

ABOUT US

Esco Aster is a contract development and manufacturing organisation (CDMO) and a young spin off with a rich 41-year history in life sciences, medical, and healthcare.

1978 - Esco was established.

2002 - We started providing process development (PD) services to clients.

2008 - We converted bench processes into closed systems.

2013 - We broadened Tide Motion applications from vaccines to biotech, biologics, and therapeutics

2017 to PRESENT - We spun out as an independent subsidiary from Esco Group of Companies and continuously working to bioengineer Tide Motion for further applications with Esco solutions/protocols.

Currently, we focus on offering vaccine-, bio-, cell- and gene-therapy development manufacturing services using primarily its proprietary Adherent Tide Motion Platform supplemented by single use suspension and fermentation, downstream bioprocessing, and custom bioengineering equipment for client specific therapeutics.

Within the *in vitro/in vivo* Dx space, we focus on developing mAb-based antigens, single-domain antibodies for radioimaging, RT PCR reagents, RCL diagnostics. We work with collaborators to provide turnkey mobile Dx labs: Aster XpressTM.

Within the chem- biopolymer- cosmetic, personal care, cosmeceuticalsegments, we excel in converting batch processes into continuous flow chemistry, closed aseptic processing within isolators and variety of skin safety/efficacy testing services.

For the COVID-19 pandemic we are working on an end-to-end trace, test, and treat platform from swab booths, to mobile labs, turnkey modular screening and treatment centres with isolation rooms as well as working on dx, therapeutics, and vaccines.

