Accelerating
cell and gene therapies
through unmatched expertise

CMC and manufacturing
expert consultant partners

Dark Horse Consulting Group comprises two business units:

DARK HORSE CONSULTING

BIOTECH LOGIC
A DIVISION OF DARK HORSE CONSULTING GROUP

Dark Horse Consulting Group is a fully-integrated global consulting practice offering services across biopharma markets. We are uniquely positioned to address a wide range of client types and challenges, offering tailored combinations of relevant expertise, resources, and engagement types.

We offer services in these domains:

CMC

REGULATORY

NONCLINICAL

CLINICAL

QUALITY & COMPLIANCE

BUSINESS ANALYTICS

Our SMEs bring expertise and experience with a wide range of product and technology types:

- Primary cells and tissues
- iPSCs, ESCs (incl. gene-modified)
- HSCs, MSCs (incl. gene-modified)
- T cells (αβ, γδ, Treg), TILs, NK cells, B cells, DCs (incl. gene-modified)
- Viral gene delivery (LVV, AdV, AAVs, RVs)
- Non-viral gene delivery (mRNA, exosomes, LNPs, etc.)
- Gene editing (CRISPR/Cas, ZFN, TALEN, base editors, etc.)
- Recombinant proteins including fusion proteins
- Biosimilars
- Complex antibodies
- Synthesized macromolecules (incl. oligonucleotides and peptides)
- Vaccines and adjuvants
- Blood-based products
- Combination products

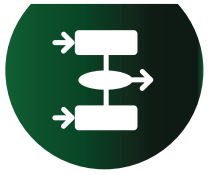
Together, we offer a wide range of customized offerings.

STRATEGIC SUPPORT

Both DHC and BioTechLogic provide strategic support, focusing on long-term organization goals and general big-picture planning: the “what” and the “why” of decision-making. All support is customized to the specific needs of each client.

OPERATIONAL SUPPORT

Both DHC and BioTechLogic also offer operational support, focused on tactics as well as day-to-day activities and processes needed to achieve operational and developmental objectives. All support is customized to the specific needs of each client.



CMC

CMC can make or break product approval, as our experts know well. Time spent on getting CMC development right will nearly always pay dividends by streamlining next steps towards regulatory approval and commercialization.

Both DHC and BioTechLogic have robust teams of CMC experts available to develop, optimize, and validate thorough, scalable, cost-effective, and compliant manufacturing processes. We offer hands-on phase-appropriate development support for all aspects of CMC and biopharmaceutical development under R&D and GMP conditions.

STRATEGIC SUPPORT

Process and analytical development support

Our team's depth and breadth of experience helps you navigate and overcome various challenges, including:

- Root cause investigation and failure analysis of processes or assays
- Analytical method and/or assay development, transfer, qualification, codification, and validation
- Process and assay evaluation and codification for formal documentation
- NGS data interpretation and off-target analysis
- Feedback on suitability of CQA (and ranges)
- Potency assay strategy development
- Stability testing support including reports
- Assay development gap analysis
- Comparability strategy review including study design and execution
- Advice on matrixed potency panels
- Remediation of analytical test failures
- GLP assays

Analytical method development & validation

Essential to CMC program success, we design phase-appropriate analytical methods, optimization and validation plans tailored to your product and processes. We recommend the utilization of fit-for-purpose assays and advanced statistical approaches to support the identification of your product's critical quality attributes (CQAs).

Process development descriptions, documentation, & reports

We support and execute the authoring of comprehensive documentation, process descriptions, data trend analysis, and supporting study reports for your product's process development and optimization journey.

Product characterization

Our consultants have a thorough command of diverse analytical techniques supporting comprehensive characterization, including functional and physicochemical assays, of your drug substance and/or drug product.

STRATEGIC SUPPORT

Full lifecycle product development planning

Our team's unmatched multi-disciplinary expertise is available to support you throughout the full lifecycle of your product development.

- CMC and nonclinical gap analysis
- Product Development Plan (PDP) and roadmap creation
- Detailed Process and Analytical Development Plans and Control Strategy
- Raw material strategy and critical supplier selection
- Milestone-based planning from FIH through to BLA readiness ('roadmap to BLA')
- Coordination of cross-functional activities

Device development support

Our team can provide support throughout the full lifecycle of device development, including:

- User Requirement Specification (URS) development
- Competitive landscape scan/analysis of existing devices
- Early-stage concept design and product strategy
- Search and selection of outsourced engineering partners
- Oversight of prototype development and testing
- Authorship of Design History Files (DHFs), Device Master Files, and Device Master Records (known as MAFs or DMRs, respectively)
- Generation of submission-ready technical documentation

Full lifecycle CMC strategy

We leverage our extensive experience gained from working on thousands of projects at all stages of development to support you with:

- Process Flow Diagram (PFD) authorship
- CMC gap analysis
- Portfolio prioritization
- High-level manufacturing strategy definition
- Capacity planning using custom quantitative models *(see pages 23 and 25)*
- Supply chain strategy development including redundancy, sourcing, and lead-time risk
- Cross-program CMC governance support
- Alignment of manufacturing timelines with clinical and regulatory strategy
- CMC roadmap
- Critical path identification

Process characterization & risk assessment

Leveraging design of experiments (DOE), we perform a systematic evaluation of your manufacturing process, establishing a thorough understanding of how critical process parameters (CPPs) influence your final product's critical quality attributes (CQAs). Additionally, our process parameter risk assessments identify the process parameters posing the highest risk to your production process to support risk mitigation planning.

