

Chapter 33

BRINGING A DRUG TO MARKET IN THE EUROPEAN UNION: REGULATORY, CORPORATE, AND TAXATION ISSUES

For businesses in any industry, the European Union (EU) is a market force to be reckoned with. Currently made up of 27 member states, the EU is the world's largest economy by gross domestic product, and it is the third largest by population. Its reach and market strength are soon to be increased by the addition of three new member states: Croatia, Macedonia, and Turkey.

Although each member state of the EU retains some sovereignty over affairs conducted within its own borders, a considerable body of law is now promulgated by the European Commission (EC) and implemented into national legislation in each member state. This harmonization of laws across the member states is designed to bolster the principle of free movement of goods, which, in brief, means that once goods have passed the borders of one member state having met its entry requirements, they are free to be circulated and imported to all other member states and sold throughout the EU.

However, in light of the health benefits and associated risks that accompany medicinal products, the movement of medicinal products in the EU is much more complicated. Medicinal products are highly regulated in the EU and are subject to a separate, complicated system of approvals that governs how, when, where, and in what form such products will be allowed to be sold. Additionally, a number of important strategic commercial and corporate considerations accompany this complex regulatory environment.

The EU is also home to a multitude of world-class research facilities, and with a large, diverse population and EU-wide clinical trial rules, it represents an excellent choice for the conduct of clinical trials.

The EU, therefore, presents interesting opportunities for life science companies, both before and after the grant of marketing authorizations. Consequently, in order for businesses in the pharmaceutical and devices sector to optimize their presence in the EU market, and to make the most of the extensive resources the EU has to offer, it is important to have an understanding of both the regulatory setting and the associated commercial issues.

Accordingly, this chapter offers insight into the EU's regulatory regime for companies wishing to conduct clinical trials or obtain authorizations for medicinal products and medical devices

in the EU. This chapter also discusses tax, commercial, and corporate considerations that will assist pharmaceutical companies plan appropriate and optimal strategies for entry into or expansion within the EU.

An Introduction to the Regulatory Framework

An Overview of the Regulatory System

The regulation of medicinal products is governed in the EU by Directive 2001/83/EC relating to medicinal products (the Directive). Also known as the Consolidated Directive, it brings many years of separate legislation together into one detailed document. It was last updated in 2005, when a number of far-reaching, fundamental, and sometimes controversial changes were made. Although it contains many complexities, the fundamental premise of the Directive is simple: No medicinal product may be placed on the market in the EU unless the relevant competent authority grants a marketing authorization.

It is also worth noting that the legislation has been adopted by the members of the European Economic Area (EEA): Norway, Iceland, and Liechtenstein. The Swiss system also mirrors EU regulation.

In addition to the requirements that must be met to obtain a marketing authorization, the Directive includes rules relating to specific categories of medicines (e.g., homeopathic and herbal medicines), manufacture, importation and distribution, labeling and advertising, the classification of medicinal products, and pharmacovigilance.

The Directive, which has been implemented into the national laws of each EU member state, is accompanied by a number of other EU directives and regulations that address specific areas of medicinal legislation, such as the Clinical Trials Directive discussed in the next section.

Preauthorization Considerations

Establishment

Both general medicines legislation in the EU and the Clinical Trials Directive (see section later in this chapter titled “Overview of the Clinical Trials Directive”) require the holder of an authorization for a medicinal product or a clinical trial in the EU to either be established itself in the EU or to have a legal representative who can act on its behalf.

In addition, for various activities that are conducted in the EU pertaining to medicines, such as manufacturing, wholesale dealing, and pharmacovigilance, EU medicines law also requires pharmaceutical companies to have a “qualified person” at their disposal to oversee certain functions. Qualified persons must meet certain specific criteria in order to be classified in this way. It is generally accepted that such qualified persons need not be employed directly and may be engaged on a contract or consultancy basis, although depending on the circumstances, direct employment may present the most attractive option. Such considerations will also have an important impact on the choices such as country and corporate vehicle.

Consequently, structuring operations in the EU, including consideration of the preferred corporate structure in the most appropriate EU country, is one of the most important decisions a pharmaceutical company can make.

There are a number of choices available for business operations. The principal corporate options are:

- A company (including a subsidiary of an overseas company)
- A branch
- A place of business

This chapter assumes that business operations will be established in the UK.

Companies (Including Subsidiaries of Overseas Companies). One option for businesses wishing to establish in the UK is to form a UK company limited by shares. The usual choice for overseas companies is a private company subsidiary of the overseas company. It is possible to establish both private and public companies in the UK—the main difference between the two is that a private company cannot offer its shares to the public. In general, public companies are also more regulated than private companies, and there are additional requirements to be met when setting up a public company.

