No Barrier/Unlimited Containment

from design to validation

www.csv-ls.com

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CONTAINMENT KNOW HOW

TOXYCOLOGY STUDIES

Experts can support clients in OEL, OEB and CPT identification and definition……

EXPOSURE CONTROL PRACTICES

Our Process Engineering , based on toxicology conclusion, can define the right exposure control strategy to target the identified CPT /OEL. These services , starts from a safety risk assessment and consist of the provision of layout analysis, HVAC/filtration design , contained process equipment , PPE and operating , maintenance , cleaning/decontamination procedure to support as the preliminary, often strategic phase in the process of developing and/or restructuring industrial sites (whether individual departments and entire manufacturing sites) designated to Highly potent compound manufacturing.

HIGH POTENT ENGINEERING

CSV High Potent Engineering aim to make real concept identified during the previous exposure control practices. Lay Outs , P&IDs and Specification will identify the final solution to be adopted . Attention will be paid on operating, cleaning and maintenance, as well as, initial and periodic validation.

CONTAINMENT SOLUTIONS

CSV provide custom made contained solutions based on flexible or rigid technology. Since 2009 CSV Life Science is the exclusive ILC DOVER agent while on 2015 represents THE CHARGEPOINT split butterfly valves. On 2016 CSV developed its own proprietary DRUM IRIS TECHNOLOGY focused on contained solutions applied to Drum handling.

SMEPAC MONITORING & VALIDATION

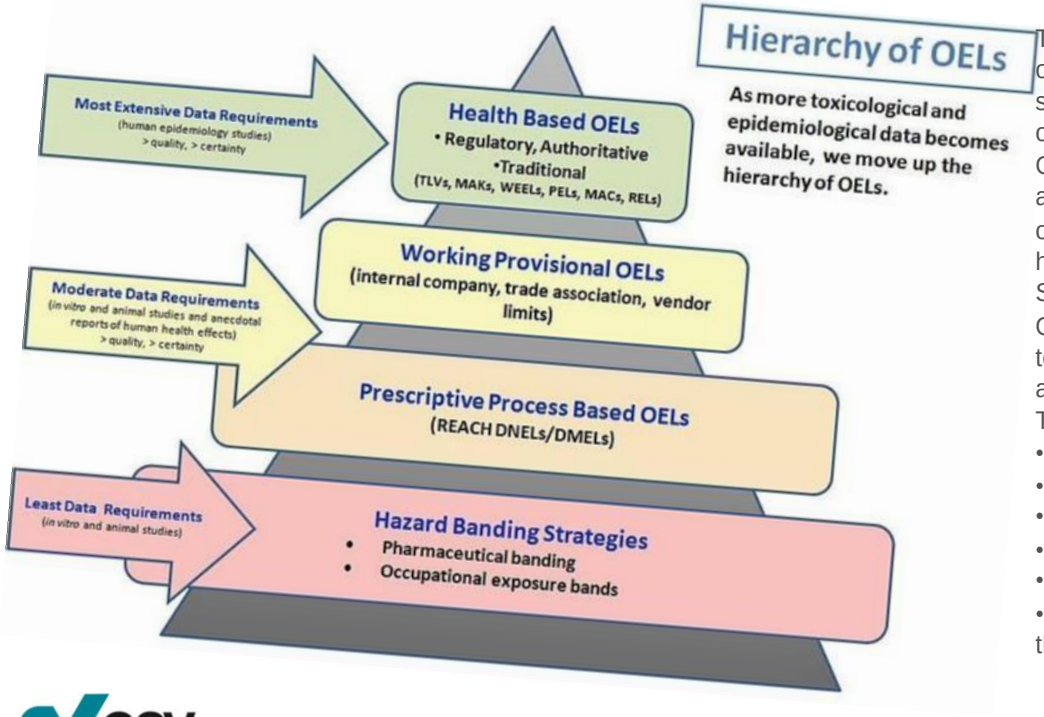
We provide the Standardized Measurement of Particulate Airborne Concentration (SMEPAC) performed according to ISPE's..

CSV Life Science

TOXICOLOGY STUDY

Occupational Exposure Limits(OEL)

To ensure effective operator protection, it is essential to contain the product on-site, from the first step in the production process until final packaging.
The critical point is often the transfer between process units and containers (containers, drums, sacks or FIBCs).