Explore CMC case studies here:

CMC
continued

STRATEGIC SUPPORT

Quality Target Product Profiles (QTPP) & Critical Quality Attribute (CQA) assessments

Creating a foundation for your product and process development program, we utilize a QbD framework to thoroughly understand the quality characteristics essential for ensuring consistent, reliable, and reproducible execution and product quality, as well as for safely delivering your drug product's intended therapeutic effect.

Project management

We oversee your project to achieve your milestones in a timely fashion, including maintaining up-to-date project timelines, organizing project team meetings, capturing meeting minutes, establishing RACI (responsible, accountable, consulted, informed) matrices, and following up on achievement of action items.

OPERATIONAL SUPPORT

Method transfer

Preparation, documentation, and oversight to ensure the seamless transfer of your method to CROs, CDMOs, and other service organization partners.

Analytical method troubleshooting

We work with you on-site or virtually to identify, diagnose, and resolve analytical problems or inconsistencies.

Regulatory compliance, SOP generation, & submission support

We support data integrity, end-to-end traceability of analytical data from collection, analysis and data management for your quality systems, regulatory filings, CMC submission summaries, and beyond. Additionally, we assist with SOP generation and management to ensure excellence in analytical execution.

Combination products CMC support

Examples include:

- Generate a Design and Development SOP or plan including templates for documentation of design inputs, design outputs, design reviews, and design verification
- Generate a Design History File SOP including a Design History File Index
- Support the generation of: User Requirements, Design Input, Design Output, and Design Verification Traceability Matrix, Design Verifications, and Design Validations
- Facilitate design reviews, act as an independent reviewer, and prepare design review documentation
- Generate a biocompatibility risk assessment
- Prepare design FMEAs (dFMEA), User Requirement Risk Assessment (URRA), and other device risk assessment

OPERATIONAL SUPPORT

Process development, qualification, & validation

Our experience managing pre-qualification, validation, optimization, and CPV for all modalities and production technologies includes managing laboratory scale processes, pilot plants, and large-scale processes. This includes the development and validation of the following: precipitation, centrifugation, microfiltration, depth filtration, cell disruption (microfluidization, homogenization), and periplasmic extraction.

- We have expertise in upstream and downstream manufacturing of: PEGylated and non-PEGylated proteins, antibody fragments, oligonucleotides, mAbs, recombinant proteins, gene therapies, and blood products. We work with both stainless steel and single use fermentors/bioreactors.
- We have developed work processes, provided on-site manufacturing support, and designed process steps using the following purification technologies: laboratory and industrial-scale liquid chromatography, high-pressure liquid chromatography, ultra-filtration/diafiltration, rotary evaporation, sterile filtration, Tangential Flow Filtration, centrifugation, chromatography, and virus inactivation & removal.
- We also manage microbial fermentation, mammalian cell culture and oligonucleotide synthesis processes for the production of biopharmaceutical products, as well as plasmid production or selection, cell expansion and plasmid transfection, and viral vector production for gene therapy.

Process material evaluations

Thorough analysis, often including an extractables and leachables risk assessment, of the impact of raw materials, excipients, consumables, and intermediates on process performance and product quality includes program design, procedure creations, external laboratory identification, results review, and mitigation strategies.

Project communication planning

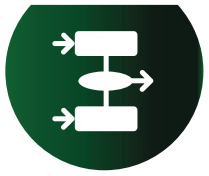
We develop detailed project communication plans and matrices, ensuring transparent and accurate communication.

Project execution, tracking, reporting, & document management

We track and report progress throughout the project, enabling all stakeholders to clearly understand the project status and upcoming activities and milestones. Along this journey, our project managers carefully track and expedite the resolution of action items, highlight critical project issues and risks, and facilitate the development of mitigation action plans.

Facility assessment, design, & capacity planning/optimization support

We offer site development and capacity planning support if you plan to scale in-house manufacturing. We also support clean room validation and personnel training. If you are working with a CMO partner operating multi-product facilities, we can thoroughly assess the facility and conduct a cross-contamination risk assessment. We're experienced in assessing and qualifying systems such as WFI/purified water, clean steam, and air handlers. If new products are being brought onsite in anticipation of audits/PAI, we assess for regulatory compliance and capacity.



CMC
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Project management

We oversee your project to achieve your milestones in a timely fashion, including maintaining up-to-date project timelines, organizing project team meetings, capturing meeting minutes, establishing RACI (responsible, accountable, consulted, informed) matrices, and following up on achievement of action items.

Manufacturing operational support

We expeditiously address operational challenges and bottlenecks, including:

- Remediation of manufacturing/testing failures (especially at CDMOs, CROs)
- Facility design consultation (for scale-up, compliance, etc.)
- Quantitative capacity planning and throughput modeling *(see pages 23 and 25)*
- Workforce development and technical training programs
- Project management support across tech transfer, scale-up, and vendor onboarding
- Interim functional leadership, e.g., QA lead, CMC director, operations head
- Support for internal GMP facility planning
- CDMO selection and evaluation support

Contract services partner selection & management (incl. CDMO/CRO)

Since CDMO selection is unique for every client, we assist based on specific project objectives and variables, including process development assistance required, needed capacity, development timelines, and tech transfer costs. If desired, we can also manage contract partner programs. Our proprietary CDMO database and established methodologies ensure a good fit for your program.

