

What Europe has to offer biotechnology companies

Unraveling the tax, financial and regulatory framework



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Foreword

by Máire Geoghegan-Quinn,
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Europe currently has a strong and fast-growing biotechnology industry and research base. However, work needs to be done in order to exploit our vast potential in this sector fully and to ensure that Europe remains competitive and a world leader for research and innovation. For that reason, I am delighted to welcome a new report from Ernst & Young and

EuropaBio entitled *What Europe has to offer biotechnology companies: Unraveling the tax, financial and regulatory framework*. The report sets out to guide biotechnology companies, particularly those in the crucial small and medium enterprise (SME) sector, investors and other involved players through the concrete measures Member States have put in place to foster and support development and growth of biotechnology in their countries.

In recent years, Europe has greatly improved the level of support for research and innovation. However, it is vital that we speed up the process of converting this research excellence into useful products and services. The global economic landscape is changing rapidly and Europe must ensure that it keeps pace. We must do our utmost to create a strong knowledge base and supportive environment for industry to remain in Europe, produce in Europe and flourish in Europe.

SMEs are critical to this process. Increasing numbers of SMEs across Europe now receive a larger share of European funding than ever before to help them grow and so create employment. Yet, if we are to capitalize on this innovation and contribute more to economic growth, we must do more support this vital industry. Only then will we succeed in translating Europe's prowess in research, development and innovation into skilled jobs and a faster rate of economic expansion.

Through initiatives such as Horizon 2020, the European Commission's proposed research and innovation funding program for 2014-20 and our recently launched Bioeconomy Strategy - *Innovating for Growth: A Bioeconomy for Europe*,¹ we aim to capitalize to greater effect on the ideas of the brightest, best and most innovative people in Europe. By advocating holistic and workable policy measures, simplifying the

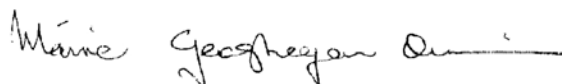
rules and concentrating our resources where they are needed and will be most effective, we aim to make European innovative companies more competitive. Among the most important, of course, are those operating in all aspects of biotechnology - from pharmaceutical to industrial and agricultural.

It is easy to see why the bioeconomy is already one of the most important and beneficial sectors in the EU. In Europe alone, the bioeconomy is already worth some €2t and employs around 22 million people across industries as diverse as agriculture and forestry, fisheries, food, chemicals and energy.² It offers Europe the potential to accelerate its transition toward a new economic model for smart, sustainable and inclusive growth, while at the same time developing a high-value, globally competitive sector capable of generating good quality jobs in rural as well as urban settings.

2012 holds the potential to be a pivotal year for biotechnology in Europe. With so many crucial policy changes in the pipeline, including the Bioeconomy Strategy, the Common Agricultural Policy reforms, the revision of the Clinical Trials Directive and of course the increased funding allocations to the bioeconomy - it is essential that Europe and its Member States align their common goals. A top priority for industry and government must be to link science and innovation more directly with society in a way that helps to improve the lives and wellbeing of people across Europe.

For this reason, I welcome the efforts of Ernst & Young and EuropaBio in explaining how the tax, financial and regulatory system across Europe affects the growth of biotechnology and the industries associated with it. Their report is a valuable resource for everybody from entrepreneurs and investors to researchers and policy-makers which I hope you will find interesting.

Yours sincerely



¹http://ec.europa.eu/research/bioeconomy/pdf/201202_innovating_sustainable_growth.pdf
²Building a Bio-based Economy for Europe in 2020

Executive summary



National governments have done much to encourage innovation, often through a web of tax incentives for research. Yet, by and large, they have done too little to ensure that these ideas are translated into new businesses, new products, additional jobs and so, in time, a faster rate of economic growth.

What Europe has to offer biotechnology companies: unraveling the tax, financial and regulatory framework is a joint report by Ernst & Young and EuropaBio. In it, we examine what European countries have to offer investors, entrepreneurs and researchers alike. We look at everything from what to take into account when determining the best location for research and development to how best exploit intellectual property (IP) within Europe's various jurisdictions.

At a time when big biotechnology companies are looking for inspiration, governments need to encourage small and medium-sized enterprises (SMEs) to take steps that may help them one day to become large firms in their own right. There is more to creating a successful industry, says the report, than putting in place the right standard of regulation. What is needed is a climate of innovation, coupled with the bricks and mortar with which to build industries around it.

Initiatives such as Horizon 2020, a program for research and innovation funding soon to be implemented by the European Commission, and the recently launched Bioeconomy Strategy and Action Plan for Europe will both contribute toward bridging the gap between people with good ideas and the investment and opportunity to make them a reality.

There is still a challenge in terms of product approval legislation in Europe for the agricultural biotech industry, which

Horizon 2020

A program for research and innovation funding soon to be implemented by the European Commission

is also a deterrent and compromises our competitiveness in this sector.

One of the most important pieces of legislation for the bio-pharmaceutical industry under revision in 2012 is the Clinical Trials Directive. A simplified and efficient regulatory framework for clinical trials is vital in order to make Europe a more attractive place for clinical research. Such a framework will benefit all stakeholders, allowing faster access to innovative treatments for patients, and reducing the administrative burden and costs for public and private sector researchers, as well as for Member States.

In an analysis of individual countries across Europe, we set out which agencies to contact for information when considering where to establish centers of research or manufacturing. We examine the tax concessions on offer in each country, some financing opportunities for SMEs and the benefits that are likely to flow from a decision to establish a research facility or start-up in a particular location.

With the economies of Western Europe seeking to remain competitive, governments are keen to encourage more investment. One tool being used is the rate of corporation tax, and another the use of tax credits for R&D. Some governments have stretched the period before tax is due; others have made sharp reductions in the overall rate for qualifying companies. In some countries, rates as low as 10%-12% can be achieved in certain circumstances.

Similar measures have been adopted by governments for investors in start-up companies by offering access to reduced rates or indeed exemptions for capital gains tax once certain conditions are met, which can be key to attracting finance.

Elsewhere, governments have refined the regimes governing the treatment of patent

or license boxes. The effective rate of tax on income derived from rights to intellectual property as well as investments in innovation, where these regimes apply, can be reduced - in some cases to as little as 5%, provided relevant conditions are met. Such steps make it easier to attract investment from private investors as well as from larger multinationals.

Even within countries whose headline rates of tax for biotechnology companies are to remain unchanged, or which are already competitive across Europe, regional authorities may offer fresh incentives to set up new operations or expand existing ones.

SMEs are also being helped through tax relief to maintain their spending on research and development (R&D). To encourage R&D, some governments now offer premiums (or the equivalent in cash) to cover the expenses incurred in developing an innovative product or process.

Because jurisdictions influence how, when and why investors in biotechnology decide to enter or exit a business, we weigh up the advantages and disadvantages of individual countries. In addition, we examine the priorities facing SMEs - those businesses which create most of the new jobs in Europe.

Too often, say those in biotechnology and allied industries, rules governing the process toward new products or processes are developed without fully appreciating and focusing on the end result. Europe may have a well-deserved reputation for innovation and the skills required to research and develop new ideas. Yet the journey from innovation to manufactured products is often labored and long.

A complicated regulatory environment makes it more difficult for businesses to assess a likely rate of return from a new product. New firms can also find it difficult to maintain the momentum needed to bring a product to market and so to begin to generate returns. Investors will only risk their capital in the first place if they see a possible return.

In today's markets, entrepreneurs may be better advised to devote their time and energies to creating a suite of products, not just a single one. In this way, says the report, firms may increase their chances of securing backing from an investor while improving the prospects of creating a product which reaches the market. History would suggest, too, that the earlier such a decision is made, the better it may be for the company as well as the investor.

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Introduction

The EU Strategy for 2020 envisages an EU economy based on smart, sustainable growth, driving high levels of employment, productivity, competitiveness and social cohesion. To reach this ambitious goal, and in order to allow Europe to prosper over the long term and deal with new crises, we require a lasting framework for industry, with support not only from EU institutions but also strong commitment from Member States. SMEs are vital to this agenda and contribute significantly to Europe's goal of becoming the foremost knowledge-based economy in the world.

Strength in biotechnology is one of Europe's most valuable industrial assets. The sector is at the core of the knowledge-based economy that is central to future European growth. Many of the innovations that have made biotechnology one of the world's most important growth sectors originated in Europe.

Biotechnology must continue to play a leading role in the growth agenda of the next decade and beyond. It is among Europe's most innovative industries and is widely acknowledged to depend in large part on the 2,000 or so SMEs operating across the continent.

These innovative companies promise a brighter future for Europe, but they require sound policy-making that supports innovation and entrepreneurial risk-taking, and regulatory structures that reward long-term investment in research and development (R&D). However, in a world of growing competition, we cannot take these assets for granted. Specifically, there is a need to attract competent entrepreneurs who can translate leading science into commercial opportunities, and for highly innovative SMEs to attract more investment.

Encouraging SMEs will create jobs and foster economic activity

Making the European Research Area a reality is a key challenge. This will require not only commitment from government for research funds under the EU's Framework Programs FP7 and the upcoming Horizon 2020 program, but policies and programs developed by individual Member States to support and encourage biotechnology SMEs.

