# Global Pharmaceutical Contract Manufacturing

## Industry Overview

Pharma IQ Sector Report & Resources:
Interviews with Industry Experts
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# Contents



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# Pharmaceutical Outsourcing, Where Do You Draw the Line?

The real issue in pharma is budget and structural change. There are no magic methods to overcome what Richard Nelson called "the simple economics of basic scientific research—patents or no patents, capturing the value that ultimately derives from fundamental research is extraordinarily difficult for profit-oriented organisations. "The world is changing fast and pharma runs an outdated business model in "*Novus Ordo Seclorum"*, where budgets for pharmaceuticals are reframed within healthcare cost containment. Outsourcing seems to be the universal answer; however there is more to the answer than meets the eye.

**Questions**: The Probability of Serendipity; the Outdated Business Model and Approaches to Innovation; the Outsourcing Answer; What Core Competencies Remain As Hallmark of Pharma Companies?

**The probability of serendipity**

"Now is the winter of our discontent, '*not*' made glorious summer": ten blockbuster patents will expire; Generics are top-level racing; pricing pressures chip away at profits; OTC's belong to the wrong industry; the R&D Productivity Paradox is a nonsensical statement; the pipelines are clogged, and pharma engages in alliances, shops for Biotech, litigates and outsources away core competencies as if they are no better than a "me-too drug".

When will pharma rethink the Value Proposition?The patent – cliff is now but the decision maker has changed; his name is "payer", lives in economic crisis, has no job, his mind is set on healthcare cost control, and wants new cheaper and faster drugs.

•Dry pipelines:

A poor pipeline has a clear secondary effect on the OTC industry. An OTC product is an ex-Rx product that has been switched from RX status (prescription only) to OTC status to extend the life- cycle with new free OTC pricing.

•The OTC industry is increasingly moving towards the FMCG industry; a few years ago, FMCG companies bought some OTC businesses. Today, OTC's are partly owned by FMCG and pharma companies.

•Pricing pressures

Unlike the US, EU countries have regulated pharmaceutical prices; to make matters worse, pricing systems are different in each country and there is no clear official guidance on how to harmonise them.

**The outdated business model and approaches to innovation**

The pharmaceutical industry has long operated on a closed model, developing and patenting new drugs, while retaining IP exclusivity. Open innovation means sourcing ideas from internal and external sources; the partnerships with biotech and CROs means sharing IP but also the cost/risk of drug development.

Companies are focusing on strategic alliances and partnerships with other companies and CROs to enhance product pipelines and manage clinical trials; pharmaceutical and biopharmaceutical companies are also joining in partnerships by licensing products to maintain revenue.

Pharma - biotech – complement strengths to compound co- development.

Biotech have high degree risk- projects with innovative approaches to diseases that may result in new pipeline products to pharma companies, which, in turn, offer expertise and resources to the partnership.

Pharma - CROs - work together in R&D for the compound development

CROs formed deep relationships, over time, with pharma companies and improved in drug development, knowledge and expertise; partnership was the logical next step.

# Pharmaceutical Outsourcing, Where Do You Draw the Line?

**The Outsourcing Answer:**

What Is Pharmaceutical Outsourcing? What Are the Most Outsourced Stages of the Value Chain? What Are the Outsourcing Countries? What Will the Impact of US Healthcare Reform In Global Biosimilars Outsourcing Be?

•What Is Pharmaceutical Outsourcing?

Outsourcing has been called “one of the greatest organisational and industry structure shifts of the century”, with special influence in pharma industry, where pharmaceutical and biotechnology companies are outsourcing at almost every stage of the value chain.

Procurement is essential to outsourcing; the right team/strategy will ensure: right service providers (CROs CMOs), communications, timelines, and contracts, due diligence, supply chain, and relationships with third parties. Sometimes procurement itself it outsourced.

•What are the most outsourced stages of the value chain?

R&D; Clinical Trials; Manufacturing; Logistics and Distribution; Supply Chain

*1.R&D , Clinical Trials and Manufacturing*

In the last couple of years, pharma witnessed a decline in R&D output ,in spite of escalating expenditures which prompted for drastic cost cuttings in order to stay competitive – outsourcing to off shore countries proved to be effective.

The emergence of virtual pharmaceutical and genomics companies granted an influx of lead compounds in the discovery pipeline and made the leap from traditional to strategic outsourcing.

CROs (Contract Research Organisations) must have good sized facilities, analytical instruments and certified quality systems, trained and trustworthy teams, knowledge of regulatory requirements, safe data storage and transfer, and be flexible enough for last-minute changes.

Written agreements with CROs are essential and should cover: protocol review; research-reporting obligations; research data ownership; auditing and monitoring rights; confidentiality of information; compliance with all regulatory obligations.