- Access to a proprietary CDMO database with selection filters by modality, scale, geography, and tech capability
- Proprietary quantitative CDMO selection methodology
- Design and management of the CDMO selection process
- Support for vendor audits, including on-site inspections and capability assessments
- Contract negotiation support (terms, deliverables, risk-sharing, etc.) including Quality Technical Agreement (QTA)
- Oversight of tech transfer activities (protocols, knowledge hand-off)
- Management of ongoing manufacturing operations at selected sites
- Person-in-plant (PiP) on-site support

See DHC DARK HORSE CONSULTING for additional CMC services:

Technology transfer & process scale up

Whether you will be scaling up your process within your own facilities or working with a contract services partner, we'll support your technology transfer plans, including technology transfer protocols, scale-up feasibility assessments, risk management plans, commercialization master plans, and guide associated studies.

Person-in-Plant & suite management

If you require real-time, on-the-ground oversight, troubleshooting, and/or remediation, we oversee execution and ensure compliance with regulations and procedures, as well as supporting gap identification. We also offer GMP training services and can be on the ground at your CMO facility during manufacturing runs.

Manufacturing troubleshooting & ongoing optimization

Grounded in sound scientific principles, decades of hands-on execution experience, and sounds science-based root cause analysis, our team supports operational performance and process troubleshooting initiatives. Additionally, we support ongoing process optimization to improve product quality, yield, and efficiency, and reduce deviation recurrence.

Interim functional leadership

For clients currently without internal leadership in this domain, senior DHC experts can provide interim expertise and hands-on leadership with the goal of enabling the clients to identify, hire, and onboard internal candidates in a timely manner.

Aseptic fill/finish

Our overall production expertise includes compounding, sterile filtration, component and equipment preparation, aseptic filling and stoppering, lyophilization, capping, labeling, and packaging operations. We have supported and managed drug product production for various biologic compounds including PEGylated proteins, PEGylated antibody fragments, vaccines, blood products recombinant proteins, and gene therapies in various forms and presentations (liquid, lyophilized products, and suspensions in vials and syringes). We can also assess & improve or implement visual inspection and inspector qualification programs for drug product manufacturers.

Project & program creation

Every project must have a defined goal, detailed plans, and an established schedule. We define and document team structures, roles, responsibilities, and what will be accomplished upon completing the project.

Mitigation & problem resolution

Even the best-managed projects and programs encounter challenges. Our project managers ensure clear, honest, and transparent communications as issues are explored, effectively prioritized, and resolved.

Teaching/training

To provide support for a remediation or to ensure future compliance, we offer customized teach-ins.

See BIOTECH LOGIC A DIVISION OF DARK HORSE CONSULTING GROUP for additional CMC services:

REGULATORY

A comprehensive regulatory strategy is key to the efficient development of complex Cell and Gene Therapies, Biologics, and Devices. Our regulatory experts integrate with our SMEs in CMC, Clinical, Nonclinical, Quality & Compliance to provide regulatory solutions customized to our clients' unique needs and regulatory challenges. We bring full spectrum strategic and operational support to guide clients through the product lifecycle from discovery, clinical trials, marketing authorization, and post market.

Global regulatory support

We are uniquely positioned to provide both strategic and tactical regulatory assistance to our clients for their global regulatory needs. We are connected with current and former staffers of multiple worldwide regulatory bodies and have supported filings for clients across a wide range of global jurisdictions and stages of development.

We work with regulatory bodies around the globe, including:

US FDA

EU (EMA and National Competent Authorities)

UK MHRA

Health Canada

PMDA (Japan)

ANVISA (Brazil)

TGA (Australia)

Israel Ministries of Health

Regulatory strategy

We help you plan for long-term success, while maintaining a pragmatic focus on near-term realities such as resource constraints and timeline objectives. We can develop your regulatory timelines for submissions and meetings and identify data that will be required for optimal outcomes at each development milestone. We provide recommendations on the programs and designations applicable to your program, such as US FDA designations and FDA expedited programs or EU special procedures and programs. Examples include:

US FDA

- Orphan drug designation (ODD)
- Rare pediatric disease (RPD)
- Fast track (FT)
- Breakthrough therapy (BT)
- RMAT designation
- Post-designation initial comprehensive multidisciplinary meeting
- CMC Readiness Pilot applications
- Advanced Manufacturing Technology designation (AMT)
- Commissioner's National Priority Voucher request

EU (EMA and National Competent Authorities) and **UK MHRA**

- Innovative licensing and access pathway (ILAP)
- PRIME (Priority Medicines) designation
- Classification as Advanced Therapy Medicinal Product
- Certification of quality and non-clinical data
- Orphan Medicinal Product

Regulatory gap analysis, filing planning, and readiness

Our support includes in-depth analysis of your current status and/or existing plan relative to requirements for your targeted milestones (e.g., readiness for INTERACT, pre-IND, Scientific Advice, IND/ CTA, BLA/MAA). We can also provide you with a detailed report summarizing all identified gaps complete with severity rating and suggested remediations.