Not all biotechnology companies operate under the same conditions. There is a wide variation in the level of politics across Europe, and the rules vary from country to country. The differences range from basic policies and regulation, which encourage financing for start-ups, to the ability to attract competent managers and entrepreneurs, and the process by which firms secure approval for their products and services to be marketed.

Given this diversity, it is important for potential investors and SMEs engaged in biotechnology to understand what instruments to support their endeavors are available across Europe. This applies not just to securing investment but also to discovering where best practices lie and how to share them to support growth.

Biotechnology in itself is a complex industry which is composed of three central applications:

- ▶ *Health care biotechnology* refers to a medicinal or diagnostic product, or a vaccine that consists of, or has been produced in, living organisms and may be manufactured via recombinant technology (recombinant DNA is a form of DNA that does not exist naturally - it is created by combining DNA sequences that would not normally occur together).
- ▶ *Industrial biotechnology* uses enzymes and micro-organisms to make bio-based products in sectors such as chemicals, food and feed, detergents, paper and pulp, textiles and bioenergy (such as biofuels or biogas). In doing so, it uses renewable raw materials and is one of the most promising and innovative

approaches toward lowering greenhouse gas emissions.

- ▶ *Agricultural biotechnology* encompasses a range of modern plant breeding techniques. For centuries, farmers have tried to improve their crops by means of crossing, relying on the random rearrangement of existing genes between two closely related parent plants. Modern agricultural biotechnology improves crops in more targeted ways. The best-known technique is genetic modification, but the term agricultural biotechnology (or green biotechnology) also covers such techniques as Marker Assisted Breeding, which increases the effectiveness of conventional breeding. Whatever the particular technology used, the crops may be destined for use for food, biomaterials or energy production.

The objective of this publication is to identify, for a selected number of European countries, policies on issues such as taxation, regulation and the availability of grants that are designed to help biotechnology SMEs set themselves up and grow in a sustainable way. Our initial focus is on those Member States of the EU with the most established track records in commercializing biotechnology. The study assesses, among other topics, the measures Member States have in place to support the establishment of SMEs in biotechnology. Such measures include the rules governing intellectual property; those applying to tax incentives for investors and entrepreneurs; systems for grants; the regulatory regimes for final products; and measures to allow young, innovative companies to accelerate their development.

Biotechnology is a capital-intensive industry with long lead times to profitability. To begin with, businesses tend to lose money as they invest in products and technologies that are mostly subject to long development cycles and regulatory approval.

Many biotechnology companies never reach profitability, but are acquired by larger companies for the quality of their products and technology once confirmed by development and regulatory approval. This is also the stage that presents one of the biggest tests. How a business negotiates its way through this period and how it competes within its designated market will determine whether it survives and how it progresses to the next stage of its growth.

Serious questions are also faced by all new start-ups. How to attract risk capital in the early and intermediate stages? How to maintain incentives for investors in early stage high-risk companies? How to attract competent managers from more secure positions with larger companies? How to make use of tax losses accumulated during the initial phases? Can such losses be applied against other taxes, such as that levied on the payroll, while the firm remains unprofitable? Will these losses be available in later years when the company starts to turn a profit?

Of particular concern is the availability of seed capital from angel investors and venture capitalists. The availability of finance at the very early and immediate stage is declining as investors become more adverse to risk.

Biotechnology firms also face difficulties replenishing their capital throughout their R&D and during trials. Some are turning to non-traditional sources such as hedge funds or the internal venture funds of larger companies. Some are seeking earlier or new types of commercial arrangements with larger companies in order to ensure they have a steady source of funding.

National governments, together with the EU, need to make sure that the policies are in place to make funding more accessible to SMEs involved in biotechnology. They need to develop ways to encourage investment in such companies and ensure that there is consistency in the application of state aid rules which do not hamper such initiatives.

It is clear from this report that some governments have recognized the importance of policies and programs that foster a strong community of SMEs in biotechnology. Other governments that are considering the implementation of such measures can draw upon the best practice that is outlined in this report. However, in the development of policies, it is important to recognize that not all products or companies will be successful.

In many cases, the costs associated with marketing, securing patents and navigating regulatory hurdles will fail to produce a product that is commercially viable. However, the willingness to accept that failure provides the long-term basis for the success of this industry is essential to ensuring a long-term commercial advantage.

Given the long timescales for product development, there must be sustained investment in strong policies and programs to support biotechnology SMEs in Europe.

The success of any long-term strategy to build a sustainable biotechnology industry in Europe depends upon consistent government policy-making that encourages start-up and development-phase SMEs. Incentives could include tax policies, grants, different forms of financing (personal as well as corporate) and longer-term tax concessions.

Encouraging SMEs at the national level - as several Member States have done by introducing Patent Boxes and other measures - will do more than just encourage the large-scale investment required to develop products in the life sciences. It will also create jobs and foster economic activity. At a time when economic difficulties have restricted government spending, such efforts have never been more important. These policies can then be complemented and integrated into programs at the EU level. This encourages cross-border collaboration and takes advantage of the abundant capabilities across Member States.

Strength in
biotechnology is one of
Europe's most valuable
industrial assets.



Biotechnology regulatory overview

Outline of regulatory framework for (bio-) pharmaceutical products in the European Union

Pharmaceutical industry explained

The pharmaceutical industry is currently facing unprecedented change. These pressures are forcing companies to refocus on ways to increase the productivity of their R&D, and consider streamlining value chain costs, such as the money spent on sales, marketing and manufacturing. The result is an industry in which specialty and niche operators (as opposed to large-volume blockbusters) are prized for their potential to reimburse investors. Activities such as marketing are being streamlined or outsourced, although the ability to manage what remain substantial risks is retained. The exponential increase in the number of mergers and acquisitions is a result of the way pharmaceutical companies assess their business models.

The industry continues to grow modestly, while adapting to changes. The global pharmaceutical market expanded by a modest 3% in 2010. In that year, total pharmaceutical sales worldwide by geographical region were as follows:¹

- ▶ North America - 39%
- ▶ Europe - 29%
- ▶ Asia, Africa, and Australia - 15%
- ▶ Japan - 11%
- ▶ Latin America - 6%

Global pharmaceutical sales are expected to grow at a compound annual growth rate (CAGR) of 3%–6% during the period 2011-15, despite the impending loss in revenue expected from the expiry of patents. This gain will largely be driven by

robust growth in emerging markets. It is anticipated that such markets will account for approximately 28% of total sales worldwide in 2015, up from only 18% in 2010. This growth is in sharp contrast to the expected CAGR of only 1%–4% for the primary drug markets of North America and Europe.

Pharmaceutical companies face many challenges and uncertainties, including heightened competition from makers of generic drugs, unprecedented pressure on pricing from payers (such as insurance companies), constraints on public sector budgets and declining R&D productivity.² The pressure to reorganize R&D, provide affordable price and marketing overhauls is intense. According to IMS Health, the big pharmaceutical companies (those with large capitalizations) are struggling to grow, with generic firms outperforming them.³ However, there are improvements in early-stage product pipelines in the pharmaceutical industry - particularly in the fields of cancer and diabetes - which offer long-term promise. In addition, an aging population and new products are likely to create a robust future for the industry.⁴

Legislative overview

A pharmaceutical product can only be placed on the market in the European Union (EU) - and the broader European Economic Area (EEA) - when one of certain conditions are met. These are:

- ▶ When an authorization has been granted by the European Commission via the centralized procedure (Community authorization) for all EU markets
- ▶ When a marketing authorization has been granted by the competent authority of a Member State for its own territory (national authorization, which can be the subject of mutual recognition between Member States)

¹Information accessed on 25 July 2011 from www.imshealth.com

²Standard & Poor's, "Industry Survey Healthcare: Pharmaceuticals," 2 June 2011, p. 13.

³Ibid.

⁴Ibid.

- ▶ When an authorization has been granted through a decentralized procedure.⁵ The marketing authorization holder must be established within the EU or the EEA.

For the purpose of this chapter, we will focus on the centralized procedure. This is the mandatory regulatory pathway for the marketing authorization of any medicinal product developed by means of biotechnological processes, such as recombinant DNA technology and monoclonal antibody methods.⁶

The centralized procedure was established in 2005 following the revision of EU pharmaceutical legislation in 2004. This procedure includes an application by the developer of a new pharmaceutical product to the European Medicines Agency (EMA), which is responsible for the scientific evaluation of the safety, efficacy and quality of the new product. Today, regulators tend to conduct this evaluation by looking at the product's benefit/risk ratio. The scientific assessment is conducted by the EMA's

Committee for Medicinal Products for Human Use (CHMP). Based on an application dossier that includes all relevant clinical data about the product, the CHMP adopts an opinion, which is communicated to the European Commission. In consultation with the Member States and the European Parliament, the European Commission is responsible for granting a marketing authorization, provided that the CHMP adopted a positive opinion in the first instance.

The active time for scientific evaluation of the marketing authorization application by the European authorities is less than 210 days. As an example, in 2010 the CHMP took an average of 167 days for the assessment of an application, and the final decision on the marketing authorization took an average of 59 days. Clock-stop time (i.e., the time given to a company to respond to questions from the CHMP) averaged 114 days.⁸

After a marketing authorization is granted via the centralized procedure, the CHMP publishes a European public assessment

report (EPAR), setting out the scientific grounds for the CHMP's opinion in favor of granting the authorization. In addition, there is a summary of product characteristics (SPC), a labeling and package leaflet (patient/user information leaflet) for the medicine and details of the procedural steps taken during the assessment process.

