

21st September 2007

Key Factors in Attracting Internationally Mobile Investments by the Research- Based Pharmaceutical Industry



NERA

Economic Consulting

A Final Report prepared by NERA for UK Trade and
Investment and the Association of the British
Pharmaceutical Industry

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Acknowledgements

We wish to acknowledge the help and advice of the Steering Committee established by our client including representatives of the government: (Raul Kharbanda, Danny Palnoch and Simon Sargent) and industry (Natacha Deschamps-Smith, Robert Jones, Catherine McGovern and Sue Middleton).

We also particularly wish to thank those who agreed to be interviewed to inform our research. These comprised 34 individuals drawn from the following companies, and range of job functions.

Companies:

Actelion
Amgen
Astra Zeneca
Bayer
Eisai
Genzyme
GlaxoSmithKline
Johnson & Johnson
Lilly
Merck & Co
Novartis
Pfizer
Roche
Sanofi Aventis

Examples of job functions of respondents:

Chief Executive
Treasurer / CFO
Senior executives in:
- research
- development
- manufacturing / operations
- industrial affairs
- European management.

Executive Summary

This report has been prepared by NERA Economic Consulting for UK Trade & Investment (UKTI) and the Association of the British Pharmaceutical Industry (ABPI). Its purpose is to identify the key factors which influence how research-based pharmaceutical companies choose where to locate their functions, and how to allocate their investments.

Our work has included a literature review and some basic analysis of data available in the area. However, the new material this report adds to the debate derives primarily from a series of interviews with 34 senior executives from 14 research-based pharmaceutical and biotech companies. The project team constructed a series of scenarios about how a company might decide to locate its investment assets. The scenarios described situations faced by a hypothetical company, and made initial suggestions as to how that company might sensibly act in those scenarios, based on economic theory and messages from the literature. Interviewees were asked whether (and why) they agreed or disagreed with the courses of action suggested in the initial scenarios. The scenarios were then used to structure a discussion about the factors that are of importance in driving investment decisions.

These interviews were extremely useful in providing rich qualitative information on why particular factors matter, as well as offering some idea of the relative importance of different drivers of investment in different contexts. However, it should be noted that this methodology inevitably relies on a degree of subjectivity in interpreting the discussions.

Our research finds that there are a number of general drivers which influence the pharmaceutical industry's investment decisions, and their willingness to invest in a particular country. Further, the factors that companies will take into account in deciding on an investment will also vary depending on the nature of the investment asset at issue.

Taking first the factors that influence the general willingness of the industry to invest in a particular location we find that:

- § **History matters:** in practice companies do not take investment decisions from a blank sheet of paper. Companies have substantial existing stocks of assets which it may be cost-effective to expand. Further new investments need to provide a good fit with this existing pattern of assets and with the culture and business style of the firm.
- § **Disinvestment may be as relevant as investment:** also reflecting the incremental nature of investments, and in light of substantial merger activity in the industry in recent years, we find that investment decisions (particularly but not exclusively in manufacturing) are as much about rationalising and consolidating as about expanding capacity.
- § **Stability matters:** a range of factors, including low tax, low bureaucracy and a can-do attitude, a flexible labour market, and political stability create an effective business environment. Demonstrating a commitment to such principles over the long term is key.
- § **Pharmaceutical market conditions may have a subtle influence:** we examined whether product market conditions (the pricing environment and rate of adoption of new technology) affect incentives to locate R&D in a country. In general we did not find credible economic mechanisms to suggest that product market characteristics were of over-riding importance when making investment decisions. Firms should locate research

and manufacturing in the best and most cost-efficient locations, then market their products globally. However, we found that firms often have a number of alternative locations for investment assets that are broadly equal in other dimensions, and in these situations market conditions can be an influence on the ultimate choice. In the case of clinical trials, we found that the economic arguments are clearer, with industry seeing limited value in familiarising opinion-leading clinicians with new medicines when returns in a local market are low anyway.

In terms of the factors that influence investment in particular industrial functions, the following drivers of investment were found to be important:

- § **Research and development:** by far the most important driver is to establish oneself in a location where one can do good science, both by accessing world leading scientists, and by accessing an adequate stock of well trained scientists to work on the programme. The former may require co-location with leading universities, although some individuals may be internationally mobile, given the right opportunities. The latter relies more on a strong commitment to science throughout a country's education system. Further, sensitive research will not be undertaken in countries that are perceived to have inadequate systems for the protection of intellectual property. Cost factors are relatively unimportant although become more relevant for simpler stages of the R&D process where more locations may offer the necessary skills. While certain investment incentives may be nice to have and affect decisions at the margin, they will be completely ineffective if the underlying scientific fundamentals are not also in place.
- § **Clinical trials:** a program of trials will always include major commercial markets, as they are an excellent opportunity to familiarise key opinion leaders with forthcoming products. Companies seek to supplement key market trials in order to create a sufficient global bank of evidence in relation to their product. This is likely to include trials in locations which are cost-efficient and can provide timely patient recruitment. Such locations may include Central and Eastern Europe, Asia, and numerous other countries, providing they have a culture of good clinical practice and can provide reliable data.
- § **Manufacturing:** very general statements about the location of manufacturing should be interpreted with caution, because the technology required depends both on the stage of manufacturing and the type of product at issue. There is an absolute need for manufacturing to deliver the required quality, and the industry is not an environment in which any mistakes can be tolerated. That said, a wide and increasing range of countries have the capability to undertake work, at least at the simpler end of the manufacturing spectrum. In these circumstances cost will be very important. In practice tax is usually a key driver of cost although labour flexibility and other components of labour cost also matter.
- § **Regional offices:** the main drivers identified for the location of regional offices were to find an area that was attractive to internationally mobile talent, and offered good transport links both within the region served and to global headquarters.

We conclude with a discussion (in Section 8) about the implications of these results for the public policy debate about the competitiveness of the UK and European pharmaceutical industry, although developing firm policy recommendations falls beyond the scope of the study.

1. Introduction

This report has been prepared by NERA Economic Consulting for UK Trade & Investment (UKTI) and the Association of the British Pharmaceutical Industry (ABPI). It also benefits from the involvement of a steering group comprising officials from the Department of Trade & Industry, the Department of Health, and those with experience of the pharmaceutical industry. Its purpose is to identify the key factors which influence how research-based pharmaceutical companies choose where to locate their functions, and how to allocate their investments.

The study takes place against a background of declining competitiveness of the European pharmaceutical industry, and its objective is to help to identify ways of slowing or reversing this trend. However, although our report will contribute to this debate it is not its place to make firm policy recommendations.

The analysis in this report draws upon and combines three strands of work:

- § A review of the economic literature addressing questions of industrial location in general, and location decisions in the pharmaceutical sector in particular;
- § Basic analysis of data covering variables thought likely to be important in explaining location decisions (although scope for such work was severely limited by data availability and technical factors);
- § A programme of interviews with senior decision makers from research-based pharmaceutical and biotech companies.

Our report primarily describes the drivers of investment decisions according to industrial function. We focus on decisions related to functions of research, development, clinical trial research and manufacturing. We also examine the factors that influence the siting of regional headquarters. A principle that underlies all decisions about investment is that there is some trade-off between cost and quality. Ensuring good quality is important across all the functions we examine, but the relative importance of cost and quality may differ between functions. The factors that allow high levels of quality to be achieved also vary.

We also identify a number of cross-cutting themes, which affect the general willingness of the industry to do business in a particular country.

The remainder of the report is structured as follows:

- § Section 2 outlines the methodology followed for the research, and explains the sources of material on which the subsequent sections are based;
- § Section 3 explores the more general themes identified;
- § Sections 4 - 7 review drivers of investment from the perspective of particular industrial functions;
- § Section 8 draws conclusions and considers the potential implications of the research from a UK or European policy context.

2. Methodology

2.1. Literature Review

We reviewed a range of literature that examined the factors that are likely to affect both how companies in general, and pharmaceutical companies in particular, choose to locate particular assets. This included literature deriving from academic economics, including searching databases such as Econ-Lit using appropriate keywords. It also included what might be termed “grey” literature such as reports prepared or commissioned by policymakers and other interested bodies. The conclusions deriving from the literature review are one input to our overall analysis, but are also consistent with the general themes and conclusions which we derive. In particular, studies in the literature consider possible drivers of location such as:

- § Labour force issues;
- § “Clustering” and co-location with other firms;
- § Government, policy and regulation; and,
- § Tax incentives;

as well as other general market considerations.

In general, both the literature and our discussions with pharmaceutical executives supported the possibility for each of these factors to influence locational decisions (although the academic literature often considers clusters in terms of their affect on society and overall growth rates through informational externalities) rather than on individual firms. However, most of the literature is primarily designed to identify whether a particular factor matters or not, whereas our interviews provided much richer qualitative information on *why* a factor matters as well as some idea of the relative priority which will be given to different drivers of investment in different contexts.

Messages from the literature and our other research are combined in the following sections.

2.2. Statistical Analysis

As part of our terms of reference for the research, we agreed to investigate the feasibility of using econometric analysis to explain trends in investment decisions made by the industry. Our general conclusion is that a number of theoretical and practical difficulties make it difficult to place great reliance on analysis of this nature, although in the light of resource constraints and the other work priorities we did not attempt a full study of the data in this area.

In brief, the difficulties in deriving robust conclusions purely from numerical data in these incidences include:

- § **Conceptual difficulties.** In particular, further work would be necessary to refine the exact question being posed. Traditional studies of investment decisions have focused on identifying the drivers of the next decision, the marginal investment by a firm (for which data on foreign direct investment flows would be useful). Alternatively, as the portfolio of a company’s assets have become increasingly internationalised and spread across the globe, it might be more appropriate to explain the pattern of location of the entire stock of a company’s assets. A decision to maintain an asset in its current location is a vote of

confidence in the country or city. Indeed, the importance of some assets to a local economy has led some European countries to develop policies on "aftercare" and "investor development" in order to retain them. Similarly, would it be appropriate to measure the capital expenditure of an investment decision, the number of jobs it creates, or the level of technological spillover the investment will provide to the local economy?

§ **Limitations on available data.** There are a wide range of variables that could be considered as being of possible importance. However, the collection of data in these areas on a consistent basis in all relevant locations is complex and unlikely to be immediately available. In particular, whether one seeks to model the existing pattern of assets (which will clearly depend on historical investment climates) or whether one seeks to model investment decisions (which depend in part on where firms already maintain a presence), the difficulties associated with data availability are magnified by the potential need for data covering lengthy historical periods.

In order to provide some illustrative analyses we undertake some basic correlation analysis, primarily making use of PICTF data. Charts describing the correlations obtained are included at Appendix A. These correlations should be interpreted with extreme caution. Apart from the general caveats surrounding empirical work in this area, as summarised above, particular caution should be paid to these charts since:

- § In many cases the accuracy of the correlations obtained is weak. In such a simplified framework it is difficult to be sure whether this is because the underlying relationship does not in practice exist, or whether the results are being distorted by the range of variables omitted from the analysis.
- § The latter issue should be regarded as a particular cause for concern, and likely explains what might be regarded as "perverse" results such as positive correlation between tax rates and the amount of investment in a country. In reality, such results reflect the fact that some countries that currently have relatively high tax rates also benefit from factors such as historic strengths in the industry and a strong and innovative science base.

Construction of a single-overarching model to investigate the accumulation of assets over time – if practical – would provide the most robust route to address these issues. Compromises would inevitably be required in the creation of such a statistical model in the light of the timeframe over which data would be required and the range of potential explanatory variables. However, the a priori selection of a restricted range of explanatory variables might facilitate some degree of analysis. Appendix B provides a range of possible explanatory variables, although it can be noted that some could potentially duplicate coverage of the same underlying drivers and could potentially be excluded. There would, however, be no guarantees that such a project would provide robust or useful conclusions.