Pharmaceutical and bio manufacturing require both high-level technology and severe regulatory compliance; CMOs (Contract Manufacturing Organisations) provide the pharmaceutical industry with services ranging from drug development through manufacture. CMOs rely on their reputation and track record to deliver quality products and services on time and at a competitive price.

EMA and FDA monitor compliance with regulatory requirements and GCP principles in clinical research conducted in off shore countries.

*2. Logistics and Distribution; Supply Chain*

Outsourcing supply chain operations to a third-party logistics (3PL) provider, allows pharmaceutical companies to retain competitive advantage and overcome the counterfeiting issue. The outsourced partner must have cold chain management specialists, securing biotech and pharmaceutical companies’ strict regulatory compliance and product control, and concur to supply chain visibility and control.

# Pharmaceutical Outsourcing, Where Do You Draw the Line?

EMEA's recent regulations make it imperative for supply chains to implement both a new process of coding to combat counterfeited drugs, and new technologies regarding the cold chain.

US current regulations: "When enforcement of federal drug pedigree requirements, originally established by the Prescription Drug Marketing Act of 1987, was put on hold by a legal challenge, some states opted to move ahead with their own requirements. As of March 2011, according to the Healthcare Distribution Management Association, 18 states had adopted final rules regarding distributor licensing and pedigree requirements, three states had enacted legislation but rules were pending, eight states had enacted legislation, one state had proposed pedigree legislation, and 20 states had no legislation or regulations on the topic." (1)

- **What Are The Outsourcing Countries?**

Off shore countries like India and China; China's regulations emulate the FDA approvals system; China is the world's third-largest pharmaceutical market.

Outsourcing to emerging markets should be the next wise step: Patent protection was reinforced in some countries; clinical trials have huge pools of patients; research has lower costs, and frankly, for pharma companies, it all comes down to collaborate with the 17 pharmerging (2) countries or face them as fierce competitors.

Emerging countries are also the next buyers. Although drug spend "per capita" is still low, the population size and economies' growth is expected to place them in a full quarter share of the global pharma market in just a few years.

- **What Will The Impact of US Healthcare Reform in Global Biosimilars Outsourcing Be?**

US Healthcare Reform creates FDA approval pathway for competing versions of already-marketed biologic drug products, under the "Biologics Price Competition and Innovation Act" (BPCIA).

The next few years are expected to portray rapid growth of the biosimilars market; however, manufacturing biosimilars requires significant financial investment, which is why biopharmaceutical companies will outsource it to CMOs and CROs. In spite of their expertise, the companies will face several challenges with biosimilar products, because the BPCIA requires the disclosure of the biosimilar application to the innovator company, which will try to delay the biosimilar approval.

- **What Core CompetenciesRemain as Hallmark of Pharma Companies?**

Pharmaceutical companies seem to be unsure of what their best choices and decisions are; is full outsourcing the answer or should there be a middle term? Should they go for partnerships or acquisitions? When is too much outsourcing? If pharma industries outsource R&D, clinical trials, manufacturing, logistics and distribution, supply chains and even procurement, what will remain of their core competencies which will acknowledge them as pharma?

The wiser answer is to repeat Chou En-Lai's reply when asked by Henry Kissinger to comment on the impact of the French Revolution: "Too early to tell."

**(1)** http://www.nabp.net/news/states-fda-pressing-forward-with-pedigree-track-and-trace-rules-and-regulations//

**(2)** http://schott.blogs.nytimes.com/2010/11/30/pharmerging-markets

# The Biggest Challenges in Pharmaceutical Outsourcing

Pharmaceutical companies are facing times of unprecedented challenge; expiring patents, generics competition, clogged pipelines, pricing pressures, huge R&D costs, all contribute to major revenue losses. Is outsourcing the “pain killer” for this highly regulated industry? What are the biggest challenges in pharmaceutical outsourcing?

**•Language Obstacles, Cultural Gaps and Time Zones**

The preferred outsourcing option is off shoring (the company providing the outsourced services is in a low-cost country far from the country where the recipient of services is located); consequently the language barrier can oftentimes slow down the communication process and lead to potentially dangerous misunderstandings.

Different time zones can be responsible for delays in data transfer and compromised deadlines.

Cultural gaps may be the source of erroneous perceptions, especially if there is not a cross- functional and cross-geographical team involved.

**•Performance, Quality and Regulatory Requirements**

When a company is looking for CRO and CMO partners it should be aware of domestic and foreign regulatory requirements.

Due-diligence auditing will be necessary to thoroughly evaluate the alignment of the two parties for the upcoming technology transfer.

Contracts must be written, and the company must conduct quality oversight of all contract manufacturers have a written quality agreement and other documents, to clearly identify the responsibilities of each party.

It is important to have a project team working together on both ends in a proactive manner, targeting dates, batches, and resources.