- CMC & preclinical gap analysis to IND/CTA & first-in-human readiness
- BLA documentation gap analysis
- Readiness assessments ahead of other regulatory submissions (e.g., designation requests, meetings)

Accelerated development and filing support

In addition to increased therapeutic complexity, leading regulatory bodies now offer many more options for accelerating development of products meeting critical unmet medical needs. We provide the expertise to navigate the multitude of approval options and manage drastically accelerated programs.

Expert witness services

Our regulatory and technical experts are available to serve as expert witness services for law firms. (Please note: DHCG does not provide legal advice.)

Explore Regulatory case studies here:

REGULATORY

continued

Project management

We oversee your project to achieve your milestones in a timely fashion, including maintaining up-to-date project timelines, organizing project team meetings, capturing meeting minutes, establishing RACI (responsible, accountable, consulted, informed) matrices, and following up on achievement of action items.

Regulatory meeting assistance

We organize and lead internal preparatory sessions for all types of regulatory meetings and also frequently attend regulatory meetings with our clients to assist them in putting their best foot forward with regulators. We provide briefing book support, pre-meeting preparatory workshops with mock regulatory authority response options, direct meeting assistance & participation, and meeting minuting.

- INTERACT meetings
- Pre-IND meetings
- Innovation Task Force (ITF)
- Scientific advice (SA) meetings
- CATT meetings
- Type A meetings
- Type B meetings
- Type C meetings
- Type D meetings
- BLA meetings
- MAA meetings

Integrated regulatory authorship

Our experienced technical writers can provide a full range of support for your filing needs, from individual sections to authorship of full dossiers. We support the full range of contents: Administrative, CMC, Nonclinical, Clinical (Modules 1-5 of the eCTD).

We also offer review, gap analysis, and editing of your existing draft documents.

In terms of publishing, our team's diverse experience spans a wide range of global jurisdictions and stages of development, from preclinical (INTERACT, pre-IND, Scientific Advice, IND, IMPD, CTA) through clinical (meeting packages, designation requests, IND protocol documents, DSUR), marketing approval (BLA, MAA), and post approval (supplements, request for variation).

Scan here for supported eCTD sections:

Scan here for a list of supported regulatory documentation across all stages of therapeutic development:

See DHC DARK HORSE CONSULTING **Regulatory services:**

US FDA Agent

We act as the US FDA Agent for clients based outside the US.

Regulatory body liaison

We offer full support, whether in response to a request for information or in managing an FDA warning letter or other communication.

Recent Regulatory Submissions

22+	INTERACT, ITF	22+	TYPE A-D, SA
46+	PRE-IND	4+	CLINICAL HOLD RESPONSE
123+	IND, CTA	44+	BLA, MAA, 315(K)
6+	CATT, AMT	2+	NDAs
6+	IMPDs	1+	PMA

Interim functional leadership

For clients currently without internal leadership in this domain, our experts can provide interim expertise and leadership with the goal of enabling the clients to identify, hire, and onboard internal candidates in a timely manner.

Combination products regulatory support

Regulatory Support for combination products includes the following:

- Generate and review the CMC sections of regulatory submissions that support combination products [e.g., 3.2.P.2.4, 3.2.P.3.3, 3.2.P.7, and 3.2.R.4: Medical Devices (Device Design Controls), etc.]

EU combination product support

- Prepare General Safety and Performance Requirements (GSPR) reports
- Obtain the opinion of a notified body

See BIOTECHLOGIC A DIVISION OF DARK HORSE CONSULTING GROUP **Regulatory services:**

NONCLINICAL

Generating a robust, focused, and convincing nonclinical (sometimes called 'preclinical') data package is critical. Failure to appropriately plan and execute a suitable nonclinical development program is a common source of regulatory application failures and delays. We can provide extensive in-house subject matter expertise to assist you in successfully planning and executing such a program.

STRATEGIC SUPPORT

Preclinical/nonclinical strategy

We help you to define and describe your nonclinical development plan as well as related safety and efficacy endpoints to optimally support your regulatory and clinical strategies.

- Development of regulatory positioning and early interaction strategy
- General planning for FIH (first-in-human) readiness such as gap analysis of current state and remediation planning
- Animal model selection and study design
- Identification of minimum viable nonclinical data package to support FIH
- Drafting or consolidation of TPP documents for regulatory filings
- Strategic interim leadership

Roadmap to FIH

An effective roadmap to FIH (first-in-human) studies considers both efficacy and safety through the lens of the client's business strategy and risk tolerance. It addresses timeline and budget, including an in-depth expectation of what the client's future capital needs will be over time.

- FIH roadmap delivery
- Gantt chart:
  fully-loaded and board-ready formats
- Timeline analysis
- Critical path identification
- Resource planning
- CRO/CDMO/vendor selection

OPERATIONAL SUPPORT

Study design and oversight

Study design and oversight can take many forms, from package design to execution, data compilation to analysis, and more.

- Design of nonclinical proof-of-concept studies
- Feedback on nonclinical test article selection and testing
- Compilation and review of nonclinical assay data
- Advisory on *in vivo* model selection and suitability
- Nonclinical study endpoint selection and study design
- Study report authorship
- De novo nonclinical package design
- Oversight of nonclinical study execution
- Nonclinical package/study gap analysis
- Quality oversight for non-GLP safety studies

CRO oversight

We work with you to understand your development strategy, pipeline asset, Agency interaction timelines, geographical considerations, and operating budget, all with the end goal of identifying, appraising, auditing, and recommending the most appropriate vendor(s) to successfully achieve your objectives.

