

The Covington Life Sciences Monitor

An annual survey of industry sector opinion

June 2005

In conjunction with mergermarket



Introduction

The Life Sciences industry, and especially the Pharmaceutical industry, is facing important challenges that will have a significant impact on how it operates. This is illustrated by this survey we have commissioned in conjunction with mergermarket. Some of the responses demonstrate how the industry and the financial community are struggling in finding the best approach to meet the challenges.

The Life Sciences Industry - Facing the challenges

The Pharmaceutical industry has always been highly regulated and the discovery and development of new products always were a risky business. Until recently, however, there was a healthy flow of new active ingredients, the main commercial markets were fairly transparent and in several instances also fairly insulated. Furthermore, the value of patents was fully recognised and as a rule resulted in higher prices, and the overall price levels supported extensive R&D as well as attractive profits. This is now changing dramatically. The search for new active ingredients is much more onerous. Patents are being challenged not only under traditional patent principles but also from an antitrust angle, and the risk being ignored in pricing and reimbursement procedures (of which the recent German “jumbo grouping” is a striking example). Also, in general, governments and other payors constantly devise new measures to cut the drug bills in light of the increasing medical costs, which in turn are the result of an aging population and the overall success of public healthcare.

In addition, like other business sectors, the Life Sciences industry has become much more global. The survey shows, for instance, that in the US the grey market threat from India and China is seen as significant as the imports from Canada, and that, in general, similar biologicals are expected to be developed predominantly in the same two Asian countries.

Contents

Introduction	02
Executive Summary	04
Survey Findings	06
• M&A Expectations	06
• Market Concerns	08
• US and European Market Considerations	14
• Research & Development	15
• Appendix: Biotechnology	16
About Covington & Burling	18
Contacts	19

The survey suggests that some players hope to address some of the challenges by striving for more international harmonisation and ultimately a globally transparent legislative and commercial pricing framework. This probably reflects a throwback to the certainties of the past, now to be pushed from a national level to the international scene. It risks, however, being illusory because the environment within which the industry must operate will probably only become more unpredictable and testing. A few examples of the new trends are:

- There will be increasing attention to post-marketing surveillance, in particular with regard to the safety of the products. The Cox-2 inhibitors experience shows the significant financial impact product decisions can have
 - More broadly, drug approvals themselves will shift from being commercial assets of a Life Sciences company to being considered more a common good, which regulators wish to manage in the interest of the public
 - Regulators increasingly enter into international dialogue and consult each other on important matters, and generally information moves almost instantly throughout the world. Even now, mere time differences between important markets, such as Europe and the US, can create logistical and legal challenges when important health related information – which may also be share price sensitive – must be reported
 - The products themselves are often more complex because of the increasing role of biotechnology and the more frequent overlap of different regulatory categories (drugs, devices, tissue engineered products, etc)
 - All these elements result in wider regulatory discretion of the authorities and more broadly in higher commercial risks
 - While markets become more international because of parallel imports and increasing worldwide activities of most companies, including the generic industry, at the same time traditionally uniform national markets can become diversified because of deregulation in the healthcare sector and the increasing role of public procurement contracts, with their specific price-setting mechanisms.
- These challenges will, however, also offer specific opportunities, provided that the industry is vigilant, flexible and proactive. Key points of attention are:
- The basic premise undoubtedly must remain that a healthy Life Sciences industry that is sufficiently innovative and competitive to develop new therapies is a prerequisite for a good healthcare system. Moreover, a strong Life Sciences industry more broadly supports a knowledge-based society, which is one of the key aims of the European Commission under the Lisbon agenda, and fertilises other sectors
 - Better medical treatment requires the industry (i) to offer innovation, which can consist of a breakthrough discovery as well as incremental innovative steps, (ii) to provide added value in products as well as services, and (iii) to ensure a high level of quality and safety
 - Companies will have to show the flexibility and alertness to react adequately to changing circumstances and new needs. At the same time, however, regulators, especially when exercising their broader discretion, must act within a legal framework that is clear and reliable with regard to key principles and that in general provides adequate procedural guarantees. A clear example of shortcomings in key legal provisions is the existing EU regime on data exclusivity, which protects against abridged applications that piggy-back on innovative approvals. The rules have been repeatedly interpreted differently by various authorities and referred to the European courts for clarification (and are now being replaced by new provisions)
 - In order to allow the industry to be flexible and assume a dynamic responsibility, existing restrictions should be reassessed and revised where appropriate. Why, for instance, can the German social security authorities publish extensive information on prescription drugs but companies cannot discuss their own products? In addition, where pricing controls apply for reimbursement purposes, they should not affect the price-setting outside the reimbursement context
 - The current trend towards more transparency of the regulatory process must be combined with adequate protection of commercial secrets. This becomes more important in light of the increasing alignment on standards for drug approvals, which results in the same or similar data being held by many regulators
 - More flexible financial market rules may be needed to ensure adequate funding of start-up companies, especially in the biotechnology sector. For instance, broader exceptions to pre-emption rights may be needed to attract sufficient new funds.

Peter Bogaert, Partner
Covington & Burling

Executive Summary

The desire to see M&A among drug developers is not a new phenomenon. Cheaper drugs from India, parallel imports from Canada and governments focused on trimming healthcare budgets no doubt have and will continue to impact Life Science business models. What makes this survey slightly different, and infinitely more interesting, is some of the recorded similarities and differences in opinions between the various different principals that work in the industry.

Whilst it is quite clear that consolidation will remain a key element of corporate strategy, the rate at which respondents believe it will happen varies. Financial Intermediaries are the most optimistic with about 88% expecting an increase in activity compared to 58% of Corporate. However 40% of Corporate respondents remain immune to the idea that the current climate is likely to act as a spur to M&A. One explanation for this result is that too often Pharmaceutical mergers have been borne from positions of weakness. For example, the recent Sankyo-Daiichi merger was arguably just as much to do with the imminent patent expiry on Sankyo's Pravachol than extraneous factors such as deregulation and biennial state-led price cuts. And inevitably there is always going to be one losing party in a transaction, as witnessed by the key positions retained by Sanofi executives on the newly formed executive board following its acquisition of Aventis. Consequently executives can view M&A as a sign of weakness and often a last resort.

