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BIOTECHNOLOGY SECTOR

Biosimilar Regulatory Pathway & IP Disputes:

Similarity Determination,
Patent Linkage,
Licensing Conflicts &
Technology Transfer

Biosimilar Regulatory Pathway & IP Disputes

Similarity Determination, Patent Linkage, Licensing Conflicts, Technology Transfer & Cross-Border Biotech JVs — The Complete Practitioner's Guide

Booklet IV of VI — Indian Biotechnology & Life Sciences Legal Series

Advocates & Legal Consultants — Ultra-Premium Client Advisory Series

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CHAPTER ONE

Biosimilar Regulatory Pathway: CDSCO Guidelines, Comparator Selection, Similarity Determination and Approval Challenges

CDSCO Biosimilar Guidelines 2016, Comparability Exercise Framework, Preclinical and Clinical Data Requirements, Indication Extrapolation and Approval Dispute Resolution

> *The Indian biosimilar market — driven by the availability of large patient populations, established biologics manufacturing infrastructure, and a regulatory framework that is more accessible than the US or EU biosimilar pathways — represents one of the highest-growth segments of the Indian pharmaceutical industry. For the large Gujarat biotechnology company investing in biosimilar*

> *development, the regulatory approval process is a multi-year exercise that intersects with patent strategy, pricing regulation, and commercial partnership structuring. The legal challenges that arise during and after the biosimilar approval process — from comparator selection disputes to patent infringement claims triggered by launch, from technology transfer agreement termination to regulatory data protection proposals — require an integrated legal practice that combines IP law, regulatory law, commercial contract law, and international trade law expertise.*

1.1 CDSCO Biosimilar Guidelines 2016: The Regulatory Architecture

The CDSCO's Guidelines on Similar Biologics: Regulatory Requirements for Marketing Authorization in India (2016) — the primary regulatory framework for biosimilar approval in India — establish a risk-based, stepwise approach to demonstrating similarity between the proposed biosimilar and the reference biologic. The guidelines require: a comprehensive quality comparability exercise (comparing the biosimilar's structural characteristics, biological activity, purity, and stability to the reference biologic through analytical methods including peptide mapping, glycan analysis, and bioassay); preclinical studies (pharmacokinetic and pharmacodynamic studies in relevant animal models); and clinical studies (Phase I PK/PD studies in healthy volunteers or patients, and Phase III efficacy and safety studies in the reference biologic's approved indication). The extent of clinical data required is calibrated to the risk level of the molecule: complex, high-risk biologics (monoclonal antibodies, recombinant proteins with post-translational modifications) require more extensive clinical data than simpler recombinant proteins (insulin, erythropoietin) where the analytical characterisation is sufficient to establish similarity. For biosimilar developers, the selection of the comparator biologic — the reference product against which similarity is demonstrated — is the most consequential early decision in the development programme: the comparator must be the originator's product approved and marketed in India (or in a comparator jurisdiction if the product is not yet marketed in India), and the comparator batches used in the comparability exercise must be representative of the originator's commercial manufacturing process.

1.2 Comparator Selection Disputes and Their Legal Implications

The CDSCO's requirement that the biosimilar be compared to the Indian-market reference biologic — rather than to the originator's product in the US or EU — creates practical challenges for biosimilar developers whose reference biologic is either not marketed in India (because the originator has not sought or obtained Indian approval) or is marketed in India in a different formulation than the global product (because the originator filed a different product specification for the Indian market). Where the reference biologic is not marketed in India, the CDSCO guidelines allow the use of a non-Indian reference biologic subject to CDSCO approval of the comparator selection — but this approval is not automatic, and the developer faces uncertainty about whether the CDSCO will accept the foreign reference biologic as the basis for an Indian biosimilar approval. For biosimilar developers who have invested in a development

programme using a non-Indian reference biologic and then face a CDSCO objection to the comparator selection, the legal challenge is framed as a writ petition: arguing that the CDSCO's refusal to accept the foreign reference biologic is arbitrary (where the foreign product and the Indian product are made by the same originator using the same manufacturing process) or procedurally defective (where the CDSCO has not given the developer an adequate opportunity to demonstrate the equivalence of the foreign and Indian reference biologics).