A company incorporated in the UK has a separate legal identity, distinct from its members (whether a parent company or individuals). As such, its members usually have no legal liability for the company's acts and obligations, except for unpaid share capital and any guarantees given in the case of companies limited by shares.

Branch or Place of Business. A “branch” is part of an overseas limited company organized to conduct business through local representatives in the UK rather than referring it abroad. Companies House, the official UK government register of UK companies (<http://www.companieshouse.gov.uk>), gives guidance on what level of activity is required to necessitate registration as a branch. Broadly speaking, if a person is able to deal directly with the UK office instead of the company in its home jurisdiction then the UK office is more than likely to be a branch.

A “place of business” is for companies who cannot register as a branch because their activities in the UK are not sufficient to constitute a branch. Such activities might include internal computer processing, warehousing, or simply a representative office. A characteristic of a place of business is that its activities tend to be incidental operations.

Clinical Trials

In order to obtain a marketing authorization to place a medicinal product on the market in the EU, it is necessary to have data demonstrating the quality, safety, and efficacy of the product in question. The results of clinical trials comprise a large part of this data, and, as such, clinical trials represent one of the largest hurdles that companies developing potential new drugs face.

Pharmaceutical companies attempting to organize a clinical trial face numerous issues. For example, depending on the disease in question, obtaining a sufficient enrollment number for clinical trials can often be a slow and difficult process, and it can be difficult to obtain the breadth and diversity necessary to ensure results are well balanced. Ethical considerations, such as choice of patient, add additional complications.

As mentioned previously, clinical trials in the EU are now governed by harmonized rules that apply to all EU member states. This enables companies conducting clinical trials to run them in a variety of countries simultaneously without the need to come to terms with a different set of rules and regulations for each country. It also means that companies have access to a larger number and a greater diversity of patients (e.g., with regard to ethnicity, lifestyle, diet).

Overview of the Clinical Trials Directive. Clinical trials are regulated in the EU by European Directive 2001/20/EC, also known as the Clinical Trials Directive (the CTD). The CTD has been implemented into national legislation in each EU member state—in the UK by The Medicines for Human Use (Clinical Trials) Regulations 2004.

The CTD applies to the vast majority of trials conducted in the EU (noninterventional trials meeting certain criteria are excluded). Under the CTD, a trial may only be started in a member state of the EU if it has been authorized by the relevant competent authority in that member state (in the UK, this is the MHRA) and has been given a favorable opinion by an ethics committee. In addition, each trial must have an identified sponsor who is responsible for trial initiation (including obtaining authorization), management, conduct, and pharmacovigilance.

To provide public health protection, the CTD sets out the requirements for obtaining informed consent from participants and, in particular, sets out the process that must be followed in relation to specific vulnerable groups. In addition, both the European Medicines Agency (EMA) and the national regulatory authorities conduct mandatory good clinical practice (GCP) inspections, and the findings from these inspections, together with details of each authorized trial, are made available on a European database for clinical studies for all other member states' regulatory authorities to see.

Failure to comply with certain aspects of the CTD may constitute a criminal offense and carry a prison sentence of up to two years, in addition to a fine.

The CTD is complemented by Directive 2005/28/EC on GCP. The GCP Directive sets forth the detailed rules and procedures that assist and guide companies involved in clinical trials.

Obtaining a Marketing Authorization

General Requirements

In order to obtain a marketing authorization, applicants must submit a full dossier to the relevant competent authority that details, among other things, the product's common or scientific name, invented name, qualitative and quantitative particulars, proposed therapeutic indications, contraindications, and adverse reactions, as well as the results of pharmaceutical and preclinical tests and clinical trials.

Marketing authorizations are valid for an initial period of five years, after which they may be renewed for a further five-year period provided they satisfy a reevaluation of the risk-benefit balance. Changes to the medicines legislation also introduced a new provision dubbed the “sunset clause,” which provides that a marketing authorization will no longer be valid if a product has not actually been placed on the market in the first three years following grant of its authorization, or if it is not on the market for a consecutive period of three years.

Once a marketing authorization has been granted, the holder is under an obligation to continually update the authorization to ensure that scientific progress and new regulatory requirements are respected, and in particular, any information that may influence the evaluation of the benefits and risks of the product. Accordingly, marketing authorization holders have a continuing duty to have in place stringent pharmacovigilance procedures and to keep abreast of developments and advances within the medicines arena.