From Earlystage Discovery to Commercial Development

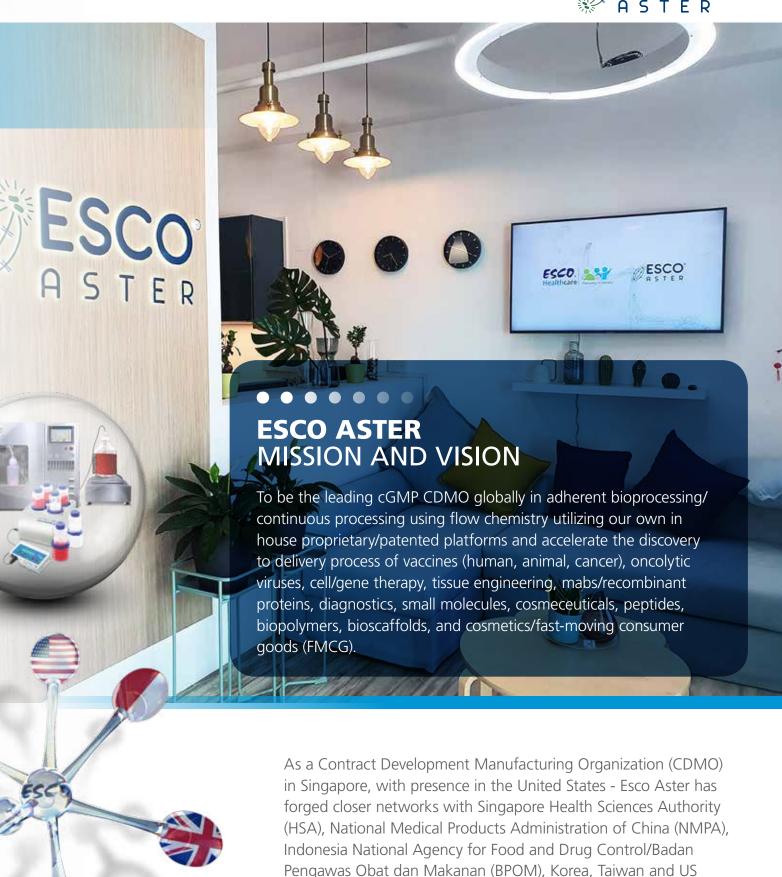


Being the first mover in scalable biomanufacturing platforms and services





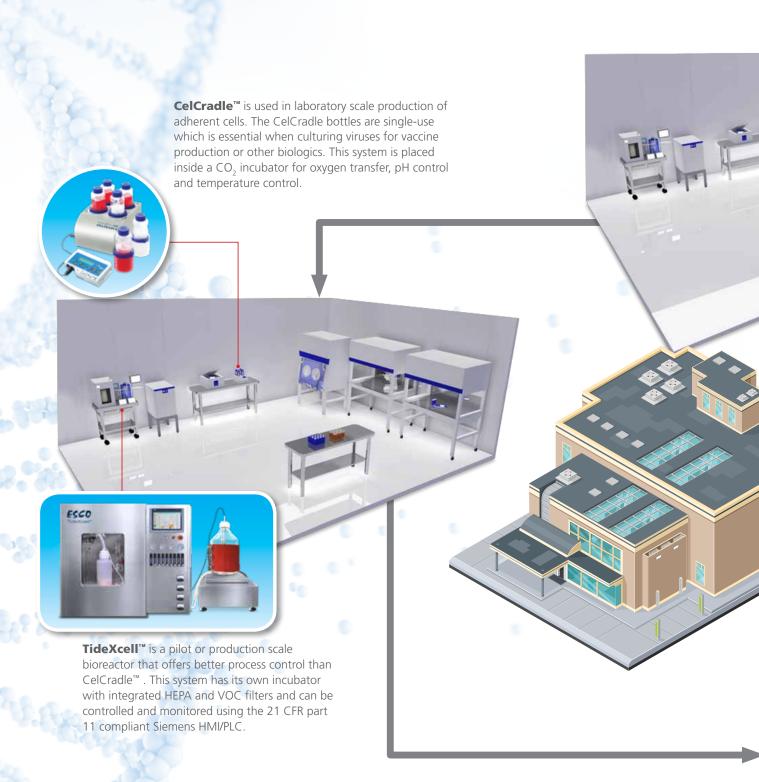




Food and Drug Administration (FDA), UK Medicines and Healthcare

Products Regulatory Agency (MHRA) and Pharmaceutical Inspection Co-operation Scheme (PIC/S) global alliance.

3



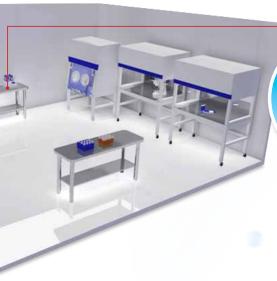


Batch Mode in TideXcell™



Perfusion Mode in TideXcell™







Batch System Useful for batch and semi-batch operation where process components are easily traceable



Continuous System Useful for continuous operation where process components are easily traceable

CelCradle™ is a single-use benchtop bioreactor perfect for high-density cell culture. It is also used as a seeding platform before scaling up to TideXcell™. This system allows the seeding of uniform concentration of cells to BioNOC™ II (a macrocarrier), while controlling the physiological conditions in the cell culture medium.





Downstream Processing Formulation and Filling

Vial QC and Sterility Testing

Cold Storage





TideXcell™ Cell Harvesting System (TCCHS) utilizes the same conventional cell harvest concept by enzymatic treatment that could digest and detach cells from being attached to substrates.



DISCOVERYFROM PRECLINICAL TO CLINICAL

As a full-range services partner, we support our global clients from early-stage discovery to market approval of clients' products.



DEVELOPMENTFROM CLINICAL TO COMMERCIAL

As a multicultural high-performing organization with established strong credibility, we have a stable operational model that delivers optimal level of performance whilst ensuring consistent cGMP manufacturing of safe, cost-effective, and reliable products.





CELL LINESDEVELOPMENT SERVICE

We work with you to provide cGMP compliant, highproducing, and stable cell lines for your protein of interest with desired post translational modifications (PTMs).

Serum-free, albumin-free, animal component-free and xeno-free VERO, MRC-5, WI-38, CEF and C8166, CHO, Sf9 and HEK 293 cell lines for commercial vaccines production, cell-based assays, and recombinant protein production.

Curated human cell lines, hMSCs, hIPSCs and umbilical-cord derived cell lines as well as extracellular vesicles such as exosomes.

Differentiated cells from hIPSCs or hMSCs such as adipocytes, hepatocytes adipose-derived MSCs, hepatocyte-derived MSCs, and others.









VECTORS PRODUCTION SERVICE

We work with you to produce large-scale viral stocks using serum-free media in a closed system, such as an isolator for your project. Our macrocarriers in our bioreactors enable a high surface area 3D cell culture. This enables a cost-effective, labor-reducing, and time saving production of viral vectors in producer cell lines. Cell lines such as HEK293T adapts well to our bioreactors, reaching a higher cell density for sustained cell growth to allow high titer vector stocks* harvesting.