- Vendor/CRO selection
- Cross-functional vendor oversight with technical program management
- CRO onsite auditing and performance monitoring

Project management

We oversee your project to achieve your milestones in a timely fashion, including maintaining up-to-date project timelines, organizing project team meetings, capturing meeting minutes, establishing RACI (responsible, accountable, consulted, informed) matrices, and following up on achievement of action items.

Technical writing

We write and/or review your study protocols, reports, and regulatory submissions, ensuring that essential items are thoroughly and appropriately addressed as well as clearly communicated. Includes preparation of briefing books.

- Review of draft regulatory documentation
- Briefing book support and authorship for INTERACT, Scientific Advice, and Pre-IND meeting interactions
- Study report and protocol content review and authorship
- Analytical methods and justification review and authorship documentation edits
- Authorship of full IND - Module 1, Module 2, Module 3, Module 4, Module 5
- Management of eCTD publishing and submission

Explore Nonclinical case studies here:

CLINICAL

Strategic and tactical support are critical to a robust and comprehensive clinical trial program in preparation for application for licensure to regulatory bodies. Without a thoughtfully structured program, regulatory applications are more subject to delays or rejection.

DHC provides support from subject matter experts with extensive experience in clinical trial design and regulatory filings.

STRATEGIC SUPPORT

Clinical development strategy, trial design, and ongoing regulatory support

We help you to define and strategize your clinical trial structure from first-in-human (FIH/Phase 1) through to Registrational (Phase 3). We can provide recommendations on the programs and designations applicable to your program, such as US FDA designations and FDA expedited programs or EU special procedures and programs. We can also assess the program's readiness for optimal timing of your submission. Example client requests include:

- Clinical trial design regulatory readiness assessment
  - Indication and patient population selection support
  - Endpoint determination support
- Clinical data review and regulatory expedited designation support
- Embedded clinical regulatory support from experts working closely with your regulatory team in an ongoing partnership

Clinical Advisory Board

When convening an Advisory Board, it's necessary to select an appropriate group of KOLs (Key Opinion Leaders) who understand both the indication in question and the unique challenges and considerations of developing a product for that indication. Working with the right group of advisors is critically important to allow for proactive identification of strengths and weaknesses in a clinical development program so as to catch any potential limitations early. Our experts work with many KOLs in biopharma and have supported convening and running of advisory boards for a range of purposes, from indication selection and clinical protocol development for therapeutics developers to opining on strength of clinical data in due diligence projects.

- Support with identification, selection, and engagement of KOLs
- Directly acting as KOLs for Scientific Advisory Boards

OPERATIONAL SUPPORT

Integrated regulatory authorship

Our experienced technical writers can provide a full range of support for your filing needs, from individual sections to authorship of full dossiers. We also offer review, gap analysis, and editing of your existing draft documents. Our team's diverse experience spans a wide range of global jurisdictions and stages of development, including clinical. Examples include:

- Clinical Synopsis, Clinical Protocol, Informed Consent Form (ICF), Long-term Follow-up Protocol, and Clinical Study Report
- Investigator Brochure (IB), Development Safety Update Report (DSUR), Annual Report, and General Investigational Plan
- Support for Expedited Designation Applications (Fast Track Designation or FTD, Regenerative Medicine Advanced Therapy or RMAT, Breakthrough Therapy Designation or BTD, Orphan Drug Designation or ODD, Rare Pediatric Disease Designation or RPDD)
- Additional support includes Module 2 clinical documents. Scan here for supported eCTD details, specifically the "Clinical module" section:
- Scan here for a list of supported regulatory documentation for clinical and beyond:

Interim functional leadership

For clients currently without internal leadership in this domain, senior DHC experts can provide interim expertise and hands-on leadership with the goal of enabling the clients to identify, hire, and onboard internal candidates in a timely manner.

Project management

We oversee your project to achieve your milestones in a timely fashion, including maintaining up-to-date project timelines, organizing project team meetings, capturing meeting minutes, establishing RACI (responsible, accountable, consulted, informed) matrices, and following up on achievement of action items.

Explore Clinical case studies here:

QUALITY & COMPLIANCE

We help you ensure that phase-appropriate compliant systems are in place so your program stays aligned with "Quality by Design" principles and ahead of the curve—without wasting resources, capital, or generating excessive bureaucracy.

Our industry-experienced experts have implemented dozens of quality systems within the biopharmaceutical, pharmaceutical, medical device, and combination product industries. We assist with organizational activities, plans, policies, procedures, and processes and provide the resources to design, implement, and maintain a quality system that delivers quality, compliant drug products.

We develop and implement quality systems in accordance with:

- FDA Phase 1 GMPs
- Good Manufacturing Practices (21 CFR 210 and 211, 600, 601, 610, 820 and 1271)
- Combination Products GMPs (21 CFR 4)
- Pharmaceutical Development (ICH Q8)
- Risk Management (ICH Q9)
- Quality Systems (ICH Q10)
- Good Manufacturing Practices for Active Pharmaceutical Ingredients (ICH Q7)
- EU Good Manufacturing Practices (Eudralex Volume 4) and EU Annex 1
- The PIC/S Guide to Good Manufacturing Practices

STRATEGIC SUPPORT

Strategic QMS design

We help you develop a Quality Management System (QMS) that meets the unique needs of your program and phase of development. Of particular interest to many of our clients is

BioTechLogic's QMS in a box.