Of the type of consolidation that is likely to feature in the coming months, most Financial Intermediary respondents dismiss the likelihood of M&A among the big caps, save for one or two exceptional cases. Instead, consolidation is expected to be typified by big Pharma companies using their balance sheets to snap up smaller biotechs. The key driving force to consolidation here is the need to fill gaps in the drug pipeline.

Clearly, however, the replacement of old drugs for new ones is the primary motivation for M&A. Over 49% of Corporate respondents feel that the single most pressing issue currently facing the Life Sciences sector is the delivery of new products. And it is not difficult to see why; drug company business models are relatively simple: the bigger the drug in terms of sales, the greater economies of scale, with everything else on the profit & loss account falling neatly into place. Indeed, sustainable margins and growing profits can only come from new drugs replacing old ones that reach maturity or lose patent protection.

Interestingly, Financial Intermediary respondents are less inclined to view the delivery of new products as a major issue, with only 29% singling this out. Instead the most pressing issue among 37% financiers is financing. Here, it is both the lack of available funding for Life Science companies, particularly at the smaller Biotech level, and the high levels of investment required to fund clinical development that are at issue. The subject of financing is also an important factor for 27% of Corporate respondents, but what is interesting is that they place less importance on the issue of R&D sunk costs. This is presumably because Corporates have become somewhat habituated to the scale of such funding requirements.

Drug R&D is an expensive business; costs have risen, on average, 17 fold over the last 25 years, yet the average approval rate has remained broadly the same in that time period. Clinical development attrition rates have also not improved with the probability of a drug reaching the market from lead validation to product approval remaining around the 10% level. Not surprisingly, both sets of respondents see a need to streamline the regulatory approval process citing shorter trials, rolling approvals and removing the need for further trials in cases when products change formats. Some respondents feel that the regulatory authorities and government bodies ought to support R&D efforts, with one obvious recent example being the issues concerning stem-cell research.

A good degree of respondents feel that the lack of qualified people involved in the approval process is a hindrance. Linked to this is the importance of developing a standardized international drug development regime that will enable the simultaneous approval of drugs across the major regions. This governing body could also presumably promote a more coordinated enforcement of patent laws and related intellectual property enforcement. About 48% of Corporate, and 34% of Financial respondents, feel that improved legislation to provide protection against illegal copycat drugs would be the best way to alleviate some of the financial pressures affecting the industry.

Copycat drugs provide a segue for another prominent issue cited in this survey, namely the increasing competition from generic manufacturers particularly from India. Analysts on average assume generic entry will cut drug revenues by 45% within six months and by 65-70% over the course of a year. Given this rate of revenue abrasion, it is not surprising that this is a concern for many respondents interviewed in this survey, particularly in light of the aggressive attempts over the last few years to invalidate patents under paragraph IV certifications.

One area in which drug developers still hold significant barriers to entry is in biologics. The last 10 years has seen significant advances in genomics, proteomics and DNA sequencing. Nevertheless, the majority of respondents, 56%, predict biogeneric competition within a three to five year timeframe, although this is largely dependent on the regulatory authorities determining how generic biologics should be tested for equivalence.

Almost a quarter of respondents feel that India remains the biggest biogeneric threat, presumably due to the obvious work being conducted by Biocon and Wockhardt in that region. China is the second hot spot. This does not discount the efforts of more established generic players such as Sandoz (which can rely on Novartis for support), Teva, Boehringer Ingelheim, Stada Arzneimittel and smaller players such as GeneMedix, all of which have established biologic research facilities.

Allied to the more prominent threat of generic competition is the pricing factors that are affecting the industry, and which many predict will force the issue of consolidation in the future. A good degree of the survey is devoted to this subject, covering issues such as parallel imports and government led price-cutting pressure.

Many respondents feel not enough is being done by governments to combat the problem of parallel trade, with over two thirds having no confidence in the EU Commission's ability to address this problem. Respondents believe that the current pricing control system in Europe has stifled R&D. One telling remark worth highlighting is that: "in the 1970s, Europe used to be the pharmacy of the world, but due to price controls this is no longer the case." And among the 32% of those who said yes to the question of whether the EU Commission will recognise the parallel trade problem, there is a view that the authorities must realise that selling drugs as commodities will lead to counterfeit drugs and associated health risks.

However the biggest concern among the industry's principals is the threat of a US government led pricing control system being put in place. Hitherto the US has been a fertile ground for drug development with market forces dictating drug pricing. Yet there is a growing reluctance among US citizens to pay for a disproportionate amount of the R&D costs of new drugs which are eventually sold worldwide. There is an even yes and no divide among the respondents polled over whether the US will itself instigate pricing controls in response to this growing consumer dissatisfaction.

The US is clearly the driving force for the Life Science industry. Drug developers in the US have better access to capital than their European counterparts thanks to a rather more supportive, value-investor base, and therefore can principally fund R&D projects better on the whole.

The US market is where drug companies make money, Europe is broadly neutral while Japan is loss making (biennial state-led price cuts and deregulation haven't helped an overcrowded market in that region). As a result, most European Pharma companies base a significant amount of their operations in the States, while Japan is only beginning to make in-roads into the US. US pricing pressures nevertheless are clearly the most obvious threat to global life sciences companies across the regions and there is a genuine feeling that this could start to pinch the defensive qualities of the sector in general. Generic competition is arguably a lesser problem since these are cyclical businesses that rely on patent expiration – most of the big blockbuster drugs have succumbed to expiration – save for those expertly placed to challenge the validity of enforceable patents. Nevertheless future generic competition, particularly in biologics, is clearly viewed as negatively influencing R&D, which in turn will ultimately lead to sub-optimal healthcare systems. These issues, in addition to the standard problems of R&D attrition rates and a fragmented industry, lead to one undeniable corollary that consolidation pressures going forward are inevitable.

Research Methodology

mergermarket canvassed the views of 100 Life Sciences corporate executives and investment bankers in Europe and the US in December 2004 and January 2005.

The aim of the survey was to garner perceptions and expectations for the sector in general, and to compare the views of our corporate and banking respondents in particular.