**•Clinical Trials, Ethics**

Outsourcing clinical trials called for pressing awareness because there are no regulatory agencies with trained people and resources to actually monitor all drug trials overseas.

There are some international and country guidelines, and laws, but their effective implementation is unclear. Companies must be assertive in discussing the outsourcing of clinical trials and provide information on their standards.

Transparency must be reinforced by the presence of ethics committees.

**•Logistics and Distribution, Supply Chain and Counterfeiting**

Logistics and distribution must grant brand security and supply chain optimisation trough product serialisation, electronic pedigree documentation andeffective tax rate (ETR).

Due to regulatory requirements and limited outsourcing options, it may be challenging, at times, to find the right supply chain strategic partner; however, once partnership is accomplished, he must comply with new regulationsto combat product counterfeiting**,** and concur to supply chain visibility and control.

The outsourced partner must have cold chain management specialists, securing biotech and pharmaceutical companies’ strict regulatory compliance and product control.

Many pharmaceutical companies that outsource major projects, can end up managing relationships at arm’s length, because distance and lack of visibility of project progress , may foster problems that will take more time to identify; often times the key to a successful outsourcing strategy in off shoring countries, lies in having a company person in place to mitigate business risks

# Cost Savings Still the Number One Reason Behind 60% of Outsourced Pharma and Bio Manufacturing

While there is normally more than one factor behind the decision of a pharmaceutical or biopharmaceutical organisation to outsource its global manufacturing, it seems the ever-important cost-saving potential remains among the main attraction of external production, particularly where emerging markets are concerned.

**The growth of global contract manufacturing**

A recent Pharma IQ survey conducted with key members of the pharma and biopharma community revealed that, while 54.5 percent of organisations outsource less than half of their global manufacturing, 18.2 percent currently use outsourcing for at least 91 percent of their output. These basic findings support a recent report by Global Industry Analysts (GIA), which predicted that the global pharmaceutical contract manufacturing market would reach a total value in excess of $40.7 billion (£24.4 billion) by 2015.

**Why outsource global pharmaceutical production?**

The analysts at GIA suggested that key factors driving such expansion included soaring demand for new drugs, increasing need for R&D productivity and efficiency, as well as the desire to make cost savings where possible. The report also noted the fact that many pharma and biotech companies simply lack sufficient manufacturing capabilities internally. In fact, the Pharma IQ research found that 70 percent of organisations cite lack of internal capacity as the number one reason for outsourcing some or all of their production.

Meanwhile, 45 percent revealed that a shortage of expertise was the key driver behind their outsourced manufacturing. Perhaps unsurprisingly, 60 percent named the potential for cost savings as global outsourcing's most appealing feature. Upon publication of its findings in January 2011, GIA commented: "Today, manufacturing capacity constraints are only one of the reasons for outsourcing.

"Pharmaceutical manufacturing entails sophisticated technology and strict regulatory compliance. Outsourcing such activities to CMOs enables a pharma company to expedite its R&D, and thus realise the potential revenues. Moreover, CMOs are increasingly offering a wide range of value-added services, which make outsourced pharmaceutical contract manufacturing an indispensable opportunity to pharma companies," the analysts added.

**Key production areas in global pharma outsourcing**

In terms of product type, it is the manufacture of finished form medicines that is most commonly outsourced. The latest Pharma IQ research indicates that 72.7 percent of organisations currently use outsourcing in global finished form production, while 36.4 percent produce APIs and 31.8 per cent manufacture biopharmaceuticals via external means.

Geographically, the US represents the largest regional market for pharmaceutical contract manufacturing globally. According to the GIA'smost-recent analysis, Europe trails behind the US, though future growth in the market is expected to emanate from developing regions, particularly the Asia Pacific. "The Japanese market for pharmaceutical contract manufacturing alone is projected to register a compounded annual growth rate of 12.8 percent during the [next four years]," the authors added.

# Cost Savings Still the Number One Reason Behind 60% of Outsourced Pharma and Bio Manufacturing

**The rise of emerging markets**

Outsourcing production to emerging global markets like Japan, China, India and Brazil is increasingly popular in the biotechnology and pharmaceutical industries. Speaking to the American Society for Biochemistry and Molecular Biology (ASBMB) in 2010, Richard Soll, senior vice president for integrated services at WuXi AppTec, agreed that it is largely these regions' potential for lower costs which makes them so attractive.

"As in many cases, economics proved to be a deciding factor; the theme for any industry is how to get the most bang for your buck. It's become a priority for the pharmaceutical industry, because they're facing some serious challenges, notably the stagnant drug development process that ends up approving only 20 to 25 new drugs a year," he said. "So, the industry is trying to retool itself, following an era of mergers and acquisitions, to bring down costs and get more drugs to market."