→ Turn to page 24 for details.

QMS gap assessment

We analyze your existing QMS, identify any gaps, and provide phase-appropriate and resource-efficient solutions to address them.

- QMS Gap Assessment
- QMS roadmap

OPERATIONAL SUPPORT

Quality operations

Hands-on operational quality support includes:

- Support with investigation, impact assessment, and resolution of GMP-related adverse issues such as environmental events, deviations, out of specification results, non-conformities, and process failures
- Execution of records and administrative activities within the QMS
- Provide quality oversight representation to external stakeholders
- Support PM of quality operations
- Good clinical practice (GCP) support
- Good laboratory practice (GLP) support

Document authoring, review, and revision

We write your SOPs, policies, and other controlled documents, or provide expert review and revision of existing documents.

- Standard operating procedure (SOP) authorship
- Quality system documentation authorship
- Quality system documentation review

Inspection readiness

To ensure successful inspections, we conduct a risk evaluation well in advance of your inspection window. This assessment may identify high-risk areas in your supply chain, informing an inspection readiness plan and effective resource allocation. Inspection readiness also runs to gap assessment against the FDA System Approach, European and other international regulations, or more specialty regulations, like Annex 1 for sterile drug production manufacturing, data integrity compliance, or good laboratory practices.

We also plan and execute these for 3rd parties.

Internal & external audits

The generation and execution of a comprehensive phase-appropriate quality audit program is critical for regulatory and developmental success. We combine specialized in-house experience and the use of a proprietary toolkit when customizing an audit for your program. Whether preparing for and supporting an external GMP audit by a global regulator [pre-approval inspection (PAI), pre-licensing inspection (PLI)] or planning and executing an internal audit, our team offers comprehensive capabilities in support of agency audits. We also plan and execute audits of third parties (e.g., suppliers and contract testing/manufacturing sites) on behalf of client sponsors. Common requests include:

- Vendor audits
- CDMO audits
- Mock pre-licensure inspection (PLI) support
- Other mock audits, including FDA inspection dress rehearsal, clinical phase GMP audit,or strategic session.

Interim functional leadership

For clients currently without internal leadership in this domain, our senior experts can provide interim expertise and hands-on leadership with the goal of enabling the clients to identify, hire, and onboard internal candidates in a timely manner.

Explore Quality & Compliance case studies here:

QUALITY & COMPLIANCE

continued

QP support

Our eligible QPs are experts in global regulatory standards. Common eligible QP client requests include training and education on the roles of QP as well as QP audits and remediation.

Please contact us for further discussion should you require batch certification or licensing support.

- QP audits and inspections
- QP batch review, certification and release
- Import/export support

Supplier oversight

We perform evaluations, risk assessments, and/or audits of critical raw material suppliers, contract manufacturers, and analytical service providers to ensure their quality standards are aligned with your needs.

- Follow-on work from audit findings
- Supplier audits
- Tech transfer oversight and management
- Person-in-plant support

QMS remediation

QMS remediation addresses gaps in US, EU, and ANVISA GMP based on guidances, regulations, directives, and norms from these regions. This includes performance of a gap assessment, a subsequent report, and preparation of inspection sub-system remediation quality plans to focus work efforts and prioritization. This can apply to any or all of the six inspection subsystems: quality system, production controls, facilities and equipment, laboratory controls, materials control, and packaging and labeling.

Global FDA/EMA remediation projects

We support comprehensive global inspection readiness remediation projects, whether a 483 remediation, clinical hold, a product complaint or adverse event, Complete Response Letter (CRL), or other.

- Quality plans for Six-System inspection readiness
- Remediation team leadership
- Conduct mock inspections
- Provide remediation services for all GMP departments
- Reorganization and establishment of a high-performance management team
- On-site support and team augmentation
- Gap assessment and reporting
- Quality remediation plans and execution

See DHC DARK HORSE CONSULTING Quality & Compliance services:

Establishing QMS excellence

Our team designs and implements quality system procedures and instructions in line with client objectives and the requirements of the leading regulatory bodies. Elements of our quality management system programs include the establishment and/or management of:

- Document control program
- Electronic document management system
- Deviation and CAPA SOPs
- External audit SOP
- Performance of GMP and GLP audits
- Establish phase-appropriate training SOP and program
- Vendor qualification, audits, and materials management programs
- Change control program
- Quality risk management (e.g., microbial control, quality risk assessment, etc.)
- Implementation of phase-appropriate quality systems from scratch
- Support for and implementation of electronic quality management systems

Project management

We oversee your project to achieve your milestones in a timely fashion, including maintaining up-to-date project timelines, organizing project team meetings, capturing meeting minutes, establishing RACI (responsible, accountable, consulted, informed) matrices, and following up on achievement of action items.