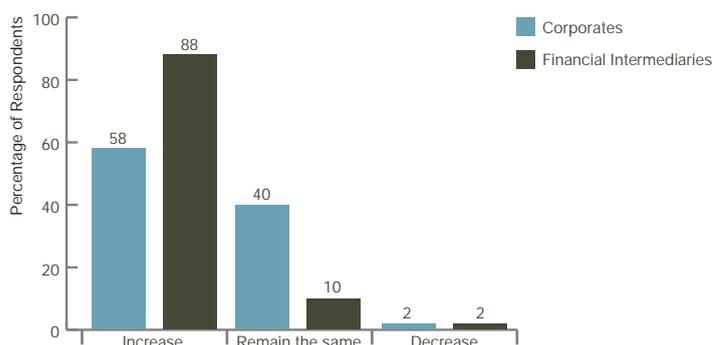
Respondent Breakdown

	Corporates	Financial Intermediaries	Total
North America	21	18	39
Europe	29	32	61
Total	50	50	100

Survey Findings

M&A Expectations

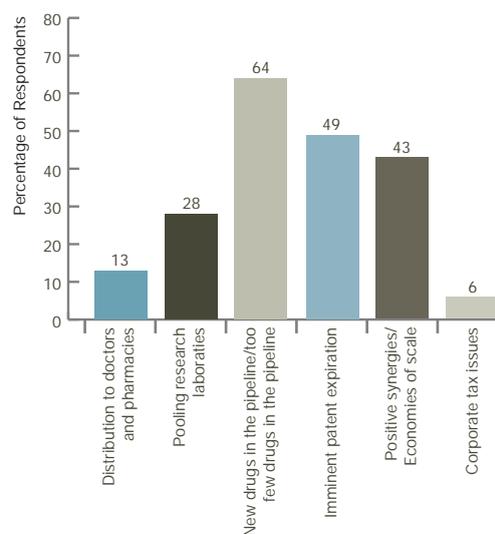
Do you expect the level of Life Sciences M&A activity to increase, decrease or remain the same in the next 12 months?



Both respondent sets expect M&A to increase in the next 12 months. Financial Intermediaries are clearly the most optimistic with 88% predicting an increase in activity compared to 58% of Corporate interviewed. A further 40% of Corporate respondents expect M&A activity to remain at current levels. Analysing by geography, US respondents are the more optimistic about M&A activity with 81% expecting an increase versus 68% of their European peers.

Despite their overall optimism, among Financial respondents there is a belief that there won't be many M&As between large Pharmaceutical companies. Instead, deals will happen on a case-by-case basis, with major Pharma companies more likely to buy up smaller Biotech companies. This is because "Big Pharma companies are short of new products, and smaller Biotech companies have actual and potential products but need financing." According to one Corporate respondent, further consolidation will occur because "the supplier base is still highly fragmented following many start-ups in the 1990-2000 period."

What do you think will drive consolidation amongst large Life Sciences companies in the next 2 years?



The issue most expected to drive consolidation for both respondent groups is new drugs in the pipeline (64%). According to respondents this is most likely to be in the form of established Big Pharma companies with access to capital (but fewer drugs in the pipeline) buying up IPO-starved Biotech companies who, by contrast, have new drugs but not enough finance to realise their potential.

After the necessity of new drugs, the next most important factors identified by respondents are imminent patent expiry and the need to achieve positive synergies. Big Pharma companies are expected to react aggressively to maintain any competitive edge lost through patent expiration, while the larger Biotechs are expected to be open to M&A in order to achieve necessary economies of scale.

M&A

"Undoubtedly there will be many acquisitions, especially of smaller Biotech companies. Similarly, however, there will remain many other arrangements for gaining access to new technology, including minority stakes, joint ventures and R&D collaborations. In addition to this we do expect some bigger mergers in the Pharmaceutical or Biotech sector."

Covington & Burling

Geographically, do you anticipate any particular M&A trends in Life Sciences?

Perhaps, unsurprisingly, the largest proportion of respondents expect to see growth into the Chinese market: “Everyone knows that China is a huge market with unbelievable potential” remarked one Corporate. Similarly, expansion by European and US companies into the Asian region in general is expected to continue: “Growth will occur, but not just in emulation but by making significant contributions to upstream R&D. This will attract a lot of western attention.”

Domestic Chinese companies are also expected to flex their corporate muscles: “There is increasing sophistication in the Chinese market. China will become a bigger player in the development of drugs... the growth of some Chinese companies will reach the point where they start to participate in global M&A activity.”

In 5 years’ time, how recognisable will the Life Sciences industry be compared with today, in terms of the number and the size of major players?

Respondents are consistent in their five-year perceptions of market structure within Life Sciences. A combined 47% agree that the size of companies will increase while the number of players will diminish through M&A consolidation. However, a further 35% of combined respondents feel the make-up of players in the market will remain unchanged.

Among those respondents anticipating ongoing consolidation, there is a degree of consensus that “one to two of the major players will disappear through consolidation.” One Corporate respondent believes the market will be characterised by a “David and Goliath syndrome – with some very big players and some small, meaning the middle will be squeezed.”

One respondent likens the expected development of Life Sciences (Biotech companies in particular) to that witnessed in the dot com industry over the last five years, echoing the general view that the range of niche players will ultimately consolidate.

Our findings regarding M&A expectations underline the critical role R&D and innovation play within the sector. The search for new and cheaper products is set to drive consolidation and geographic expansion.

What do you think is the single most pressing issue currently facing the Life Sciences sector?

In light of the critical role R&D is expected to play in the sector’s M&A decision making, it is perhaps unsurprising that the delivery of new products is cited as the top issue for 63% of Corporate respondents. It is the “life-blood of the Life Sciences industry”, and a high proportion of respondents develop their comments to underline the need to streamline the regulatory approval process in particular. The delivery of new products is, as one respondent describes, “the conversion of research into highly innovative products and services despite increasing cost pressure from governments and patients/consumers.”

While investment banking respondents also mention the importance of new product delivery and R&D issues (37%), they equally highlight how financing is affecting the sector (38%). The lack of funding for Life Sciences companies and the difficulty in attaining external financing are mentioned, as are the high investment levels required by the industry, the higher sunk costs of R&D compared to other industries, and the high associated risk with product ROI. The latter R&D-specific financing issues are also cited by 22% of Corporate respondents.