Efficient, large-scale production of lentivirus, retrovirus, adenovirus-associated, adenovirus stocks compared to cell factories and other 2D culture systems.

Actual results may vary, depending on viral vectors used and transfection reagents/ techniques adopted. We advise client to seek our advice and recommendations whereas appropriate.

RECOMBINANT PROTEIN EXPRESSION AND PRODUCTION SERVICES

Recombinant Protein is a form of protein that is artificially made using recombinant DNA technology. It is made to be produced in large quantities, to be used throughout biomedical science, and to be manufactured for useful industrial applications.

Eukaryotic systems, specifically mammalian and insect cell culture systems, are very viable system for the production of both monoclonal antibodies and recombinant proteins. Our laboratory uses highly productive cell lines such as Chinese hamster ovary cells (CHO) and Sf9 cells which stably express antibodies/recombinant proteins which have been subjected to process optimization techniques for more improved expression and consistent high yield protein production.

Our capabilities ensure a seamless workflow that inludes:

- Engineering of Expression Vectors
- Host Cell Transfection
- Clone Selection
- Single Cell Clone Isolation and Expansion
- **Cell Banking**
- Evaluation of Growth Characteristics and Process Optimization





The specific advantages of the CHO cell culture system are:

- High cell density achievable in our Tide Motion Bioreactors
- Survival in serum-free media during the production phase
- Rapid and high protein yields –up to several hundred mgs/L

Besides CHO lines, we also use HEK 293 lines which are grown to high densities and in turn, offer:

- Small-scale construct screening
- Transient transfection or stably integrated genes
- Rapid and high protein yields –up to several hundred mgs/L

For Baculovirus expression system using Sf9 cells, we employ consistent and high protein yield with post-translational modification (PTMs) workflow, they are as follows:

- Cloning of the Transfer Vectors
- Generating a Recombinant Bacmid
- Production of P1 Virus Stocks
- Virus Amplification
- Virus Titer Determination -Plaque Assay
- Cell Expansion and Infection with Baculovirus
- Protein Purification





- Time of infection
- Multiplicity of Infection
- Cell Density at the Time of Infection
- Cell Density at the Time of Harvest
- Insertion of Kozak sequences, signaling peptides (to enhance production and secretion of protein) and fusion tags for ease of purification in the transfer vector





UPSTREAM PROCESSING DEVELOPMENT SERVICE

With our in-depth understanding of the Asian market, we adopt a customisable approach in delivering sustainable risk-adjusted returns to our clients.

We support an integrated approach to service delivery to increase viral expression titer, multiplicity of infection (MOI), and increase cell viability at high-density cultures. On the average, we have obtained at least 5x10⁹ (for mammalian cell lines) and 2x10⁸ for stem cell lines.

We are the industry's leaders and expert in Upstream Processing (USP) development using our Tide Motion™ bioreactors.



CHO library suits the expression of recombinant proteins, monoclonal antibodies, and biosimilars implemented with our proprietary bioreactors in a small footprint



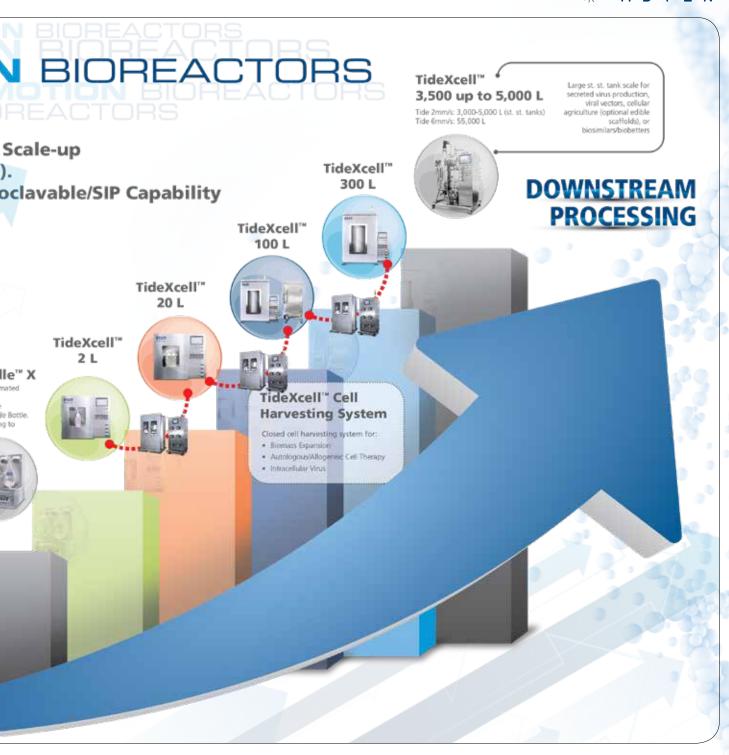
Bioprocess optimization using Design-of-Experiments methodology in optimizing cultivations and unit operations