1.3 Indication Extrapolation: The Regulatory and Legal Battleground

Indication extrapolation — the practice of seeking approval for a biosimilar in all of the reference biologic's approved indications based on similarity data generated in only one or a subset of indications — is one of the most commercially valuable and legally contentious aspects of the biosimilar regulatory pathway. A biosimilar of a monoclonal antibody that is approved for multiple indications (such as a TNF-alpha inhibitor approved for rheumatoid arthritis, ankylosing spondylitis, Crohn's disease, and psoriasis) need not conduct separate clinical trials in each indication to seek approval in all of them, if the CDSCO accepts extrapolation of the similarity data from the primary indication studies to the extrapolated indications. The originator's challenge to indication extrapolation — through scientific submissions to the CDSCO arguing that the mechanisms of action differ between indications and that extrapolation is not scientifically justified — is a standard defensive strategy that delays the biosimilar's approval across the full indication set and limits its competitive threat to the primary indication only. For biosimilar developers, the indication extrapolation strategy must be built into the clinical development plan from the outset: the choice of primary indication, the design of the comparability exercise to generate extrapolation-supporting data, and the pre-submission engagement with the CDSCO on the extrapolation scientific rationale are all decisions that affect the ultimate scope of the approval and the product's commercial positioning against the reference biologic across the full indication spectrum.

CHAPTER TWO

Patent Linkage in Biosimilars: Originator Patent Claims, Freedom-to-Operate Analysis and Pre-Launch Legal Strategy

Biologic Patent Landscape, Process vs Product Patents, Section 3(d) Application to Biologics, Freedom-to-Operate Analysis and Pre-Launch Patent Challenge Strategy

2.1 The Biologic Patent Landscape: Product, Process, and Formulation Claims

The patent landscape for a reference biologic is significantly more complex than for a small molecule drug: while a small molecule drug may have a primary compound patent, a few formulation patents, and some process patents, a reference biologic can have hundreds of patents covering the protein sequence (if filed before the 20-year term expired), the cell line and expression system used in production, the fermentation and purification process, the formulation, the device (prefilled syringe or autoinjector), and the dosing regimen. The freedom-to-operate analysis for a biosimilar developer must cover this entire patent landscape — not just the obvious product patents — because infringement of any one patent in the portfolio can expose the biosimilar to an injunction that blocks launch regardless of the biosimilar's regulatory approval status. For Indian biosimilar developers, the patent landscape analysis is complicated by the fact that many biologics' composition-of-matter patents have either not been filed in India (because the originator's Indian filing strategy predated the biosimilar commercialisation era) or have not been maintained in India (annual renewal fees not paid), creating gaps in the Indian patent portfolio that provide freedom to operate not available in other jurisdictions. Systematic analysis of the Patent Office's patent register — searching by the originator's name, the INN (international non-proprietary name) of the molecule, and the relevant therapeutic category — is the starting point of every biosimilar freedom-to-operate analysis, and the identification of lapsed patents (where renewal fees were not paid) provides immediate freedom to operate without any challenge proceeding.

2.2 Process Patent Infringement: The Manufacturing Process Challenge

Even where the reference biologic's product patent has expired or was never filed in India, the originator may hold process patents covering the cell line, fermentation conditions, or purification steps used in the reference biologic's manufacture — and a biosimilar developer whose manufacturing process replicates the originator's patented process is at risk of process patent infringement even though the end product (the biosimilar protein) is itself not patented. Section 104A of the Patents Act reverses the burden of proof in process patent infringement cases: where a patented process is used to produce a product, the defendant (biosimilar

manufacturer) must prove that its process is different from the patented process if the plaintiff (originator) has demonstrated that the biosimilar product is identical to the product of the patented process. This reversed burden is particularly onerous for biosimilar developers whose manufacturing processes are not disclosed publicly and whose process development documentation would need to be produced in litigation to establish the non-infringing nature of their process. For biosimilar developers, the process independence strategy — deliberately designing the biosimilar's manufacturing process to differ from the originator's patented process in a material and documented way — is both a patent risk mitigation measure and a critical litigation preparation step: the documentation of the process design choices and the rationale for departing from the originator's approach is the evidence that will be needed to discharge the Section 104A reversed burden if the originator asserts a process patent infringement claim.

CHAPTER THREE

Biosimilar Licensing Agreements: Cell Line Access, Know-How Transfer, Manufacturing Sublicences and Royalty Structures

Cell Line Licensing, CHO and HEK293 Cell Line Access Issues, Know-How Transfer Obligations, Manufacturing Sublicence Restrictions and Royalty Computation for Biologics