Specialized EMA Committees such as the Committee for Orphan Medicinal Products (COMP) and the Committee for Advanced Therapies (CAT) are responsible for preparing a draft opinion on each specific product's application that falls under their expertise, before the CHMP adopts a final opinion on the granting of the marketing authorization.

To help applicants better understand the efficacy, quality and safety requirements and prepare their marketing authorization applications, the CHMP and specialized committees develop scientific guidelines. These guidelines, drawn up in consultation with national regulatory authorities, can be general or product-specific, and they provide a basis for practical harmonization of how Member States and the EMA interpret and apply the detailed requirements provided by the Community legislative framework on pharmaceuticals.⁹

In 2005, an SME Office at the EMA was created to help small and medium-sized companies to navigate the regulatory maze of marketing authorization applications and guidelines. Companies complying with the EU criteria for granting the statute of SME,¹⁰ can receive administrative and procedural assistance; fee reductions for scientific advice and inspections; fee exemptions for certain EMA administrative services; and assistance with translation of the product information documents.

After marketing authorization is granted, the holder is subject to pharmacovigilance

Table 1: Product approvals by EMA, 2000-11⁷

	Total approvals	Generics	Biosimilar
2011	77	26	0
2010	50	22	1
2009	109	41	2
2008	51	6	3
2007	65	3	5
2006	36	0	2
2005	19	0	0
2004	34	0	0
2003	14	0	0
2002	30	0	0
2001	34	0	0
2000	27	0	0

⁵ Notice to applicants. Volume 2A; Procedures for marketing authorisation; Chapter 1: Marketing Authorisation; November 2005

⁶ Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

⁷ Statistics available from the EMA website, at www.ema.europa.eu

⁸ EMA 2010 Annual report

⁹ The rules governing medicinal products in the European Union. EUDRALEX. Available at: <http://ec.europa.eu/health>

requirements, as provided in the new legislation on pharmacovigilance.^{11,12} The new post-authorization requirements aim to improve the pharmacovigilance system in the EU, making the reporting of side-effects easier and introducing special provisions for medicines that need additional monitoring. The legislation also aims to ensure that the public becomes better informed about the benefits and risks of taking medicines. A new EMA Committee - the Pharmacovigilance Risk Assessment Committee (PRAC) - was created to provide recommendations to the CHMP on questions relating to pharmacovigilance activities and on risk management systems. While acknowledging that patient safety is paramount, the impact of the new pharmacovigilance legislation on SMEs with products on the market will need to be closely monitored to ensure that these companies are not subject to unnecessary administrative burdens.

Since the adoption of new EU pharmaceutical legislation in 2004, regulators have adapted their science to the fast pace of biotechnological advancements. The regulatory framework plays an important role in bringing fast access to innovative medicines. Recent reflections on (re-) new(ed) regulatory processes, such as accelerated assessment or progressive approvals, pave the way to even faster approvals. This benefits innovation and patients.

Outline of regulatory framework for agricultural biotech products in the European Union

Agricultural biotechnology explained

Worldwide, the agricultural biotech industry grew by 8% in 2011. Last year, crops were planted on a total of 160m hectares. Some 16.7m farmers around the world planted these crops, which was also a rise of 8% over 2010. Indeed, 2011 was the 16th year in which biotech crops have been commercialized. It is the fastest-growing crop technology in modern times.

According to market research and consultancy provider Cropnosis,¹³ in 2011 the market value of biotech crops worldwide was more than €10b, up from approximately €8.8b in 2010. This represents more than one-third of a commercial seed market worth €28b.

Of the 29 countries planting biotech crops in 2011, 19 were developing economies and 10 were industrialized nations. In terms of biotech crop cultivation, the five leading developing countries are China, India, Brazil, Argentina and South Africa. Collectively, they grew nearly half of global biotech crops in 2011, and are home to 40% of the world's population.

In Europe, only two biotech crops are authorized for cultivation: an insect-resistant maize and a potato for industrial use. Such crops were grown in eight countries across Europe during 2011: Spain, Portugal, the Czech Republic, Germany, Slovakia, Romania, Poland and Sweden. The number of hectares of the only genetically modified (GM) maize permitted to be cultivated in Europe increased from 91,643 to 114,607 in

2011 - an increase of more than 20% over the previous year.

Europe is a net importer of biotech crops in the form of feed and food because of its relatively small output. Some 22 biotech crops are currently awaiting authorization for cultivation in the EU, including maize, soybean, potato and sugar beet. The approval process remains the biggest challenge for the industry. Compared with other countries around the world, it is slow and cumbersome. Because of the uncertainty facing the industry, the number of agricultural biotech companies in Europe is understandably small.

In October 2011, the world population reached seven billion. Experts predict that the world will need to almost double its food production by 2050. Agricultural biotechnology offers a way to reach this goal while preserving natural resources, thanks to lower CO² emissions, the improved quality of the soil and higher productivity. There is an urgent need in Europe for appropriate decisions, based on science, that support the production of more food while respecting the environment and encouraging small and medium-sized companies to enter the market.

¹⁰ User guide for micro, small and medium-sized enterprises (SMEs) on the administrative and procedural aspects of the provisions, laid down in regulation (EC) No 726/2004, that are of particular relevance to SMEs. Available at: www.ema.europa.eu

¹¹ Regulation (EU) No 1235/2010 amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products

¹² Directive 2001/84/EU amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use

¹³ www.cropnosis.com

Table 2: Global area of biotech crops in 2011: by country (million hectares)**

Rank	Country	Area (million hectares)	Biotech crops
1	USA*	69.0	Maize, soybean, cotton, canola, sugarbeet, alfalfa, papaya, squash
2	Brazil*	30.3	Soybean, maize, cotton
3	Argentina*	23.7	Soybean, maize, cotton
4	India*	10.6	Cotton
5	Canada*	10.4	Canola, maize, soybean, sugarbeet
6	China*	3.9	Cotton, papaya, poplar, tomato, sweet pepper
7	Paraguay*	2.8	Soybean
8	Pakistan*	2.6	Cotton
9	South Africa*	2.3	Maize, soybean, cotton
10	Uruguay*	1.3	Soybean, maize
11	Bolivia*	0.9	Soybean
12	Australia*	0.7	Cotton, canola
13	Phillippines*	0.6	Maize
14	Myanmar*	0.3	Cotton
15	Burkina Faso*	0.3	Cotton
16	Mexico*	0.2	Cotton, soybean
17	Spain*	0.1	Maize
18	Colombia	<0.1	Cotton
19	Chile	<0.1	Maize, soybean, canola
20	Honduras	<0.1	Maize
21	Portugal	<0.1	Maize
22	Czech Republic	<0.1	Maize
23	Poland	<0.1	Maize
24	Egypt	<0.1	Maize
25	Slovakia	<0.1	Maize
26	Romania	<0.1	Maize
27	Sweden	<0.1	Potato
28	Costa Rica	<0.1	Cotton, soybean
29	Germany	<0.1	Potato

* 17 biotech mega-countries growing 50,000 hectare, or more, of biotech crops

** Rounded off to the nearest hundred thousand

Source: Clive James, 2011

Legislative overview

EU legislation on genetically modified organisms (GMOs) has been in place since the early 1990s. This specific legislation follows two main objectives:

1. Managing possible human health and environmental risks
2. Ensuring the free movement of approved GM products in the EU

The entire corpus of GMO legislation was amended in the early 2000s, leading to the creation of a new legal framework which can be summarized as follows.

GM crops cannot be put on the market without prior EU approval, whether for importing a food or feed product made from GM crops or for planting GM seeds. The EU approval system is widely recognized as one of the most stringent in the world and covers both deliberate release (i.e., cultivation under Directive 2001/18/EC), and import and processing of GM food and feed through Regulation 1829/2003. Directive 2001/18/EC and the accompanying regulations are transposed and translated respectively into national laws across the EU so that each Member State may carry its specificities. Biotech crops that are produced without using genetic modification (as listed in Annex I of Directive 2011/18/EC) do not fall under the above-mentioned legislation.

The following steps provide an overview of the GMO approval system:

1. Risk assessment is done on a case-by-case and step-by-step basis, fulfilling the requirements laid out in the legislation (Directive 2001/18/EC for cultivation and Regulation 1829/2003 for import and processing of GM food and feed).
2. When the European Food Safety Authority (EFSA) has completed the environmental,

human and animal health safety assessment based on the risk assessment, its opinion, if positive, forms the basis of a Draft Decision. This is subject to approval by the European Commission after voting in Standing Committees, which are composed of representatives from the Member States.

3. Post-release monitoring plans need to be approved prior to marketing the product. Traceability is ensured by labeling and administrative records throughout the food chain. Food that contains more than 0.9% GMO or GMO-derived content must be labeled.

4. Throughout the approval process, information is provided to the public.

In the EU, unlike the above-mentioned approval system, coexistence between GM, conventional and organic farming is governed by the principle of subsidiarity.¹³ That means that Member States are to adopt their own national strategies to promote coexistence.