Animal component free media adapted to USP processes and lowering impurities







Customizable and reprogrammable fed-batch, continuous, and perfusion mode(s) in hypoxia and/or anaerobic conditions



Robust proprietary technology platform that is scalable up to 5,000 liters capacity



SUSPENSION CULTURE SERVICES

Our suspension services can be used for various cell culture applications such as bacteria, insect cells and mammalian cells in batch, fed-batch, and perfusion modes. We utilize single-use cell bags of up to 50L capacity allowing an easy set-up with no cleaning required and less susceptible to issues such as cross-contamination. The various advantages of the system include convenience, reliability, flexibility and versatility.



Key Applications are as follows:

- Monoclonal Antibody (mAbs) Production
- Hybridoma Cell Culture
- Insect Cell Culture
- Cellular Agriculture



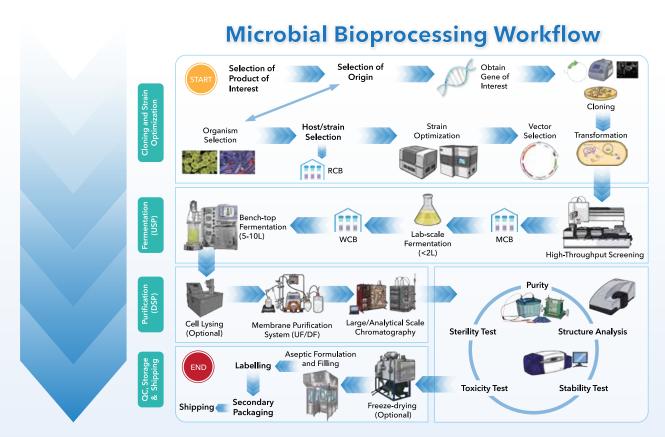
FERMENTATION SERVICES

Esco has vast experience in bioreactor designing and offering fermentation service to the clients for different cell lines. A series of bioreactors and bioprocessing equipment of laboratory (5L-10L) to large scale are utilized for the following services:

- Strain Development and Optimization
- Recombinant DNA Technology
- Microbial Fermentation (e.g. Bacteria, Yeast)
- Large-scale Contract Fermentation (50L)
- Fermentation Process Optimization for Expression/Production of:
 - Recombinant Proteins
 - Peptides
 - Enzymes
 - Active Pharmaceutical Ingredients (APIs)
- Fermentation Process Validation

- Biomass Generation
- Cellular Agriculture
- Alternative Proteins

Below is an overview of the Esco Aster's Microbial Bioprocessing Workflow:



DOWNSTREAM PROCESSINGDEVELOPMENT SERVICE

We have a modular setup to optimise efficiency in obtaining a pure and high concentration of your product whilst recovering as much as 80% product of interest (POI) with minimal waste. Our bioengineers will propose the most feasible downstream processing systems (DSP)* tailored for your project development.

A. FILTRATION SERVICES

We incorporated tangential flow filtration systems (TFF) as a first downstream concentration/ purification step in different pipelines:

Microfiltration: Applications where the harvested cells are the final product, TFF combined with a clarification step will consolidate the final downstream platform.

Ultrafiltration (UF)/Diafiltration (DF):

- a. Applications where the final product are biological, such as:
 - Extracellular Vesicles (EVs)/Exosomes
 - Viruses as Intermediate Products (CAR-T)
 - Protein Purification

Applications where the final product are synthetic nanoparticles such as:

- Biocompatible Polymer Particles
- Liposomes
- Polysaccharides

We provide an upstream to downstream bioprocessing and end-toend modular approach that are able to achieve suitable concentration/ purification factors to meet your final product specifications.

