Risk Assessment Solutions
Services Available

Toxicology Safety/ Product Assessments	**Extractables and Leechables**
Cleaning Validation	**Workers Compensation Expert Consultatoin**

Toxicology Safety/Product Assessments

PharmEng Technology's Toxicology division offers a comprehensive solution for conducting risk assessment of a therapeutic. A risk assessment is conducted to categorize active pharmaceutical ingredients to prevent recalls and ensure patient safety; worker safety; pharmaceutical cleaning limits; and an overall banding characterization of a product. Our board-certified toxicologist and team have conducted more than 250 toxicology risk assessment categorization and banding for both contract manufacturers and owner companies with traditional pharmaceutical therapy and biotechnology products.

MORE INFO

Extracables & Leachables

PharmEng aligns cleaning validation with toxicological evaluation to provide tools to meet regulatory expectations, implementing results in compliance, and patient safety. Customized solutions for cleaning validation are created and include health-based exposure limits (HBEL) considering identification of hazards and evaluation of the dose-response relationship.

MORE INFO

Cleaning Validatoin

PharmEng consultants will work alongside you to evaluate your manufacturing process, container closure systems (CCS), and packaging to assess materials and contact chemicals that have the potential to produce extractables and leachables (E&L), which may be inherently toxic and can contaminate drug products.

MORE INFO

Worker's Compensation Expert Consultation

PharmEng provides case review, written assessments, and expert testimony for worker's compensation cases.

MORE INFO

We look forward to the opportunity to work with you to provide toxicological technical support ranging from categorizing active pharmaceutical ingredients based on toxicity and established criteria to worker's compensation expert consultation.

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Toxicology Product Assessment

Product specific evaluations to help prevent product recalls and ensure patient safety; ensure worker safety; pharmaceutical cleaning limits; and an overall toxicological assessment for product development, manufacturing process, and laboratory testing.

Toxicological Product Assessments include:

- Product characterization
  - API or product mechanism of action (MOA)
  - Pharmacokinetics – absorption, distribution, metabolism, excretion (ADME)
- Disease or ailment etiology
- Summary of pre-clinical & clinical trials (if available)
- Summary of Personal Protective Equipment (PPE) for worker safety
- Determination of manufacturing product via standard stainless-steel manufacturing vs. single use technology (SUT)
- Risk assessment of product, Health-Based Exposure Limit (HBEL)– categorization of overall toxicity and Permitted Daily Exposure (PDE, µg of API/day) & Occupational Exposure Limit (OEL, µg of API /m3) (data permitting)
- Safety Training provided per request

Regulatory & Guidance Governance Documents:

- ICH Q3C(R6)
- ICH S6(R1)
- EudraLex, Vol 4 GMP Guidelines, Part 1, Chapter 5
- EudraLex, Vol 4 GMP Guidelines, Part 1, Chapter 3
- EudraLex, Vol 4 GMP Guidelines, Annex 15
- EMA/CHMP/CVMP/SWP/169430/2012
- ISPE Baseline Guide Volume 7, Second Edition, Risk-based Manufacture of Pharmaceutical Products
- Active Pharmaceutical Ingredients Committee (APIC): Guidance on Aspects of Cleaning Validation in Active Pharmaceutical Ingredient Plants.
- Technical Report No. 101: Guidance for Setting Occupational Exposure Limits: Emphasis on Data-Poor Substances

Biologic Evaluations Experience:

Viral Vectors:

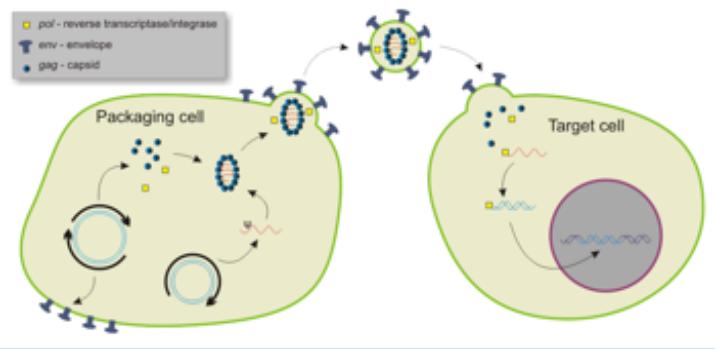
- Adenovirus
- Adeno-associated virus (AAV)
- Lentivirus
- Poxvirus
- Baculovirus