2.3. Interview Program

2.3.1. Interviewees

We selected a sample of fifteen research-based pharmaceutical companies, and invited each of them to nominate up to three senior executives from a range of functions in their organisations who we could interview about their views on how and why they allocate their assets in certain ways.

Our sample of pharmaceutical companies was designed to be broadly rather than statistically representative. It included a number of major European research-based companies (UK and other European), a number of similar US-based companies, one major Japanese based company and a number of smaller companies including biotechnology companies.

Across our sample of companies we sought to interview individuals with a range of responsibilities. These included general management responsibilities such as Chief Executives or regional heads, and individuals holding senior positions in individual functions, including research, development, manufacturing, and finance.

In all we completed interviews with 34 senior executives from 14 companies. Our acknowledgements section provides a list of the companies who participated in our research, and an illustration of the range of job titles of our interviewees.

2.3.2. Nature of the interviews

It was decided that a formulaic “tick-box” style of questionnaire would reveal only a limited amount of information. This partly reflects the complexity of some of the issues, and the potential richness of experience required to provide a true grounding for understanding the key drivers of decision making. It also reflects the difficulty of obtaining a statistically robust sample size, particularly once controlling for different backgrounds of individuals and companies being interviewed. Finally, a number of the elements being tested in the research are the subject of some controversy, where positions publicly taken by some pharmaceutical companies are hard to reconcile immediately with predictions that would be derived from basic economic or business theory. In these cases, the explanations of the rationale for the positions taken by those companies are of more interest than a straightforward restatement of those positions.

To this end, the project team constructed a series of scenarios that described situations faced by a hypothetical company, and made initial suggestions as to how that company might sensibly act in those scenarios. Interviewees were asked whether (and why) they agreed or disagreed with the courses of action suggested in the initial scenarios. The scenarios were then used to structure a discussion about the factors that are of importance in driving investment decisions.

It should be acknowledged that this methodology relies on a degree of subjectivity on the part of the project team in terms of guiding discussion and interpreting the results. A core script was not rigorously followed for the interviews: for example theories and arguments put forward by earlier respondents were sometimes tested and examined with subsequent interviewees. Equally, judgements sometimes need to be made between the extent to which particular positions were put forward in interviews, and the interviewers’ impressions of the strength of the arguments put forward to support those positions. We attempt to reduce this subjectivity by providing anonymised quotes from the interviews so that readers can have an opportunity to form their own opinion about the views expressed.

2.3.3. The scenarios

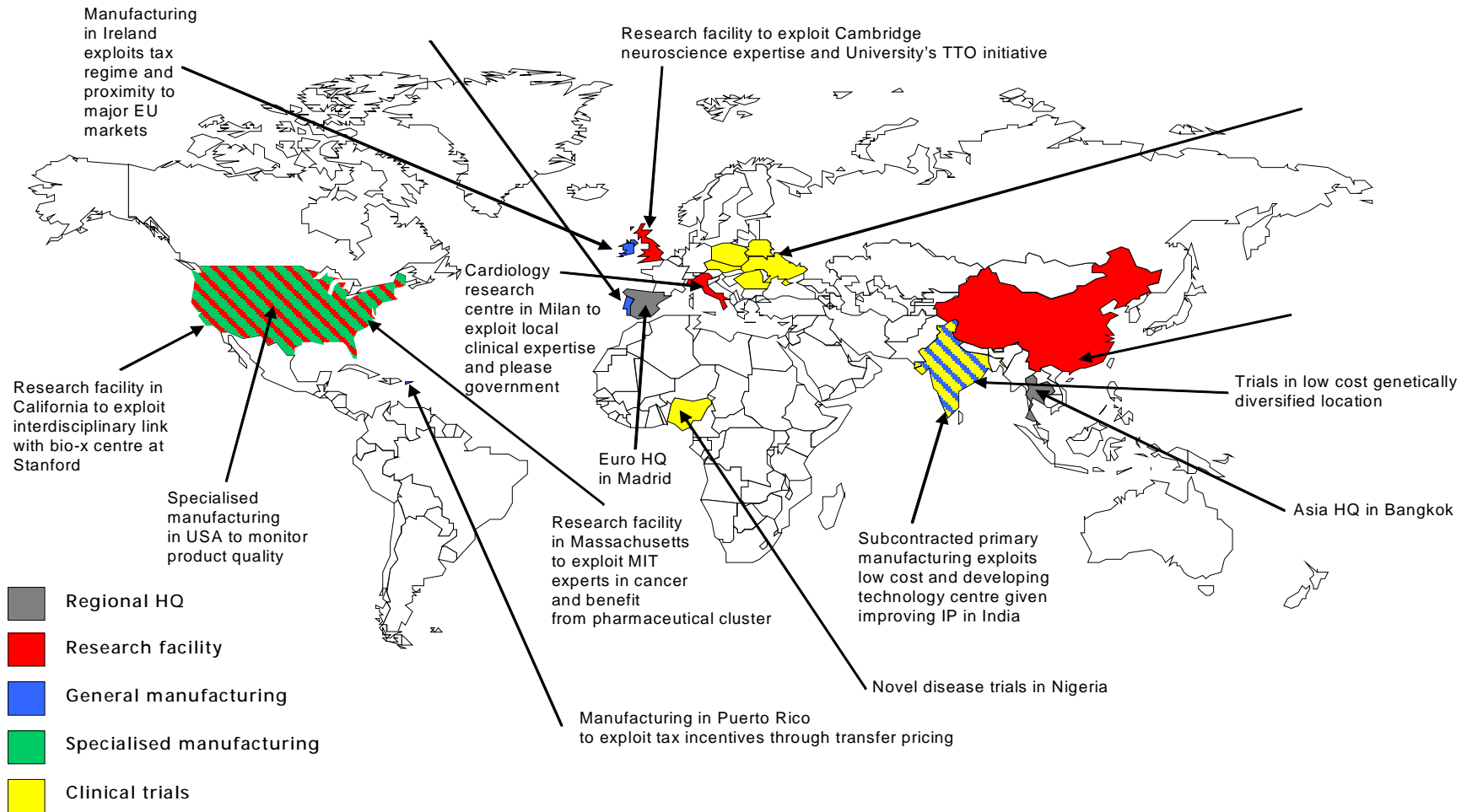
Five scenarios were constructed, although their applicability depended in part on the scope of experience of individual respondents. In many of the interviews, discussion of the issues arising from Scenario 1, provided a natural route to cover material that could otherwise have been discussed in subsequent scenarios.

In summary, the scenarios covered the following ground:

1. A broad thought experiment that posed the general question that if a medium-sized research-based pharmaceutical company were to have an opportunity to re-establish itself without taking account of its history, how would it divide its assets and where would it locate them. Information provided to respondents included the number of disease areas the company was engaged in research within, and the extent of its existing portfolio of assets. A distribution of these assets was hypothesised (see Figure 2.1 overleaf), and the views of respondents on the degree of distribution of assets, and the sensibleness of their location were sought.
2. A situation where a decision had to be taken as to where to locate production of a blockbuster product that required dedicated investment in new or expanded capacity. Issues discussed in the scenario included tax issues, possibility of co-location with existing assets, political issues, transportation issues, cost issues and the technological base required.
3. A scenario covering a situation where a company was keen to work with a research team that was currently based in a location that was inconvenient for the company's existing spread of other assets. It was assumed that the team was unwilling to relocate, and the scenario considered options such as building research assets around that team, working with the team on a remote or 'virtual' basis, or abandoning the plan.
4. A situation where a cash-constrained company was forced to abandon one of a number of research programmes. Programmes were outlined both in terms of attractiveness of the location where they were sited, degree of maturity, perceived likelihood of success, co-location with other assets of the firm and political factors.
5. A question around choosing the site of a single regional office for a company that currently had two European bases as a result of a recent merger, and needed to consider the political, strategic, business continuity and other factors that may arise from selecting one of the two offices, or even a third new location as a choice for the regional office.

We note that in part the answers to the scenarios proposed by the project team were intended to be 'correct' – to the extent that single correct answers can be suggested for questions of this nature – and in part they were intended to be controversial in the expectation of sparking debate with interviewees.

Figure 2.1



2.4. Engagement of Respondents

We discuss in the following sections the detailed responses made by interviewees. However, in general, respondents engaged actively with the scenarios as presented, and in many cases discussion of the first scenario was sufficient to cover the full scope of material that was relevant to the interviewee.

A number of general themes arose in the context of the discussion and need to be borne in mind in interpreting the conclusions from the interviews. These included that in practice, all companies take decisions against their historical background. Alternatively, if the scenario is understood as pertaining to a newly established company, the issues it faces in terms of engaging financing and establishing a geographical footprint might mean that the company makes decisions differently from more established firms which have, for example, more options in terms of managing risk. It also needs to be understood that the hypothetical nature of the scenarios inevitably limits the detail with which responses can be made. However, in most cases the scenarios provided a good basis for engaging in debate.

Notwithstanding the themes discussed in the remainder of this report, respondents generally suggested that the outline of assets suggested in Scenario 1 provided a sensible starting point for discussion. Particular issues where significant numbers of respondents disagreed with suggestions made in the scenario included that:

- § While the research locations were broadly sensible, they might possibly be spread too thinly for a company of this size, and they are not the only sensible locations. In particular a range of other European countries were suggested as possible locations, and as locations that might be preferable to Italy; (Section 4);
- § Clinical trials would be likely to be undertaken in a broader range of locations, including the USA, Western Europe, Japan, and potentially other locations with a culture of good clinical practice. Nigeria would only be likely to be used as a trial location if disease-specific factors meant that there were few or no alternatives; (Section 5);
- § A number of alternative models for integrating or dividing the various stages of manufacturing within the manufacturing function, and with development functions were described. While interviewees generally felt the suggested pattern was sensible many were already committed to manufacturing in costlier more mainstream locations. While these locations would often not be considered as candidates if a new greenfield site was required they would still be maintained and expanded. Product-specific technological issues make it difficult to draw very general conclusions in this area; (Section 6);
- § Madrid and Bangkok proved controversial choices for the location of regional offices; (Section 7);
- § The omission of any functions (particularly but not exclusively manufacturing) from Singapore was repeatedly mentioned as being surprising.
- § Marketing was excluded from the scenario (on the assumption it would occur everywhere). Some suggested that while sales forces had to be organised on a national basis there was some scope to regionalise more strategic aspects of the marketing function.

2.5. Interpretation of Responses

It is necessary to acknowledge that interviewees, being senior representatives of the pharmaceutical industry, will have views on which types of government policy would be of most benefit to the industry. Indeed, as well as understanding decision making criteria and processes, part of the benefit of this study lies in identifying views on preferred directions for policy development. However, this also means that interviewees have an interest in the outcome of the exercise, and hence could have an incentive to offer the answers that they believe would secure the most benefit, and not necessarily the most accurate answers.

In part, our methodology is designed to address this concern. Basing interviews around discussion of scenarios rather than a “tick-box” questionnaire, offers the project team an opportunity to question and to assess the rationale for the positions put forward, and we critique responses in the text of this report, particularly where this tension is most likely to be acute. However, we also acknowledge that it is not possible to avoid these issues completely. For example, there remains a risk that even where plausible mechanisms to support a link suggest can be identified, this might reflect ex post rationalisation of the discussion rather than the accurate underlying facts.

