KEMWELL
Keeping You Competitive

KEMWELL INTRODUCTION

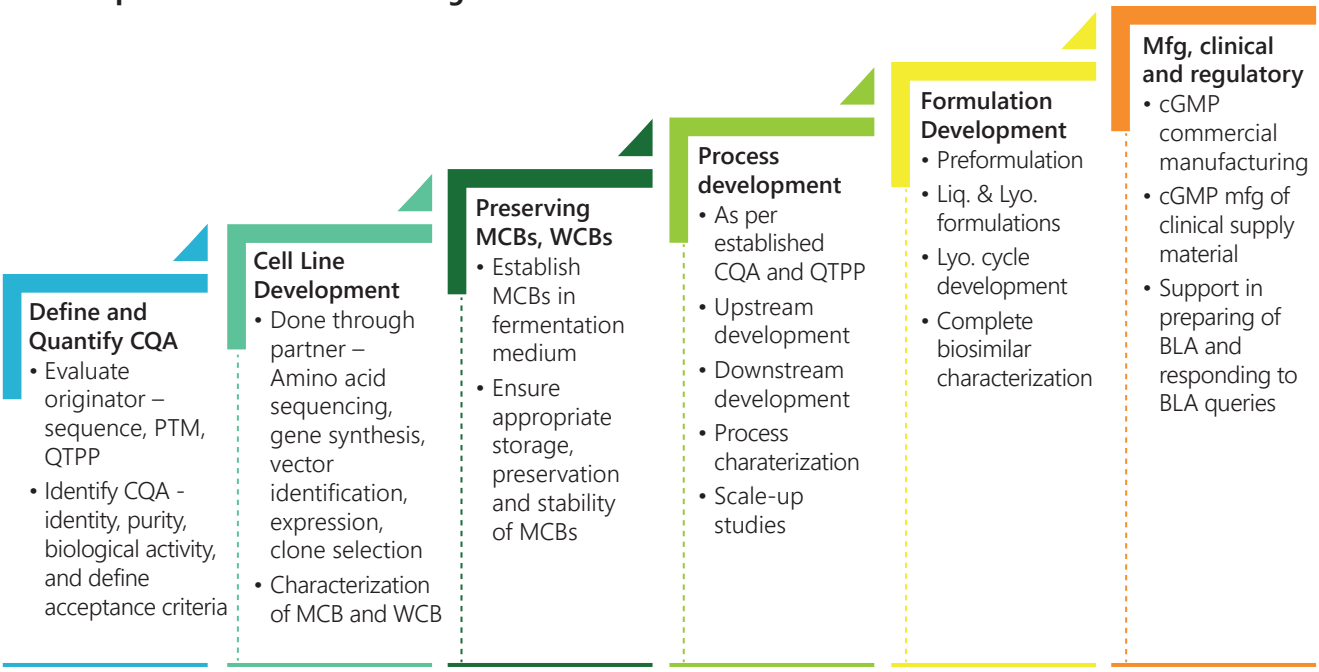
Kemwell is a contract biologics development and CMO company which provides services to global biopharmaceutical organizations. The 15,000 sq. m. facility consists of a cGMP drug substance manufacturing area with over 4000L bioreactor capacity, a sterile fill and finish area for cGMP drug product manufacturing and process development laboratories to support production of protein therapeutics from mammalian-cell culture – monoclonal antibodies, bi-specific antibodies, fusion proteins, etc.. Kemwell is capable of supporting novel, bio-better and biosimilar programs' preclinical development, clinical development, cGMP clinical manufacturing and cGMP commercial manufacturing.

