Granulation. (FIBC Dispensing, Facility Design)
- OEB4 Bulk API Facility Containment Upgrade (UHC SBV IBC Transfer)
- OEB5 FIBC Containment for Large Scale NPI

These Projects Covered Areas:

- Process & Facility Upgrades for API & Secondary Process
- Lab Containment & Handling
- Warehouse Dispensing
- Sampling Waste management
- Cleaning & Maintenance Activities.

Our Capabilities

We design,
manage & deliver
projects for a broad
spectrum of clients
in the following
Industries

PHARMACEUTICAL

BIOTECHNOLOGY

MEDICAL DEVICES

To find out how we can tailor our service
to meet your business goals give us
a call or visit our website.

- BRIEF BPE OVERVIEW
- HIGH CONTAINMENT EXPERIENCE

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DESIGN MANAGE DELIVER

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