3. Overarching Themes

- § Pharmaceutical companies make incremental rather than revolutionary investment decisions, which are affected by their history and existing asset base.
- § “Investment” decisions (particularly about manufacturing) are at present often to do with consolidating and rationalising capacity, rather than new investment as such.
- § A stable general climate for doing business, such as low bureaucracy, an industry-friendly government low taxation across the board rather than dependent on limited circumstances are attractive.
- § Interviewees had mixed views on the subject of whether conditions in the pharmaceutical product market affected their willingness to invest research or manufacturing resources in that country. Economically robust mechanisms driving such a link are limited. However, where companies have a number of other sensible potential investment locations, perceptions about a market could influence the final choice.

3.1. History Matters

If one seeks to explain the current worldwide distribution of pharmaceutical assets, historical factors would be the pre-eminent explanatory factor. There are several reasons for this, all of them important:

- § The existing stock of pharmaceutical assets has been built up as a result of a series of decisions over previous years and decades. Since investment in these assets typically takes place according to a lengthy time horizon, and it is difficult and costly to relocate assets, there is a strong element of path dependence in the distribution of these assets. The difficulties involved in this were a common theme of interviews. However, one company with experience of moving these assets disagreed, suggesting that provided a successful strategy was in place to retain key talent shifting locations was not necessarily as difficult and expensive as is commonly assumed.
- § Reinforcing this, when pharmaceutical companies consider new investment, all potential sites do not start on an equal footing. In many cases re-engineering or expanding an existing facility will have cost-efficiency advantages compared to a completely new site. Using existing sites may harness economies of scale and scope, and drive better value out of the existing assets. For example, not all manufacturing sites may be running at full capacity, so expanding capacity at existing sites rather than investing in new sites may be cost effective. Some interviewees described the process of obtaining planning permission to locate in particular areas and the need for environmental permits etc, and suggested that often it is easier to expand existing sites rather than start this process from scratch.
- § Pharmaceutical companies develop a corporate culture over decades of doing business, which is likely to strongly reflect the company’s home, and this in practice is a significant influence on the company’s strategy and decision-making.

3.2. Investment and Disinvestment

Capacity decisions taken by the industry should generally be represented as a series of incremental changes to existing patterns of assets (both in terms of investment and disinvestment) rather than swift dramatic reorganisations and investments. Especially in the light of merger activity in the industry over recent years, the issues faced by the industry, are as much to do with capacity rationalisation and disinvestment as they are to do with investment. This applies as a general observation, although it has particularly relevant in terms of manufacturing.

In large part, the factors that drive investment and disinvestment are similar: the factors that make a location a good candidate for investment are largely the same as those that make it a poor candidate for disinvestment. However, labour flexibility is an important factor that may operate on an asymmetric basis. Companies may be reluctant to invest in locations with inflexible labour laws that impose high costs on exist and redundancy, but they may also be reluctant to disinvest from those locations when engaged in an overall downsizing exercise. Labour market flexibility was a theme that occurred consistently in our interviews as being important. However, some respondents suggested that whilst there are additional costs to pulling out of markets with tight labour laws, with planning and negotiation many of the costs can be mitigated. Further, it was suggested that if a rationalisation strategy is designed to achieve synergies following a merger, incurring higher transitional costs that can be written down as part of the organisational reform is unlikely to have a significant adverse effect on a company's share price.

It should also be noted that moves towards rationalisation and disinvestment will speed up the process of shifting from an asset distribution reflecting historical factors to one reflecting current drivers. In particular, assets in high cost locations whose existence reflects historical factors are at increased risk in such a context.

3.3. Clustering

We discussed the benefits and drawbacks of locating in a cluster with several respondents. This is a topic which is debated in the economic literature in which theorists suggest that that regions where informational externalities occur will exhibit higher rates of growth.¹ These externalities effectively allow the transfer of information and know-how between firms, either through direct observation, cross-hiring or drawing on a common support base. Porter suggests that this can increase labour productivity by increasing incentives and performance rewards and creating competitive pressure to innovate.² However, from the perspective of an individual firm the costs and benefits of clustering are more mixed, with firms potentially needing to balance the risk of resources and knowledge outflowing from their company against the range of benefits which being within a cluster can offer. In particular, market leaders and followers may have different perspectives on such questions.

¹ Furman, Jeffrey L., et al (2005) "Public and Private Spillovers, Location and the Productivity of Pharmaceutical Research".

² Porter pp 65-7 *Location, Competition and Economic Development: Local Clusters in a Global Economy*, reprinted in Cantwell (ed) *Globalization and the Location of Firms*.

The industry in practice exhibits a high degree of clustering. Examples of such clusters include manufacturing centres in Singapore, Ireland and Puerto Rico, leading-edge research clusters such as Switzerland, Massachusetts or the West Coast in the USA or Cambridge in England. However, the potential variation in attitudes to clustering and recognition of both advantages and disadvantages suggested in the literature was reflected in our discussions with interviewees.

Most respondents agreed that clustering in the pharmaceutical industry is prevalent because many firms wish to access what happen to be the best locations for tax or knowledge reasons, rather than because the industry deliberately sees significant advantages in clustering.

Respondents in general saw the benefits of clustering as having the potential to outweigh the drawbacks, as summarised in the following table. Some felt that the potential risk to the continuity of their research programme, through locating somewhere that makes staff turnover relatively easy, was a serious drawback. A more common view was that avoiding this risk by locating in an unconventional location would be more likely to make it too difficult to attract a quality workforce in the first place.

Table 3.1
Advantages and Disadvantages of Clusters

Advantages	Disadvantages
Existing stock of qualified staff who can be recruited.	Knowledge base and know-how exposed to poaching by other firms.
Perception that it is easier to attract talent to a cluster (as they and potentially their family enjoy other future options).	Risk of losing key staff to other firms.
Existing infrastructure eg local firms supplying supporting functions.	Resources can become scarce and cost can be "bid up".

3.4. Co-location

There are various advantages to co-locating certain functions within the industry. Partly this relies on exploiting economies of scale and scope in ensuring minimum efficient scale, and not duplicating overheads such as management between different locations. Particular functions where benefits of co-location were anticipated were:

- § Various stages of research and development, where synergies were anticipated;
- § Late stage development and launch manufacturing, where especially for products requiring more complex manufacturing it is helpful for these activities to be undertaken in parallel, perhaps prior to the transfer of full-scale manufacturing to an alternative facility.

This combination of potential complementarities requires companies to consider carefully how to manage knowledge transfer prior to scale-up to full commercial production.

3.5. Stability

Respondents repeatedly emphasised the importance of stability in the general business environment as a general factor underlying the decisions taken by the industry. This should be regarded as distinct from the stability and favourability of conditions in the market for pharmaceutical products, which we discuss below. Rather, this concerns, the general business environment for any industry.

Respondents cited a range of factors which helps to define a business environment which is favourable from this point of view, including:

- § Low tax
- § Low bureaucracy and a “can-do” attitude
- § Flexible labour market
- § Political stability
- § Above all, given the timescales to which the industry operates, a demonstrable commitment to such principles over the long term.

As well as specific tax incentives offered, Singapore was frequently cited as an excellent example of a country which has successfully achieved significant levels of investment as a result of its delivery of an environment which matches these principles.

3.6. Product Market Characteristics

3.6.1. Background

There has been persistent tension in the public policy debate, about the possible links between conditions in the pharmaceutical product market in a particular country and firms’ incentives and willingness to invest in assets in that country. On the one hand, it can be argued that research (especially) and manufacturing (substantially) are global functions and the optimal strategy for a firm is to locate these facilities in the location that provides the best balance between quality and cost, in respect of the investment at issue. In the face of minimal distribution costs, this should be independent of where final sales will be located. On the other hand, industry executives have suggested that it is in practice unrealistic to expect pharmaceutical companies to bring valued investments to countries which do not value and provide realistic prices and market access for the innovative products which the industry develops. A further argument is that “deals” may be explicitly or implicitly made that link a company’s investments in a country with the terms on which its products will access the market there.

A certain amount of grey literature has already considered these questions in the context of the pharmaceutical industry. For example, diversity of European national healthcare systems has been argued to limit the operation of a unified EU market, generating inconsistencies, inefficiencies and distortions in market function.³ This could make Europe a less attractive

³ Gambardella, Alfonso, et al (2000) “Global Competitiveness in Pharmaceuticals: A European Perspective: Report Prepared for the Directorate General Enterprise of the European Commission”.p58.

site for R&D investment when compared to the United States⁴ (although the US market is itself complex and multi-layered).

Government price intervention is an alleged deterrent for R&D investment. While it is clear that total expected profits may be lower in countries with cost containment instruments CRA have suggested that R&D expenditures will probably also be lower in such countries.⁵ It has been claimed that a 1 per cent decrease in drug prices causes a 0.68 per cent fall in R&D expenditures⁶, although extensive difficulties in undertaking such work robustly mean that such estimates need to be treated with caution.⁷

3.6.2. Interviewees' comments

Interviewees varied in their consideration of how product market conditions impact on investment decisions. In particular:

- § A small number of respondents suggested (generally when asked) that product market conditions were essentially irrelevant to decisions about functions such as research or manufacturing, and that these decisions were purely driven by underlying fundamentals.
- § The largest group of people suggested that decisions were largely driven by underlying fundamentals. However, when underlying fundamentals were similar enough that the industry had a number of realistic choices, executives' perception of market conditions is an additional variable that can become an important factor in the overall choice.
- § A material minority of respondents suggested that product market characteristics were a key factor at the forefront of their minds when making all investment decisions. This would not prevent them locating in a country that was far out in the lead on technical or financial grounds, but the industry usually has some credible alternative choices about location decisions and market conditions are an important driver influencing these.

It was also noted that political change may mean that the location of favourable markets changes more quickly than industry's investments can realistically adapt.

3.6.3. Analysis and mechanisms

Those who suggested that product market characteristics were a key factor did not generally supply credible mechanisms, which could be tested against economic principles, through which such links operated. Three general issues were raised in such discussion:

⁴ EFPIA www.efpia.org

⁵ Charles River Associates (2004) "Innovation in the Pharmaceutical Sector: A Study Undertaken for the European Commission". p 95.

⁶ Charles River Associates (2004) "Innovation in the Pharmaceutical Sector: A Study Undertaken for the European Commission". p 84, cites HEHS (1994) "Prescription Drugs: Spending Controls in Four Countries"

⁷ In particular, the original research studies the effect of drug prices in different markets, on R&D undertaken by firms domiciled in those markets. We are not convinced that such an approach adequately reflects the global nature of the industry, and it does not address the question of whether there is a relationship between prices in a country and R&D undertaken there. Further, the authors themselves acknowledge that the size of the effect is difficult to measure and their own estimates suggest that the 0.68 per cent figure could plausibly be in a range from 0.1 - 1.2 per cent.

- § Some interviewees turned the question around and asked instead, why should the industry invest in countries which do not value its output? They suggested that it makes more commercial sense to invest in the countries which offer higher overall product returns. *NERA does not see that this provides a robust economic rationale for location decisions.*
- § In practical terms, when choices are fairly equal it is natural that product market characteristics create perceptions about a country that influences decisions. It can be difficult to justify investment in a country to senior management who are struggling to deal with product market conditions there when there are a number of acceptable alternative locations for investment. *Although this argument is not generally subject to testing against economic theory we would not discount it and understand that it might become important in certain circumstances.*
- § Industry will usually complete clinical trials in the major markets, partly because it may help speed regulatory approval but more importantly because it familiarises local key opinion leaders with the value of a new product. When the product market environment is difficult, there is less value to the company in completing clinical trials in these markets. *NERA sees this as a logical and robust argument, although one which is applicable only to one particular sphere of activity.*

The other general theme that was explored was that companies who locate in a particular market may receive favourable treatment in terms of pricing or access in that market. Respondents generally suggested that conversations of this nature happened, sometimes explicitly, and even suggested examples of: non-EU countries where local manufacturing was a de facto requirement.⁸ There was, however, also a perception that drivers of this nature were declining in importance, at least in the EU. The fact that a local industry manager wishes to leverage a bargaining position may once have driven investment in some countries but was now much less likely to do so. However, the perception remained that, even if there is no commitment which is easy to quantify, in some EU countries a local research or manufacturing presence has the potential at least to smooth the course of such discussions. The point was made that if such deals are to affect the terms on which access to the market can be obtained, in either theory or practice, the size of the market at issue will be an important criterion – there is little value in negotiating such a deal in relatively small countries. The diversity of European markets may suggest that EU markets are in practice sliced too thinly to remain attractive from the perspective of such “deals”. A weaker version of this hypothesis suggests that the knowledge that a company has invested in a country creates goodwill of a more general form which can ease sales and marketing activities.