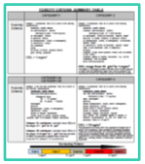
The OEB (Occupational Exposure Band) value relates to the toxicity of the substance itself. The aim is to evaluate the toxicity of the substance in order to select production units and processes that are optimally suited to the product hazards.
OEL (Occupational Exposure Limit) is an upper limit on the acceptable concentration in the workplace air for a particular material or class of materials. The exposure times are averaged for eight hours (8-hour TWA) and 15 minutes (short-term exposure limit STEL).
Once workplace limits have been defined for a chemical, the required technical procedure can be defined thereby minimizing investment and operating costs.
The study provides:

- Collection, evaluation and analysis of toxicological data
- Data gaps filling by *in silico*, *in vitro* and *in vivo* methodologies
- PDE (Permissible Daily Exposure) assessment
- OEL quantitative assessment
- OEL qualitative assessment
- Proposal of the most appropriate containment strategy based on the potential exposure of the operator

EXPOSURE CONTROL PRACTICES

TOXICOLOGY STUDY → EXPOSURE CONTROL PRACTICES → ENGINEERING DESIGN → CONTAINMENT SYSTEM → SMEPAC & VALIDATION

Whenever there is a new CONTAINED plant or a major refurbishment, this is a strategic activity to define the CONTAINMENT STRATEGY to fit the investment purpose technically, economically and from temporal point of view. It is divided in several steps:



1. OELs ASSESSMENT REVIEW

The Output of the Toxicology Study is analyzed in order to group products in classes based on the identified OELs and the relevant batch sizes.

2. BATCHES SIZES IDENTIFICATION

In order to target the Production capacity and then size the facility any product batch size is defined

3. PROCESS OPERATIONS ANALISYS

Operations , containers, volume and weight , as well as , frequency and duration of each manufacturing step is investigated in order to associate a CPT to each product belonging to any OEL class

4. TRANSFER OPERATIONS ANALYSIS (FREQUENCY, VOLUMES, CONTAINERS)

Particular attention is paid to Transfer In/Out operations either for manufacturing, Sampling or Maintenance/cleaning operation.

5. EQUIPMENT PRE-SELECTION

When finally defined the facility/system CPT target the relevant suitable technology can be identified . Previously performed study results are considered during the equipment selection.

6. LAY OUT/ ARCHITECTURAL REQUIREMENTS

As well as contained equipment, lay out are designed considering the the high compound safety risks introduced by potent to be manufactured;

lay out are then drawn considering manufacturing operations and maintenance/decontamination activities.

7. MATERIAL / PERSONNEL FLOWS

To mitigate contamination risks material and personnel flow s are usually design as one way . Avoid or Minimize clean and dirty cross flows is a must

8. HVAC, UTILITIES TREATMENT

HVAC Once trough and HEPA filtered air supply and exhaust has to be considered as well as drainage and waste treatment

HIGH POTENT ENGINEERING DESIGN

TOXICOLOGY STUDY → EXPOSURE CONTROL PRACTICES → HIGH POTENT ENGINEERING → CONTAINMENT SYSTEM → SMEPAC & VALIDATION

These activities define better the equipment/facility, always from a technical, SAFETY & Quality, economical and temporal point of view.

1. LAY OUT , MATERIAL& PERSONNEL FLOWS

We coordinate all branches, to assure a proper quality/safety of design, to meet

milestones and to guarantee proper communication and control of changes or modification during the design development.

2. ISOLATION EQUIPMENT SPECIFICATION

We produce all the drawings, specifications, information, and equipment/systems URS needed to subcontract or to order accordingly Working Break Down Structure (WBS) defined for the plant realization. Designs are related to all engineering branches; some of them might be executed by Local Engineering Company.

3. COST ESTIMATE

Then a Cost Estimate (± 5÷10% accuracy) is provided. If TIC (Total Installed Cost) overrun the budget a Value Engineering activity can be executed to optimize costs without affecting the final plant quality.

4. SCHEDULING

It includes procurement, construction, commissioning, and SMEPAC/validation. During those phases a level 3, or Project Control Level Schedule is developed, integrating EPC MV activities for the entire project scope of work based on a Critical Path Method (CPM) using a network scheduling technology with detailed input of all major milestones.

5. REPORTING

Along all the engineering development, Project Manager issues

Reports, indicating the work progress, delays, recovery action to reduce delay, budget overrunning, etc.

6. GMP / SAFETY REVIEW

The presence of personnel experienced in containment engineering and dedicated to SMEPAC/Validation let CSV execute GMP & SAFETY review of existing equipment, facility and sites under design or under construction. The purpose of this activity is to identify, trough procedures, and comparing with norms and guideline, if an equipment/facility or site is installed, being installed or designed accordingly to GMP/SAFETY rules/requirements.

7. INTERACTIVE SESSIONS

We run an interactive planning, a structured approach to review engineering development in order to ensure the constant interaction with our clients.