Which Authorization?

One of the most important decisions a pharmaceutical company has to make when bringing a drug to market in the EU is which marketing authorization to apply for. Previously, there were only two possible routes to authorization, but since changes to the legislation in 2005, applicants now have three possible choices: the centralized procedure, national marketing authorizations, or the mutual recognition procedure and decentralized procedure.

Prior to the introduction of a uniform, EU-wide system, each member state had responsibility for granting and regulating medicinal products within its borders. Updates and amendments to EU legislation governing medicinal products over the years have resulted in the harmonization of the approvals system to help facilitate the free circulation of authorized medicinal products throughout the EU. However, as is illustrated by the following, in many ways the approvals system remains somewhat disjointed.

Depending on a product’s eligibility, each of the authorization routes offers various advantages and disadvantages.

The Centralized Procedure. The centralized procedure is compulsory for products developed by means of certain biotechnological processes, orphan drugs, and new active substances for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, and, beginning May 1, 2008, autoimmune diseases and other immune dysfunctions and viral diseases. In addition, the centralized procedure is open to medicinal products containing a new active substance never before authorized in the EU; medicinal products that can be proven to have a significant therapeutic, scientific, or technical innovation; and medicinal products in which the authorization would be in the interests of human or animal health.

Products authorized pursuant to the centralized procedure are granted marketing authorizations that cover all EU member states and the EEA. A further distinguishing feature of this route includes the requirement for the marketing holder to also secure a single EU-wide trademark for the

product. However, the convenience of the centralized procedure is also accompanied by fees that are significantly higher than the national procedure's.

National Marketing Authorizations. With the exception of products granted a marketing authorization under the centralized procedure as set out in the previous section, all products are granted marketing authorizations on a country-by-country basis by the competent authorities in each member state. Such marketing authorizations permit the holder to market the product in question in the member state concerned, subject to any restrictions or requirements that accompany the authorization.

The Mutual Recognition Procedure and Decentralized Procedure. Medicines legislation also foresees the possibility that most pharmaceutical companies will wish to market their products in more than one EU country and provides two mechanisms to applicants that avoid the need to submit full marketing authorization applications in each country.

The first of these, the mutual recognition procedure, enables pharmaceutical companies who already hold a marketing authorization in one EU member state to ask additional member states to recognize the marketing authorization that has already been granted. The procedure involves the preparation of an assessment report by the original member state that is forwarded to the additional member states for their consideration. Assuming the other member states agree with the report, a marketing authorization will then be issued for the product in the member states concerned. However, the mutual recognition procedure often sees disagreements between member states that can hold up the procedure and lead to delays. For such occasions, there is a detailed disputes procedure that must be followed.

The decentralized procedure, which was introduced during the changes to the legislation in 2005, aims to avoid some of the potential disputes between member states and the resulting delays to authorization by engaging each of the member states the applicant wishes to apply to at the time the first marketing authorization is made. Consequently, this procedure is only open to products that have not yet been granted a marketing authorization in the EU. Under the decentralized procedure, the applicant chooses one member state to be its reference member state. The chosen reference member state then prepares a draft assessment report that is submitted to the other member states for their consideration and approval. For disputes, the decentralized procedure follows a course of action that is similar to that of the mutual recognition disputes procedures.

Data and Market Exclusivity

Once a product has been granted a marketing authorization in the EU, the holder's thoughts will unsurprisingly turn to maximizing market share for the product and ensuring it is adequately protected. EU medicines legislation has created a protection mechanism for original products that is entirely separate from patent protection and allows innovative products a set period during which they enjoy exclusivity on the market.

Data exclusivity refers to the period in which generic product applicants cannot rely on the dossier of the original product (the reference product) for the purposes of obtaining a marketing

authorization. Prior to changes to the legislation in 2005, this protection period was set at either 6 or 10 years, depending on the country in question.

However, one of the changes made in 2005 was to introduce a new, uniform 8 + 2 + 1 protection period throughout the EU. It is important to note that this new protection period only applies to products granted after the changes came into force. Under the new system, the data protection period is now set at eight years, meaning that the marketing authorization holders of reference products enjoy a protected period of eight years before applicants may submit applications for generic products that rely on the original data in the reference product's dossier.

Following this initial eight years, even though generic applicants can begin preparing generic versions of an existing product by submitting their abbreviated applications, they must wait a further two years before being able to actually start selling generic versions of a reference product.

This 10-year data and market protection period can be further extended by one year, if, during the first eight years, the reference product authorization holder seeks and obtains authorization for one or more new therapeutic indications that represent a significant clinical benefit when compared with existing therapies.