Host Cell Platforms:

- HEK-293
- CHO
- Sf9
- MDCK
- Vero
- C6
- ARPE-19

Expression Systems:

- Vaccine Antigen Expression Systems
- Virus Replication Platforms
- Viruses & Vectors



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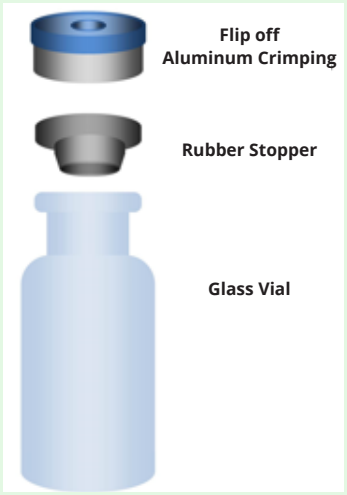
Extractables and Leachables (E&L) Evaluations

What are E&L?

- Extractables are species released from surface of components used in manufacturing & storage of drug product under laboratory conditions (accelerate temps)
- Leachables are species released from surface of components used in manufacturing & storage of drug product under normal conditions

Where do E&L Come From?

- Manufacturing process
- Container Closure Systems (CCS)
- Packaging
- Drug Delivery Devices



Why evaluate E&L?

- Drug product not altered in identity, safety, strength, quality, or purity due to E & L
- Prevent product recall
- 21CFR211.94
- 21CFR211.160
- 21CFR600.11 (b)(h)

E&L Evaluations Include:

- Evaluation of potential of E&L across manufacturing process by a board-certified toxicologist (DABT)
- Provide assessment of materials & contact chemicals that will not elicit E&L along with list of materials & contact chemicals in which production of E&L is unknown & requires further investigation
- Document all findings via a report & table/spreadsheet
- Zipped file of all references uses in evaluation

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Cleaning Validation (CV)

- Aligning cleaning validation with toxicological evaluation provides tools to meet regulatory expectations, implementing results in compliance, and patient safety.
- Modern cleaning programs focus on patient safety and must include health-based exposure limits (HBEL) considering identification of hazards and evaluation of the dose-response relationship.

Deliverables include:

- Customized solution for your CV Master Plan
  - Cleaning Process Design & Development
  - Cleaning Process Performance Qualification
  - Cleaning Process Verification
- Author/revise CV SOPs
- Evaluate toxicity of biopharmaceutics, therapeutic proteins, chemicals, and active pharmaceutical ingredients
  - Determine No Observed Adverse Effect Level (NOAEL)
  - Calculate Permitted Daily Exposure (PDE)
  - Determine Acceptance Criteria that take account of limits for the carryover of product residues with consideration to toxicological evaluation.

Regulatory & Guidance Documents:

- FDA 1993, Validation of Cleaning Processes, Guide to Inspections Validation of Cleaning Processes
- EudraLex, Vol 4 GMP Guidelines, Annex 15
- European Medicines Agency: Guideline on setting Health
- Based Exposure Limits for Use in Risk Identification in the Manufacturer of Different Medicinal Products in Shared Facilities
- ICH Q3
- ISPE Baseline Guide Volume 7, Second Edition, Risk-based Manufacture of Pharmaceutical Products
- PDA TR 29, Points to Consider for Cleaning Validation
- PDA TR 49, Points to Consider for Biotechnology Cleaning Validation

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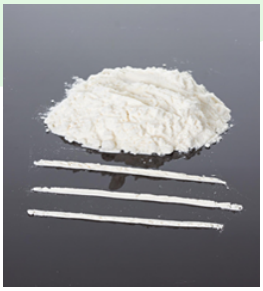
Toxicology Services: Worker's Compensation Expert Consulting

Drugs of abuse in biological samples have a wealth of literature with clear endpoints. However, drugs of abuse are commonly taken with prescription medications or alcohol which can alter the biologic effect. Drugs identified in blood samples provide quantitative levels (amount or concentration) of the drug within the body. However, drugs identified in urine are qualitative with a cutoff level, present or not detected.

Case review, written assessments, and expert testimony from a Board-Certified Toxicologist (DABT).

Evaluations Include:

- Verbal preliminary case review
- Written evaluation with conclusions supported by weight of evidence
- Impairment determination based on quantitative (amount) data from blood samples
- Zipped file of all references used



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