Service spectrum for Novel programs:

Cell Line Development	Process Development	Manufacturing for toxicity studies	Clinical and commercial manufacturing
• Kemwell works with leading cell line researchers for preparing cell lines	• Experience of working with CHO, NS0 cell lines • Upstream process development • Downstream development • Extensive analytical, characterization • Stability Studies • Process characterization • Viral clearance studies	• Manufacturing and supply for toxicity assessment studies • Equipment used in Development labs same as in case of GMP scale at 80 L scale (eases transfer from non-GMP to GMP condition and further scale up)	• cGMP commercial manufacturing • Scale-up activities for clinical manufacturing • Manufacturing and labelling services for clinical studies • Experience in IND clinical manufacturing • USFDA, EMA and other global regulatory compliant facility

Kemwell is flexible to focus on individual activity or undertake complete development responsibility based on the requirement of its partners

Service Spectrum for Biosimilar Programs:



ANALYTICAL DEVELOPMENT AND TESTING

Kemwell provides analytical method development and method validation services. Development approach covers all aspects for intended use of the method (stability indicating, process development support, limits of detection/ quantitation, etc.)

Analytical method development and optimization for various assays including:

Process related impurities & identity	Protein related impurities and variants	Invitro Bioassays	Miscellaneous
• CHO HCP quantification – ELISA • Residual DNA determination • Q-PCR & Pico-Green method • Protein A contaminant qualification by ELISA • Mycoplasma by RT- PCR • BET test • Kinetic chromogenic lysate assay • Gel clot assay • Identity • Peptide mapping • Immuno blotting • Electrophoretic techniques	• Charged variant by CEX & cIEF • Size related impurities by SEC, SDS-PAGE (NR) & CE- SDS (NR) • Degraded protein by – SDS-PAGE, CE-SDS (NR) • Oxidised and reduced impurities by RP-HPLC • IgG purity – quantification of free heavy chain and light chain, non-glycosylated IgG, Intact IgG and other fragmented species by Capillary Electrophoresis • Isoform variants by IEF, CZE and IEF with western blotting • Glycan profiling by Capillary Electrophoresis and UPLC	• Cell proliferation assays • Anti-proliferation assays • CDC Complement Dependent Cytotoxicity) assays • Cell based cAMP release assay • Binding assays • Reporter gene assay	• Compendial methods for parenteral i.e. Sterlity, Endotoxin, Visible and sub-visible particulate matter, Degree of coloration and opalescence • Content assays by absorbance, Colorimetric and HPLC based methods • Raw material analysis including moisture content, melting point, refractive index, FTIR and various identity and assay methods

Biacore, MS, biophysical characterization tests are outsourced to a partner and managed by Kemwell

PROCESS DEVELOPMENT AND FORMULATION DEVELOPMENT

Process Development

Kemwell provides extensive mammalian cell culture based products' development services. Each project is individually customized to match the customer's requirements.

Kemwell routinely provides the following development services:

- Upstream and Downstream process Development
- Analytical methods and formulation development (including lyophilized formulations)
- Clone screening and selection
- Cell line stability studies
- Media and cell culture optimization
- Optimizing mfg. processes to improve process time and increase yields/outputs
- Achieving efficient process scale-up
- Reducing of manufacturing costs and time – through process improvements
- Process characterization
  I. Establishment of scale-down models
  II. Univariate and multivariate DoE studies
  III. Studies to define critical and key process parameters, establishment of design space, etc.
  IV. Control strategy

- Head to head comparability studies of biosimilars
- Development stability studies
- Preclinical manufacturing capabilities at 5L, 10L and 80L scale

Upstream Process Development

Kemwell's team of experienced scientists and analysts specialize in mammalian cell culture process development. We use well versed techniques such as design-of-experiments approach for process optimization to reach optimal titer values and generate superior quality products. We strive to develop a robust, efficient, scaled up manufacturing process to deliver consistent product quality.

Downstream Process Development

Kewell's purification process development team develops robust, economical processes for mammalian cell culture products. The design-of-experiments approach for process optimization and process characterization is used in order to achieve optimal yields. Our foremost goal is product quality and we strive to generate superior quality products. A close collaboration with analytical method development scientists ensures in-process testing scheme development.

Formulation Development

Kemwell offers formulation development services for early and late stage clinical development and commercial products based on target formulation profiles.