Consequently, authorization holders of reference products enjoy, under the recently updated system, a protection period of at least 10 years.

Patent Protection

It is important to note that data and market exclusivity are entirely separate from patent protection; although, in order to accommodate the two-year market protection period, patent legislation has been amended to make it clear that submitting a generic application and conducting the necessary preparatory work to do so will not be deemed patent infringement.

As further incentive to innovator pharmaceutical manufacturers, the EU also allows such companies to apply for supplementary protection certificates (SPCs) in respect of new products. SPCs can only be applied for once a patent and marketing authorization have been granted in respect of a particular product, and they cover the time lapse between the date of patent application and the grant of a marketing authorization up to a maximum of five years (resulting in a monopoly of up to 15 years on marketed drugs). They cover a combination of what was claimed in the patent in relation to the marketed drug and what is covered by the marketing authorization.

Taxation Issues

In determining the optimal business structure, it is important to consider the taxation consequences that may arise. As discussed previously, an EU "establishment" may be required, or otherwise a "legal representative" in the EU. From a structural perspective, the choice is between the establishment of a subsidiary or a branch, or alternatively, the non-EU entity could enter into a contractual relationship with an EU entity or individual. Each of these alternatives will have different

tax consequences, as will the precise arrangements between the EU entity/presence and the non-EU company.

The following sections discuss important tax issues that should be considered when establishing a presence in the EU.

Different Structures for the Establishment of an EU Presence

General

Both the CTD and the general medicines legislation in the EU require that the holder of an authorization for a medicinal product or a clinical trial in the EU either be established in the EU or have a legal representative in the EU that can act on behalf of the non-EU entity (the parent company). This requirement may be satisfied by the parent company entering into a contractual relationship with an unrelated third party to act as the legal representative or, alternatively, establishing its own branch or subsidiary.

It is generally preferable from a taxation perspective to establish a structure that avoids the imposition of tax in jurisdictions other than the home jurisdiction of the parent company. The advantage of only paying tax in the parent company's home jurisdiction is that there should be no risk of double taxation, which may arise, for example, if tax paid in a jurisdiction outside the home jurisdiction is not fully creditable in the home jurisdiction (because, for example, the parent company has tax losses, so it pays no home jurisdiction tax, or because the tax rate in the foreign jurisdiction is higher than the rate in the home jurisdiction, so an excess foreign tax credit results).

Assuming that the parent company is situated in a country that has a double tax treaty with the relevant EU jurisdiction, the parent company should only be subject to tax in that EU jurisdiction to the extent that it carries on business in that jurisdiction through a "permanent establishment." Most double tax treaties are based on the OECD Model Convention, including the U.S./UK double tax treaty (the Treaty), so broadly the analysis should be similar for each jurisdiction. For the purposes of the discussion in this tax section, it is assumed that the parent company is a U.S. corporation that is entitled to benefit under the Treaty, and that the EU jurisdiction for the establishment is the UK.

The Treaty defines a "permanent establishment" as a fixed place of business, which includes a branch, an office, or a place of management, but does not include an agency, unless the agent has, and habitually exercises, a general authority to negotiate and conclude contracts on behalf of the principal. Notwithstanding this general rule, an agency will not give rise to a permanent establishment if the principal operates through a broker or an independent agent, where that person is acting in the ordinary course of his or her business.

Contractual Relationship

If the parent company was simply to enter into a contractual arrangement with an unrelated third party to act as its representative in the UK, then provided that the representative had no power to enter into binding contracts on behalf of the parent company, no permanent establishment should

exist and the parent company should not be subject to corporate tax in the UK. The parent company would be required to purchase services from third-party providers—for example, the clinical trials could be carried out by a contract research organization (CRO), and marketing and product support could also be purchased. The parent company would sell any products developed directly to customers.

While a contractual relationship may produce a desired tax result, there may be a number of commercial reasons why such an arrangement may be unattractive. In particular, it may be difficult to find someone willing to act as a representative for clinical trials, given the liabilities that may arise. In addition, the parent company may be concerned about leaking information into the market place, especially if no patent is obtained—as a consequence, the parent company may prefer its own employees to perform the work, rather than a third party, as this may permit it to obtain stricter employee noncompete and confidentiality agreements. Further, the parent company may wish to establish a UK presence under its own name to provide greater credibility in the UK, to demonstrate a commitment to the UK market, to provide greater name recognition, and so forth.