All of our interviewees discussed such “deals” in contexts where their own company received some form of product market return as a result, and where such enhanced returns would not be available to a competing firm that had not invested. However, it might also be hypothesised that the industry might make investments in markets that provide a product market which is attractive to the industry overall. Such investments might be intended to “reward” policy makers that pursued policies which were attractive to the industry or “incentivise” the maintenance and development of such policies. Although there is an

⁸ For example, interviewees suggested it would be extremely difficult to obtain licences to engage in business in Brazil without (potentially subcontracted) local manufacturing.

underlying economic rationale to such an argument, it needs to be interpreted with some caution because:

- § It is not clear that policy makers respond in this way, or how pharmaceutical companies would have formed this view;
- § We would have expected interviewees to outline this link if they believed that it was important. (It could have been raised at various stages in interviews and although it is consistent with a general desire to invest with friendly governments which was sometimes expressed, this underlying mechanism was never raised);
- § It is not clear that this strategy would offer a better return than seeking a more company-specific arrangement. More generally, there would be a concern about the stability of such a position since the possibility of free-riding would need to be addressed. This is because any individual company would retain an incentive to invest in the location that best suited its internal priorities, while hoping that other companies did enough to please policy makers and ensure an attractive overall environment.

3.7. Quality and Cost

Respondents generally described the process of making location decisions as one of trading off factors influencing quality and factors influencing cost in search of the best overall, or most cost-efficient, outcome. It should be borne in mind that:

- § the relative importance of quality and cost may vary substantially according to the investment being considered;
- § exactly what drives quality and cost may differ according to the nature of the investment at issue;
- § both the cross-cutting influential factors discussed above and the function specific factors discussed in following sections can contribute to quality and to cost.

3.8. Exchange Rates

Exchange rates have an important influence on trade in all industries and the pharmaceutical industry can not be regarded as an exception. In part, this affects individual investment decisions – investing in a location whose currency seems overvalued seems bad business sense – although the timescale of pharmaceutical investments counts against over-reliance on this. There may be some value to companies in ensuring that their cost base and revenue base are denominated in the same currency.

4. Research and Development

- § The key driver of R&D location decisions is to establish oneself in a location where one can do good science. This means a location where world-leading scientists are currently based, or a location to which it is possible to attract internationally mobile talent. Equally, it relies on the (less mobile) factor of the quality of a country's science base as a whole.
- § Intellectual property acts as a limiter more than a driver of R&D investment. Companies would be very careful about which activities they place in countries where there remains scepticism about the IP environment (in theory or practice). Investment in China or India remains constrained by this, although the situation is evolving.
- § Public funding of a basic medical and science base, backed with appropriate incentives to diffuse technology and encourage interchange between the academic and commercial sectors can have a strongly positive influence on research output.
- § Cost factors are of relatively limited importance in driving such decisions. Incentives such as R&D tax credits are nice for the industry to have and may have some influence, but can be too small, bureaucratic or unstable to be highly significant, especially in light of the pre-eminent importance of quality.

4.1. Description of Activities

The process of research and development consists of a range of activities, from the earliest stages of drug discovery, through compound screening, identification and development of robust production processes, and undertaking clinical trials and other experiments to demonstrate the safety and efficacy of a product. The rationale for the location of human (and particularly large-scale) clinical trials is discussed in Section 5. This section considers the range of other activities associated with research and development, although we note that issues vary slightly according to the exact nature of the function at issue.

4.2. Drivers of Investment Location

4.2.1. Quality of science

Overall, respondents were clear that the quality of science which can be delivered in a particular location is the most important and fundamental driver of location decisions for R&D facilities. In practical terms, the quality of science deliverable in a particular location depends on two key factors:

- § Ability to recruit a small number of world leading scientists to lead the research;
- § Ability to recruit a significant number of competent well trained scientists to support the research.

4.2.1.1. Access to leading scientists

Access to world leading scientists is one of the factors underlying whether a location offers a base for successful research. In practice, access to such scientists depends importantly on three factors:

- § Being based in a location where scientists are already located;
- § Being based in a location which is sufficiently attractive to entice these scientists to move there;
- § Local academic facilities (both in terms of the strength of those departments, and the extent to which commercialisation of research resources is encouraged or discouraged).

The literature supports the view that close proximity to leading institutions can give a firm access to talented human capital that can strengthen the research basis scientifically and financially.⁹ Pharmaceutical firms locating in that cluster can benefit from the potential spillovers to and cooperation with such prestigious institutions. The benefit of proximity varies, however, particularly on the flexibility of the nation's academic system and the possibility of commercial exploitation of university research.¹⁰

A desire to work with particularly well respected scientists was common to most interviewees, although the strength of this pressure varied. In particular, we were told of two examples where a company had, more or less, sited a new research facility solely in order to work with a particular individual. However, when exploring such a strategy in interviews the majority of respondents felt that this behaviour was too extreme. Although leading scientists can make the difference, a research programme organised around a single key individual is widely regarded as being simply too risky because:

- § Where will the other resources come from?
- § A research programme is a commitment whose length makes it impossible to rely on an individual. Replacement and the future of the programme need to be considered.

For these reasons, access to the expertise of a number of leading scientists would be an important driver for location decisions, but access to a single individual, or even a single research group would be unlikely to be a major factor. In our interviews we explored a scenario testing how firms would seek to work with a leading research team established in a remote location. Persuading the researchers to move was the favoured strategy. Should this not be viable, attempting to collaborate with the researchers on a remote basis – perhaps supplemented by visits or by integrating some of the company's own personnel with the team for periods of time – was generally the preferred option.

In addition to the option of locating where scientists are already based, respondents generally suggested that a viable option was to locate in an attractive site that would induce scientists to move. This would particularly be the case at leading edges of science, although there was

⁹ Ando, Ken-ichi (2005) *Japanese Multinationals in Europe*, Edward Elgar Publishing Limited, United Kingdom, 2005pp 80-81.

¹⁰ Gambardella, Alfonso, et al (2000) "Global Competitiveness in Pharmaceuticals: A European Perspective: Report Prepared for the Directorate General Enterprise of the European Commission". p. 70.

some perception that the scientific workforce is becoming slightly less internationally mobile than, say, a decade ago. Factors driving the attractiveness of a location included being in a cluster (offering career options without relocating again, and employment opportunities for a partner who may work in the industry), and the existence of a community and infrastructure (such as schooling) to support an ex-pat lifestyle.

Co-locating in an area where universities had strong complementary scientific interests was in general viewed highly favourably. In part this was because such areas are likely to offer an accessible stock of scientists (newly trained as well as more senior) in order to develop the facilities. However, direct knowledge transfer from research groups was also viewed as a driver – the strength of which depended largely on attitudes within the academic community to the commercialisation of research findings. Respondents generally took the view that the USA offered the best environment from this perspective and that the UK remained somewhat behind, albeit that culture was changing markedly in this direction.

4.2.1.2. A strong general scientific base

The other key determinant of the quality of science which can be delivered in a particular location is the strength of the general scientific base, from which the bulk of a facility's workforce is derived. In practice, this is likely to correlate closely with the quantity of suitably trained scientists available (and in part also the quality of such training). Since the general scientific base is less internationally mobile than particular leading individuals, it is likely that it is, if anything, a more important driver of location decisions.

Commitment to science throughout the education system was perceived as being the key driver of a strong general scientific base. Many respondents expressed some concern about this in the context of the UK, where matters such as the potential closure of chemistry departments were viewed as serious threats to the future research potential of the country. This was partly balanced by a view that these factors are not specific to the UK, but rather reflect trends towards less technical education which are evident in many significant industrialised economies, and as such the UK's relative position may not suffer unduly. However, this also needs to be understood in the context of large economies without a track record of pharmaceutical research who nonetheless wish to develop industry in this area. In particular, several respondents mentioned China as an attractive location, with a key factor underlying this being very large quantities of well trained scientists trained by the Chinese education system.

Where the overall process of R&D is considered in terms of its components, there exist some more commoditisable tasks (chemical synthesis was mentioned as an example) which can be closely scripted and it is reasonably practical to undertake in any location with a good supply of well trained scientists. At present these are the sort of functions that are currently being exported to countries such as China. Further development in the sophistication of research tasks exported in such a manner is expected.

4.2.2. Intellectual property

Literature suggests that Intellectual Property (IP) regimes may be significant, as the rules and their enforcement can affect the willingness of companies to invest in skills, research

technology, and upgrading other capital.¹¹ It is also suggested that not only current IP laws should be considered, but a country's history of IP regulation. Previous years of inconsistency and IP law loopholes (patent protection under process, not formula) have created scepticism around India's more recent standardised IP laws, for example.¹²

In practice in interviews, IP regimes were perceived as being not so much a driver of location decisions but rather as placing limits and identifying elements of research that would **not** be undertaken in certain locations. This may primarily reflect the adequacy of the regimes in most countries in which research was undertaken.

The main exceptions to this were China and India, where the IP environment was perceived as a factor limiting investment in research in those countries. While many companies were happy to farm out simpler more commoditisable stages of research to those countries, there remained substantial reluctance to do the same with cutting edge research from which key IP rights and industrial knowledge would be derived.

While some suggested that this attitude was overly risk averse and the number of stages involved in research and production of an innovative new medicine made the risks small, most either perceived the risks as larger in the context of the developing science base in those countries, or felt that it was not worthwhile to accept even small risks in such an important context. That said, respondents did perceive that the environment was changing and IP protection was being strengthened, in China and India, both in theory and in practice. While the present situation may not yet convince international investors, it was thought likely that in 5-10 years this would have changed. In other words, introducing appropriate IP law is important, but a track record of its enforcement is also needed before companies will have full confidence.

4.2.3. Spread of facilities

The basic interview scenario discussed with respondents suggested that a company undertaking research in four disease areas would operate four distinct research facilities, with each in effect being sited in order to access local scientific expertise.¹³ Some respondents argued that this was unnecessarily diverse for a company of the size discussed, and that co-locating research programmes (into say two centres) was of value. This value would derive from two sources:

- § It is possible to generate knowledge spillovers between research programmes in different disease areas. The likelihood of this depends somewhat on the nature of the disease areas, and is particularly strong where medicines are based on similar scientific platforms;
- § Co-locating research programmes avoids the need to duplicate costly supporting overheads such as management, security, some testing functions and so forth.

¹¹ Porter p 65 *Location, Competition and Economic Development: Local Clusters in a Global Economy*, reprinted in Cantwell (ed) *Globalization and the Location of Firms*.

¹² ATKearney (2004) 'Pharma Explores Uncharted Territory', *Executive Agenda*, Vol. 7, No. 4, Fourth Quarter 2004. p 47

¹³ One choice was based around clinical rather than scientific expertise and this was perceived as being a much less relevant factor for primary research.