In more specific comments, respondents highlight the need to improve the governmental and regulatory environment, with one noting the importance of the “globalisation of drug development regimes and ability of companies to get products licensed in the US and European markets simultaneously”, and another feeling that, “the government should facilitate US biologics and there should be rewards for innovation.”

Survey Findings

Market Concerns

Given the crucial importance of R&D innovation and the resultant need to deliver new products quickly, regulatory authorities and their processes attract significant attention from our respondents.

What steps do you think the European and US authorities should take to modify the approval process for new drugs?

For the largest proportion of both respondent groups the most important step is to streamline, shorten and simplify the review process. Respondents cited shorter trials and fewer patients, more procedures for provisional approvals, rolling approvals, and removing the need to conduct trials when products change format.

Furthermore, respondents feel that more mutual recognition and better communication would improve the process, particularly in the US. Companies criticise the authorities for their lack of clarity on what is required for approval, and feel that interaction with the regulators is poor during both development and review. One respondent noted that the authorities "should support R&D instead of cramming them into tight corsets", while another explained that "we need to work in partnership; currently they act like police."

Perhaps underpinning many of the issues raised above is the lack of a globally transparent legislative and commercial pricing framework for the industry, which was mentioned as a solution to the timing problem.

Staffing appears to be a concern for many respondents with Corporates in particular wishing for more and better qualified people to be involved in the approval process.

Do you think we will see any fundamental changes in the criteria used to approve new medicines in the next 5 years?

Respondents are almost evenly split on expectations for a criteria change in the drug approval process, with 47% overall predicting significant movement. Corporates are somewhat more pessimistic with 60% believing there will no change in the approval criteria over the next five years.

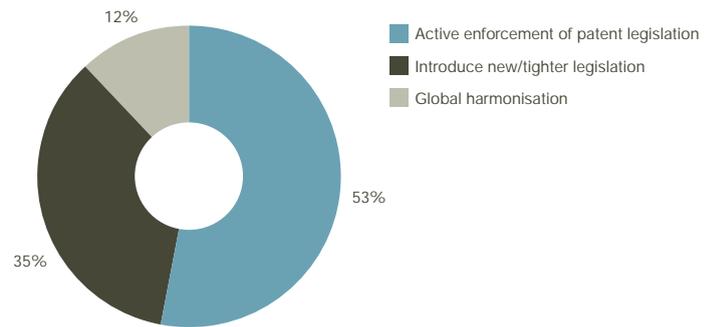
Among those respondents believing that changes will occur, improved safety and post marketing approval study requirements are cited, especially in the light of recent high profile product withdrawals. However, other respondents completely disagree, claiming that "the current criteria are already pretty good" and that "the FDA is still catching-up with ICH, and EU is still catching-up locally with the recent EMEA initiative."

How highly do you rate the issue of drug approval process?

The majority of respondents (56%) consider the issue of drug approval as very important (Grade 4 on a scale of 1 to 5), while a further 20% rate it as the most important. This again underlines how crucial R&D issues permeate the sector's concerns.

Given the perceived difficulties in gaining regulatory approval for new products, there is added pressure to maximise revenue before patent expiration, to reduce risks from grey market, and to deal with pricing issues. Again the regulatory authorities play a key role in ensuring that Life Sciences' investment in R&D innovation develops profitably.

How do you think the Life Sciences industry should best counter patent threats across the board?



Clearly the need to protect patents is a key issue for respondents and one where a large proportion are looking to the authorities for protection. 53% note that Life Sciences companies and regulators need to be firm on patents, exerting political pressure to compel countries to recognise and enforce patents where necessary.

35% of respondents feel more strongly, and demand new tighter legislation to protect their R&D investment and commitment to developing new and truly innovative products that minimises the effect of generics.

The remaining 12% of respondents favour global harmonisation and alignment of patent regimes: in particular, "by working with governments, and super national bodies, such as the WHO."

Where do you believe the biggest grey market threat for US Life Sciences companies exists?

For 33% of respondents the biggest grey market threat to the US comes from its neighbour Canada. The second and third most cited areas are China (17%) and India (16%) where, with the benefit of lower manufacturing costs, generic competitors are developing rapidly. Collectively, Asian countries account for 44% of responses and the continent is now viewed by the largest proportion of respondents as the greatest grey market threat to US companies.

What do you think is the best way to minimise the grey market threat?

As a whole, there are two broad approaches discernible from the responses we received. The first is a more internationalist desire for equitable trade among nations by eliminating pricing differences and by enforcing international patent laws and related intellectual property legislation. The second approach is a more protectionist approach that aims to tighten the US market from grey imports. Respondents suggest this can be achieved by providing tax relief for US researchers and manufacturers, and through a greater control of product distribution and the termination of parallel imports. Other respondents emphasise the need to educate Government and consumers that lower quality grey imports with dosage instructions in foreign languages place end users at risk.

Once again we see respondents looking for regulatory and governmental assistance in tackling issues of concern.

What responses are likely to come from the industry to the grey market threat?

As well as lobbying for the regulatory reform outlined above, respondents believe that attempting to compete with cheap imports via cost reductions is also a viable approach, and one that the industry itself can proactively pursue. Expected ways of doing this are US firms relocating production overseas, as well as reducing research budgets and improving the supply chain. Some respondents also expect firms to diversify more fully into the growing generic drugs business, although some accept that this would probably cannibalise their branded sales somewhat.

Many respondents chose to limit their responses to dealing with Canada, partly due to its grey market role, but also as it is one of the few countries that can be influenced. These respondents expect Canada to be pressured through the threat of product withdrawal and price increases.

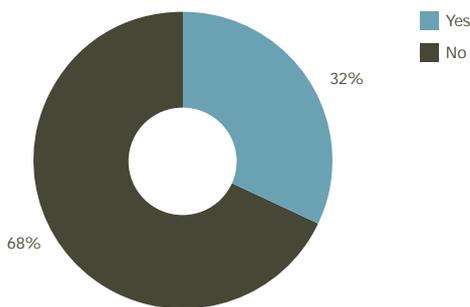
Within the European market the Life Sciences sector faces a range of different issues, these include parallel trade, bureaucracy and government price controls that stifle the incentive to conduct ambitious R&D. It is, perhaps, not surprising then that regulatory issues are again prominent among respondents' concerns.