Mr Soll went on to suggest that, for many organisations, a short-term solution is merely to outsource the early stages of drug development, such as screening and validation, where savings can be made with overseas CROs. Over the past decade or so, the ever-intensifying battle for cost-effective drug development has seen this mentality permeate the entire process. As a result, emerging markets now represent a core target for a huge number of pharmaceutical manufacturers.

**Which emerging markets and why?**

The recent Pharma IQ survey backed up the latest GIA analysis, indicating that the Asia Pacific region will in fact play a major role in the future development of global pharmaceutical contract manufacturing. In fact, 76.9 percent of pharma and bio firms named India as the country in which they outsource production the most. Not far behind with 53.8 percent of responses was China, while Russia and Latin American nations, most notably Brazil, each accounted for 15.4 percent.

**The future of global pharmaceutical contract manufacturing**

In recent years, the global pharmaceutical industry has been witnessing unprecedented waves of dramatic change. Most significant have been the increased competition in generic markets, declining R&D productivity, shrinking average patent life and mounting government pressure to reduce drug prices. At the same time, the drug development process is already known to extend as far as anywhere between eight and 15 years, with the cost of bringing a single new molecule to market exceeding $800 million.

With so few new blockbuster drugs emerging, the decisive factors for growth and sustainability are unquestionably quicker development and cheaper production. As a result of the latter, the global market for pharmaceutical contract manufacturing continues to witness robust growth. With the recent economic recession, which severely impacted drug makers across the world, firms have increasingly sought ways to find ways of minimising their costs.

Though manufacturers will be hoping that the most challenging times are behind them, it is reasonable to suggest that the global market for outsourced drug production will continue leaping from strength to strength. If constraints on drug development remain as they are – or indeed worsen – the future could hold magnificent prospects for the emerging markets that have already saved swathes of the industry from the threat of extinction

# Additional Resources

## INTERVIEW Need for Access to Enabling Technologies Drives Growth in the Contract Biomanufacturing Market


Eric S. Langer, Managing Partner, BioPlan Associates, joins Pharma IQ, to address how the contract manufacturing sector is adapting to the changing needs of pharma and biotech, the need for access to enabling technologies and how contract manufacturing organisations (CMOs) are increasing their client services capabilities- focusing on not only how to meet technical and scientific challenges but also how to deliver value more effectively to the client.

## INTERVIEW Choosing a New CMO? The Cost of Change is Critical


Richard Loughlin, Director, Contract Manufacturing Business Development North America, Commercial & External Partnerships (CEPiA) sanofi aventis, joins Andrea Charles from Pharma IQ, to discuss contract manufacturing trends and the advantages of using a CMO to enter a new market. Loughlin also shares his top 3 tips for choosing a new outsourcing partner. Sanofi-aventis engages in API custom synthesis and drug product contract manufacturing services through its CEPiA organisation.

## INTERVIEW Working with an Overseas CMO to Gain FDA Inspection and Approved Status


Pharma IQ speaks with Earl Sullivan, Chief Executive Officer, Landela Pharmaceutical, about working with an overseas CMO to gain FDA inspection and approved status.

## WEBINAR Outsourcing: Challenging the Project Management System at Your Organisation


Join Jubilant HollisterStier Senior Manager, William Allen, as he evaluates what to consider when reviewing the project management capabilities of your current CMO, potential CMO, and the internal PMO system at your organisation. Mr. Allen will review successful outsourcing parameters, due diligence, evaluation of project management capabilities and expectations from CMO project management.


Following the success of Pharma IQ's Global Pharmaceutical Contract Manufacturing event in London last month, we bring you an exciting industry first, **Global Pharmaceutical Contract Manufacturing Online**, the only online event dedicated to addressing the current challenges in this constantly evolving field.

**Global Pharmaceutical Contract Manufacturing Online** will deliver all of the information that you need in order for you to create new and nurture existing CMO relationships across the globe. This series of interactive webinars will demonstrate how to overcome the challenges of contract manufacturing and will help to identify the strategies needed to ensure you reap the benefits in terms of cost, time and quality.

**Gain access to the leading authorities in contract manufacturing who will share their knowledge on:**

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- Working successfully with overseas CMOs to **maximise your market reach**
- Best practice strategies in **operational and financial risk mitigation**
- Utilising your CMOs innovative technologies to **extend your marketed product lifecycle**
- Integrating your internal and external supply chains to **streamline your manufacturing processes**
- Strategically choosing your CMO in order to **consolidate your position in emerging markets**

*6 webinars, 4 days, 0 travel expenses!*

In order to accommodate your schedule, the series will run live from 1st - 10th November but all sessions will also be available **on-demand,** allowing you to catch up on any missed sessions at a time convenient to you.

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- **Richard Loughlin**, Director, Contract Manufacturing, **Sanofi-Aventis**
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- **Richard Fazackerley**, Director, Global Technology Strategy, **Eisai**
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