CSV Life Science

CONTAINMENT SYSTEMS

TOXICOLOGY STUDY → EXPOSURE CONTROL PRACTICES → HIGH POTENT ENGINEERING → CONTAINMENT SYSTEMS → SMEPAC & VALIDATION

CSV develop and realize High Containment solutions dedicated to High potent manufacturing in API and pharmaceutical industry

1. PRELIMINARY SURVEY / DISCUSSION - FRONT END DESIGN

The aim of this phase is to reflect all of the client's project-specific requirements involving operators in the preliminary solution design. Exposed operations to be contained are analyzed paying particular attention to background environment, (ATEX or GMP) areas classification, spaces , batch size, containers volume/weight, transfer operations , sampling , cleaning/decontamination and maintenance procedure

2. CONTAINMENT ENGINEERING

Based on the preliminary discussion & survey and the identified CPT/OEL target CSV proceed with the containment system conceptual design, Client comments are collected in order to eventually improve/modify the suggested solution and proceed with the creation of a prototype called MOCK UP

3. 3D MODELING – MOCK-UP – ERGONOMIC TEST

Site Mock Up Installation is crucial in space critical application. Factory Mock up is

anyway suggested before proceed with construction
In both scenario manufacturing operators involvement is strictly recommended .
No solution can work without the final owner contribution

4. DESIGN REVIEW - MANUFACTURE

After having tested the Mock Up and collected any comments from the final owner CSV can proceed with containment system 3D design and , when

ILC DOVER

5. FLEXIBLE CONTAINMENT – REACH – GMP- HAPI

CSV since 2008 is exclusively representing ILC DOVER a worldwide recognized flexible containment technology company. Using flexibles, CSV can create any kind of solution to enclose exposed operations, particularly when classic/rigid solutions can not be applied.
By using flexible containment CSV can rapidly upgrade existing equipment to handle potent compounds, guaranteeing reduced capital costs, ergonomic design/operations and faster project start-up.

6. RIGID ISOLATOR

When working with highly potent compounds and cytotoxic products, rigid wall isolators provide an extremely safe working condition for operators and a specific environment can be more easily maintained. The rigid isolator has a high resistant to strong cleaning agents and neutralizing agents
As THE CHARGEPOINT split valve Agent , CSV can guarantee High Contained

ChargePoint

Powder Transfers, during charging, offloading and sampling while using RTP and

Continuous liner can realize contained transfer and BAG In/Out ,

7. CSV DRUM IRIS TECHNOLOGY

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SMEPAC MONITORING & VALIDATION

TOXICOLOGY STUDY → EXPOSURE CONTROL PRACTICES → HIGH POTENT ENGINEERING → DRUM IRIS TECHNOLOGY CONTAINMENT SYSTEMS → SMEPAC & VALIDATION

This activity is multifaceted activity, and includes several supports that might be provided to the client. Below an excerpt of support activities that CSV Life Science can provide:

1. SMEPAC MONITIORING SAMPLING & VALIDATION PLAN

The purpose of the Plan is to provide an overall strategy for the SMEPAC monitoring and validation efforts, identifying , placebo and describing test activities and studies that will be carried out to demonstrate that contained systems /facility have been properly built and installed and are able to work in a reliably and repeatedly manner, according to pre-established requirements and safety/quality.

2. RISK ANALYSIS

Containment expert let CSV execute RA, GMP & SAFETY review of existing equipment, facility, sites under design or under construction. The purpose of this activity is to identify, trough procedures, and comparing with norms and guideline, if an equipment, facility or , plant is installed, being installed or designed accordingly GMP/SAFETY and to determine which systems and/or system components/functions should be subject to SMEPAC/Qualification

3. SMEPAC MONITORING & VALIDATION PROTOCOL

CSV can write and execute Qualification and SMEPAC (DQ IQ, OQ, PQ) protocols, as well as Process Validation Protocols. This activity is applicable to all production forms and branches.

5. CONTAINMENT SUPPORT

CSV Life Science can provide also H&S, QA support, including: process validation, cleaning/Decontamination validation, SOP writing, maintenance, QA and QC SOP review, etc.

6. CONTAINED SYSTEM FAT / SAT AND INSTALLATION

CSV Life Science can execute or provide any assistance during Factory or Site testing on contained systems

7. SMEPAC MONITORING / VALIDATION EXECUTION

CSV has all necessary references, skills, procedure and I field instruments to perform any validation activities and SMEPAC monitoring

Assessing the particulate containment performance of the equipment /facility is required in order to: Establish if the systems used to contain the products is suitable for that purpose - Identify critical points - Evaluate potential exposure of personnel during production operation

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