4.2.4. Public funding of basic research

Government sponsoring and promoting of research and innovation will presumably increase the incentives for investment. Firms will want to locate near sponsored universities and research centres because of the possible cost-sharing and risk reduction opportunities.¹⁴ Literature also provides a number of examples of how publicly funded basic science and commercial development can interact in an appropriate regulatory environment to deliver innovation for patients.¹⁵

Although only a small number of respondents discussed this topic they did express the view that public funding of basic research was an important driver behind the construction of an environment that is conducive to effective commercial research. This helps both by *acting as a catalyst for the rate of change of understanding in areas such as biology*. In the US, the National Institute for Health (budget \$28 billion)¹⁶ *is an enormous help in itself and in light of the contribution made to training scientists and developing a culture of scientific innovation*.

Disease-specific data suggest that the UK and Europe do not match such levels of funding. For example, the European Cancer Research Survey found that public spending per person on cancer research in the USA was around 6-7 times the average across the EU. Expressed in terms of a percentage of GDP, spending in the US remained four times higher than the EU average.¹⁷ However, the PICTF indicators suggest that the UK is second to the USA in terms of the government's spending on overall health R&D, as a percentage of GDP.¹⁸

Bearing in mind the general caveats expressed earlier about undertaking correlation analysis, the available statistics do support the idea that public spending on medical and scientific research makes it more likely that private spending will increase in this area (Figure 4.2). This correlation is shown on a cross-country basis, although it should be acknowledged that the USA (top-right corner of graph), with both a strong science base and strong public funding may have a marked influence on the results, even though there are other possible explanations for its scientific strength.

¹⁴ Charles River Associates (2004) "Innovation in the Pharmaceutical Sector: A Study Undertaken for the European Commission". p 96.

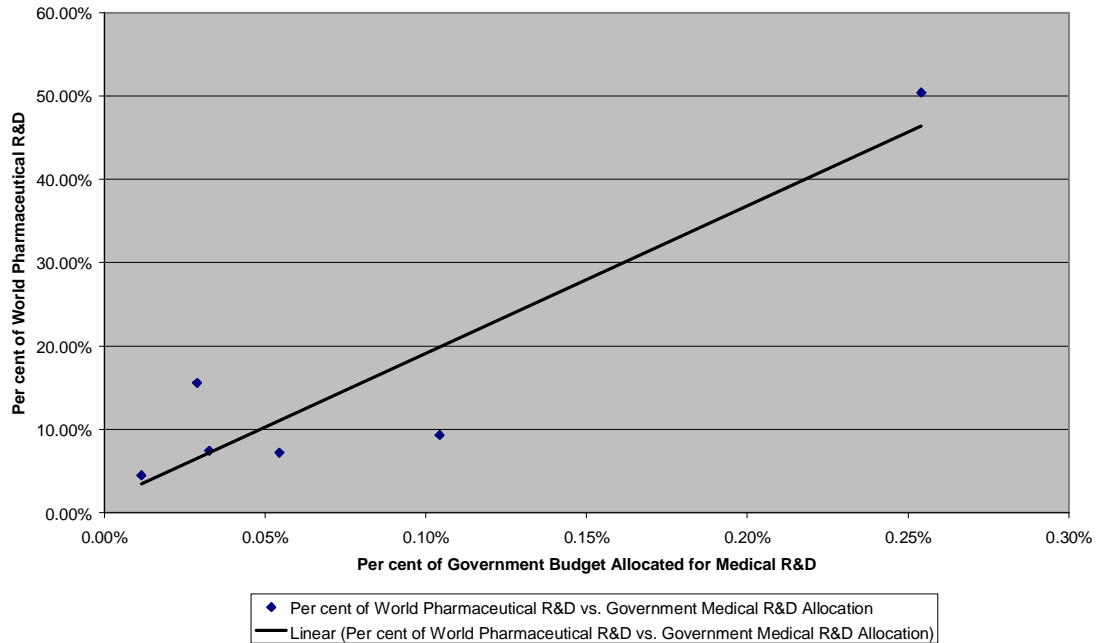
¹⁵ Rozek and Dickensheets: Encouraging cooperating between the academic, government and private sectors in US biomedical R&D; in Pugatch (ed) *The Intellectual Property Debate*; Edward Elgar

¹⁶ <http://www.nih.gov/about/> accessed 30 October 2006.

¹⁷ <http://www.medicalnewstoday.com/medicalnews.php?newsid=47531> ; accessed 20 November 2006.

¹⁸ Pharmaceutical Industry Competitiveness Task Force: Competitiveness and Performance Indicators 2005 (Indicator 9)

Figure 4.1
Per cent of World Pharma R&D vs. Per cent of Government Budget
Allocated for Medical R&D 2003



4.2.5. Cost factors

Cost factors were perceived as being relatively unimportant to location decisions about research programmes. In contrast, quality was perceived as an overwhelmingly dominant factor: *The most expensive research programme is one that delivers no successful output*¹⁹. In other words, although decisions are in principle made in terms of trading off cost and quality factors, in practice quality tends to dominate. Only if choices are broadly equivalent in terms of quality is it likely that cost or broader commercial considerations come in to play. Commercial benefits tend to be *nice to have but unlikely to drive location decisions in this area*.

Incentives which were discussed included:

§ **R&D tax credits:** these were perceived to be of some value, but this value was quite limited for a number of reasons:

- They generally involve relatively small sums in the context of a major pharmaceutical company's research budget;
 - *A major company might have a research budget of \$3.5bn, making a tax credit of, say \$20m of limited attractiveness. At \$200m companies may start to engage seriously, and at \$2bn their full attention will be gained.*
- The process of claiming them can be bureaucratic and the outcome uncertain;

¹⁹ In these sections italics represent quotes from interviews that broadly reflect main views of respondents.

- Tax credit regimes are subject to change, and there is scepticism about the maintenance of such credits over the commercial life of a research programme (25 years or more).

§ **Capital grants:** these were perceived as being of too low value to be of material relevance to established firms (although might be valued by start-up firms where cash flow is likely to be of much greater importance).

If quality considerations are sufficiently similar that commercial priorities might have a serious influence on the location decision, participants suggested that alterations (even relatively small) in parameters that have an overall influence on their business, such as the general rate of corporation tax would be likely to be more significant considerations. The general perceptions of the attractiveness of product market conditions in a particular country, and the potential to leverage R&D investment to improve them are also likely to fall into this category.

Table 4.1, below, illustrates the R&D tax incentives offered by a range of countries.

Table 4.1
R&D Tax Incentives

Country	R&D Tax Incentives
Australia	125% deduction for R&D expenses Plus a 175% deduction for R&D expenditures that exceed a base amount of the prior year's spending
Canada	Permanent 20% R&D tax credit Provincial governments also offer refundable credits for R&D activities
China	Foreign investment offered a 150% deduction, provided it has increased 10% from previous year
France	50% R&D credit (10% flat credit and 40% credit for R&D in excess of previous two years average)
India	100% deduction of profits for 10 years if engaging in scientific R&D
Ireland	Offers a 20% R&D tax credit Plus a full deduction And a low 12.5% corporate income tax
Japan	Flat 10% R&D tax credit (15% for smaller firms) in addition to other incentives
Korea	Tax holidays, up to 7 years, are provided for high-tech business Variety of tax credits also provided for R&D expenditures
Singapore	R&D and Intellectual Property Management Hub Scheme: Offers U.S. companies a 5-year tax holiday for income earned with respect to Singapore based R&D
United Kingdom	125% deduction for R&D expenses (150% for SMEs)
United States	Allows a maximum 10% incremental credit for qualified R&D expenditures in excess of some base Alternative Incremental Research Credit formula is also used for a three-tiered credit percentage Business deductions for R&D must be reduced by the amount of any R&D credit

Source: NERA from various sources

4.2.6. Regulatory factors

The regulatory environment underpinning development research was suggested by respondents as a driver of location, in particular in the case of animal rights. A number of respondents suggested that it was an inevitable fact that some animal use was required in testing the safety of pharmaceutical agents. However, it was also suggested that it is not

always possible to divorce the location of such research from other aspects of the development process. Interviewees suggested that pressure against such activities from the animal rights movement has in the recent past placed in serious jeopardy the maintenance of R&D in the UK. However, they also acknowledged that legislation has substantially assisted the industry in dealing with these pressures.

The other area where ethical or regulatory factors was (less commonly) suggested to have the potential to constrain the development of R&D was in the area of research on stem cells deriving from embryos in the US, where it was suggested that the current US approach to government funding of such research was a barrier to the further development of the science base in this area.

4.3. Implications for the UK and the EU

The strong historic science base of many EU countries is a major factor in the historic strength of the European industry. Being a function that is primarily driven by quality with cost factors having a relatively marginal effect, the EU may be in a better position to retain and develop R&D than some other functions within the industry. Possibilities of enhancing these prospects can be improved by:

- § Renewed commitment to excellence throughout scientific education to promote an adequate supply of well qualified scientists (as well as stars at the cutting edge of research);
- § Adequate public funding of basic scientific and medical research, and promoting flexible interchange of personnel and knowledge between academic and commercial sectors;
- § Maintaining the integrity of intellectual property rights;
- § Providing a regulatory environment that safeguards personnel working in the industry and does not present unnecessary bureaucratic barriers to launching trials.

Countries may also help to attract R&D through schemes such as R&D tax credits. However, such schemes might possibly add to, but in no way substitute for, the provision of an underlying high quality environment.

5. Clinical Trials

- § A pre-eminent requirement for the location of clinical trials is a culture of good clinical practice, producing reliable data in an environment based on informed consent. Without such a culture, the process of bringing an entire product to market may be undermined. However, this is achievable in a wide variety of locations.
- § Interviewees had mixed views as to whether local regulators required, preferred, or were indifferent to the existence of local clinical data. In practice, companies are always likely to undertake some of their trials in key commercial markets because of the opportunity to access key opinion leaders which results.
- § Trials in key markets are likely to be supplemented in other locations that allow rapid patient recruitment at reasonable cost in order to create an overall global store of data which supports the product's launch.

5.1. Description of Activities

Clinical development and human trials cover a range of trials of increasing scope and size. Phase 1 trials focus on monitoring the safety of the drug in small populations of healthy volunteers, whereas Phase 3 trials aim to establish the safety and efficacy of the drug on the basis of statistical significance, generally through multi-centre double blind randomised controlled trials. The size of such studies is determined by the expected statistical power of the trial, but it may include several thousand patients. Since cost and the impact of a function being located in a particular country will both be correlated with the scale of a trial, this section of the report mainly considers later stage large scale clinical trials.

5.2. Drivers of Investment Location

5.2.1. Culture of good clinical practice

An underlying requirement for a location to be considered as a trial site was a culture of good clinical practice. A badly undertaken trial can place a significant burden on a firm, risks derailing the timing and strategy for a product, and can not be risked. However, there is a wide range of countries in which good quality can be achieved. These suggestions included locations as diverse as the USA, Western Europe, Central and Eastern Europe, Japan, Brazil, Australia, Israel, South Africa, Morocco, and Egypt.

5.2.2. Access to key opinion leaders

Respondents overwhelmingly suggested that clinical trials were an important opportunity to access key opinion leaders and familiarise them with the potential of their products. For these reasons, respondents suggested that they would always undertake a proportion of clinical trials in the USA and in the industry's major markets in Western Europe, even though these locations are relatively expensive compared to some possible locations. The commercial benefit of influencing key opinion leaders by demonstrating the products' efficacy to them at an early stage outweighs the additional costs involved.

A partial caveat was, however, suggested about the benefits of undertaking activity in the UK in this context. The benefit of accessing key opinion leaders largely derives from the potential to increase uptake more quickly upon launch. However, the UK is historically a country which has seen relatively slow adoption of technologies, and NICE at least in part removes clinicians' control about prescribing decisions in relation to new innovative products. As a result, the benefits of influencing key opinion leaders may be lower. On the other hand, some UK clinicians are of sufficient stature to exert an influence on global opinion. Although the UK was the country referred to by respondents, the general principles would appear to apply to any country that limits the diffusion of innovation by strategies that distance the decision to adopt it from individual clinicians.