- Number cells/ml: Recovery yields of as much as 87% depending on the product-of interest
- Nanoparticles/ml: Recovery yields that enable the production of nanoparticles in concentrations required to meet biological outcomes in clinical studies
- Identity, Potency, Morphology: Cell viability and proliferation as much as 98%
- Purity: Removal of protein impurities and microcarriers to meet quality attributes for final product



DSP development is not limiting to single-use concentrators or chromatography or microfluidics-size exclusion methods. We advise clients to seek our advice and value-added services in conjunction to USP development.





B. PREPARATIVE CHROMATOGRAPHY

Esco has capabilities in the downstream purification of wide range of biologics like recombinant proteins, viruses, virus-like particles (VLPs), and monoclonal antibodies (mAbs) using different chromatographic techniques based on the requirement of the product of interest.

- These techniques include:
 - Affinity Chromatography (e.g. antibody, specific group, tagged group)
 - Ion Exchange Chromatography
 - Multimodal Column Chromatography
 - Hydrophobic Interaction Chromatography
 - Reverse Phase Chromatography
 - Size Exclusion Chromatography
 - With these, we offer specific services in downstream bioprocessing such as:
 - Optimization of process variables using Design of Experiment (DoE) analysis
 - Process development for the production of biologics (e.g. viral vaccines, recombinant proteins, viruses, VLPs, antibodies)
 - Scale-up and scale down of the bioprocessing platform from laboratory to industrial scale
 - Access to bioprocess expertise with dedicated scientist(s)



ANALYTICAL TESTINGAND VALIDATION SERVICES

Nowadays, the biopharmaceutical industry relies on analytical service providers to come up with an excellent platform for core testing needs so they can back up their internal resources at their best.

At Esco Aster, we understand the importance of providing a robust platform to support our clients during process development and product manufacturing. To meet industry needs for high-quality, rapid, cost-effective, and top-of-the-line services, we are now offering extensive analytical expertise, including:

- Analytical Method Development, Validation and Transfer
- Bioassay Transfer and Validation
- Product Characterization and Biochemical Comparability
- Reference Standard Characterization
- Pre-formulation Studies
- Final Product Stability Studies
- Forced Degradation Studies



- **Sterility Testing**
- Product-related Impurity Testing
- Microbiology Testing
- Particulate Matter Testing
- Nanoparticle Characterization
- Process Characterization/ Validation:
 - Characterization of Cells
 - Cell Bank Characterization
 - Process Limit Studies
 - Product-specific Assay Validations
 - Process Performance Consistency Studies
 - Evaluation of DNA Reduction
 - Stability of Process Intermediates
 - Cleaning Validation
 - Sterile Process Validation



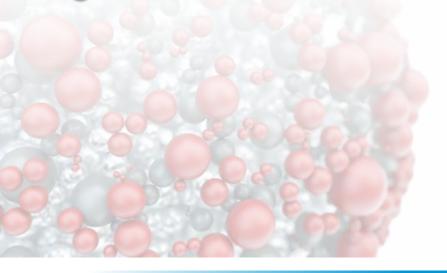


(BIO)POLYMER ENCAPSULATION SERVICES

For those customers that require enhancing the half-life and stability of their final drugs or bioactives, Esco Aster offers a cutting edge encapsulation technology based on biocompatible polymers, polysaccharides, and other macromolecular or lipid-based carriers.

Our scientific and bioengineering teams have the knowledge and years of experience to support our clients with different encapsulation approaches during R&D, drug development and manufacturing for several applications, namely:

- Encapsulation of Fat-Soluble Compounds
- cGMP- compliant Nanoparticle Purification using Tangential Flow Filtration Systems
- Research and Development: Plain and Encapsulated Liposomes, Polymersomes, Polymer Nanoparticles and other Formulations
- Customized Surface Modification of Nanocarriers
- Custom Formulations
- Encapsulation of Small Molecules, Therapeutic Agents, Bio-actives and Nucleic Acids
- Encapsulation of Vitamins and Supplements
- Nanoparticles Production Process Control
- Analytical and Characterization Services: Analysis and Reporting





OTHERCUSTOMIZED SERVICES

Our manufacturing facilities are world-class built in accordance to PIC/s and upcoming HSA CTGTP guidelines. Our facilities are ready for batch, recirculation, and perfusion in single-use bioreactors or stainless steel fermenters. Our USP and DSP platforms, when used in conjunction with an integrated quality control system, total quality management and Supervisory Control and Data Acquisition (SCADA) deliver the best-in-class manufactured products. All this, combined with our talented bioprocessing scientists, we develop the full process validations, product characterization, and production for all clinical trial phases.