Establishment of a Branch

If the parent company did require an actual presence in the UK, then it would have to choose between the establishment of a branch or a subsidiary. It is assumed that, given the role to be played by the UK entity, a place of business would not be appropriate.

The simplest and cheapest form of presence would be for the parent company to establish a branch in the UK. The first issue is to determine whether the activities of the branch create a permanent establishment of the parent company in the UK. No permanent establishment will be created if the activities of the branch are limited to collecting information. In addition, no permanent establishment would be created if the activities in the UK could be characterized as “preliminary or auxiliary” to carrying on business. Under the old Treaty (which was superseded a few years ago), this exemption specifically included scientific research activities. The view of the UK tax authorities was that research activities in which no product had been developed would fall within this exemption, but that once a product had been developed, any future research was enhancement of an existing product and was therefore not “preparatory” in nature, as there was a product that could be exploited. The scientific research exemption was deleted in the current Treaty, and thus it may be difficult to argue that it applies. In any event, by the time a parent company conducts clinical trials in the UK, it is likely that the product would have been developed to a stage where the “preparatory and auxiliary” exemption is unlikely to be available.

Assuming that a permanent establishment is created, what are the consequences for the parent company? The main consequence is that the parent company would be subject to UK tax on the profits attributable to the activities of the permanent establishment. Initially, while clinical trials are being conducted, it is likely that there will be losses generated, and thus UK tax should not be an issue. In addition, the parent company should be able to use the losses to reduce its taxable income in its home jurisdiction (assuming of course that there are sufficient taxable profits available), although

as will be discussed later, a U.S. parent company should be able to achieve the same result by establishing a UK subsidiary and filing a check-the-box election, electing to disregard the UK subsidiary for U.S. tax purposes.

However, when a marketing authorization is obtained, and products are sold in the EU, the UK permanent establishment is likely to become profitable. The principal issue at this time will be to calculate the profits that are subject to UK tax—namely, the profits generated by the activities of the UK permanent establishment. In theory, the profits of the permanent establishment are calculated as if the UK branch was a separate and distinct enterprise—this sounds like a simple concept, but the level of profit is often difficult to determine, particularly given the fact that there are no formal arrangements in place between the UK branch and the parent company. (Such arrangements are not possible, as the parent company and the UK branch are legally the same entity, and an entity cannot contract with itself.) This may lead to long and expensive negotiations with the UK tax authorities before an acceptable level of profit is agreed.

The advantages of establishing a branch include the fact that it is fairly simple and inexpensive to establish, with low ongoing costs. It may be possible to operate free from UK tax for a period of time, and the parent company should be able to utilize initial losses to reduce its taxable income in its home jurisdiction. Disadvantages include exposure of the parent company to unlimited liability in the event of a claim against the branch (although the parent company could establish a special purpose subsidiary to shield it from such claims), potentially long and expensive negotiations with the local tax authorities to determine the level of profit that is subject to local tax (which may not necessarily result in a favorable determination), and the need to disclose the accounts of the parent company in the UK.

Establishment of a Subsidiary

As an alternative to the establishment of a branch, the parent company may decide to establish a UK subsidiary. As a UK resident company, the subsidiary would be subject to UK tax on its worldwide income and capital gains. The standard UK corporate tax rate is 30%, while small companies that have income less than £300,000 are subject to tax at only 19%. A tapered rate applies to companies with income between £300,000 and £1,500,000. The subsidiary may pay dividends free from withholding tax to the parent company, and providing that certain criteria are satisfied, the subsidiary may also pay interest on borrowings from the parent company without any withholding tax charge.

The establishment of a subsidiary has a number of benefits. It is a separate legal entity, and any claims including product and employee liability claims may only be made against it, and not against the parent company. In addition, there is greater certainty as to the level of profit that is subject to UK taxation, especially through the use of an inter-company services arrangement (see next section). From a practical perspective, it will be easier to acquire premises in the UK through a local company, and there is no requirement to disclose the accounts of the parent company. A further benefit arises if the exit strategy involves the sale of the UK business—shares in the subsidiary may

be sold free from UK tax, whereas the sale of branch assets in the UK will be subject to UK tax on disposal. The disadvantages of a subsidiary include increased establishment and ongoing costs. In addition, the parent company cannot use initial losses to reduce the taxable profits (absent a check-the-box election; see section later in this chapter titled “Check-the-Box Election”).

The amount of tax payable by the subsidiary will depend on the role it plays. Will the subsidiary merely provide services to the parent company, or will the subsidiary act as a principal in the development and ongoing conduct of business in the EU?