Finally, the EU legislation is in line with WTO international trade agreements (it is clear, transparent and non-discriminatory) and with the trans-boundary movement rules of the UN Cartagena Protocol on Biosafety.

How long do applications take and what do they cost?

It takes on average almost four years for a GM import approval to be completed in Europe, which is roughly twice as long as in other jurisdictions. Such a time lag between European approvals and those in the rest of the world have led to trade disruptions which, in turn, have led to WTO cases against the EU. All but one of the WTO cases have been settled at this stage. Europe tends to have even longer waiting periods for GM cultivation applications, partly due to political differences between the Member States.

Costs for applicant companies arise mainly from the large number of studies required and vary from €7m to €15m per crop.

An overview of agbiotech legislation

- ▶ Directive 2001/18/EC on the deliberate release into the environment of GMOs.¹⁴ This Directive is the main legislation which governs experimental releases and placing GMOs on the market. Compared with the former legislation (Directive 90/220/EEC¹⁵), the criteria for determining permission for commercial releases of GMOs into the environment is tightened up. This includes limiting the period of authorization to a maximum of 10 years and requiring post-market monitoring of the organisms' environmental impact. The Directive provides for a step-by-step approval process on a case-by-case assessment of the risks to human health and the environment. The environmental risk assessment and risk management of GMO relies on pre-commercialization biosafety research and post-commercialization monitoring.
- ▶ The placing on the market of GMO food and feed, or food and feed products containing or consisting of GMOs, is regulated by Regulation (EC) No 1829/2003 on genetically modified food and feed.¹⁶ The regulation pursues the global objective of ensuring a high level of protection of human life and health; animal health and welfare; and environment and consumer interests in relation to genetically modified food and feed, while ensuring the effective functioning of the internal market.
- ▶ GMOs and food and feed products derived from GMOs which are placed on the market must also satisfy labeling and

traceability conditions. These conditions are laid down in above-mentioned Regulation (EC) No 1829/2003, Regulation (EC) No 1830/2003¹⁷ concerning the traceability and labeling of GMOs and the traceability of food and feed products produced from GMOs, and amending Directive 2001/18/EC.

Regulation (EC) No 1830/2003 is a complement to Regulation (EC) No 1829/2003. This regulation introduces a harmonized EU system to trace and label GMOs and to trace food and feed products produced from GMOs. In particular, the requirements are that business operators must transmit and retain information about products that are covered by the scope of the Regulation at each stage of their placing on the market. This means that operators shall have a traceability management system in place to identify to whom, and from whom, products are made available. Regarding labeling, Regulation 1830/2003 stipulates that all food and feed containing or consisting of GMOs, food and feed produced from GMOs and food and feed containing ingredients produced from GMOs, must be labeled. The presence of GM material in conventional food and feed does not have to be labeled if it is below 0.9% and if it can be shown to be adventitious or technically unavoidable.

In the presence of a food and feed product containing GMOs or consisting of GMOs, the applicant has, in reality, a choice. It can submit the application in its entirety, subject to Regulation (EC) No 1829/2003, applying the "one door, one key" principle, in order to obtain an authorization for the deliberate release of GMOs into the environment in accordance with the criteria laid down by Directive 2001/18/EC, and the authorization

¹³ Defined as the principle that the EU does not take action on a particular subject unless it is more effective than action taken at national, regional or local level

¹⁴ Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC. Official Journal of the European Communities L 106, 17.4.2001, p. 1.

¹⁵ Council Directive 90/220/EEC of 23 April 1990 on the deliberate release into the environment of genetically modified organisms. Official Journal of the European Communities L 117, p. 15-27.

¹⁶ Regulation (EC) No. 1829/2003 of the European Parliament and of the Council of 22 September 2003 on genetically modified food and feed. Official Journal of the European Communities L 268, 18.10.2003, p. 1-23.

¹⁷ Regulation (EC) No 1830/2003 of the European Parliament and of the Council of 22 September 2003 concerning the traceability and labeling of genetically modified organisms and the traceability of food and feed products produced from genetically modified organisms and amending Directive 2001/18/EC. Official Journal of the European Communities L 268/24, 18.10.2003 p. 24

to use this GMO in food or feed in accordance with the criteria laid down by Regulation (EC) No 1829/2003. Alternatively, the application – or part of the application – can be submitted both under Directive 2001/18/EC and Regulation (EC) No 1829/2003.

In practice, the main difference between the two procedures concerns the risk assessment. Under Directive 2001/18/EC, this is done by the competent authority of the lead Member State, in which the application for authorization is filed. EFSA only takes part in cases of disagreement of other national authorities and acts as an arbitrator. Under Regulation (EC) No 1829/2003, EFSA performs the risk assessment itself (only for the environmental risk, EFSA has to ask a national authority to make a primary assessment). In addition, dossiers under the Regulation are considered by a different Regulatory Committee and, subsequently, in the Agricultural Council, not in the Environment Council.

Intentional and unintentional movements of GMOs between Member States and third countries are regulated by Regulation (EC) No 1946/2003 on trans-boundary movements of GMOs, with the exception of intentional movements within the EU.

Other legal instruments have been adopted in connection with the legislation described above. These include:

- ▶ Commission Regulation (EC) No 641/2004, which details rules for the implementation of Regulation (EC) No 1829/2003 of the European Parliament and of the Council as regards the application for the authorization of new genetically modified food and feed, the notification of existing products and adventitious or technically unavoidable presence of genetically modified material which has benefited from a favorable risk evaluation.¹⁸

- ▶ Commission Regulation (EC) No 65/2004, which establishes a system for the development and assignment of unique identifiers for GMOs. All operators in the food and feed production chain shall transmit and retain specified information on the GMOs. As a means to specify the identity of GMOs, a system of "unique identifiers" has been developed in this regulation.¹⁹
- ▶ Commission Recommendation 2004/787/EC, which issues technical guidance for sampling and detection of GMOs and material produced from GMOs as or in products in the context of Regulation (EC) No 1830/2003.²⁰
- ▶ Regulation EC 619/2011, which harmonizes implementation of the zero-tolerance policy on non-authorized genetically modified material in feed

entered into force on 15 July 2011. It addresses EU businesses' uncertainty when marketing feed imported from non-EU countries.

Outline of regulatory framework for industrial biotechnology in the European Union

The bioeconomy explained

The bioeconomy in Europe is currently worth more than €2t a year and employs over 22m people, predominately in rural areas and often in SMEs. The term "bioeconomy" refers to the sustainable production and conversion of biomass into a range of food, health, fiber and industrial products, as well as energy. Renewable biomass

Table 3: The bioeconomy in the European Union²²

Sector	Annual turnover (€b)	Employment (thousands)	Data source
Food	965	4,400	CIAA
Agriculture	381	12,000	COPA-COGECA, Eurostat
Paper/pulp	375	1,800	CEPI
Forestry/wood ind.	269	3,000	CEI-BOIS
Fisheries and aquaculture	32	500	EC***
Bio-based industries			
Bio-chemicals and plastics	50 (estimation*)	150 (estimation*)	USDA, Arthur D Little, Festel, McKinsey, CEFIC
Enzymes	0.8 (estimation*)	5 (estimation*)	Amfep, Novozymes, Danisco/Genercor, DSM
Biofuels	6**	150	EBB, eBio
Total	2078	22,005	

* Estimation for Europe for 2009 ** Estimation based on a production of 2.2 million tonnes bioethanol and 7.7 million tonnes of biodiesel at average market price in Europe *** EC, *Facts and figures on the CFP, Basic Statistics Data*, ISSN 1830-9119, 2010 Edition

¹⁸ Same name, OJ L102, 7.4.2004, p.14-21.

¹⁹ Commission Regulation (EC) 65/2004 of 14 January 2004 establishing a system for the development and assignment of unique identifiers for GMOs. OJ L 10, 16.1.2004, p. 5-1.

²⁰ European Commission (2004). Commission recommendation 2004/787/EC of 4 October 2004 on technical guidance for sampling and detection of genetically modified organisms and material produced from genetically modified organisms as or in products in the context of Regulation (EC) No. 1830/2003. Official Journal of European Union, L348, 18-26

²² www.oecd.org

encompasses any biological material as a product in itself or as a product to be used as a raw material. Estimates by the Organization for Economic Cooperation and Development (OECD) suggest that industrial and plant biotechnology will overtake health biotechnology by 2030 and account for 75% of the total gross value added by the biotechnology sector (*The Bioeconomy to 2030: designing a policy agenda*, published by the OECD).

Industrial biotechnology continues to grow in the EU, thanks to a relatively supportive regulatory and financial system. Sales of bio-based products in Europe in 2007 amounted to €48b, equal to 3.5% of total chemical sales. In 2012, the total is expected to increase to €135b, or 7.7% of chemical sales; and, by 2017, sales are estimated to be €340b, totaling 15.4% of all chemical sales.²¹

Although Europe is one of the largest economies in the world, most activities aimed at supporting the development of the bioeconomy have, until recently, been conducted at a national level. Europe is currently a world leader in the bioeconomy. Yet, for that to remain so, and for the industry to continue to expand, it requires supportive and holistic regulation. In 2012, the European Commission Bioeconomy Strategy will begin to roll out, contributing to a policy framework that is not only more coherent but aims to pave the way for more innovation, a more efficient use of resources and competition across Europe. The strategy will build on the EU Framework Programmes for Research and Innovation funding known as FP7 and Horizon 2020.