- Formulation development studies, including conditioned media for cosmetics or wound healing purposes
- Transdermal and topical emulsion-based formulation development
- Inhalation and nasal formulation development
- Oral-dispersing film and sustained-release development
- Customized homogenizing needs for oral tablets
- Drug substance and excipient development
- Micro-/ Nano-encapsulation technologies for tasting or smelling masking, increase bioavailability
- Shelf-life and stability testing under accelerated conditions for pharmaceutical or skin products
- 2 3D in vitro technologies for cosmetic products testing
- 2 3D in vitro lung efficacy studies for compounds/ ingredients testing
- 2) 3D organoids using miniaturized bioreactors for diseases modelling
- Technology transfer and process validation
- Compilation of regulatory dossier and documentation to a regulatory body of interest

CONTINUOUS FLOW PROCESSSERVICES

As an emerging contract development and manufacturing organisation (CDMO), we have focused our attention on continuous flow processes. We have the expertise, local collaborations and state-of-the-art facilities to address your process requirements pertaining to Active Pharmaceutical Ingredient (API) synthesis or multistep synthesis of functional organic molecules.

SPECIALIZATION:

- Synthetic Route Scouting
- Chemical Process Safety Assessment
- Process Optimization













HIGH-END FACILITIES

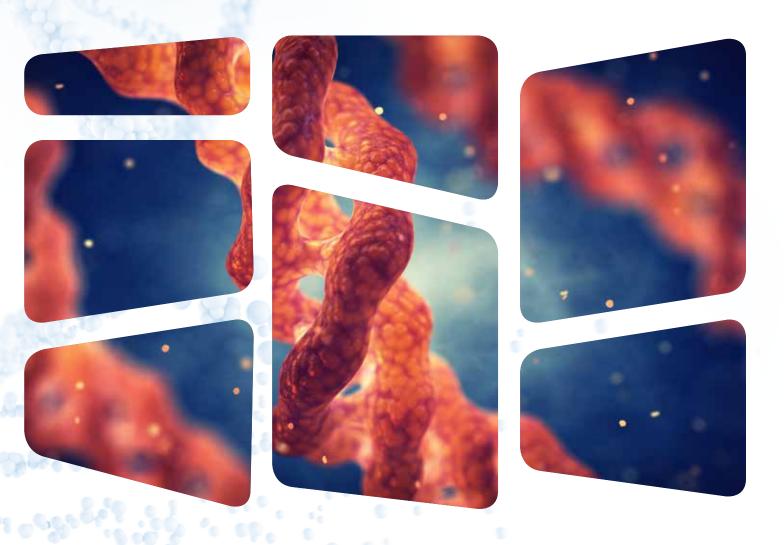
We are equipped with flow chemistry equipment, parallel reactors, high performance liquid chromatography (HPLC), flash purification systems, peptide synthesizers and can optimize/ develop batch reactions to make them suitable to run on a continuous platform. We have the facilities for the following class of reactions:

- Metal-mediated cross coupling reactions
- Substitution reactions
- Condensation reactions
- Functional group transformations and rearrangements
- Amide coupling

We are in the process of upgrading our facilities to accommodate other organic transformations.

CAPABILITIES

- Appropriate standard modules to handle different reactions and batch sizes
- Development and optimization of synthetic routes suitable for Flow Chemistry
- Streamlining and automation of multistep reaction sequences of APIs
- Diversification of API synthesis using common key intermediates
- Establishment of a safer alternate way for hazardous reactions
- Peptide synthesis, intermediates for API and compound libraries
- Appropriate standardized modules to handle multiple batch sizes.



PEPTIDE MODIFICATIONSERVICES

We understand that peptide development is filled with challenges. Due to hydrophilicity, peptides exhibit limited ability to cross physiological barriers and are confronted with efficient hepatic and renal clearance. Also, once inside the systemic circulation, peptides typically have rather short half-lives due to aggressive degradation by multiple digestive proteases. These aspects have led to difficult administration routes which resulted to low patient compliance.