Preformulation Studies

- Evaluation of biophysical characteristics
- Assessment of 'thermodynamic stability'
- Identification of critical factors that impact stability

Formulation Screening Studies

- Formulation screening studies to select optimal formulation for the molecule
- Integrated formulation and analytical method development team to ensure right methods are available forevaluating degradation routes of molecule to enable formulation screening studies

Lyophilization Cycle Development

- Lyophilization cycle development for molecules that may have inherently lower stability in liquid form
- Optimization of each phase of the cycle to ensure an efficient, robust and scalable process

cGMP MANUFACTURING

Kemwell Drug Substance and Drug Product Manufacturing facilities are audited by reputed global multinational clients, European QPs, former USFDA inspectors and regulatory agencies. A USFDA Pre-Approval Inspection (PAI) for a BLA filing is expected by early next year. As one of India's largest and most preferred contract manufacturer of biopharmaceuticals, Kemwell operates multiple world-class GMP manufacturing facilities for the production of mammalian cell culture based biopharmaceuticals- monoclonal antibodies, fusion proteins, etc.

Drug Substance cGMP Manufacturing

Over 4000L of bioreactor capacity is available for both clinical trials and commercial drug substance supply.

Core Competencies

- Mammalian cell culture
- Product types – monoclonal antibodies and other cell culture based recombinant proteins
- Clinical and commercial manufacturing
- GMP cell banking
- Integrated with process development and drug product manufacturing capabilities
- Comprehensive analytical support

Capabilities

- Upstream – Bioreactor train of 80L, 400L and 2 x 2000L stainless steel bioreactors
- Expansion plan for additional 12,000L bioreactor capacity in available shell place
- Harvest – Continuous centrifugation and/ or lenticular filtration
- Downstream – Multiple chromatography and TFF steps; pre-and post-viral segregation – call to action
- Hybrid design – Stainless steel and single use equipment
- Flexible and adaptable to different process requirements
- Designed for purifying high titer cultures
- State-of-the-art equipment with CIP, SIP capability
- Central data management system with 21 CFR part 11 compliance
- Process validation
- Cleaning validation

DRUG PRODUCT cGMP MANUFACTURING

Kemwell provides fully automated final drug product formulation and filling under cGMP conditions as per by the worldwide regulatory agencies including US FDA, EMA, and agencies from other countries or regions such as Japan, Korea, Taiwan, Singapore, Australia and India.

Capabilities

- Both liquid and lyophilization formulation and fill in vials and PFS(planned PFS line)
- Both biologics and aqueous non-cytotoxic and non-antibiotic small molecule parenterals
- Multiple validated container & closure configurations (from 2ml to 50ml)

Liquid Vial Capacity

Vial Size (ml)	Max. Batch Size (vials)
2	42,000*
5	33,600*
10	30,000
20	15,000
50	6,000

Lyophilized Vials Capacity

Vial Size (ml)	Max. Batch Size (vials)
2	29,000
5	15,000
10	13,000
20	8,000
50	4,000

* 1-shift operation; Maximum batch size: 300L (Formulated bulk)

STABILITY STUDIES

Kemwell provides complete stability storage and testing standalone services for biologics in all recommended ICH conditions as well as custom temperature, humidity conditions. We work with customized client protocols or develop one for clients and conduct development and commercial stability studies Stability programs cover design of the study, generation of stability protocol, execution, statistical data evaluation and preparation of reports.

In addition to routine stability studies as per ICH requirements, various exploratory studies are also executed.

These include:

- Comparative / non-comparative force degradation stability studies to evaluate the product degradation pathways under different stress conditions such as high temperature, freeze thaw, pH, oxidation, agitation etc.
- In-use stability
- Hold-time stability

At Kemwell, our cGMP stability storage facilities include 21 CFR part 11 compliant walk–in and reach–in chambers, which are:

1. Qualified as per cGMP conditions
2. Monitored on-line
3. Equipped with multiple sensors
4. Provided with back-up power supply

The following stability chambers are available:

- 2-8°C walk-in chamber
- 25°C walk-in chamber
- -80°C chamber
- -20°C chamber
- 30±2 °C/ 65 ± 5% RH walk-in chamber
- 40±2 °C/ 75 ± 5% RH chamber

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