Legislative overview

Industrial biotechnology includes a series of processes involving biotechnological steps, often, but not exclusively, via the use of micro-organisms. EU legislation has been in

place since the 1990s to cover the contained use of genetically modified micro-organisms (GMMs), as described below:

Contained use of GMMs

Directive 2009/41/EC lays down common measures for the contained use of GMMs, aimed at protecting human health and the environment.

The Act

2009/41/EC of the European Parliament and of the Council of 6 May 2009 on the contained use of GMMs.

Summary

Member States are required to take all measures necessary in order to avoid the contained use of GMMs having negative consequences on human health and the environment.

The Directive does not cover:

- ▶ Genetic modifications resulting from the use of certain techniques or methods listed in Annex II, part A.
- ▶ Contained uses involving the GMMs listed in Annex II, part C. GMMs on this list meet the criteria laid down in Annex II, part B, establishing their safety for human health and the environment.
- ▶ The transport of GMMs by road, rail, inland waterway, sea or air
- ▶ The storage, culture, transport, destruction, disposal or use of GMMs which have been placed on the market in accordance with Directive 2001/18/EC on the release of GMOs or pursuant to other Community legislation which provides for a specific environmental risk assessment similar to that laid down in the said Directive, provided that the contained

Sales of biotech products

2007: €48b (3.5% of total chemical sales)

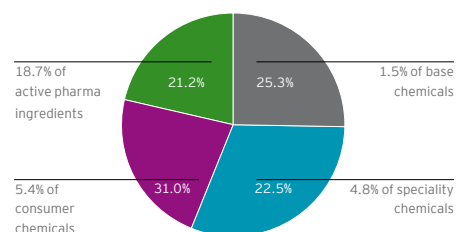
2012: €135b (7.7% of total chemical sales)

2017: €340b (15.4% of total chemical sales)

Source: G. Festel (EFIB 2009, Lisbon, October 2009; OECD workshop, Vienna, January 2010)

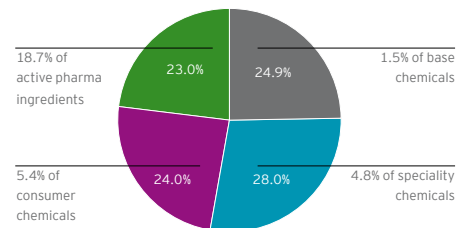
Biotech sales per segment 2007

100% = €48b



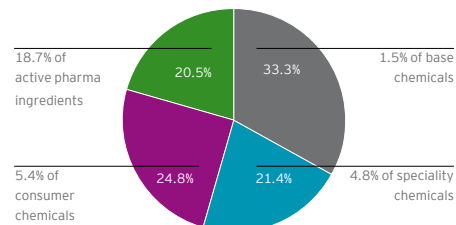
Biotech sales per segment 2012

100% = €135b



Biotech sales per segment 2017

100% = €340b



Legend: Base chemicals (green), Speciality chemicals (grey), Consumer chemicals (purple), Active pharma ingredients (blue)

use is in accordance with the conditions, if any, of the consent for placing on the market.

The assessment of GMM records shall result in a risk hierarchy of the contained uses, consisting of four classes. The containment measures to be applied shall also be classified in a four-level hierarchy:

- ▶ Class 1: No or negligible risk, level 1 containment
- ▶ Class 2: Low risk, level 2 containment
- ▶ Class 3: Moderate risk, level 3 containment
- ▶ Class 4: High risk, level 4 containment

The contained use of GMMs requires an examination of the containment and protection measures taken to avoid a release.

When contained uses are to be carried out in premises for the first time, the user shall be required, before commencing such use, to submit to the competent authorities a notification containing at least the information listed in Annex V, Part A, B or C, as appropriate. Following notification to the competent authorities of a class 1 contained use, subsequent class 1 contained use may proceed without further notification. Users of GMMs in class 1 contained uses shall be required to keep a record of each assessment, which shall be made available to the competent authority on request.

If the premises have been the subject of a previous notification to carry out class 2 or a higher class of contained uses and any associated consent requirements have been satisfied, the class 2 contained use may proceed immediately following the new notification. However, the applicant may himself request from the competent authority a decision on the grant of a formal

authorization. The decision must be made within a maximum of 45 days from the notification.

If the premises have not been the subject of a previous notification to carry out class 2 or a higher class of contained uses, the class 2 contained use may, in the absence of any indication to the contrary from the competent authority, proceed 45 days after submission of the notification, or earlier with the agreement of the competent authority.

A class 3 or higher class of contained use may not proceed without the prior consent of the competent authority, which shall communicate its decision in writing:

- ▶ At the latest, 45 days after submission of the new notification, in the case of premises which have been the subject of a previous notification to carry out class 3 or a higher class of contained uses and where any associated consent requirements have been satisfied for the

same or a higher class than the contained use with which it is intended to proceed

- ▶ At the latest, 90 days after submission of the notification in other cases

The Annexes to the Directive detail the criteria for assessing the risks of GMMs to health and the environment, as well as the protective measures for each of the four levels of containment.

If they so wish, Member States may provide for groups or the public to be consulted on any aspect of proposed contained use.

Before a contained use commences, Member States shall ensure that:

- ▶ An emergency plan is drawn up in order to react effectively in the case of an accident
- ▶ Persons at risk of being affected by an accident are informed of all aspects related to their safety

Key terms of the Act²²

Genetically modified micro-organism: a micro-organism in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination; within the terms of this definition:

- ▶ Genetic modification occurs at least through the use of the techniques listed in Annex I, Part A.
- ▶ The techniques listed in Annex I, Part B, are not considered to result in genetic modification.

Contained use: any activity in which micro-organisms are genetically modified or in which such GMMs are cultured, stored, transported, destroyed, disposed of or used in any other way, and for which specific containment measures are used to limit their contact with, and to provide a high level of safety for, the general population and the environment.

Accident: any incident involving a significant and unintended release of GMMs in the course of their contained use which could present an immediate or delayed hazard to human health or the environment.

²² Directive 2009/41/EC; Entered into force on 10.06.2009; published in Official Journal OJ L 125 of 21.5.2009

If an accident occurs, the user should immediately inform the competent authority and communicate the information necessary for assessing the impact of that accident and for taking the appropriate action. The Member State shall also inform the Commission and any Member State that may be affected by the accident.

The Commission shall create a register of accidents including an analysis of the causes of the accidents, the experience gained and measures taken to avoid similar accidents.

The Commission shall be assisted by a Committee, which is to rule on matters related to the application of the Directive and adapting it in light of technical progress.

Context

This Directive replaces and repeals Directive 90/219/EEC. It is a formal amendment aimed at bringing together the original Directive and its successive amendments into a single act, without any changes to the fundamental provisions nor any new transposition into national law being made.

Finally, this Directive lays down the minimal standards applicable to the contained use of GMMs. Member States are permitted to take more stringent measures. They may also extend the scope of the Directive to contained uses involving genetically modified plants, animals or fish.



Part A:

The establishment of a company:
a country-by-country overview of start-up considerations

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Sweden	61
Switzerland	65
The United Kingdom	69

	Rate	Use of losses	R&D tax credits	Patent/ innovation box	Intellectual property regime	Capital gains tax (CGT)	Other incentives	Incentives - grants/finance support
Austria	25%	Yes - capped at 75% of income	10% to a cap of €100,000 (cap to rise to €1m)				6% and 20% training expenses	€200,000 non refundable and €1m loan
Belgium	33% (lower rate 24.25% to 34.5% up to €322,550)	Yes	13.5% and 20.5%	Yes - 80% of gross income, maximum effective tax rate 6.8%		CGT rollover relief available in certain cases	Notional Interest Deduction which allows a tax-free return on qualifying equity	
Denmark	25%	Restrictions on carryforward - 60% to DKK1m	Yes - can receive refund of DKK 1.25m			Possible introduction of exemption where 10% equity held for 3 years		Public funding DKK750,000 (€100,000)
France	33.33%	Yes - limit €1m, plus 60% above this limit	30%		15% rate - amortization and financing cost allowed	Young Innovation Enterprise (YIE) - CGT exemption		
Germany	Effective rate 15.825% with municipal (7% - 18%)	Yes - limit €1m, plus 60% above this limit	No					National Research Strategy and Health Research Framework
Hungary	19% and 10% on first €1.7m	Yes - up to 50% of tax base	Yes - restricted deductions up to 50%		50% dispensation for royalty income	Yes - CGT - on certain shares		VIP cash grant €10m/EU investment cash grant €3.4m
Ireland	12.5% and 25% (passive)	Yes - full relief	Yes - 25% (effective deduction 37.5%)		Deduction for broadly defined IP		Three-year exemption from corporation tax for start-ups	Enterprise Ireland €650,000
Italy	31.4%	Yes - up to 80% of tax base	Yes - 2011 and 2012, on 90% of investment 2008 and 2010 base year			Investor relief from CGT where proceeds rolled over into new investment	3% notional return on equity available as a deduction	
The Netherlands	25% and 20% on first €200,000		Available in limited situations and proposal to amend	Effective tax rate of 5%		CGT exemption or rollover available		International innovation - maximum grant €750,000
Norway	28%	Yes - carry forward indefinitely	Yes - 18% or 20% - maximum tax credit NOK2.2m			No CGT for non-resident		Innovation Norway
Poland	19%		Yes - 20% with cap of €200,000				Exemption from tax in special economic zone	Maximum cash grant available PLN4m
Portugal	25%	Yes - carry forward for 4 years	32.5% on expenses, capped €1.5m and 20% in investment, cap €5m				Reduced rate 5%/10%/15% in disadvantage areas	National Strategic Reference Framework (NSRF) - for example, incentive of 75% attainable on global investment
Spain	30% and 25% on first €120,202	Yes - for a period of 18 years	Yes - general rate 25% (42% can be achieved)	50% of income exempt, capped at 6 times cost of the asset				Proyectos de investigacion y desarrollo (PID) - zero interest rate with budget of at least €240,000
Sweden	26.30%	Yes - carry forward indefinitely and available in group	No				Corporate/lower rate 20% for individual "close company"	Security-free loan SEK250,000
Switzerland	12%-25%	Yes - carry forward 7 years	Capitalised expenditure - write off or amortize	Canton of Nidwalden - effective rate of 8.8%			Tax holiday, 10 years - canton	Swiss National Science Foundation supports for 7,200 researchers annually
United Kingdom	25% (20% on first £300,000)	Yes - carry forward full relief	Yes - small and medium-sized enterprises (SME), 200% of qualifying expenditure	10% rate		Entrepreneurs' Relief - 10% rate for lifetime gains up to £10m	Substantial shareholding exemption for companies	www.businesslink.gov.uk/finance