- **1. Synthetic Services:** capabilities to synthesize a broad range of therapeutic peptides/proteins through:
 - A novel continuous flow approach with the latest technology
 - Conventional Solid Phase Peptide
 Synthesis/ Liquid Phase Peptide Synthesis
 (SPPS/LPPS)
 - Combo Technology
 - Fermentation
 - Recombinant DNA methodology



- **2. Comprehensive Peptide Modifications**: capabilities to increase their half-lives.
 - Attachment Chemistry
 - Polyethylene Glycol (PEG) Modification
 - Linkers
 - Spacers
 - N-terminal and Side-chain Modification
 - PEGylation
 - Acetylation (lipopeptides)
 - Formylation

- Peptide Stapling
 - Ring Closing Metathesis (RCM)
 - Thioether Formation
- Peptide Macrolyzation



ANTIBODY-DRUG CONJUGATE SERVICES

Our capabilities are directed towards the synthesis of payloads/lead compounds providing the design, synthesis and development of novel and stable cleavable linkers with desired properties for the overall stability, solubility, and potency of antibody-drug conjugates (ADCs).

We are unique because our biochemistry labs can either provide: (1) large molecules for small molecule companies (2) linker/payload for large molecule companies and/or (3) combination of both for virtual companies.

Our services are as follows:

- Design and Synthesis of Chemically Cleavable Linkers
 - Acid-cleavable Linkers
 - Reducible Disulfide Linkers
 - Exogenous-responsive Cleavable Linkers
- Design and Synthesis of Enzyme-cleavable Linkers
 - Dipeptide Linkers
 - Glycosidase-cleavable Linkers
 - Phosphotase-cleavable Linkers

In addition, we offer suitable methodologies for the chemical conjugation of antibodies thru the strategic attachment of (1) linkers tethered with the payload or (2) a suitable handle with a reactive functionality of which the payload can be conjugated. Our recent focus on continuous flow chemistry for the multistep synthesis of API and advanced intermediates gives us a great advantage to carry out the synthesis of payloads on a continuous platform which has the inherent advantage of a linear scale-up.

Methodologies are listed below:

- Lysine Amide Coupling
- Cystine Coupling
- Synthetic Amino Acid Incorporation by Genetic Engineering into Monoclonal Antibodies (mAbs) and Subsequent Chemical Conjugation





STEMISTRY:DEVELOPMENT and SERVICES

Harnessing the full potential of stem cells is one of the major challenges in medicine and healthcare nowadays. Stem cells are specialised human cells that have the ability to develop into many different cell types. They have the ability to repair damaged tissues and have a great potential in various clinical applications. Over recent years, small molecules have emerged as essential tools for understanding, regulating, and manipulating stem cells—stemistry, is what they call it.

The continued interests for small molecules targeting in vivo aspects of regeneration, including adult stem cells, stem cell niches, and mechanisms of homing, mobilization, and engraftment as well as somatic cell proliferation have been the new emerging paradigm in the field of research. Esco, a CDMO company, offers an integrated multi-instrumental approach that exploits the potential of several techniques to provide sound evidential support in terms of synthesis, characterization, and screening of small molecules for both phenotype-based and target-based screening.

Our services are as follows:

- Synthesis of reported small molecules and their close analogues (discrete structural modification) targeting specific cell signalling pathways (target-based screening) using modified synthetic schemes, conventional, and continuous flow chemistry methods. Able to synthesize the reported compounds up to a gram scale with high purity (>95%) based on clients' needs.
- Synthesis of a novel small molecule chemical libraries from commercial building blocks for phenotype-based screening
- Characterization studies involving observation of cell-specific phenotypes by visualization of cell morphology using appropriate methods such as Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM).
- Characterization studies involving the detection of specific marker proteins by antibody immunostaining
- Hits identification and Hit-to-Lead Studies: Transfection of cells appropriate reporter genes for initial screening of small molecules and the use of suitable imaging methods to shortlist Hits and activate reporter gene. Identification of the right molecule(s)/Lead(s) from the initial screen using immunostaining and reverse transcription polymerase chain reaction (RT-PCR) analysis.
- Lead Optimization Studies: Focused structure-activity relationship (SAR) for design and synthesis of analogues with specific structural modification based on molecular modelling studies.

As part of a growing CDMO business, we plan to extend our capabilities and services with affinity chromatography techniques, drug affinity responsive target stability (DARTS) to explore the target protein of small molecules, and the use of DNA chips or regulators (or a combination of both) in studying their effects on a particular signalling pathway.



FILL AND FINISH SERVICE

Our fill and finish services cater to preparations in which the end product is in liquid, cell, or vial form. This production of clinical trial ready product can be done in a ready-to-use vial filling line with integrated freeze drier integrated in an isolator. The same cGMP-compliant process can be applied to client's dosage, formulation and filling requirements defined in the dossier submission package.