3.1 Cell Line Access: The Foundational IP in Biologics Manufacturing

The production cell line — the genetically engineered Chinese Hamster Ovary (CHO), NS0, Sp2/0, or Human Embryonic Kidney (HEK293) cell that expresses the target biologic protein — is the foundational IP asset in any biologics manufacturing operation. Unlike small molecule synthesis (which can be replicated by any chemist given a structural formula), biologics production requires access to the specific expression cell line, and the performance characteristics of the manufactured protein (glycosylation pattern, charge variant profile, aggregation tendency) are determined by the cell line's genetic characteristics. Cell line licences — agreements that provide access to a proprietary cell line (such as the DHFR-deficient CHO cells developed by academic institutions and licensed through technology transfer offices) or to an originator's own proprietary cell line (in the context of a contract manufacturing or biosimilar co-development arrangement) — are therefore one of the most commercially critical licensing agreements in the biotech sector. The key legal issues in cell line licensing disputes are: the scope of the licence (does the cell line licence cover the manufacture of the specific biologic for which the cell line was provided, or can the licensee use the cell line to develop and manufacture new biologic molecules?); the sublicensing restrictions (can the licensee sublicence the cell line to its own contract manufacturing partner in India or offshore?); the improvement ownership provisions (who owns genetic improvements or adaptations made to the cell line during the development programme?); and the termination consequences (what happens to the cell line — and to the biologics manufacturing programme built around it — when the licence is terminated?)

3.2 Know-How Transfer Obligations: Defining What Must Be Transferred and When

A technology transfer agreement for a biologic product — whether an originator-to-Indian-manufacturer licence for domestic supply, a biosimilar developer's sublicence to a contract manufacturing organisation, or a foreign partner's technology transfer to an Indian JV — includes an obligation on the technology owner to transfer the know-how (the manufacturing process knowledge, analytical methods, quality specifications, and process troubleshooting expertise) that enables the recipient to reproduce the manufacturing process. The know-how

transfer obligation is frequently the most contentious element of a technology transfer dispute: the transferor argues that it has discharged its obligation by providing process documents, training sessions, and process validation support; the recipient argues that the know-how transfer is incomplete because the process does not run reliably in the recipient's facility (yield shortfalls, product quality failures, process inconsistency). The legal analysis of know-how transfer completeness requires: identifying the specific know-how defined in the agreement's schedule; determining whether the documents and training provided correspond to the scheduled know-how; assessing whether the recipient's process failures reflect a genuine know-how deficiency (transferor's failure to transfer critical process parameters) or a recipient facility issue (recipient's failure to replicate the process correctly despite adequate transfer). Practitioners handling technology transfer disputes must retain a process development expert — an independent consultant with experience in the specific biologic's manufacturing technology — to assess the technical adequacy of the know-how transfer independently of the parties' competing characterisations.

CHAPTER FOUR

Technology Transfer Disputes: Milestone Non-Payment, Termination and Development Agreement Enforcement

Development and Licence Agreement Milestones, Payment Triggers, Breach and Termination Rights, Injunction Against Termination and Arbitration Clause Enforcement

4.1 Milestone Payment Disputes: Definitions and Triggering Events

Development and licence agreements for biotech products typically structure the consideration as a combination of upfront licence fees, development milestones (payments triggered by specific regulatory or technical achievements), and royalties on commercial sales. Milestone payment disputes — disagreements between the licensor and licensee about whether a specific milestone triggering event has occurred — are among the most commercially significant contract disputes in the biotech sector, because milestone payments can individually run to tens or hundreds of crores and the triggering event definitions are frequently drafted with insufficient precision to cover the actual development pathway. Common milestone trigger definition disputes include: whether a "successful Phase II clinical trial" (a milestone trigger) has been achieved when the Phase II shows a positive trend but does not reach the pre-specified primary endpoint with statistical significance; whether a "regulatory filing acceptance" milestone is triggered when the CDSCO acknowledges receipt of the filing (a purely administrative acknowledgement) or when the CDSCO formally accepts the filing for substantive review; and whether a "first commercial sale" milestone is triggered when the first invoice is issued to a distributor or when the first sale to an end customer is recorded. Practitioners drafting milestone triggers must anticipate these definitional ambiguities and specify the exact objective criteria that constitute each milestone — including the statistical threshold for clinical success, the specific regulatory communication that constitutes filing acceptance, and the channel in the distribution chain at which a "commercial sale" is deemed to occur.

CHAPTER FIVE

Reference Biologic IP and Market Exclusivity: Regulatory Data Protection Proposals, Orphan Drug Designations and India's Position

TRIPS Article 39.3 Obligations, India's Proposed Data Exclusivity Debate, Orphan Drug Policy, Rare Disease Treatment Access and Patient Advocacy in Regulatory Proceedings

5.1 India's Data Exclusivity Debate: Status and Commercial Implications for Biosimilar Developers

The proposal to introduce a data exclusivity regime for new biological entities in India — providing a period (typically 5-8 years in other jurisdictions) during which biosimilar developers cannot rely on the reference biologic's regulatory submission data to support their own approval — has been a recurring and contentious policy debate in India's pharmaceutical sector since the 2000s. As of 2024, India has not implemented data exclusivity for biologics or any other category of pharmaceutical product. This regulatory status quo is commercially critical for India's biosimilar industry: the absence of data exclusivity enables biosimilar developers to obtain CDSCO approval by referencing the originator's publicly available clinical data (published in scientific journals and regulatory submissions) to establish the safety and efficacy profile of the reference biologic, without independently repeating the originator's full clinical programme. If data exclusivity were introduced for biologics, every new biologic approved in India would carry a period during which no biosimilar approval could be granted based on the reference biologic's data — a significant delay in biosimilar entry that would reduce competition and maintain originator pricing power during the exclusivity period. For large biosimilar developers in Gujarat (and in India generally), monitoring the data exclusivity policy debate and engaging with the Ministry of Health, Department of Pharmaceuticals, and CDSCO through industry associations and direct representations is a material commercial risk management activity — a regulatory policy change could affect the approval timelines of every biosimilar in the development pipeline.