Austria

The entrepreneurial culture

The federal and regional governments of Austria provide a variety of financing for early-stage companies and start-ups in biotechnology. This is complemented by other measures (such as trade fairs, support for intellectual property and business plans).

1. Austria Wirtschaftsservice (AWS; www.awsg.at) provides financing for biotech start-ups through its promotional program Life Science Austria (LISA) which comprises financing as well as tailor-made advice and awareness measures. In the home market, LISA acts as a resource for all companies engaged in life sciences within Austria as well as companies wishing to move to the country. It also plays a part in helping new companies get started through its Preseed (€200,000 non-refundable) and Seedfinancing (€1m, refundable once profitable) grants. Every two years, it runs a life science business plan competition called Best of Biotech (BOB, www.bestofbiotech.at) as a way of fostering a culture of excellence. On the international front, LISA promotes Austria as a country known for the excellence of its life sciences. It maintains a presence at international conferences and exhibitions on life sciences. Organized through the regional life science clusters ecoplus, Health Technology Cluster, LISAVienna, human.technology.styria and Cluster Life Science Tyrol, LISA represents companies in the therapeutic, medical technology and diagnostic sectors as well as providers of enabling technologies and related service companies.
2. Forschungsförderungsgesellschaft (FFG; www.ffg.at) makes available project financing for companies conducting research and development (R&D).

Most federal states in Austria have regional funding banks, which provide additional

funding. The academic incubators in the federal states - "AplusB-Centers," www.aplusb.biz - also give advice and financing for the founders of businesses.

Other organizations, such as the investment agency, Austrian Business Agency (ABA; www.investinaustria.at), as well as the Austrian Chamber of Commerce (WKO; www.wko.at) or the Austrian Biotech Industry Association (ABI; www.biotechindustry.at) offer a variety of support for businesses. ABA-Invest in Austria, the national company for investment, provides consulting services to firms interested in setting up operations in Austria. As a government agency, it focuses on all issues relevant to selecting an appropriate location. In addition, it provides information free of charge about Austria as a business location.

Taxation

Corporate income tax

All companies resident in Austria, and foreign companies with a branch or permanent establishment in the country, are subject to corporate income tax at a rate of 25%. Taxable income is based on the profit or loss shown in financial statements, which must be adjusted in accordance with special rules set out in the tax act. Note that the regime for group taxation allows parents and subsidiaries to consolidate their taxable income in certain circumstances.

A recent comparison of the effective tax burden in Austria compiled by economic researcher and consultancy BAKBASEL and the Center for European Economic Research (ZEW) concludes that the country has a total tax burden of 22.1%.

Austria's network of double taxation treaties ensures minimal taxation at the source for dividends, interest and licensing fees. In addition, firms may claim an education

10%

Cash premium can be claimed for R&D expenses

€200,000

Maximum amount of non-refundable financial support

allowance of up to 20% or claim a 6% credit for expenditure on education.

Tax losses can be carried forward indefinitely, but losses cannot be carried back. Under a general restriction, 75% of income can be set off against losses carried forward. So, 25% of the income remains subject to tax, even if there are sufficient losses carried forward. In certain exceptions, 100% of the income can be set off against tax (e.g., gains on the sale of a business unit pre-group tax loss carryforwards at a group member level).

A change in ownership may jeopardize tax losses carried forward. Indeed, this may be true if there is a material change in ownership, management or business. The tax losses carried forward are also at risk after a reorganization if the assets or business units that generated the losses do not exist at the effective date of a reorganization.

Although, in general, shareholders are free to determine whether to finance their company with equity or loans, the tax authorities may reclassify loans granted by shareholders as equity if funds are transferred under legal or other circumstances, which typify equity contributions.

For third-party acquisitions only, interest expenses can be deducted against tax for debt financing in Austrian as well as foreign corporations.

Incentives

Companies may claim a premium (or cash equivalent) for R&D equal to 10% of certain expenses on research or experimental development. Currently, a legislative proposal has been issued that provides for a governmental expertise institution (Österreichische Forschungsförderungsgesellschaft mbH) to be addressed to decide on whether certain expenses qualify for a premium. The R&D must be conducted by an Austrian

company or the local arm of a foreign one permanently established in Austria. The R&D premium may also be claimed for contractual research conducted by third parties (Auftragsforschung). In such cases, however, the qualifying expenses are capped at €100,000. Based on the current legislative proposal, this cap shall be raised to €1m. Furthermore, the third party must be registered in the European Union or European Economic Area, while the R&D must be its main business. An R&D premium cannot be claimed if the third party is under the control of the principal or if the companies belong to a tax group.

Similarly, a premium of 6% can be claimed for training expenses. Instead of the premium, the company can deduct an additional, fictitious expense of 20% of the training expenses in its tax return. Annual fees for pending patents are levied only from the 6th to the 20th year.

Landscape for investors

i. Tax groups

Companies are allowed to establish a tax group, so that a parent company and its subsidiaries can consolidate their income. The group's parent requires a majority of capital and voting rights in its subsidiaries from the beginning of the subsidiary's fiscal year. With a shareholding exceeding 50%, the parent company can claim 100% of the taxable profit or loss of the domestic group member, irrespective of the percentage of the shareholding. If a company leaves a tax group before the end of a three-year period, the whole period is rolled up and the entities are taxed on a stand-alone basis (i.e., profits and losses are reallocated to the individual member of the group).

Available pre-group tax loss carryforwards can be fully offset against available profits

at the level of the individual member. The parent's loss carryforwards, as well as those suffered within the tax group, are restricted by the rules on minimum taxation.

If an Austrian corporation acquires shares in an Austrian operating company from a third party and subsequently enters into a tax group, the (negative or positive) goodwill is amortized for tax purposes at the level of the buyer over 15 years. The goodwill is determined as the difference between the purchase price and equity of the target company, reduced by hidden reserves in non-depreciable assets. The goodwill is further capped at 50% of the purchase price.

ii. National dividend exemption/ international participation exemption

Dividends received by an Austrian company from another such firm are exempt from corporate income tax (and no minimum holding is required). Capital gains derived from the sale of shares in Austrian companies are treated as ordinary income and so are subject to corporate income tax.

An Austrian company is entitled to an international participation exemption (for dividends and capital gains) if, for more than a year, it holds at least 10% of the share capital of a foreign corporation that is comparable to an Austrian corporation. A reduction in the value of an international participation and capital losses is not tax deductible, but an Austrian company can opt for such tax deductibility. Capital gains are tax exempt under the international participation exemption; if an option was exercised, capital gains are subject to corporate income tax.

Under the anti-abuse rule, the international participation exemption does not apply if (i) the subsidiary earns primarily specified types of passive income, i.e., interest, income from

€1m

Maximum AWS start up loan

leasing property other than land and buildings and capital gains, and (ii) the subsidiary is not subject to income tax at an effective rate of more than 15% in its home country.

iii. Advance ruling

Since 2011, it has been possible to obtain binding information from the tax authorities on actions that have yet to be realized (i.e., an advanced ruling). Based on an application filed by the taxpayer, the tax authorities issue an assessment related to the specific case. The authorities are then bound to this legal opinion in future. The system is limited to certain issues, i.e., reorganizations, tax grouping and transfer pricing.

Landscape for entrepreneurs

Austria's rates for individual income tax for 2010 are progressive and vary between 0% and 50%.

Finance

Austria Wirtschaftsservice (AWS)

Focusing on start-up ideas in biotechnology and medical devices, AWS provides financial support with its funding measures "PreSeed LISA" and "LISA Seedfinancing." PreSeed LISA (www.preseed.at) provides funding for the phase before a life science company is set up. Costs related to the scientific implementation and the economic application of a project can be funded. The maximum amount of this non-refundable financial support is €200,000.