- Automatic sterile aseptic filling of liquid vials and cells cryopreserved vials ready for clinical trial or biobanking
- Various customized filling lines depending on product types
- Complete QA/QC release
- E Labelling, packing, and shipping of clinical samples

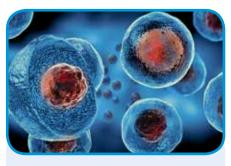
TAKE PRIDE WITH THE

We are a leading manufacturer and provider of integrated Tide Motion platform technologies and solutions which allows us to solve process development/commercial-scale manufacturing bottleneck, thereby enabling faster and lower COGS translation for our collaborators and partners for their different applications towards:



Animal Health

- Livestock, Poultry, & Aquaculture
- Companion Animal mAbs & Vaccines
- Zoonotic Vaccines
- Cell Gene Therapy & Tissue Engineering
- Animal Conservation



Cellular Therapy

- Autologous/Allogeneic Cell Therapy
- Skin Tissue Mass Production
- Exosomes
- Stemistry



STRATEGIC ALLIANCES

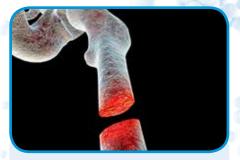
We adopt an innovative R&D model that encourages external industry and academia collaborations to accelerate open innovation, advance science and technology, and expand market growth opportunities. We collaborate, on a global basis, to complement our CDMO value-added services. Mostly importantly, we encourage the building of new relationships to build new application notes using our tools and technologies.



Water Treatment



Vaccine Production



Bone Regeneration



Biosimilars/Biobetters

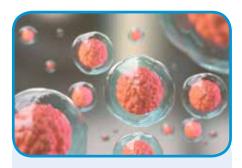


Cosmeceuticals



Cellular Agriculture

- Acellular Products
- Cellular Products



Cell Lines

- Adherent Cell Lines
- Suspension Cell Lines



Gene Therapy

- Integrative Viral Vectors
- Nonintegrative Viral Vectors
- Organic and Inorganic Vectors



Diagnostics

- mAbs for Diagnostics
- Disease Diagnostics

ESCO.
WORLD CLASS. WORLDWIDE

1978

Esco was founded in Singapore and began to pioneer cleanroom technology in Southeast Asia



Expansion of Esco life science and medical products

2007



Esco earns first EN 12469 cert. for BSC

2001



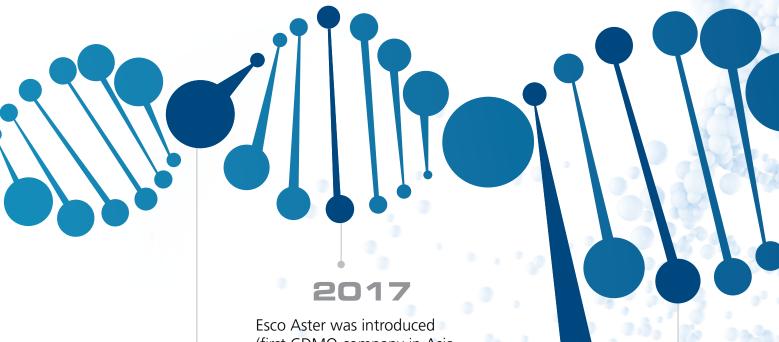
Esco earns onsite UL accreditation

2006

Esco expands distribution to pharmaceutical life science biotech and medical research markets

1990





Esco Aster was introduced (first CDMO company in Asia utilizing its own proprietary Tide Motion technology)

Esco Aster and Instittute of Molecular Cell Biology announce a collaboration to accelerate preclinical development of a hand foot and mouth vaccine

Esco Aster and Bioprocessing Institute sign a Memorandum of Understanding to innovate on continuous manufacturing platform



2018

Esco Aster and National University of Singapore announce a development of single-use bioreactorbased stem cells for bone regeneration.



Esco VacciXcell was introduced

2015

2019

Esco Aster continues to grow with the outfitting of a cGMP-compliant PD, GLP, Phase 1 and 2 clinical trial facility.









PRE-CONSULTATION







SERVICE AGREEMENT SIGNING



PROJECT COMPLETION



PROJECT DELIVERY



PROJECT COMMENCEMENT





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