



REACHUP REGULATORY NETWORK ITALY

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OUR SERVICES FOR PHARMA

ToxHub is a group specialized in ensuring the safety of its Customer's products and their regulatory compliance with an extensive and proven track record in Toxicological Risk Assessment in the pharmaceutical, chemical and health care area.

Genotoxic Impurities (ICH M7)	Services for CDMO
Toxicological Risk Assessment and Safety Limits' definition ✓ Database search for experimental genotoxicity data; toxicological review and relevance ✓ In-silico assessment identification for genotoxicity structural alerts compliant with ICH M7 ✓ Classification ✓ Purge factor	Services dedicated for drug substance intermediates and data-poor substances ✓ PDE for shared facilities ✓ OEB: banding characterization and strategy based on GHS H-CODES or performing <i>in silico</i> assessment and <i>in vitro</i> testing ✓ Impurity specification in the drug substance ✓ Leachables risk assessment from bulk containers ✓ DMF/ASMF 3.2.S.3.2/3.2.S.4.1/3.2.S.4.5 and 2.C.1.2.6 support
Non-Genotoxic Impurities (ICH Q3/A&B)	Environmental Risk Assessment
Toxicological Risk Assessment of impurities or degradation products above the qualification threshold ✓ Database search for toxicological data (NOAEL/LOAEL) ✓ Definition of a qualification study plan for data-poor-substances ✓ Definition of safety limits ✓ Qualification report	Phase I ERA compliant with EMEA/CHMP/SWP/4447/00, and relevant Q&A ✓ Comprehensive literature search using public and commercial databases. ✓ Estimation of environmental exposure; Persistence, Bioaccumulation and Toxicity (PBT); calculation of the Initial Predicted Exposure Concentration (PEC). ✓ Possible refinement of the market penetration factor (Fpen) based on market data. ✓ Data gap analysis under consideration of non-testing approaches. ✓ Identification of intelligent testing strategies, design and management of testing programmes. ✓ ECHA-guideline compliant assessment of endocrine disrupting properties.
Leachables & Extractables	Training
Toxicological Risk Assessment of L&E from primary packaging ✓ Database search for toxicological data (NOAEL/LOAEL) ✓ In silico assessment or Cramer Classification ✓ Definition of analytical evaluation thresholds and safety concentration thresholds	Specific training session client customized
PDE	Non-Clinical Regulatory Documentation
Hazard identification and PDE calculation compliant with EMA CHMP/CVMP/SWP/169430/2012 guideline ✓ Database search for toxicological data (NOAEL/LOAEL) and identification of "critical effects" ✓ Different routes (i.e. topical, intravitreal)	Non-clinical sections of INDs/NDAs in legacy and eCTD format Investigator's Brochure.
Occupational Limits (OEL/OEB)	QSAR Assessment
Banding categorization and strategy based on qualitative or quantitative data derived from database search for relevant toxicological data ✓ Derivation of OEL/OEB according to international standards ✓ methodologies developed by NIOSH/COSHH HSE ✓ In silico assessment and in vitro testing for skin and eye irritation skin and respiratory sensitization	Consultancy services based on <i>in silico</i> methods using free-available or commercial tools: Lhasa® (Derek, Sarah); Leadscope®