The taxation analysis can vary quite significantly depending on the role the subsidiary plays. The subsidiary could simply provide services to the parent company in return for an arm’s-length fee. In this capacity, the subsidiary would be providing services in the same way as a third party may be contracted by the parent company to provide services—for example, a CRO that conducts clinical trials for the parent company in return for a fee. Any rights that are developed from the activities carried on by the subsidiary would belong to the parent company, which would itself exploit the rights, enter into contracts with customers, and receive the revenue from the sales. In these circumstances, the subsidiary is unlikely to receive substantial income. Going forward, the subsidiary could be engaged by the parent company to provide support services and/or marketing services, for which it would receive an arm’s-length fee. Again, it is unlikely that the subsidiary would earn substantial profits.

Alternatively, the subsidiary could act as the principal in its own right. This would involve the subsidiary taking an entrepreneurial risk in exchange for a share of the future rewards. Thus the subsidiary would pay for the clinical trials, potential additional research and development activities, and future marketing activities. If a product were to be developed that was marketed and generated revenue, then the subsidiary would expect (and the UK tax authorities would require) that it would receive a share of the revenue earned from the exploitation of that product. The main issue would be to determine the reward (namely which rights) that the subsidiary should receive in exchange for taking the entrepreneurial risk on the clinical trials, research and development, and marketing activities. Clearly, if valuable rights are developed, the consequences of the ownership of some or all of these rights being given to the subsidiary would need to be carefully considered, especially as it should result in the subsidiary earning substantially more income than if it acts as a service provider.

It would be fairly typical for the subsidiary to incur expenditures on research and development or clinical trials in return for specified distribution rights—for example, the subsidiary could receive the UK distribution rights to any product that is developed from the activities it performs. Alternatively, consideration could be given to rewarding the subsidiary with a percentage of the net cash proceeds from sales in the UK of the product that is developed, which may be appropriate if the subsidiary is engaged in marketing activities on behalf of the parent company. If both the parent company and the subsidiary engage in the relevant activities, then the revenue generated could be divided between them, with the parent company and the subsidiary each receiving a portion of the net cash proceeds from sales of the product in the UK, based on their respective contributions.

Clearly, the appropriate reward for the entrepreneurial risk that is taken will depend heavily on the precise factual circumstances and will need to be considered on a case-by-case basis.

It should be noted that any expenditure incurred by the subsidiary on research and development, clinical trials, marketing, or any other activities should give rise to UK tax losses, which should be available to reduce future taxable income earned by the subsidiary.

Providing the subsidiary with a share of future benefits may help to overcome one of the major disadvantages of the traditional structure, where a UK entity is paid a fee for providing services, such as clinical trials. The problem arises because the tax authorities would expect a third party that is providing services to an unrelated party to earn a profit from the provision of those services—thus the subsidiary should earn a profit from providing services to the parent company. This profit would be subject to tax in the UK. However, if the parent company has no product to sell, it will not be earning any income. Consequently, the group (as a whole) may be paying tax at a time when it is earning no income and has no product to sell, and it may never develop and sell any product from which it can earn income.

In these circumstances, the inter-company pricing rules may be satisfied by an arrangement whereby the parent company funds the expenditure of the subsidiary, and the subsidiary receives some distribution rights (or a percentage of the revenue generated) for any product that is developed from its activities. Such an agreement should provide the subsidiary with an arm's-length reward for the entrepreneurial risk that it has taken and should therefore satisfy the inter-company payment rules.

Another point to note is the ownership of any rights that are developed. Generally, by the time clinical trials are undertaken, the initial research has been completed and the parent company should have a patent on the product. Accordingly, it is unlikely that any intellectual property (IP) will be developed that will be owned by the subsidiary, but any inter-company documentation should make this point clear. If IP is to be licensed to an EU entity, then the royalty paid by the EU entity must be an arm's-length royalty. In addition, consideration will need to be given to any local withholding tax on royalty payments.

Inter-Company Arrangements

Regardless of the precise role the subsidiary plays, the relationship and transactions between the parent company and the subsidiary will need to be carefully considered. First, it will be necessary to ensure that the subsidiary's activities do not create a permanent establishment of the parent company in the UK (thus potentially exposing the parent company to UK tax). Second, the UK tax authorities (and the IRS) will require that any dealings between the parent company and the subsidiary be conducted on an arm's-length basis, with a full arm's-length price paid for any goods or services that are supplied between the two companies.

It should be possible to manage these two issues through the use of an inter-company services agreement. An inter-company services agreement can be used to limit the power of the subsidiary,

particularly to ensure that the subsidiary cannot enter into binding contracts on behalf of the parent company, thereby reducing the risk that the subsidiary may be treated as a permanent establishment of the parent company.