Grey market threats

"The grey market does not provide a constructive contribution to the healthcare systems. As demonstrated by the recent London School of Economics study, parallel imports mainly benefit the arbitragists. Price differentials between major markets will undoubtedly remain in place in the foreseeable future but there must be legal ways for the companies to prevent prices imposed on the industry by government intervention in one market spilling over into other markets."

Covington & Burling

Do you believe that the EU Commission will recognise and take measures to address the parallel trade problems in Europe?

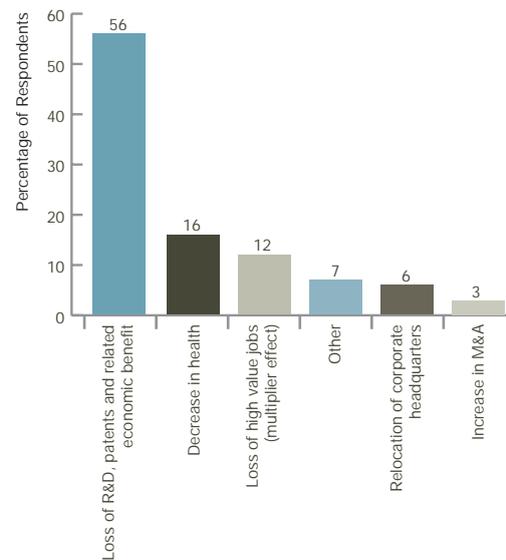


Over two thirds (68%) of respondents are not confident that the EU will address parallel trade problems. Among respondents who answered 'no', the main reason was the enormous bureaucracy of the EU Commission which would render any solution impossible. As one Corporate respondent says, "there are 25 countries and too many 'conductors' with different opinions and their own healthcare systems." Furthermore, free trade, of which parallel imports are a manifestation, is an aim of the EU and a fundamental part of the EU Constitution. This view is underlined by respondents who believe the EU Commission does not necessarily view parallel trade as a problem, or at least not one it is required to solve.

Other respondents believe parallel trade will become less of an issue over time as drug prices increasingly converge. Some respondents feel that parallel trade has more to do with national politics and cannot be dealt with at an EU level. Other respondents claim that the Euro currency has already decreased the problem somewhat.

Among those who did answer 'yes', there is a belief that the EU Commission needs to recognise that Pharmaceuticals are being repackaged and traded like commodities leading to counterfeit products and associated health risks. These respondents believe there will be a serious attempt to resolve parallel trade and it will be relatively successful despite the inherent difficulties. Other respondents feel the best way will be for the EU to follow the lead of the US – if and when it acts on parallel imports – and mimic its legislation accordingly.

What do you consider to be the most significant disadvantage of price control systems / bureaucracy for major European markets?



For both respondent groups (63% of Corporate and 50% of Financials) the most significant disadvantage of price controls for European markets is the loss of R&D and related economic benefits: "price controls are stifling R&D, investment, innovation and creativity." Another perceived disadvantage of price controls for 15% of Financial respondents and 17% of Corporate respondents is reduced public health levels. This is because reduced R&D spending will probably mean new drugs are of a lower standard.

Another drawback of European price controls is the resulting brain drain of talent to more dynamic US based companies. This has a negative economic multiplier effect on overall European GDP because the trickle-down wealth of a dynamic Pharmaceutical industry and the secondary expenditure of its highly paid employees moves overseas. As one respondent says, "in the 1970s, Europe used to be the pharmacy of the world, but due to price controls this is no longer the case."

Dealing with the Commission

"The rules on parallel trade are an application of the general principle of the free movement of goods, which is one of the pillars of the EU single market. There is, however, growing understanding that when low prices are imposed on companies in certain Member States, there is an inherent unfairness when companies are denied legal methods to prevent low priced goods being exported from these Member States throughout the EU. In addition, such an environment stifles innovation and undermines the overall objectives of the Lisbon agenda, which aims at making the EU the 'the most dynamic and competitive knowledge-based economy in the world' by 2010."

Covington & Burling

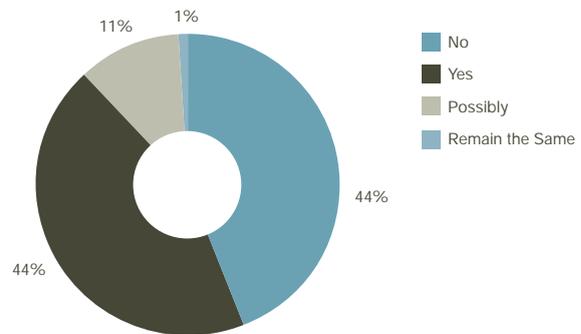
What can or should be done to improve the differing effects of drug pricing across countries?

The majority of respondents (58%) agree on the need to create a harmonised pricing system across Europe and/or on a Global scale. As one Corporate respondent says: "The EU and other national authorities should recognise that the current system of reimbursement pricing is unsustainable." Some respondents, however, are more laissez-faire about the route to harmonisation: "Companies are striving to achieve unified pricing across Europe and I think that over time prices will largely converge even in the absence of government initiatives." In total contrast, the next largest proportion of our respondents (14%) believes that the free market should be allowed to prosper and that mechanisms designed to prevent it should be removed. For example, one respondent noted that the "German reference pricing system is insane."

Compared to Europe- – where government subsidisation swallows the true cost of drugs – the US market more transparently passes on the cost directly to domestic consumers. However, this apparently freer market raises complicated issues for Life Science companies when they interact with overseas markets.

Do you believe that the US Federal government will enforce a stricter drug price control regime in the next five years?

The issue of US drug pricing is a key concern. High domestic prices are clearly perceived by respondents to be paying for the R&D costs of new drugs that are sold worldwide. One Corporate respondent believes, "the expense of R&D costs to the customer should be shared globally." Another adds that, "the US public is clearly increasingly frustrated about the fact they pay the highest prices worldwide for prescription medicines" – especially for non-generic drugs.



Both respondent groups are evenly divided over US Federal policy direction with regard to price control – 44% predict stricter control and 44% expect no change. However, a further 11% think some kind of control is a possibility, implying that overall momentum is towards stricter price control in coming years.

Within the 'yes' camp, there is a belief that any kind of price control introduced by the Bush administration will be indirect and relatively minor, possibly through control of parallel imports. As one Financial Intermediary says, "price controls will probably not follow the European subsidisation model." Another respondent believes that any controls "are more likely to be at a State rather than Federal level."

