GVK BIO

Accelerating Research

Analytical Services

WORLD CLASS SERVICES TO MEET GLOBAL NEEDS

GVK BIO offers a broad range of analytical development services for complex research needs. We perform method development, validate and transfer Good Manufacturing Practice (cGMP) compliant methods for a broad spectrum of pharma compounds. We also perform stability analysis of drug products and active ingredient (APIs), packaging as per ICH, quality control testing and release as per cGMP requirements.

Our team is capable of providing documentation support – CMC, IND-CTA, MAA and DMF in line with the regulatory requirements across the globe.

Equipped with one of the best infrastructure in India for Analytical Development, GVK BIO is well positioned to meet the needs of complex analytical challenges.

OUR CAPABILITIES

- A wide range of chromatographic separation techniques (HPLC, UPLC, GC, SFC and IC) and detection techniques (UV, FL, MS, ELSD, RI, FID, TCD, CAD, etc.) to meet the requirement of different types of compounds including the ones that are non-chromophoric in nature
- Stability-indicating assay and / or related substances methods for drug substances and products (stress stability testing as per ICH)
- Dissolution (IR, ER and MR)
- Residual solvents by HSGC
- Enantiomeric separation by normal phase HPLC & GC
- Clinical comparator assay and dissolution
- Method development, qualification, validation and transfer
- Release and in-process testing
- Stability protocol development and program management
- Stability storage, testing and data trending
- Compendial testing (USP, EP, BP, JP, etc.)
- Microbiological testing
- Analytical support for cleaning validation & process validation
- Isolation of impurities and purification of compounds using Preparative LC & SFC
- Reference standard characterization & qualification, Materials characterization, Thermal analyses, Particle-size distribution, Spectroscopy (NMR, Mass, FTIR, GC-MS, UV, etc.)

METHOD DEVELOPMENT

A robust analytical method is one of the keys to quality product development and faster regulatory approval. We develop product specific analytical methods, which are best suited for intended use of application with an approach of 'right first time'. We help our partners globally in developing various analytical methods at efficient costs and meeting global quality and regulatory standards.

We have expertise in developing analytical methods for:

- Reverse engineering
- Identification
- Assay
- Related impurities
- Chiral purity
- Preservative anti-oxidant content
- Residual solvents
- Particle size distribution
- In-vitro dissolution
- Physicochemical and wet chemical methods

Various advanced and conventional analytical techniques & instruments are adopted for developing analytical methods like:

- Chromatography (HPLC, UFLC, GC and TLC)
- Spectrophotometry (UV-visible)
- Laser Diffraction Technology (Particle Size Analyser)
- Potentiometry (Auto & KF titrator)
- USP-1 and USP-2 Dissolution Tester (Automated & Manual)
- Titrimetry

We develop all analytical methods based on a thorough scientific literature search and review, which leads to appropriate selection of analytical technique and development design for the targeted product/analyte. Performance of instruments is ensured throughout the experimentation, which is handled by highly trained and skilled analysts. Robustness testing and key preliminary validation performance parameters are integral to our development design method.

We excel in development of In-Vitro dissolution methods, which plays a critical role in drug development process especially for solid oral dosage forms where absorption of drug is necessary.

We take great care while establishing a discriminating dissolution method with emphasis on following key elements:

- Dissolution media selection based on pharmacokinetic parameters
- Relevance to In-vivo performance
- Sink conditions
- BCS Classification of API
- Selection of relevant analytical technique

METHOD VALIDATION

Method validations are carried out as per latest regulatory guidelines for assay, related impurities, chiral purity, preservative & anti-oxidant content, residual solvents, particle size distribution, in-vitro dissolution, physicochemical and wet chemistry methods.

Analytical method validations are executed in alignment with stringent SOPs, which are based on **ICH Q2 guidelines** and in adherence to **cGMP requirements.**

Validation experimentation includes:

- Specificity
- Forced degradation studies
- Precision
- Accuracy
- Linearity
- Quantitation limit / Detection limit
- Stability of analyte in solution
- Robustness studies
- System suitability

Good documentation practices are followed throughout the process and an exhaustive and scientifically documented validation report is provided to the customers.

FORCED DEGRADATION STUDIES

At GVK BIO, forced degradation studies are an integral part of our method development and validation in order to establish stability indicating behaviour of methods and product characteristics. Forced degradation studies include exposure of analyte to harsh hydrolytic, oxidative, photolytic, thermal and humidity conditions.

METHOD TRANSFER

We ensure successful method transfer to our client manufacturing sites with:

- Validated robust analytical method
- Scientific rationalised scope with predefined limits
- Active involvement from qualified analysts

All the analytical methods are transferred through protocol bound study in accordance with latest regulatory guidelines such as USP (1224).

STABILITY STUDIES

We execute protocol bound stability studies for both NCEs and generic formulations as a part of our global business in accordance with ICH Q1 and custom requirements. We provide a wide range of studies, which supports the critical understanding of API and formulation.

The stability testing support can be provided to IND, NDA, ANDA and prototype formulation stability. Stability studies are routinely performed at various stages under storage conditions of different temperature and humidity (Real time, Accelerated and Stress studies as per ICH guidelines).

GVK BIO performs comprehensive stability services virtually for every dosage form. We support the customers at various stages of drug product lifecycle:

- Early formulation development
- Formulation development
- Clinical supplies
- Drug product registration / marketing authorisation
- Post approval stability

Stability Studies are performed to understand the compounds/formulation in development:

- Physical & Chemical properties of API and drug product
- Drug and excipient compatibility
- Impact of manufacturing process steps
- Interactions with packaging materials
- Assignment of shelf life

ICH STABILITY ZONES

Stability chambers are available for following conditions with climatic zones I-IV.