The setting-up of an innovative and internationally competitive high-tech company needs a lot of know-how, courage and capital. LISA Seedfinancing (www.seedfinancing.at) supports the start-up phase of high-tech companies with up to €1m, combined with tailored advice and support.

Once the company is making profit or is sold, financial support must be refunded. Customary securities usually needed for bank loans are not necessary. However, the company must be partly and adequately funded through private capital.

With temporary management (www.awsg.at/maz) AWS supports start-up high-tech companies, which are already funded through the seed program, to overcome critical competence gaps. With up to €50,000 or a maximum of 50% of the costs, external advice in the areas of finances, sales or technology can be funded. The this support measure usually lasts six to nine months.

Later on during a company's life, there are a number of loans and guarantees available through outlets such as Forschungsförderungsgesellschaft: Basisprogramme (which may provide up to €1m per year). Regional agencies and the academic incubators AplusB-Centers may also step in to help.

Availability of capital

Biotech companies in Austria are financed to a large extent by venture capitalists mainly from France, Germany, the Netherlands and the UK. In addition, AWS offers with i2 - the business angels exchange - the only nationwide cooperation exchange between companies looking for equity and business angels. AWS performs a pre-selection on behalf of the business angels based on personal, technical and economic criteria, while companies looking for equity receive access to an exclusive circle of business angels. Through this program, private investors provide both fresh equity and valuable business know-how. In 2011, AWS initiated a second round of the Venture Capital Initiative, providing €5m in risk capital for start-ups through venture funds active in Austria.

Regulatory environment and incentives

Regarding patents, the Directive on Biotechnological Inventions has been implemented without national amendments. The London Agreement has not been implemented.

Market access regarding chemicals is based on the REACH System. Regarding reimbursement of Pharmaceuticals, please refer to www.pharmaconsulting.at. Marketing of GMO is partly restricted and does not follow EU rules. Cultivation of GMO crops is hampered by a strict liability scheme and by public opinion.

Structuring for the future

A common structure scheme is to establish an Austrian holding company for the acquisition of an Austrian target company. In the case of a third-party acquisition, related interest expense would be deductible at holding level. If the holding and target company enter into a tax group, a consolidation of taxable profits and losses is possible (as regards foreign group members, however, only aliquot losses can be considered). Additionally, if the operating Austrian entity was acquired from a third party, capitalized goodwill has to be amortized at group parent level over 15 years.

Dividends distributed from the target to the acquisition vehicle are tax exempt under the national dividend exemption. At both levels, dividends and capital gains from foreign participations may qualify for the international participation exemption. Dividends distributed from the acquisition vehicle to its foreign shareholder(s) may benefit from Austria's excellent treaty network.

Belgium

The entrepreneurial culture

Belgium is considered by many to be a prime location for business. Situated in the center of Europe, some 60% of the European Union's buying power is concentrated within a 500-kilometer radius of the country.

Not only does Belgium have the densest network of road and rail in the world, its waterways link Antwerp, Europe's second-largest sea port, to industrial clusters across the rest of the country and beyond. As well as being home to the European Union, Brussels is headquarters to NATO and many other European and international organizations.

Belgium has no fewer than 16 universities as well as world-class centers of innovation and research. It is no surprise therefore that it was voted the best country within the Organization of Economic Cooperation and Development (OECD) for biotechnology in the organization's Science, Technology and Industry Outlook for 2008. The country was also placed sixth in the Ernst & Young European Investment Monitor 2011.

Business and the academic world also have a tradition of working together. Two examples are WB and Welbio. WB, which receives nearly €75m a year in funding, brings together four of the five Dutch-speaking universities as a point of contact for research in Flanders. Welbio, on the other hand, combines three Walloon academies training scientists and helping to speed up the pace of research. As a result, spending on R&D as a measure of employment is high in relation to the country's size. It is fourth highest in the world, according to the OECD, in terms of spending per firm on research into biotechnology and the third highest within Europe for research per capita in business.

Moreover, Belgium's federal government provides incentives to foster R&D and innovation. Various organizations provide advice and guidance to those wanting to start (or to expand) their activities in Belgium.

Foreign companies considering setting up there may contact the Service for Direct Investments. Contact is possible via the following websites:

- ▶ ib.fgov.be
- ▶ www.investinlanders.be
- ▶ www.investinwallonia.be
- ▶ www.investinbrussels.com

There are also various industry federations. Essencia, an umbrella organization, represents the field of chemicals and life sciences. Pharma.be, or the Belgian Pharmaceutical Industry Association, represents the country's pharmaceutical interests. Bio.be is the Belgian association for bioindustries. It aims to develop a climate for companies to expand their businesses, make new investments and have access to markets. In doing so, Bio.be enables the various regions to attract investments into biotechnology. Bio.be is a member of EuropaBio.

At a regional level, there are bodies such as FlandersBio and Biowin. The former, with 240 or so members, specializes in life sciences and is the largest organization of its kind in Europe. Biowin is a cluster based in Wallonia. It supports activities such as training and development.

Taxation¹

Corporate income tax

Companies resident in Belgium are subject to tax on their worldwide income. Non-resident companies are subject to tax on income sourced from Belgium only. A company is resident in Belgium if its central management or registered address is located in the country.

The normal rate of corporate income tax is 33% for both resident companies and branches of overseas ones. Income below €322,550 is taxed at rates ranging from 24.25% to 34.5%.

Belgian companies and foreign firms with a permanent establishment in the country can benefit from a tax deduction equal to a percentage (3.435% for the tax year 2012) of their qualifying equity (or risk capital). The deduction is not reflected in the financial accounts. Risk capital equals total equity, including retained earnings as reported in the non-consolidated closing balance sheet of the financial year preceding the relevant tax year. This excludes items such as the net tax value of the company's own shares and shares held in other companies that are accounted for as fixed assets.

An advance ruling is a unilateral written decision by the Belgian tax authorities at the request of a (potential) taxpayer about the application of the fiscal law in a specific situation that has yet to occur. The purpose of such a ruling is to provide certainty to the taxpayer. A ruling typically takes three months. This period may be extended in complex situations. A ruling may be valid for a period of five years.

A meeting can be scheduled with the tax authorities before an application is filed. In principle, a verbal indication may be obtained during the meeting. At this point a taxpayer can still choose whether to file a formal application.

The net amount of capital gains (after deducting administrative expenses) is exempt from tax if the dividends on such shares qualify for the Dividend Received Deduction. To qualify for the capital gains exemption, only the taxation test needs to be satisfied. Neither a minimum holding period nor a minimum share ownership is required.

In Belgium, all other capital gains are taxed at the ordinary rate. If the proceeds are reinvested in depreciable fixed assets within three years (or five years subject to certain conditions) and if certain other conditions are met, taxation of the capital gains is deferred over the period of the newly acquired assets.

Under the Dividend Received Deduction, 95% of the dividends received by a qualifying Belgian company or the Belgian branch of a foreign one are exempt from tax. The remaining 5% is subject to the standard rate of corporate income tax. However, it can be partly or fully eliminated by deductible expenses, such as interest expenses incurred upon the acquisition of the underlying shares.

The exemption applies only if a minimum participation test and a taxation test are satisfied. To satisfy such tests, the recipient must own a minimum of 10% or a participation with an investment value of at least €2.5m. Furthermore, the shares must be held for at least one year. The subject-to-tax test contains a number of clauses that look at the regime of the direct subsidiary, its income, the income from its branches and those of its subsidiaries.

The normal rates of withholding tax for dividends paid by Belgian companies are 15% and 25%.

Exemptions or reduced rates are available under the country's tax treaties or domestic legislation. Withholding tax is not imposed on dividends distributed to a qualified treaty parent (i.e., one which holds, or commits itself to hold, a shareholding of at least 10%

in a Belgian company for an uninterrupted period of 12 months). A withholding tax of 10% on dividends is imposed if a company is liquidated or the shares are redeemed.

In principle, depreciation rates are determined on the useful economic life of the assets. The following straight-line rates are generally accepted:

- ▶ Office buildings: 3%
- ▶ Industrial buildings: 5%
- ▶ Chemical plants: 8% to 12.5%
- ▶ Machinery and equipment: 10% to 20%
- ▶ Office furniture and equipments: 10% to 15%

The declining-balance method and rules of accelerated depreciation are also allowed in certain circumstances. Income derived from a permanent establishment abroad may be exempt under the provisions of a tax treaty. A Belgian company that receives interest income from foreign sources and royalties subject to a foreign withholding tax can claim a credit in Belgium if certain conditions are met.

Tax losses can be carried forward indefinitely if a company remains a going concern. Of particular relevance to those in life sciences and biotechnology is the fact that all R&D expenses in principle can be deducted fully against tax. However, prior losses cannot be recaptured. Belgium has no rules on tax consolidation or grouping. There is also no carryback available.

Belgium has no strict rules on thin capitalization. A debt to equity ratio of 7:1 applies to payments made to a foreign entity which is either not subject to tax or which is subject to a regime which is significantly more advantageous than Belgium's (unless the taxpayer is able to demonstrate that the payments are related to effective and genuine transactions not exceeding market rates).