Combination products quality support

BioTechLogic assists companies by supporting the registration of drug-device combination products. BioTechLogic's team can guide you through the matrix of requirements. The following are examples of services to help support combination products throughout product development and into commercialization:

- Quality System Mapping and Quality Planning for products, gaps in the quality system, or transitions to new regulatory requirements
- Establish new QMS in accordance with GMP for Combination Products (21 CFR Part 4)
- Provide on and off-site quality system support including reviewing documentation, generation of system procedures and forms, corrective and/or preventive action recommendations, management review system and training

Teaching/training

To provide support for a remediation or to ensure future compliance, we offer customized teach-ins.

See BIOTECH LOGIC Quality & Compliance services:

BUSINESS ANALYTICS

Our Business Analytics Service Domain includes all service offerings previously listed under the Core Capabilities of *Due Diligence & Business Strategy, Market Expertise*, and *Quantitative Modeling*. Whether you're in the process of developing a tools & tech offering, are a company seeking funding, or are an investor considering investing in the CGT or biopharma spaces, our experts are available to provide due diligence, strategic support, market research, and quantitative modeling services.

STRATEGIC SUPPORT

Due diligence technical assessments

We are frequently called upon by investors to perform due diligence on companies in the CGT space. Alternatively, for companies seeking investment, our mock diligence service can help ensure you are prepared for questions investors may raise.

Landscape scanning

Our knowledge of the biopharma landscape can help you identify investment targets that are well-aligned with your portfolio objectives.

Teach-ins

Are you an experienced investor who is new to the complex world of CGT? Or an existing pharma or biotech company that has recently acquired a cell and gene asset? We provide customized CGT teach-ins.

Message optimization and market positioning

Our unique combination of deep technical expertise and investor relations experience allows us to provide a candid assessment of your program and strategic planning for an optimal 'pitch.'

Voice-of-customer (VOC) surveys

Knowing the right questions to ask and the right respondents to contact is the secret to getting actionable survey results that speak specifically to your product and the market. Our experts have more combined years of experience in the CGT field than any other consulting practice; in fact, many of us have been in the space since the very beginning. There is no substitute for direct experience and meaningful connections when building a survey or a set of respondents.

VoC Research

Would you like to lend us your voice? Join our VOC community here!

STRATEGIC SUPPORT

Capacity planning

Predict facility size requirements, instrumentation needs, and FTE by department over time under the full range of reasonable input assumptions to enable robust scenario planning even in environments of great uncertainty.

Cost of goods (COGs) analysis

Evaluate the range of likely product COGs over time and evaluate key levers for cost reduction based on the impact of various input assumption on overall product COGs.

Market analysis

Determine current and project future market size for your product or services based on inputs such as patient/user/customer type, indication prevalence, and assumed market penetration.

Profit margins/business use case

Model profitability scenarios based on COGs, OpEx, CapEx, and market size inputs.

These offerings are delivered via Pegasi, DHCG's proprietary data-modeling application, which is designed to model uncertainty. *See page 25 for additional details.*

Needs assessment/market research

Our unmatched experience in this industry means that we have a deeper understanding of existing offerings and competitive environments than your company can get anywhere else. An informed assessment of market needs gets far beyond the buzzwords and the latest trends, aligning unmet needs with opportunities for future therapies and the tools & tech necessary to create those therapies. Having watched this industry for decades, we've also seen a range of typical pitfalls and oversights and are equipped to help you avoid those.

Commercial (marketing) strategy

We both are your target customers and work with your target customers every day. Living amidst the technical details of this space has provided us with an understanding of what your customers are looking for, what their pain points are, and what messaging will resonate with them. We know how to strategize effectively in biopharma, no matter what your stage of market readiness may be.

Explore Business Analytics case studies here:

Centauri

Centauri is a growing suite of proprietary resources, tools, and service frameworks developed to enable greater access to the expertise offered by Dark Horse Consulting and BioTechLogic. Informed by decades of experience working with global clients across all stages of development, services delivered through Centauri have been optimized to maximize efficiencies of cost, timeline, and resources, while still delivering the highest value, quality, and expertise you'd expect from us. Additional frameworks are under development. Current offerings include:

Integrated regulatory authorship

Our experienced technical writers can provide a full range of support for your filing needs, from individual sections to authorship of full dossiers. We support the full range of contents: Administrative, CMC, Nonclinical, Clinical (Modules 1-5 of the eCTD)

We also offer review, gap analysis, and editing of your existing draft documents.

In terms of publishing, our team's diverse experience spans a wide range of global jurisdictions and stages of development, from preclinical (INTERACT, pre-IND, Scientific Advice, IND, IMPD, CTA) through clinical (meeting packages, designation requests, IND protocol documents, DSUR), marketing approval (BLA, MAA), and post approval (supplements, request for variation).

Delivered by both BIOTECHLOGIC and DHC DARK HORSE CONSULTING

QMS in a Box (phase-appropriate)

QMS in a Box is a foundational framework of core procedures, forms, and templates designed to support smaller US-based start-up companies currently using an outsourced supply chain model. We provide an established, phase-appropriate, and customizable QMS based on FDA's Phase 1 GMPs that utilizes recognized cloud-based electronic document and learning management systems (integrated EDMS-LMS) to enable release of Phase 1 GMP clinical trial material.

This enables Sponsors to initiate vendor qualification of GLP CROs, review and approve Quality Agreements, and conduct audits of CDMOs either through their own internal resources or via a contracted QA resource provided by BTL/DHC. Ultimately, these procedures will be necessary for use by the Sponsor company's Quality representative to formally release the early phase clinical lot to the clinic.