SN	Zone	Type of Climate
1.	Zone I	Temperate zone
2.	Zone II	Mediterranean / subtropical zone
3.	Zone III	Hot dry zone
4.	Zone IVa	Hot humid / tropical zone
5.	Zone IVb	ASEAN testing conditions hot / higher humidity

For OSD and Injectables (not packed in semipermeable containers), we cover stability study for all Zones and product storages, which are:

1.	25 ±2°C / 60 ±5%RH	Covers Zone I, II and III
2.	30 ±2°C / 65 ±5%RH	
3.	40 ±2°C / 75 ±5%RH	
4.	30 ±2°C / 70 ±5%RH	Covers Zone IVA(LT)
5.	30 ±2°C / 75 ±5%RH	Covers Zone IV B, Brazil, ASEAN (LT)
6.	5 ±3°C (for products to be kept in refrigerator)	
7.	-20±5°C (for products to be kept in freezer)	

In case of products packed in semipermeable containers, following stability conditions are maintained in addition to the above:

- 25 ±2°C / 40 ±5%RH (LT)
- 40 ±2°C / NMT 25%RH (ACC)
- 30 ±2°C / 35 ±5%RH (Intermediate)

We can programme the stability chambers to customised requirements for the following:

- Temperature and humidity
- Cold
- Photo-stability

The various offerings as per ICH guidelines on stability studies are listed below:

- Exhibit / submission batches
- Validation batches
- Commercial batches
- Support for SUPAC filing

We also offer contingency stability programmes as risk management approach to the clients.

SCIENTIFIC STUDIES INVOLVING DRUG SUBSTANCE & DRUG PRODUCTS

These studies are meant for gaining in–depth understanding of scientific concepts in relation to API and/or drug product stability. These are aimed at supporting customers in:

- NCE Research
- Early formulation development
- Clinical supplies
- Generic product development

SALIENT FEATURES

Process Driven Stability Programmes

- Stability studies are conducted in strict adherence to GVK BIO's internal standard operating procedure, meeting global quality guidelines (ICH Q1, CDER and WHO)
- Stability studies are governed by well designed, client approved stability protocols, which are prepared focusing onto geographic zone specific recommendations of ICH and factors in the dosage form specific aspects
- Concurrent documentation of loading and withdrawal of stability samples in to / from stability chambers
- Traceability of each and every stability sample ensured by documented positions
- Stability chambers are maintained and monitored / alarmed through computerised systems
- All the stability chambers have 24x7 back up power supply
- Efficient and scientifically driven OOS and OOT investigations

Consultative Approach

GVK BIO actively involves in design of stability protocols and shares its expertise in deciding:

Bracketing & Matrixing Strategy

We offer our expertise in Q1D guidelines of ICH to design and implement bracketing and matrixing strategies for stability programmes to the clients. We study the various factors that include strength, similarity of composition of the products, container closure sizes, manufacturing process employed and applicability, as well as potential risks, before suggesting possible means to reduce number of test samples by a suitable bracketing or matrixing approach.

Interpretation of Results

We share a critical view on stability results in relation to the product composition, manufacturing process, polymorphism, packaging configuration, Q3 guidelines of ICH on residual solvents and impurities with emphasis on maximum daily dose permitted, and significance of the actual results in view of these guidelines.

EXTRACTABLE & LEACHABLE

We offer Analytical support for extractable and leachable testing as per PQRI guidelines:

- Our dedicated and highly specialized team has more than 15 years of experience supporting numerous studies for various container/closure selections as well as process qualification and validation for different manufacturing processes
- Extractable/leachables program to support Injectables, OINDP studies and as well other packaging materials
- Controlled extraction studies with LC-MS, GC-MS direct injection and GC-MS headspace injection sample analyses with data interpretation and toxicity assessment services
- Leachables method development and validation studies
- Material qualification for polynuclear aromatic hydrocarbons (PAH), N- nitrosamines and other toxicologically concerned compounds
- Leachables monitoring for stability studies and routine extractable testing

ANALYTICAL CHEMISTRY

GVK BIO supports extensively structural chemistry services for small and large molecules that include:

- Impurity and degradation product identification and structural elucidation
- Characterization of API, product, reference standard and other pharmaceutical ingredients
- Molecular weight determination for large biomolecules
- Support for regulatory documentation for IND, MAA, DMF, etc.
- Analytical reference standards qualification

ANALYTICAL INSTRUMENT DETAILS

HPLC with PDA, UV, ELSD and RI, CAD detectors	FT – IR
UPLC with PDA and ELSD, FLD detectors	pXRD
LC-MS & LC-MS / MS – UPLC-PDA and ELSD	Malvern Particle Size 3000 PSD
LC-MS – HPLC Ion trap	TGA
LC-MS / MS Q-TOF	Auto titrator
Preparative LC with PDA and ELSD	CHNS Analyser – Elementor
MS directed Preperative HPLC	UV spectrophotometer
NMR (300, 400 and 500 MHz)	Ion Chromatography with Conductivity & Ampirometric detectors
Head Space – GCMS & HS-GCMS	Dissolution tester with Auto sampler
GC with Head-space – FID	Melting point apparatus
SFC – Analytical	Refractometer
SFC – Preparative	Disintegration test apparatus
DSC	Friability tester

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