The 'no' camp firmly believes price control is unlikely as long as the Republican Party is in office, especially as, "the Government is under pressure to cut healthcare costs."

Other reasons respondents offer for not controlling prices are less political, namely beliefs that it would stifle innovation and competition in the sector.

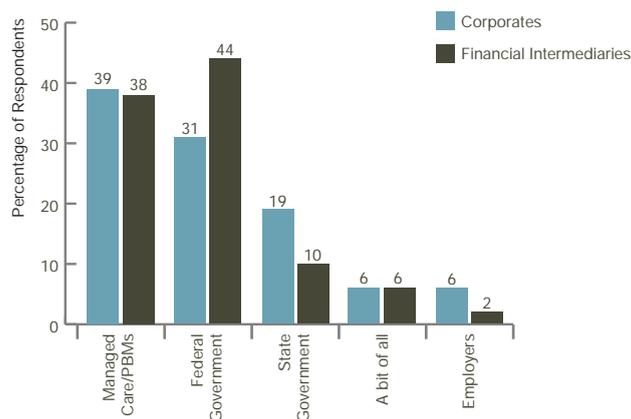
What do you expect the response of large Life Sciences companies to be, given stricter drug price controls?

Given stricter price controls both respondent groups expect Life Sciences will have to adapt. For 24% of Financial respondents the form of this adaptation would take the form of ‘cost control’. A further 9% expect there would have to be some consolidation among Life Sciences companies. Although one Financial respondent feels further M&A is unlikely among more than one or two large players as “they are already big enough.”

Among Corporate respondents, again only 7% expect industry consolidation to result, while the largest proportion of respondents (17%) believes restructuring of costs is more likely. Cost control and a decrease in research are viewed as other likely outcomes. According to one such respondent: “Cost control would come in the form of outsourcing of manufacturing and, if everything fails, a reduction in R&D.”

Other recurrent strategies suggested by respondents are a need to “focus on volume”, and with more aggressive and targeted research, market drugs with mass market potential rather than niche products. Cost savings could also be sought by speeding up the development process and pressure could be put on the FDA to shorten product approval time.

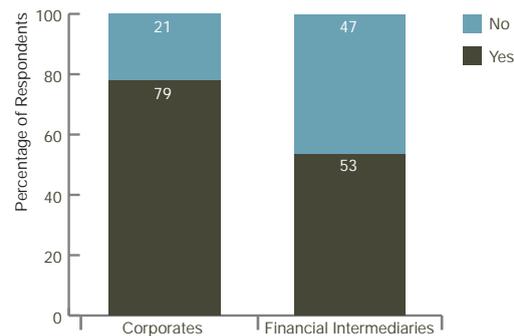
Who do you see as having the greatest pressure on drug pricing in the US?



Among 44% of Financial Intermediaries, the Federal Government is viewed as having the greatest influence on drug pricing in the US. Managed Care /PBMs are closely behind with 38%. State government is viewed as relatively uninfluential with only 10%.

For Corporate respondents, State government is given more influence with 19% of responses. Interestingly though, only 31% of Corporate respondents believe Federal Government has most influence. Instead, Managed care/ PBMs are given 39%. This is perhaps slightly surprising considering the prominent lobbying of Federal Government by Life Sciences companies.

Will a tiered system of drug pricing lead to tiered products?



Our respondent groups differed significantly on the issue of tiered pricing leading to tiered products, with Corporates believing this more likely to occur than their Financial counterparts (79% to 53%). Respondents who believe that cost differences will naturally lead to tiered products either welcome a flexible system where prices increase from generic to branded drugs, and where the customer has more choice, or believe that the practice already occurs.

The remaining respondents, however, query the economic sense of the proposed situation, claiming that companies will be unable to develop different drugs for two different price regimes.

Tiered products

“Tiered product ranges seem unavoidable to some extent, but efforts should obviously be made to make proper care available to as many patients as possible. The more dynamic the industry can be, the higher the chances of reaching this goal.”

Covington & Burling

Survey Findings

US and European Market Considerations

What is the role of the US in the global Life Sciences market versus that of Europe?

Both groups of respondents provide a unanimous verdict on the dominance of the US market in global Life Sciences – 89% of Corporate respondents and 96% of Financial Intermediaries back the US.

Among Financial Intermediaries there is a perception that the US is five to ten years ahead of the European Pharmaceutical market. According to respondents this US maturity is manifested in both the size of the massive homogenous domestic market and the scale and ready access to substantial financing from its capital markets.

Culturally the US Life Sciences market is also ahead. According to one Financial Intermediary the US has “a more entrepreneurial spirit” compared to Europe in the sector. This is embodied in more active R&D into new drugs and more intensive marketing to bring products to commercial fruition. One Financial respondent summarises this cultural difference as follows: “European R&D is driven by more scientific claims, whereas American R&D places more emphasis on delivering shareholder value.”

This pursuit of shareholder value underlies what both respondent groups describe as a more free market approach to drug pricing in the US. As one respondent puts it, “markets outside of the US are government controlled, so the US is a leader in innovation.” However, both sets of respondents admit that Europe has the ability “to close the gap”, and one Corporate respondent believes that, “Europe has more market potential due to its greater combined population.” Clearly though, to do this it will have to increase harmonisation of its markets and introduce a more openly commercial culture similar to that of the US market.

European potential

“There is significant potential for the European Life Sciences industry, notwithstanding the clear gap with the US and the strong build-up in India, China, and certain third world countries. This will require higher investment and also a better recognition of the role the industry can play in the knowledge-based society. Furthermore, it will be necessary for authorities to allow financial incentives to play their role. Unfortunately, the opposite trend is visible in the context of orphan drugs where there is growing pressure to reduce the market exclusivity from ten to six years whenever the product in question is sufficiently profitable. This undermines the basic incentive scheme since the potential for significant profits is intended to stimulate the development of new products, and such profits have to finance research in numerous other products that either fail or are less successful.”

Covington & Burling

Survey Findings

Research & Development

Unsurprisingly, respondents endorse the importance of R&D as a core driver of innovation and future profits within the Life Sciences Industry. Furthermore, with the escalating threat from emerging markets and generic products, leading Life Sciences companies will increasingly lean towards the cutting edge of R&D in order to maintain their competitive advantage.