5.2.3. Influencing regulatory authorities

Respondents discussed the possibility that including local clinical data for a product might accelerate or ease its approval by the local regulatory authorities. While there was widespread agreement that this would be highly beneficial in some contexts (Japan was mentioned and sub-populations may require study where disease profiles might differ), in the context of the major Western markets there was a significant divergence of view with opinions being expressed including that:

- § Regulators will base decisions on the quality of the data, and what it says about products, and not the location of trials;
- § Regulators would not admit that the location of trials was an important consideration, but in practice those without local data will at least be subject to closer scrutiny;
- § Having local data is an important consideration in seeking regulatory approval.

Since companies have other commercial reasons for undertaking trials in markets where timely regulatory approval is most important, the practical significance of these different positions may be regarded as marginal.

5.2.4. Speed and cost

Subject to undertaking a sufficient proportion of trials in key markets and only using locations that deliver good clinical practice, the key drivers of trial location are speed and cost. By the time that large scale trials are being undertaken the "patent clock" for a product will be running and companies have a significant interest in bringing products to market quickly. One way of doing this involves shortening the duration of the clinical trial process. Ensuring that trials are undertaken in locations where significant volumes of patients can be quickly recruited helps to achieve this. Locations such as Central and Eastern Europe and India were confirmed by respondents as offering access to material numbers of patients on such a basis, and the fact that those populations tend to be less highly medicated than those in Western countries reduces the risk that patients will be unsuitable for the trial due to the possibility of drug interactions.

Beyond these considerations, cost is likely to be an important consideration. One respondent suggested that *the cost of trials varies substantially; Western European trials incurring twice the cost of Eastern Europe, US trials incurring twice the cost of Western Europe, with Japan in turn being twice as expensive as the USA.*

Regulatory issues also involve the conduct of trials. Respondents suggested that in the UK, bureaucracy and need for multiple ethics committee approvals makes it difficult to get studies off the ground. This increases the overall time required and hence provides a disincentive to doing trials in the UK. However, an appropriate regulatory framework was perceived as being necessary – many respondents commented in response to a suggestion in our basic scenario that they would only consider trials in a country such as Nigeria if suitable patients could only be secured in such locations. The potential that regulatory regimes might be laxer risks compromising the study's credibility and would not be a driver of decisions.

5.3. Implications for the UK and the EU

Continuance of incentives to undertake trials in the UK and EU requires nations to maintain their culture of good scientific and clinical practice, and to minimise unnecessary bureaucracy in getting trials off the ground. Ensuring that markets remain attractive to the industry, and that clinicians exposed to products in trials will have an opportunity to use them post-launch will further maintain and develop these incentives. This is the area where the regulatory environment in the product market has the most direct effect on the incentives to undertake research in a country, and the use of HTA by bodies such as NICE in the UK is perceived as a potential barrier to allowing clinicians such opportunities.

6. Manufacturing

- § Very general statements about the drivers of manufacturing location should be approached cautiously as it is a multi-stage process, and because the technical skill base required may be very different for different products. Compromising on the required level of skills is not an option.
- § Firms have different strategies, either to link together manufacturing stages, or to link manufacturing in a product's early years to its late-stage development.
- § There is a substantial range of products which it is technically feasible to manufacture in a wide range of locations. Where this diversity of choice in the light of required quality is available, accessing a low-tax environment is the primary driver of location choices.
- § The flexibility of the labour force and labour law appear to be more significant drivers than labour costs per se in influencing location decisions.

6.1. Description of Activities

Manufacturing covers a range of processes. In very simple terms this ranges from primary bulk manufacturing of active pharmaceutical ingredient (API), through secondary manufacturing involving combining API with excipients and producing tablets or other formulations of the product, to tertiary manufacturing, or packaging. It should also be noted that different degrees of technical sophistication are required in the manufacturing of different products. One relevant distinction is in the manufacturing of new compared to old products – difficulties in the production process are more likely to be identified for new products. Another distinction is between chemical (small molecule) and biological (large molecule) manufacturing, where the latter can be substantially more difficult to manufacture.

6.2. Drivers of Investment Location

6.2.1. Quality

Quality tends to play a different role as a driver of manufacturing decisions than as a driver of research decisions. In particular, for manufacturing there is less need to seek to secure the best quality available anywhere in the world as a driver of the success of one's programme. This is not to say that quality is not important – a dependable level of quality remains vital in manufacturing. Production difficulties or supply interruptions could have a major impact on both patients and the company, and this is not an environment where mistakes can be tolerated. However, once a certain required level of quality is obtained, the benefits of investing in even higher quality may be rather limited.

Access to a sufficiently skilled workforce is the main factor underlying the achievement of this quality. This depends both on skilled specialised professionals to undertake key roles in the factory as well as access to a generally efficient and qualified workforce to fill the bulk of operational positions.

The question then arises as to what level of quality is in practice required, and how many countries can deliver it. This question can only be truly answered on a product-specific basis. For example, the level of technical expertise required to produce a new biological product using an innovative delivery device may be very different to that required to produce a traditional chemical based product in tablet form. However, when one considers the diversity of pharmaceutical production sites operated by major research-based companies at present (some companies suggested they owned, or had owned not far short of a hundred facilities in a wide range of countries), it is clear that the necessary quality to produce medicines is achievable in many locations. Advancing scientific standards in previously less developed countries are further widening this range.

6.2.2. Taxation

Once a sufficient degree of quality is obtained, cost factors are likely to dominate the decision as to where to locate manufacturing. Rates of taxation are likely to be the single most important factor in this decision, particularly where the technology required for successful manufacturing is available in a wide variety of locations. This is reflected in both the discussion with respondents and their specific answers to the likely location of key manufacturing capacity – respondents agreed that locations such as Puerto Rico and Ireland were sensible candidates and almost uniformly suggested Singapore as a further candidate. Tax reasons are not the only reason why these locations are desirable; for example they have made substantial investments and commitments to ensuring that the required technical resources are available, but taxation is a major underlying advantage. Table 6.1, below, illustrates the differences in corporate tax rates between selected countries, and hence provides an indication of the potential savings. Box 6.1 discusses transfer pricing issues and highlights how these reinforce the benefits of ensuring that key mobile steps in the pharmaceutical value chain are located in tax-efficient locations. It needs to be understood that these provide a simplified overview of the issues involved, and in practice decisions will need to be undertaken in light of a company's overall tax strategy. Other elements that will be important include the location where key steps of IP are taxed, and the rules for taxing IP in the relevant jurisdiction, as well as the overall level of taxes.

Table 6.1
Main corporate tax rates (1 Jan 2005), selected countries

Country	Tax Rate
Japan	40.69%
USA	40.00%
Germany	38.31%
Italy	37.25%
India	36.59%
Canada	36.10%
Spain	35.00% *
Belgium	33.99%
France	33.83%
China	33.00%
Netherlands	31.50%
Luxembourg	30.38%
Australia	30.00%
UK	30.00%
Denmark	30.00% *
Sweden	28.00%
Czech Republic	26.00%
Austria	25.00%
Switzerland	21.30%
Singapore	20.00%
Poland	19.00%
Hungary	16.00%
Ireland	12.50%

Source: KPMG Corporate Tax Rate Survey, 2005; at http://www.kpmg.com/om/PDF/212792%20Global%20Tax%20Rate_fin.pdf (accessed 30 November 2006)

* 2004 rate

Box 6.1 Transfer Pricing

The taxation of profit accruing to pharmaceutical companies is complicated by the fact that, although the end-market where revenue is achieved may be clearly identifiable, the functions which need to be undertaken in order to generate those sales tend to be spread over a multiplicity of tax regions, as well as over long periods of time.

Transfer prices are those prices at which a multinational trades within itself and between its subsidiaries. A company's transfer prices may have a substantive effect on the jurisdiction where revenue is taxed (and hence on post-tax profits given the divergent tax rates noted in Table 6.1, above).

As a result, a pharmaceutical company has incentives both to ensure that as much activity as possible is undertaken in tax-efficient locations, and to ensure that its transfer prices, where justifiable, assign profit to those locations. On the other hand, tax authorities are keen to ensure that what they see as a fair or sufficiently high proportion of a company's profit is taxed in the authority's regime. This divergence of interests can lead to conflicts between companies and tax authorities regarding the appropriateness of transfer prices although the potential for these is reduced by the adherence to common principles for establishing fair transfer prices such as the OECD guidelines, which are in turn similar to US practice.

In essence, the practice of transfer pricing deals in *risks* and *functions*. It asks *which functions* are being undertaken in *which jurisdictions*, *which risks* are incurred in *undertaking those functions* and what economic reward is appropriate in light of this contribution to the overall value chain.

The question then naturally arises as to what proportion of value typically occurs at various stages of the journey of a medicine from laboratory concept to patient. Hard and fast answers to this question are not possible, in large part because different corporate structures can lead to different risks being undertaken by different functions, and the simplified stages identified in this report can be further subdivided if necessary. However, a NERA expert suggests that in very broad terms it would be typical for 15-20% of revenue to accrue to an R&D function, and around 35-40% of revenue to accrue to a full risk-bearing marketing subsidiary, with the balance accruing to manufacturing. Of course, estimates will in practice need to be made on a case by case and the exact division of risks between subsidiaries (eg what if a manufacturing subsidiary assumes certain responsibilities for late-stage development and product liability?) may affect the rates in any given example. Exactly which manufacturing steps accrue value, and how intellectual property revenues are complex matters that will need to be evaluated in the light of an individual company's transfer pricing strategy.

Acknowledging these caveats, the importance of transfer pricing and the benefits to an overall transfer pricing strategy of locating manufacturing in a low tax environment can be clearly illustrated in light of this report. The choice of research location is strongly influenced by the quality of the science base, and most marketing realistically takes place in or near the end market. Hence manufacturing, and risks and rewards that can be integrated with this function represent a pharmaceutical company's main opportunity to book revenue in a tax-efficient manner through an effective transfer pricing policy.

6.2.3. Labour flexibility

Labour market policies and the incentives for workforce development also play a role in location decisions.²⁰ Europe may not be as appealing as the United States, for example, because of the organisation of labour and company law, which inhibits the ability of firms to ‘hire and fire’ staff or rapidly cut sub-performing assets.²¹

Interviewees stressed the importance of labour flexibility in the context of their decisions about locating manufacturing capacity, and suggested it was of more importance than headline labour costs. In practice, the impact of labour law on the company’s ability to deploy its workforce flexibly, to reconfigure or to exit a particular location will be of substantial importance. The financial impact of these regulations has the potential to be extremely significant, and was widely described as being a more important driver of decisions than factors such as the general level of wages. Particular concerns about these costs in relation to several continental European countries were expressed, although the UK was perceived as offering a more flexible environment in this regard.

It should be noted, as described in section 3.2, that the impact of labour flexibility may not be symmetric, and whereas inflexibility may be a significant barrier to new investment, it may also act as a barrier to disinvestment from a particular location.

6.2.4. Labour costs

Where cost is driving decisions to move to a particular location, it is natural to consider the role of labour costs as one variable which distinguishes location. Respondents suggested that this was a factor of some importance, although usually of less importance than taxation or labour flexibility. One reason that it is constrained is that for technical manufacturing processes the cost of the plant is an important consideration and regardless of the physical location of the manufacturing plant that equipment is likely to need to be purchased from the same source at the same cost.