In addition, the inter-company services agreement will also state the consideration to be paid for the inter-company services and goods. This agreement will provide written evidence to support the inter-company pricing methodology that has been chosen. Provided that the pricing methodology chosen is reasonable and supportable, it is unlikely that the UK tax authorities will challenge the inter-company pricing methodology.

The acceptable inter-company pricing methodology will depend upon the precise services to be provided. If the services are similar to those provided by a CRO or are support services that could easily be purchased from a third party provider, then it is likely that a cost-plus fee should be acceptable. By contrast, marketing services would usually require a fee calculated by reference to a percentage of sales.

Check-the-Box Election

As was discussed previously, losses generated by the activities of a branch are generally available to reduce the parent company's taxable income, whereas losses generated by a UK subsidiary are not. This general rule may be modified when the parent company is a U.S. corporation that files a check-the-box election with respect to the subsidiary. The effect of a check-the-box election is that the subsidiary is disregarded for U.S. tax purposes. The parent company is therefore treated as carrying on business in the UK through a branch, and any losses generated by the subsidiary should be available to reduce the parent company's taxable income for U.S. tax purposes. The check-the-box election has no effect for UK tax purposes, and thus the subsidiary will continue to pay UK tax on its worldwide income and capital gains. The UK corporate tax paid by the subsidiary should be available as a credit against the U.S. tax payable by the parent company.

While the filing of a check-the-box election may provide a benefit while the UK operations are loss-making, a disadvantage may arise once the UK operations become profitable, as any opportunity to defer recognition of the subsidiary's income for U.S. tax purposes will no longer be available (as a corporation, subject to the application of the controlled foreign corporation rules, the income of the subsidiary should only be subject to U.S. tax when the subsidiary pays a dividend to the parent company). There are two advantages to deferring the recognition of income for U.S. tax purposes. First, the parent company could take advantage of the differential in tax rates. This savings in tax could be quite significant, and the funds saved can be used to provide funding for the non-U.S. operations, such as funding growth in the EU. Second, if the subsidiary is a corporation for U.S. tax purposes, there will be greater flexibility over the timing and use of tax credits in the United States for corporation tax paid by the subsidiary.

Raising Future Funds: How AIM Can Help a Company Fund Its Future Growth and Raise Its Profile in Europe

Why AIM?

One of the challenges that any company faces is raising money to fund future growth. This pressure is vastly increased for life sciences companies that are required to fund costly clinical trials. AIM is the London Stock Exchange's market for smaller companies. While AIM membership is available to companies from all sectors and from all over the world, AIM, with its flexible approach to regulation and streamlined admission process, has proved exceptionally attractive to life sciences companies looking to raise capital and enhance their profile within Europe.

A company joining AIM gains all of the benefits of flotation on a public market, in addition to the advantages of being quoted in London, including:

- Exposure to the deepest pool of global capital in the world, both at the time of flotation and later through further issues
- The creation of a market in the company's shares, broadening its shareholder base and potentially providing an exit for existing shareholders
- The flexibility to raise its profile with a view to expanding its operations into new overseas markets
- Access to international investor expertise through a unique globally respected market
- A flexible yet internationally respected regulatory regime
- Currency for and easier rules on acquisitions
- Eligibility for a range of tax benefits

At the end of June 2007, there were 1,656 companies trading on AIM with a total market capitalization in excess of £107 billion, of which 45 were U.S. companies and 75 were life sciences companies.

Admission Requirements

Whatever the company's country of origin, the AIM application process remains the same, with the key requirement being that the company must be appropriate for the market—a decision made by the company's Nominated Advisor (or NOMAD).

There are no restrictions on the size of the company or its specific activities. Furthermore, there are no restrictions on the number of shareholders, no minimum number of shares required to be in public hands, and no required trading track record.

The Admission Process

NOMAD

Each company must appoint and retain a NOMAD at all times. The NOMAD will be one of a number of firms of experienced corporate financiers who are approved by the London Stock Exchange. There are a number of NOMADs whose experience is specifically in the life sciences field and whose help and support would be invaluable to any life sciences company seeking admission to AIM.

The NOMAD is appointed by the company but is responsible to the London Stock Exchange for the confirmation that the company is suitable for admission to AIM and for ensuring the company's compliance with the AIM rules after admission. The NOMAD is responsible for coordinating the admission process with the assistance of the company and its lawyers, accountants, and other advisors.