What new Research & Development technologies are you aware of and how successful have they been?

Genetics/gene and cell therapy/stem cell research were most frequently mentioned by our respondents. Perhaps understandably, however, respondents are unsure how successful such nascent technologies have been so far.

One respondent in particular, claims the question is too general to answer and "there are many technologies, such as genomics, proteomics, computational chemistry, antibody technology, and fragment-based chemistry. But because they are so new it is hard to say how successful they are. Nevertheless, they will have major impact."

How economically viable are large Life Sciences companies' investment in genetics?

Half of respondents feel that investments in genetics by Life Sciences companies are ultimately viable: "Large companies need to invest in genetics as this is the road to commercially relevant clinical diagnostics for early intervention and pharmacogenomic tests." However, a third demanded caution and scepticism in the short term of the financial benefits: "We are still a decade away from seeing any true genetic products. So such investment is important but should only be a modest fraction of R&D. Big companies had better focus on what they are good at doing, and let more fertile Biotech companies do more about genetics." Another respondent claims "investments in genetics to date have been very defensive and in most cases unlikely to create economically compelling assets."

What cutting edge technologies do you believe will play a major role in the future of the sector?

Once again Genetics/gene and cell therapy/stem cell research are the dominant technologies mentioned by half of our respondents.

What area of healthcare (e.g. oncology, diabetes) will see the next big breakthrough? What technologies will be used?

For both sets of respondents cancer is the area most selected for a breakthrough – chosen by 45% of Corporate and 67% of Financial respondents. Respondents expect gene and cell therapy to be used extensively in this field. Diabetes and Alzheimer's were also widely selected by respondents.

What does the development of mass-produced pharmacogenomic products versus designer specialised drugs mean for the Life Sciences industry as a whole?

There is something of a divide between Financial and Corporate respondents over the development of mass produced pharmacogenomic products. The largest proportion of Financial respondents (20%) view it as a threat, compared to only 4% of Corporates. Instead, 19% of Corporate respondents believe it will lead to more niche products.

Other Corporate respondents are more dismissive about the prospects of pharmacogenomic products, stressing they are still a long way off.

Many Corporates (40%), however, are more negative, pointing to price pressures, higher costs, lower margins, and cheaper alternatives.

One respondent went further by saying that "mass produced pharmacogenomic products will mean lower revenue per unit, and wider distribution and access for more people; and some specialised drugs will not get developed."

Other respondents are more upbeat about future developments, insisting it will lead to more individualised and specialised treatment – "a better outcome for everybody." Another respondent also endorses this view saying, "Targeted therapies are the future and are better for patients in terms of effectiveness and reduced side effects."

One likely future scenario envisioned by some respondents is "a two-layered market comprising one wider mass-market for traditional proven products and one for tailored (pharmacogenomic) approaches for a premium price."

Survey Findings

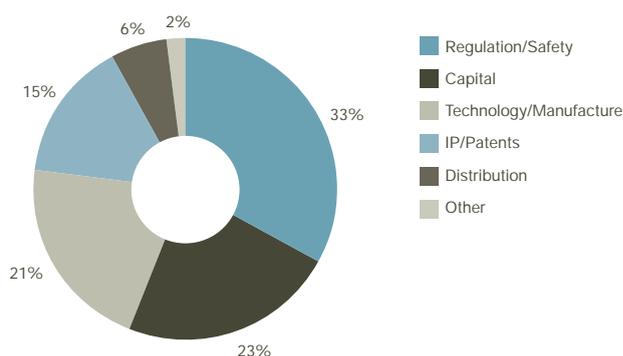
Appendix: Biotechnology

The Life Sciences Industry is betting on Biotechnology to provide most of the innovative new products that will secure its future profits. It is the pursuit of this market advantage that is attracting the large sums money currently being sunk into Biotech R&D – despite the general uncertainty of if, and when, any reward will materialise.

When do you expect to see more generic competition in the Biotech market?

Generic competition in the Biotech market is not expected in the short term, with the majority of respondents (56%) predicting a three to five year timeframe, and a further third expecting it in 2010 and beyond.

What is the greatest barrier to entry for the generic Biotech market?



Responses varied on the barriers for entry into the generic Biotech market, predominantly along our respondent group lines.

Corporates appear to be cautious mostly on account of the regulatory and technical hurdles that exist, most pertinently in respect of the necessity to prove equivalence. As one respondent summarises: "Regulatory authorities have not been able to determine how generic biologics should be tested to show clinical equivalence."

Financial respondents, while acknowledging the technical difficulty in reproducing Biotech drug manufacturing processes and the complexity of production, also draw attention to the cost of development and the limited capital available.

Both respondent groups underline the IP and patent issues. As one Corporate noted, "the risk of investment is considerable: we're now competing in a sector where companies have far more experience and patent protection."

Generic Biotech

"The key principle is that there are no Biotech generics. Follow-on Biotech products cannot be approved on the basis of a quality dossier that is supplemented with bioequivalence data, but will require extensive non-clinical and clinical testing before and in some cases also after approval. In addition, there will always be differences between the follow-on product (the "similar biological product") and the reference product, which will require a clear differentiation in product name, labelling and reporting."

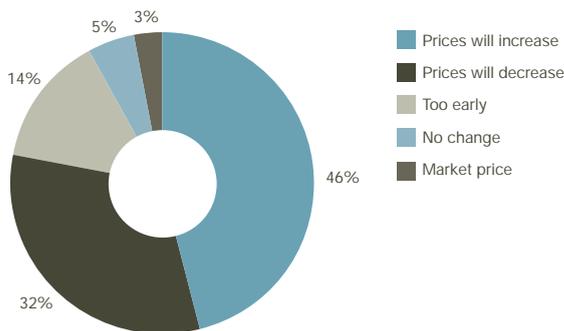
Covington & Burling

What will the relationship be in the medium term between Big Pharma and Biotech companies with regard to:

Licensing: Almost all respondents agree there will be an increase in licensing, with most underlining the view that Big Pharma and Biotech companies rely on each other: "Big Pharma will also continue to spin out compounds for Biotech companies to develop...it strengthens their pipeline."