Delivered by BIOTECHLOGIC

EXCLUSIVELY BY DARK HORSE CONSULTING GROUP

Pegasi

DHCG's proprietary quantitative modeling platform can help model uncertainty by applying customized input assumptions to quantitatively describe a range of probable outcomes. Use cases span our full range of clients, including:

Tools & Tech Developers

Use cases include market forecasting and COGs modeling

- Understand potential market size for a product
- Understand size of potential customer base by therapeutic area
- Understand impact of product on client's COGs

CDMOs & Service Providers

Use cases include capacity planning, operating expense, and revenue analysis

- Optimize facility design for operational and financial efficiencies
- Plan labor and capacity allocation strategies based on potential client mix and inflection points
- Understand size of potential customer base by therapeutic area

Therapeutic Developers

Use cases include market forecasting, COGs analysis, and capacity planning (internal or external)

- Understand potential market size for a therapy
- Plan capital allocation strategy based on COGs, workforce, and production requirements
- Assess implications of build vs buy decisions
- Inform fundraising timelines

Investors

Use cases include market forecasting and cost timelines for capital projects

- Understand market opportunity for a potential investment
- Understand size and growth rates of specific CGT market segments
- Optimize facility design for operational and financial efficiencies

ICMC™: Initiative for Certification of Manufacturing Capabilities

WHY ICMC?

The current Cell and Gene Therapy (CGT) CDMO landscape is rapidly expanding. Contract Development and Manufacturing Organization (CDMO) claims about ability to provide compliant and scalable manufacturing services are typically not proactively verified by the relevant regulatory bodies, leaving therapeutic developers challenged with evaluating credibility of prospective CDMO partners. This is causing fragmentation and a perception of diminished value in the CDMO market.

WHY PARTICIPATE?

Certification of CDMO capability claims by a credible independent party allows therapeutic developers to more robustly evaluate CDMO partners. Additionally, it allows CDMOs to build credibility and differentiation in the marketplace and introduces a level of standardization that is currently lacking.

WHY DHCG?

With an industry-leading track record of cross-functional experience and expertise in supporting both CGT therapeutic developers and manufacturing organizations, Dark Horse Consulting Group (DHCG) is uniquely positioned to act as the credible, expert, and unbiased party to perform such evaluations, as evidenced by the success and recognition of our global CDMO database and CDMO selection service offerings.

ICMC™
Initiative for Certification of Manufacturing Capabilities

Learn More

Unbridled Excellence webinars

UNBRIDLED EXCELLENCE

Learn from our experts! Each webinar in this series takes a deep dive into a particular topic of interest to those in the CGT industry. View the entire library on-demand by scanning here.

Episode #1: **Streamlining Manufacturing Partner Selection**
One of the most important early decisions you will make is the selection of your CDMO partner.

Episode #2: **Inspection Readiness, Management, and Response**
How ready are you for inspection?

Episode #3: **Phase Appropriate Analytics to Support CGT Development**
Phase-appropriateness may influence your strategy for release and characterization testing.

Episode #4: **Regulatory Roundup LIVE 2023**
Our unparalleled team of former FDA regulators discussed the regulatory news of the day.

Episode #5: **2023 Takeaways, 2024 Predictions**
DHC Managing Partners discussed their top big-picture takeaways from 2023 and what-to-watch predictions for 2024.

Episode #6: **Navigating Route to Market for CGT Enabling Technologies**
A practical discussion on how to understand and navigate key issues facing CGT tech companies.

Episode #7: **Navigating Nonclinical Development for CGT Products**
As an increasing number of CGT products reach the clinic, we can look back to identify common non/preclinical pitfalls and how to overcome them.

Episode #8: **Implementing Advanced Characterization Techniques into rAAV Release Panels**
Best practices and trends for implementing advanced methods for empty/full analysis, next-generation sequencing, and post-translational modification analysis

Episode #9: **Recommendations for IND Authorship**
A survey of the recommended best practice for structuring and authoring a CGT IND, plus what to expect after submission.

Episode #10: **Unique Considerations for Development of IND Strategy for Viral and Non-Viral Gene Editing**
A look at the evolving gene editing and delivery landscape, including LNPs and AAV.

Episode #11: **Cell Therapy Facility Management: Reducing Costs Through Operational Streamlining**
Key considerations for driving production efficiency while improving manufacturing efficiencies and mitigating costs.

DARK HORSE CONSULTING

Since DHC's founding in 2014, we have remained focused on the field of CGT. Over the last decade, the range and depth of the collective strategic and tactical knowledge of DHC's hand-picked consulting team has grown rapidly. We apply best practices from across this and other industries to address the varied needs of our clients, who range from biopharmaceutical companies to tools & tech providers to venture capital and private equity investors.

To request a complimentary initial consultation, visit www.darkhorseconsultinggroup.com/consult/ or scan this QR code.

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BIOTECHLOGIC
A DIVISION OF DARK HORSE CONSULTING GROUP

For more than 20 years, BioTechLogic has been a leading industry voice for biopharmaceutical CMC and manufacturing consulting excellence. BTL offers strategic, practical, and hands-on experience to help clients bring products to market quickly and successfully by augmenting and optimizing each organization's technical, manufacturing, analytical, and regulatory resources.