Broker

Each company must appoint and retain a broker at all times. The broker is a securities house that is a member of the London Stock Exchange. The broker may be the same firm as the NOMAD, or an independent broker may be chosen. The broker takes responsibility for dealings in the company's shares.

Admission Document

A company joining AIM must publish an admission document containing the information required by the AIM Rules of the London Stock Exchange.

While it is possible to have shares admitted to AIM without raising money, most companies will take the opportunity to raise money by way of a placing of new shares. Following the implementation of the EU Prospectus Directive, a company may not make an offer to the public in the UK without producing a prospectus that is first approved by the UK Listing Authority, unless such an offer is an "exempt" offer. To be exempt, the offer must satisfy certain prescribed criteria, which include not making the offer to more than 100 persons, other than "qualified investors" as the term is defined in the relevant legislation. The NOMAD will seek, if at all possible, to ensure that such criteria are met. Accordingly, it is likely that the applicant company will be required to produce only an admission document, compliant with the AIM Rules. This document may look like a prospectus, but it will contain much less information and, most importantly, will not need to be approved by the UK Listing Authority.

An admission document provides details about the company and its securities that are to be admitted to AIM so that investors can assess the value of the securities and make an informed judgment as to their future performance in the market. In addition to information on, *inter alia*, the history and background of the company and its products, business, and directors, there are certain specific requirements that the admission documents must contain, including:

- Annual audited accounts for the last three years (or less if the company has been trading for less than three years)
- Financial information on any business or company that the company intends to acquire
- A statement that the company has sufficient working capital for its present requirements (at least 12 months from the date of the Admission Document)
- The name of any person who has received, within the previous 12 months, any fees, securities, or other benefits with a value of £10,000 or more
- Details of any lock-ins
- Details of any significant shareholders (3% or more)
- Detailed information requirements covering, *inter alia*, each director's interests in shares, employment terms, other directorships, and insolvencies in which the director has been involved
- A responsibility statement confirming that each of the directors accepts responsibility, individually and collectively, for the information contained in the document, and that *"to the best of the knowledge and belief of the directors (who have taken all reasonable care to ensure that such is the case), the information contained in the admission document is in accordance with the facts and does not omit anything likely to affect the import of such information"*

General Duty of Disclosure. The applicant company must include in the admission document "any other information which it reasonably considers necessary to enable investors to form a full understanding of:

- (i) the assets and liabilities, financial position, profits and losses, and prospects of the applicant and its securities for which admission is being sought;
- (ii) the rights attaching to those securities; and
- (iii) any other matter contained in the admission document."

Who Has Responsibility for an Admission Document. The persons responsible for an admission document include (i) the company, (ii) each director of the company at the time it is published (this includes shadow directors, i.e., people in accordance with whose instructions the directors of the company are accustomed to act, regardless of their official position), and (iii) every person named in the admission document as a proposed director.

The admission document must contain the responsibility statement discussed previously.

Placing/Introduction Agreement

The company and its directors will enter into a placing or introduction agreement with the NOMAD and the broker, under which the NOMAD and the broker agree to perform their respec-

tive functions (including placing the company's shares, if relevant), and the company and its directors undertake to fulfill their roles in the placing and give warranties and (in the case of the company) indemnities in relation to the company.

"Fast Track" Designated Markets Route

The London Stock Exchange has introduced a "fast track" procedure for companies already listed on one of the designated markets. Both the NYSE and NASDAQ are designated markets for these purposes. The procedure is designed to simplify the AIM admission process for companies that have been traded on certain major markets (known as AIM Designated Markets) for at least 18 months. These companies can use their existing annual report and accounts as a basis for a complementary quotation on AIM.

Tax Benefits for Investors in AIM Companies

In certain circumstances, a quotation on AIM can provide the opportunity for UK tax-paying investors in non-UK companies to take advantage of UK tax benefits. This relief mostly applies to unquoted companies, and for this purpose, qualifying companies traded on AIM are regarded under UK tax legislation as unquoted. The relief may not apply where the company is listed on another recognized stock exchange. These benefits include capital gains tax benefits, inheritance tax benefits, and continued relief under the Enterprise Investment Scheme and Venture Capital Trust rules.

Time and Cost

The admission process for AIM (other than for companies on the fast track designated markets route) usually takes approximately three to four months. The length of time is largely dependent on the complexity and type of the company involved, how well organized the company is, and therefore how quickly information is supplied and how accurate it is, which will have an impact on the amount of time spent by the lawyers and other advisors carrying out due diligence and verification processes.

Costs comprise fees for the various members of the admission team and will generally amount to between 8% and 10% of the amount raised.