6.2.5. Differences between products and stages

Differences between the technological requirements necessary for different products and for different stages of manufacturing make it difficult to draw extremely general conclusions about the drivers behind the selection of “manufacturing location”. On the one hand, respondents were generally clear that tax considerations would be likely to preclude EU locations other than Ireland as candidates for the construction of a new greenfield facility undertaking basic chemical manufacturing. On the other hand, consolidation within the industry makes such new investments of limited relevance for many firms in any case. The level of technology available within EU countries would make them realistic candidates for new or sustained investment in more advanced manufacturing processes.

One strategy regarded as useful was to make a major investment in a flexible manufacturing facility close to development facilities. This could then be used to launch a sequence of

²⁰ Porter p.65. *Location, Competition and Economic Development: Local Clusters in a Global Economy*, reprinted in Cantwell (ed) *Globalization and the Location of Firms*.

²¹ Gambardella, Alfonso, et al (2000) “Global Competitiveness in Pharmaceuticals: A European Perspective: Report Prepared for the Directorate General Enterprise of the European Commission”. pp73-74.

products in turn, ensuring that the process and scale-up is fully developed in a site with access to expertise and development staff, prior to migrating ongoing production to a lower cost location.

6.3. Implications for the UK and the EU

Given the range of tax-efficient and otherwise low cost locations, and widening spread of countries that are developing IP protection and enhancing manufacturing quality, the UK and EU's position as a major player in pharmaceutical manufacturing appears mainly as a result of historical factors. However, as we have discussed, these historical factors can be exploited. Particularly for more complex manufacturing processes (eg biological manufacturing), products based around innovative delivery mechanisms or scale-up from development to full commercial manufacturing the quality available in Europe may form the basis for an attractive environment. Moves to reduce taxation would be of further benefit in terms of attracting such investment, but would need to be significant to allow most Western European companies to be competitive in terms of post-tax costs alone.

7. Regional Offices

- § The primary drivers of locating a regional office are to locate somewhere that is attractive to internationally mobile talent (eg benefits from good international schools) and possesses good transport links, both across the region to be served and to an organisation's global headquarters.
- § More limited advantages were seen in locating close to key regulators, and locating in a country where other functions are already located to help to create critical mass.
- § Depending on a company's overall tax strategy, the choice of a regional HQ might have tax implications.

7.1. Description of Activities

The activities undertaken in regional offices vary between companies. In practice the extent to which regional offices are a meaningful layer of management, as opposed to a route to head office rather varies. Functions could include local marketing, strategy, management of distribution and regulatory affairs, but it is also possible for some of those functions to be undertaken either globally or from separate regional locations. Most respondents suggested that relative to the company as a whole, the size of a regional office is likely to be small.

7.2. Drivers of Investment Location

7.2.1. Location attractive to international talent

One of the two over-riding drivers of regional office location was to be in a location that is suitable for the recruitment of internationally mobile executive talent. Characteristics that make such a location attractive include:

- § An infrastructure that supports the needs of an ex-pat community, particularly the existence of high quality international (and often English-language) schooling;
- § A pleasant environment that is attractive to live in;
- § Possibly, low rates of personal taxation;
- § Particularly from the perspective of American companies, the common language makes England an attractive location for a regional office.

7.2.2. Transport links

The other over-riding driver of regional office location was to be in a location which was well connected through the region (either in a hub that is central to the region, or at least a location with good transport links throughout the region). In practice, in a region such as Europe several locations are likely to meet this criterion.

Some respondents also brought up the need for a regional office to have good intercontinental transport links to their global head office. Obviously, whether this presents a serious extra

constraint depends somewhat on where precisely the global headquarters is located but in some cases it has the potential to narrow substantially the range of choices available.

7.2.3. Proximity to regulators

Respondents saw some advantages in locating regional offices so that they were close to regulators, although this was not cited as a major driver of location decisions. In particular, several respondents pointed out that if one sees a need for a regulatory affairs department to be located in proximity to a regulator, it is not necessary for it to be located within the regional office.

7.2.4. Strategic positioning

Some respondents noted that there was more discretion and flexibility in where to site a regional office than is present for research (driven largely by science quality) and manufacturing (driven largely by tax considerations, subject to appropriate quality). Hence, if a firm is seeking to expand its presence in a particular market from a strategic point of view, the regional office is one logical candidate for placement there.

7.2.5. Critical mass

Respondents suggested that placing the regional office in a country in which the company already undertakes business functions was a sensible step. In particular, this would allow overheads and management structures to be shared. Generating critical mass in this way might also allow the company to make best use of any political leverage offered by its investments.

7.2.6. Taxation

The issue of taxation arose, and the question of whether a regional holding company may accrue profit, necessitating consideration of the tax position of the local environment. In part, this depends on the transfer pricing strategy adopted by the company. It was also suggested that in practice the location of the global holding company would be of more relevance from this perspective. As a result, although this should not be ignored as a potentially important factor in particular situations, it seems unlikely to be an important driver across the industry.

7.3. Implications for the UK and the EU

The apparently most important drivers for the location of regional offices, such as transport infrastructure and an environment attractive to internationally mobile talent may be difficult for governments to influence in the short term, although there could be potential for countries to, in effect, market themselves, as strategic choices based on these factors.

8. Conclusions and Policy Implications

This section develops conclusions and the potential implications for policy which flow from our research. It would be inappropriate to describe these as being policy recommendations. For example, to make unqualified recommendations as to whether a policy change designed to attract certain forms of investment was worthwhile, one would also need to consider the value of the benefits of attracting that investment. Those considerations are beyond the scope of this report.

There is no single factor that determines the attractiveness of a region as a location for all elements of the pharmaceutical value chain, but there are general things which a government can do in order to create an attractive climate for investment. The most important revolve around the creation of a general business environment which offers stability, low bureaucracy, a long term commitment to low taxation, and generally the provision of business-friendly environment. There is evidence that countries such as Ireland and Singapore have succeeded through such an approach. In part this may reflect economic development being viewed as a national strategic priority to which a co-ordinated approach is taken. Some countries, including the UK, at times take a less co-ordinated region-driven approach to this area, which our interviews suggested is less likely to deliver attractive results.

A more pharmaceutical-specific element of the general attractiveness of a country from an investment point of view relates to the attractiveness of the market for pharmaceutical products in that country. The theoretical economic rationale for believing that such factors influence investment decisions (except to the extent that investment is implicitly or explicitly tied to prices or market access) is weak, given that the industry in effect seeks to recoup its global research, development and manufacturing expenses through the sales of a product in a global market.

Interviewees had mixed attitudes to this question, but did not generally provide *economically* robust arguments to challenge this theoretical view. A limited exception to this point is the case of clinical trials, where it was pointed out that the benefits of familiarising opinion-leading clinicians with new medicines will not be high if cost-cutting bodies are to prevent clinicians prescribing them anyway. A more general exception – although one not readily susceptible to economic testing – is that where the industry has a number of realistic choices for investment, perceptions of the product market in a country could become *psychologically* important in making those decisions.

Table 8.1, overleaf, summarises the factors that matter most from the point of view of particular industrial functions. This needs to be considered in combination with the factors underlying the attractiveness of the investment climate in a particular country. It also needs to be acknowledged that such tables can provide only a broad indication of the scope of investment decisions – in any individual case questions such as how an investment fits **incrementally** with a company's existing asset base will be important.

Table 8.1
Function-Specific Investment Drivers

	R&D	Clinical Trials	Manufacturing
Quality	Paramount. Affected by: - co-location or attractability of leading scientists - a strong general science base - public funding of basic research and scope for crossovers from academia	Site must have culture of good clinical practice and achieve credible data (but there are many). Trials will always include key markets due to benefit of accessing key opinion leaders. <i>Possible</i> regulatory benefit of local data.	Sufficient quality to deliver the task at issue is a must-have. What this means in practice is highly product-specific. For many products, required quality is available in a wide (and probably increasing) choice of locations.
Cost	Limited importance. Incentives such as R&D tax credits could affect choice at margin, but often limited by size, claim process and uncertainty of duration	Cost an important criterion in adding to key market trials to create a global bank of data. Speed of patient recruitment a key factor in overall commercial decision.	Key criterion, once required quality achieved. Heavily influenced by tax, particularly for key steps in light of overall tax and transfer pricing strategy. Labour flexibility more important than wage cost alone.

Source: NERA

In terms of a strategy for the UK or EU to maintain or enhance its position as a destination for investment by the research-based pharmaceutical industry, a number of points require consideration:

- § Investment decisions are made with long run time horizons in mind, and in the light of the opportunities offered by maintenance and incremental addition to the existing stock of assets. This may mask the effect of declining underlying competitiveness of an economy. It also creates a risk that an underlying trend may gain significant momentum before it becomes apparent in outcome measures. Competitive strength – once lost – may be difficult to regain.
- § A strong science base – if maintained and renewed – provides an opportunity to maintain a strong R&D base, particularly combined with the pharmaceutical tradition and historical asset base located in the UK and other parts of the EU. Increased publicly financed investment in basic biomedical science, combined with appropriate incentives for cross-fertilisation between academic and commercial sectors could strengthen this further.
- § For the simpler elements of pharmaceutical manufacturing, where cost is at a premium, the EU is looking increasingly unattractive in terms of post-tax returns, and many would not consider it as a site for new greenfield investment in this area. However, there is scope for a strategy that leverages the existing asset base in this area, and the country's strong scientific and manufacturing skills, to preserve and expand a manufacturing base at the more complex end of the spectrum. This could cover factors such as biological manufacturing, products requiring innovative delivery mechanisms, and launch manufacturing sites designed to facilitate scale-up and technology transfer from the development process.

To a greater or lesser extent, many European countries share the opportunity of a historically strong domestic industry and science base, and the challenge that the position of this industry is increasingly being eroded by competition from outside the EU. This policy challenge should be seen in light of the fact that competition within the industry increasingly takes place on a global basis and a trend towards a more globally diversified pattern of assets is increasingly visible. A number of our interviewees stressed the point that competition now takes place on a global basis, and suggested that regulation designed to level the competitive playing field within the EU, risk further strengthening the hand of those who compete with rather than within Europe.

Appendix A. Correlations Obtained from PICTF Data

This section presents selected graphs from the correlation analysis discussed in Section 2.2. Readers are referred to that section for a discussion of the various caveats which must be applied to any analysis of this nature, particularly when it is undertaken in simplified form. These figures should primarily be regarded as being indicative of the methodology and type of results achieved rather than drawing firm conclusions. We note that in several cases the effect of the USA as an outlier, with high levels of pharmaceutical industry activity, may have a substantial (and sometimes counterintuitive) effect on the results. One approach to this would be to exclude the USA from the analysis, but this would not address the underlying problems, which would still be present in the data for several other countries.

Bearing these caveats in mind we note that:

- § Figure A.1 suggests that pharmaceutical production is positively related to high taxation (counter-intuitive) while Figure A.2 suggests a positive relationship between production and labour market flexibility (as expected). The US influences the results as a high producer with high tax rates and a flexible labour market.
- § Figure A.3 suggests a counterintuitive negative relationship between pharmaceutical R&D and scientific papers or citations per head (as a measure of research quality). Figure A.4, on the other hand, suggests a positive relationship between pharmaceutical R&D and the prevalence of graduate scientists in the labour force. However, in both occasions, the correlation obtained is very poor – the data primarily appear to be random or explained by other factors.