Generic biologic: Most respondents (68%) felt that there was no relationship between Big Pharma and Biotech in relation to generic biologics, as the larger companies are not expected to enter the market.

Given the expected legal and regulatory hurdles, what effect will this have on pricing for generic biologics?



Respondents are divided on how the pricing of generic biologics will develop, with 46% expecting an increase due to the risks associated with development and route to market, while 32% highlight the fact that by definition generics will be relatively cheaper.

Those backing price increases point to the fact that only half of companies will produce generic biologics and they will therefore be able to set higher prices. Other respondents claim the higher risks involved will raise prices, ("high regulatory hurdles will lead to oligopolistic pricing"), but gradually costs will fall provided competition increases.

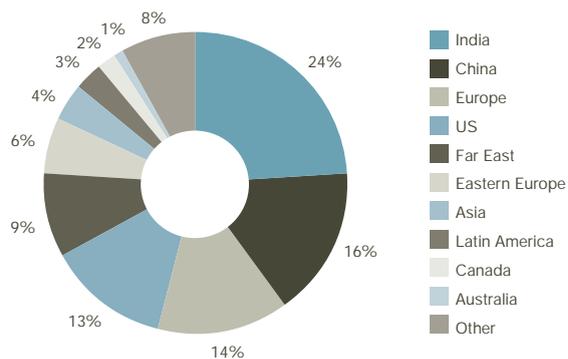
Some respondents, however, claim it is still too early to predict which way pricing will go for generic biologics.

What will be the effect of generic Biotech competition on large Life Sciences companies?

Respondents again seem unsure about how this aspect of competition will develop. While 20% of respondents (predominantly Financial Intermediaries) believe generic Biotech development will have a negative effect on large Life Sciences companies by reducing market share and forcing a reduction in prices, many respondents see it as stimulating Big Pharma, reducing R&D costs and development times, and increasing National Medical Enterprises. As one respondent pondered: "It depends on whose perspective one is looking at it from: competition can be detrimental in the short term but in the long term, it is good."

In terms of a timeframe, most respondents believe the generic Biotech market will become a viable alternative in three to five years, by which time many companies will have become integrated in mainstream Life Science businesses via acquisitions in any case. Elsewhere, respondents stress again that much regulatory and technical work is required before Biotech generics can truly become a viable alternative to existing Life Sciences products.

From which countries do you expect to see the most competition in the generic Biotech market for US and European companies?



India is the market expected to present the most competition in the generic Biotech market by 24% of respondents, while China takes second spot overall, backed by 16%. One Corporate describes how competition has emerged from India and China "due to limited regulations and patent laws, which have allowed them to leap ahead in development." However, another respondent believes that "ultimately companies in these countries will have to decipher the regulated market."

About Covington & Burling

Integration

Corporate

"Clients singled out this 'responsive' team for its ability to 'give you the impression that you are the only client'." (Chambers 2005)

Collaboration

"Covington & Burling has developed an impressive corporate partnering practice (both Pharma and Biotech) to match similarly broad regulatory expertise." (Global Counsel magazine, November 2004)

Regulatory

Voted No. 1 firm for regulatory worldwide by industry in an independent survey conducted by Global Counsel.

Intellectual Property

"Covington & Burling has an outstanding reputation in this sector in America." (Legal 500 2005)

Commercial

"Clients rely on the group for its 'trustworthy and current advice,' with particular emphasis on the life sciences and Pharmaceuticals sectors." (Chambers 2005)

Competition

Highly recommended for competition/antitrust in EU. (Life Sciences Handbook, Practical Law Company)

Litigation

The firm's reputation for quality extends to a litigation team that has been described by competitors as "professional and worryingly smart." (Chambers 2005)

Worldwide

An integrated approach with global reach

"Among those that have been at the forefront of this multi-disciplinary approach are... Covington & Burling." (Global Counsel magazine, November 2004)

Covington, a full service firm of over 500 lawyers in London, Brussels, Washington, New York and San Francisco, is one of the leading international life sciences law firms in the world. The firm was ranked among the top three firms in the Life Sciences Super League law firm rankings, published in Global Counsel magazine's November 2004 issue. These overall life sciences rankings assess a broad range of legal services, including corporate partnering, IP, competition and antitrust, product liability, regulatory and commercial law. In addition, the firm topped the Life Sciences Regulatory Firm in 2004 for the third year running.

Covington has a multi-disciplinary and multi-jurisdictional practice that integrates its extensive corporate, transactional, regulatory, intellectual property, litigation, competition and trade law expertise to meet the specialised needs of life sciences companies around the world. One of the key strengths of the practice is its ability to handle complex cross border transactions and multi-jurisdictional regulatory issues.

Contacts

Covington & Burling

265 Strand
London
WC2R 1BH
England
www.cov.com

Richard Kingham
London
T: +44 (0) 20 7067 2018
E: rkingham@cov.com

Peter Bogaert
Brussels
T: +32 (0) 2 549 5243
E: pbogaert@cov.com

John Hurvitz
Washington
T: +1 202 662 5319
E: jhurvitz@cov.com

Scott Smith
New York
T: +1 212 841 1056
E: ssmith@cov.com

Jim Snipes
San Francisco
T: +1 415 591 7071
E: jsnipes@cov.com

mergermarket

91 Brick Lane
London
E1 6QL
England

Simon Anam
T: +44 (0) 20 7059 6124
F: +44 (0) 20 7059 6101
E: sa@mergermarket.com
www.mergermarket.com

This publication contains general information and is not intended to be comprehensive nor to provide financial, investment, legal, tax or other professional advice or services. This publication is not a substitute for such professional advice or services, and it should not be acted on or relied upon or used as a basis for any investment or other decision or action that may affect you or your business. Before taking any such decision you should consult a suitably qualified professional adviser.

Whilst reasonable effort has been made to ensure the accuracy of the information contained in this publication, this cannot be guaranteed and neither Covington & Burling, mergermarket nor any of its subsidiaries nor any affiliate thereof or other related entity shall have any liability to any person or entity which relies on the information contained in this publication, including incidental or consequential damages arising from errors or omissions. Any such reliance is solely at the user's risk.

© Mergermarket

Published by
Remark
91 Brick Lane
London E1 6QL

+44 (0)20 7059 6100
www.remarkeurope.com