CHAPTER SIX

Cross-Border Biotech JVs: FDI Compliance, Joint IP Ownership, R&D Agreement Structuring and Dispute Arbitration

FDI in Biotech Sector, Automatic Route Eligibility, Joint IP Ownership Agreements, FEMA Compliance for Royalty Payments and International Arbitration in Biotech Licensing Disputes

6.1 FDI in the Biotech Sector: Regulatory Framework and Structuring Considerations

Foreign Direct Investment in India's biotechnology sector is permitted under the automatic route (without government approval) up to 100 per cent, subject to compliance with FEMA, the Companies Act, and sector-specific regulations applicable to biotechnology activities. Biotech sub-sectors that attract additional regulatory scrutiny include: genetically modified organism (GMO) related activities (subject to the Environment Protection Act, Genetic Engineering Approval Committee — GEAC — clearance, and the Rules for the Manufacture, Use/Import/Export and Storage of Hazardous Microorganisms / Genetically Engineered Organisms or Cells, 1989); human genomics and clinical genomics activities (subject to the ICMR's national guidelines on human genome research); and clinical trial activities (subject to NDCT Rules' requirement for CDSCO approval of clinical trials involving foreign collaboration). For a foreign biotech company establishing a joint venture in India for biosimilar development — a common commercial structure where the foreign partner provides the technology and the Indian partner provides the manufacturing infrastructure and market access — the FDI structuring must address: the foreign partner's equity stake (within the automatic route limit); the valuation of the technology contribution (whether the foreign partner's technology can be capitalised as a non-cash equity contribution, and at what FEMA-compliant valuation); and the ongoing royalty structure for technology use (which must comply with FEMA's pricing guidelines for royalty payments to foreign technology providers and attract withholding tax at the applicable treaty rate).

6.2 Joint IP Ownership: Governance, Exploitation, and Dispute Resolution

A biotech joint venture that jointly develops new intellectual property — new molecules, manufacturing processes, analytical methods, or clinical data — must address the governance of jointly-owned IP from the outset of the JV agreement, since the default rules for joint IP ownership under Indian patent law (which grant each co-owner the right to exploit the jointly owned patent without the other's consent) are commercially unworkable for a structured JV relationship. The Patents Act Section 50 provides that where a patent is granted to two or more persons, each of them is entitled to an equal undivided share of the patent — and, unless the

patent instrument otherwise provides, each co-owner may exploit the patent without the other's consent and without accounting to the other for any profits. This default position — which allows either JV partner to independently license the jointly-owned patent to a third party (including a competitor) without the other's agreement — is typically modified in the JV agreement by: requiring mutual consent for any exploitation of jointly-owned IP by either party; specifying the territory and field restrictions within which each party can exploit the jointly-owned IP; establishing a licensing committee with both partners' representation to approve third-party licences; and providing for the apportionment of licensing revenues between the partners on a specified basis. Practitioners drafting JV agreements for cross-border biotech collaborations must ensure that the IP ownership and exploitation provisions in the JV agreement are consistent with the applicable patent law in each relevant jurisdiction — since different countries have different default rules for co-owned patent exploitation, and a multinational joint venture may need jurisdiction-specific IP assignment or licensing structures to achieve the intended commercial result in each market.

Booklet IV Complete Summary: The biosimilar sector sits at the intersection of regulatory law, patent law, licensing practice, and cross-border investment — creating a practice area that demands the full spectrum of life sciences legal expertise. The CDSCO's biosimilar guidelines define the regulatory pathway; the patent freedom-to-operate analysis defines the commercial risk; and the technology transfer agreement's milestone, know-how, and cell line provisions define the contractual relationship that must perform reliably over a development timeline of 5-10 years. The data exclusivity policy debate and the CCI's competition enforcement in biologic markets add regulatory and policy dimensions that sophisticated practitioners must track proactively. Cross-border JV structures — with their FEMA compliance requirements, joint IP governance obligations, and international arbitration provisions — require the integration of corporate, IP, regulatory, and international commercial law expertise that characterises the highest-value biotech legal mandates in Gujarat's growing life sciences sector.