Figure A.1
Pharmaceutical Production vs. Corporate Tax Rate 2003

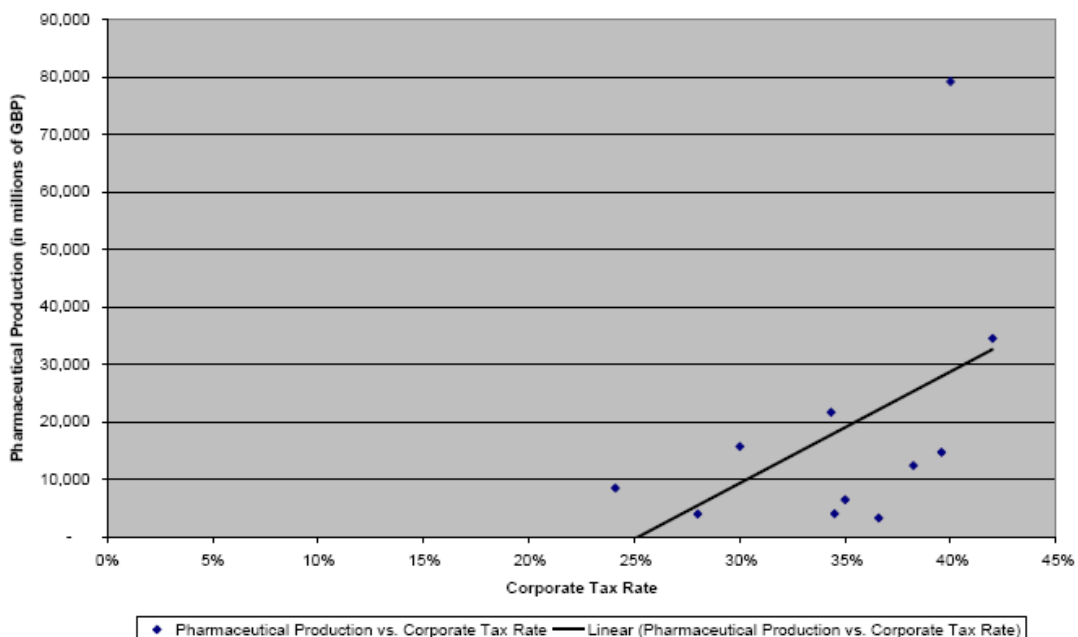


Figure A.2
Pharmaceutical Production vs. Business Executive Perceptions of Labour Market Regulation 2003

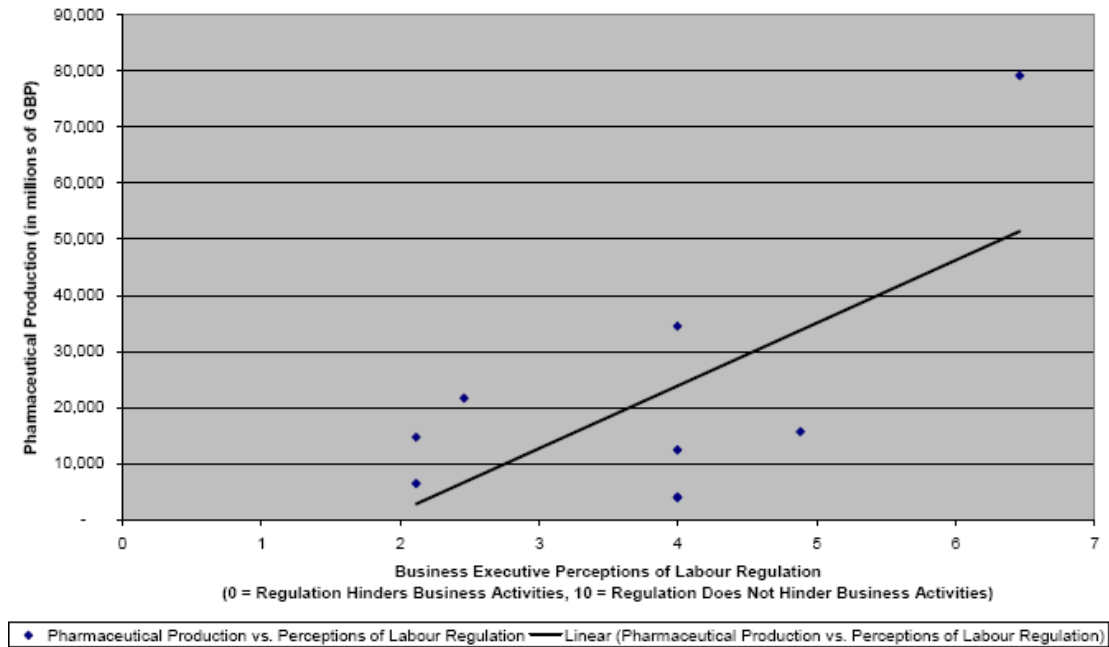


Figure A.3
Per cent of World Pharmaceutical R&D vs. Papers / Citations Per Head 1994 - 2003

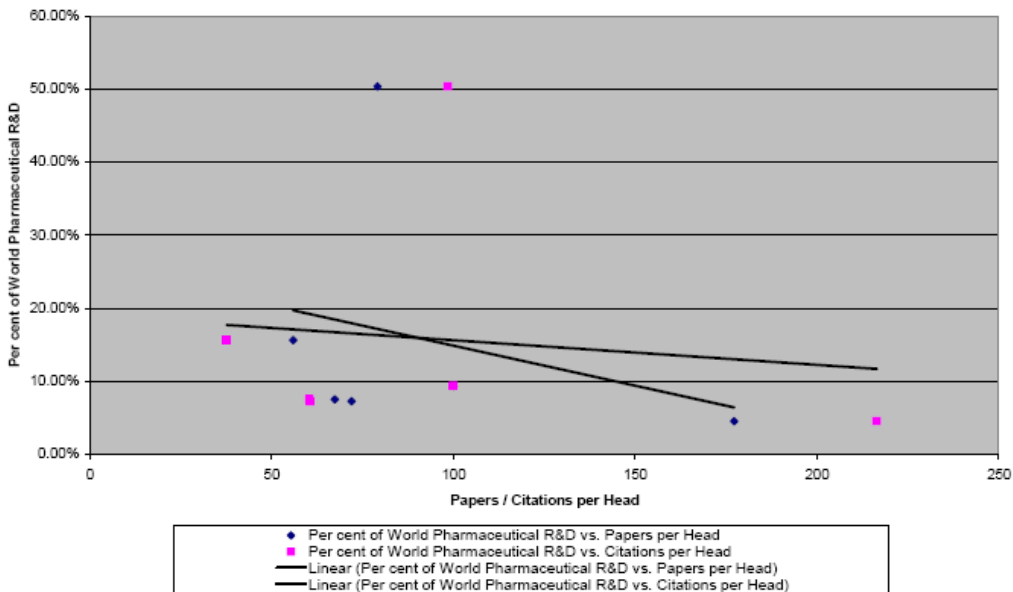
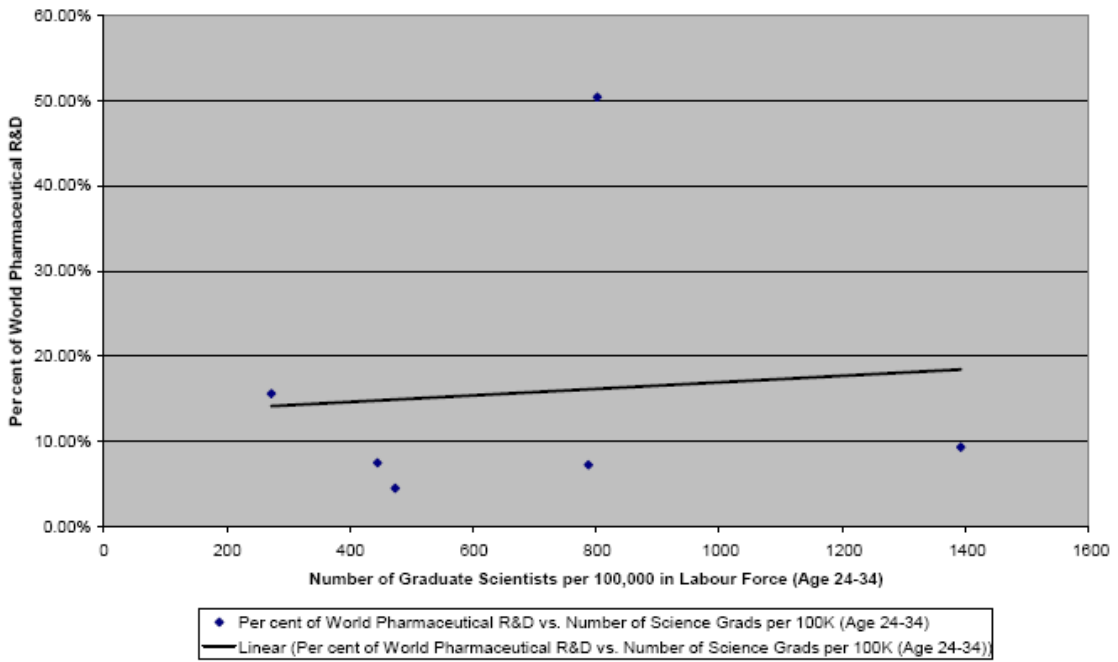


Figure A.4
Per cent of World Pharma R&D vs. No. of Grad Sci per 100K in Labour Force
(Age 24-34) 2003



Appendix B. Potential Data Requirements for an Econometric Assessment of the Drivers of Investment

If numerous conceptual and practical difficulties were resolved, an econometric exercise could seek to regress ‘the change of investment’ on a wide range of explanatory factors. The following are examples of the range of factors which could potentially be relevant to such an exercise:

- § A measure of innovation, such as the number of patents or publications
 - If the measure of innovation is related to the number of patents, then it may be necessary to adjust it to compensate for the propensity to patent, using for example a revealed technological advantage index relating patents in a technological subdomain as a share of the global total to a country’s overall share of world patents.
- § Number of research centres and universities
- § A measure of agglomeration, or clustering
 - Number of similar firms in location
 - Proximity to biomedical inputs
- § Population – as a measure for size of country
- § Scale economies
 - Labour cost index
 - General cost differences
 - Rising cost measure – to account for future cost burden
- § Pharmaceutical imports and exports
- § Measures of economic stability and growth
 - Economic growth rate
 - GNI per capita
 - Exchange rate (stability)
- § Per capita expenditure on healthcare
- § A measure of skilled labour
 - Number of tertiary level students enrolled in technical subjects
 - Number of scientists affiliated with nearby universities, research centres or firms

- Scientists per capita
- § Financial sources for start-ups/new ventures and R&D innovation
 - Percent of firms receiving funding from each of the various sources
 - Total amount of government subsidies/grants in past year(s)
- § Number of field trials performed in the locale
- § History of labour discord
 - Number of or change in frequency and days lost due to strikes over previous years
- § Ease of academic (institution and star scientist)-company collaboration in locale
 - Dummy variable or numerical measure of frequency of collaborations or technology transfers over past years or for ease of co-operation
- § Firm history with FDI
 - Existing subsidiaries/affiliates abroad
 - ú Return on past investment
 - ú Labour at home versus abroad
- § A measure of FDI confidence
- § Firm size and success
 - Number of employees
 - Previous years' profit / growth / other factors
- § Distance to centralised or regulatory authority
- § IP laws
 - Number of patent infringements and ratio outcome of infringement
 - Recognised index that scores the strength of statutory IP protection (eg Ginarte-Park IP index)
- § Is this firm a new entrant in this location or geographic market? (dummy variable)
- § Tax incentive measurement
 - Credit vs. deduction (dummy variable)
 - ú E.g., Some firms may value immediate tax relief differently than a credit to be given in the next period

- Percent deduction for R&D expenses
- Additional income tax deductions
- Tariff deductions
- Corporate tax rate

§ Government intervention in pharmaceutical price

- Dummy variables to compare severity of price-fixing across countries
- Number of price control mechanisms used by the government
- Other measure of drug price difference using some average reference price

§ Ease of drug authorisation (eg duration of approval process)

Firm specific dummy variable

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