¹ This information may change as a result of the 2012 Belgian budget measures

6.8%

Maximum effective tax rate under PID

A debt-to-equity ratio of 1:1 applies to payments to non-resident directors. Interest borne in order to acquire shares is generally considered a tax-deductible expense.

Tax incentives

i. Patent Income Deduction (or Patent Box)

Under the Patent Income Deduction (PID), 80% of the gross income of a qualifying patent can be deducted from the net taxable basis of a Belgian company or the Belgian branch of a foreign one.

This leads to a maximum effective tax rate of 6.8% or lower since the PID applies to the gross income and other tax attributes which may further reduce the taxable income.

To qualify, intellectual property (IP) must be developed by the companies themselves or to those acquired and licensed by them. The same applies to protective certificates and connected know-how. Acquired or licensed patents must be improved in an "R&D branch" in Belgium or abroad.

Although the PID applies to patents not commercialized before 1 January 2007, it may apply to those granted or acquired before then. This is especially true of patents in life sciences.

The types of income to which it may apply include that from licensing patents to related or unrelated parties and royalties (i.e., royalty income). Also covered is income from patents embedded in the sales price of a product or service. This is determined by comparing it to a situation where a royalty would be charged to an unrelated party to manufacture the product or to deliver the service.

Capital gains are excluded from the regime but advance planning can limit taxation when exiting the investment. In such cases, the PID applies to the gross income related to the

patent. With acquired or licensed patents, the gross income is adjusted for depreciation or royalties paid (i.e., the depreciation or royalties paid are deducted from the gross income from the patent before the PID is applied).

In addition, qualifying income from patents is not reduced by interest or other expenses. If the deduction for 80% of (adjusted) gross income from the patent exceeds the total net income, the excess can be used to offset other taxable income. It is also important to note that there is no cap or minimum threshold. Nor can development costs which have previously been deducted be recaptured.

ii. Tax credit or deductions for R&D

A tax credit or deduction for R&D (i.e., a refundable credit or a deduction from taxable income) is available for qualifying capitalized assets under Belgian's generally accepted accounting principles (GAAP). Assets which qualify include those used in Belgium to promote the development of new products and forward-looking technologies which do not harm the environment, or those whose purpose is to reduce damage to the environment (green investments). New patents also qualify.

The deduction can be calculated as a percentage of the acquisition value (a one-shot deduction) or as a percentage of the annual amortizations (which spreads the deduction). For the tax year 2012, the rates amount to 13.5% (for one-shot deductions) and 20.5% (for those which are spread). Certain investments in energy saving may not qualify for the spread deduction.

Unused tax credits can be carried forward for five years, and will effectively be reimbursed if not used by the end of the five-year period. Unused investment deductions may be carried forward indefinitely, but with certain limitations.

Exemptions from wage withholding tax for qualified personnel (i.e., researchers) are also available. This incentive lowers the cost of a salary for the employer and is neutral for the employee concerned.

There is also a special tax regime for foreign executives and researchers who are temporarily employed in Belgium. Under this regime, such people are taxed only on income related to professional activities performed in Belgium. Moreover, certain allowances which relate to the temporary nature of their employment are exempt.

Tax landscape for investors

As mentioned above, there are incentives for those investing in Belgium. These include the Notional Interest Deduction which allows a tax-free return on qualifying equity. Belgium also boasts such measures as the Patent Income Deduction (PID), a deduction for investment in R&D and other credits.

i. Principal companies

A low effective rate of tax can also be achieved in Belgium by applying a combination of the following: patent income deductions; notional interest deductions; transfer pricing based rulings; the use of a mixed holding company; and what is known as the Belgian branch principal.

The transfer pricing based approach is based on a transfer pricing provision, which introduced the internationally accepted arm's length standard to Belgium's tax legislation. It provides a downward revision of taxable profits to the extent that these can be considered "excess profits" (i.e., those which would not be realized by a stand-alone entity).

The anticipated benefits are a low effective tax rate and certainty based on a ruling.

ii. Holding companies

Belgium has a long history of attracting holding companies. This makes it a classic jurisdiction for such companies in Europe, not least because of its extensive network of tax treaties (amounting to 90 in all) as well as other attributes. There are no capital duties, stamp duties or taxes on net worth.

Under Belgium's regime of participation exemption, qualifying capital gains are 100% exempt. There is no minimum holding period, nor a participation threshold. Subject to certain tests, qualifying dividends are also 95% deductible. Belgium has no domestic withholding tax on dividends paid to qualifying parent companies in any of the 90 countries with which the country has a tax treaty.

There is no legislation concerning what are known as controlled foreign corporations (i.e., those owned and controlled from outside the country but registered to do business in Belgium). Companies may adopt a foreign currency for accounting purposes. They are also eligible for check-the-box elections, a simplified system for declaring tax in the US. In Belgium, too, interest paid on loans to finance the acquisition of shares is also tax deductible (subject to certain requirements). There are no rules on thin capitalization. And there are many exemptions from withholding tax for both domestic and overseas companies.

Finance

Various subsidies are available at a regional level in Belgium to stimulate scientific research. Such subsidies may be granted as direct financial support or through subordinated loans with favorable terms and conditions. The grants or loans depend on several criteria (e.g., the size of the company and the activity for which the support is requested). The amount of support may also depend on the region where the work is to be done.

Support may be requested for everything from feasibility studies for innovative ideas to the recruitment of researchers, research related to the application of an idea or the field of development. Also covered may be efforts to evaluate new processes and products, tests involving universities and research institutions, research in pursuit of new processes, products or services, or to improve existing ones.

In many of the regions, support for small and medium-sized enterprises receives priority. In Flanders, for instance, this includes help for a start-up to the point where it files a patent. As well as supporting individual firms, bodies such as IWT (Agency for Innovation through Science and Technology) provide a focal point for collective research in areas highlighted by industry groups such as FlandersBio or CNBIOS.

In the south of Belgium, companies can receive subsidies of up to 30% and 80% respectively of the total amount invested. Biowin offers subsidies of up to 100% of the cost of research by universities, up to 70% for small companies and up to half for larger ones.

Availability of capital

According to the European Union's Innovation Scoreboard for 2010, not only is 28% of venture capital invested in Belgium deployed in life sciences; the average amount invested is also the largest anywhere in the European Union. The Belgium Government supplies seed capital for qualifying ventures through the Flemish Innovation fund, managed by PMV. The latter also runs a new Transformation, Innovation and Acceleration fund (TINA), which was approved by the Flemish Government in 2010. In addition, the Government holds a 27% interest in GIMV, an investment company with shares listed on Euronext Brussels. GIMV, which specializes in private equity and venture capital, focuses mainly on Europe and is an important investor in life sciences.

Regulatory environment and incentives

Biotech for health care

Compared with other countries in the EU and the US, the cost of clinical trials in Belgium is lower, although competition with Eastern Europe and Asia is increasing. About 85% of the clinical studies in Belgium are initiated by pharmaceutical companies; the remainder by academics. Belgium's Federal Agency for Medicines and Health Products (FAMHP) is known for its effective and speedy procedures. Applications for medicinal products involving biotechnology (including Advanced Therapy Medicinal Products) follow a centralized route and are covered by the relevant EU directives and regulations. In addition, the Directive on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and the distribution of human tissues and cells, as well as the Belgian law of 2008 (on the procurement and use of human biological material for medical applications and scientific research) which implements this Directive, define the framework for operations performed with human cells and tissues.

It is the role of Bio.be in technology and pharma.be in biopharmaceuticals jointly to propose changes to the country's federal rules and laws in science. Bio.be and pharma.be consult their members on a definition of what needs to change in order to sustain the pace of innovation. The outcome then influences negotiations with the relevant minister to change the existing legislation.

Biotech for industrial use

Belgium is adopting and adapting European legislation to improve its sustainability. Yet some responsibilities are regional, not federal.

For those generating electricity, Belgium has set up a scheme of green certificates and has guaranteed minimum prices to support the development of energy generated from renewable sources, including biogas made from waste. To promote biofuels including bio-ethanol in transport, the federal authority has set up a scheme of biofuel quotas which are exempt from tax. It has also introduced the mandatory use of biofuels in mixes of fuel. This has resulted in the development of a viable industry producing over 500,000m³ of bioethanol.

Biotech in agriculture

Agriculture is a matter for Belgium's regions. In Flanders, universities do the research and so may succeed in optimizing the genetics of plants. As a result, the regional government there is receptive to the use of biotechnology in agriculture. Wallonia is different. It is opposed to such things. Result: the rules in each region are different.

Belgium ranks second in the world (after the US) in the strength of IP relating to biotechnology, according to research by the Scientific American. Unsurprisingly, therefore, Belgium has an effective system for enforcing such rights. It has sophisticated procedures to implement the IP Enforcement Directive (Dir. 2004/48/EC).

Structuring for the future

If an idea proves successful, Belgium is also a good place in which to plan for the future. First, prepare a sound business case and ensure that the company has a presence in the country. Then design the business carefully including how you intend to distribute the product or service. Make use of the available tax incentives such as the NID, PID and the "excess profit" incentive. Also consider whether other businesses or processes could be transferred to Belgium in order to create extra leverage or synergies.

Tax-efficient structuring

Later on, too, there are ways to structure an investment so that any gains can be protected if it is sold. As well as exemptions in certain circumstances from capital gains, companies may consider a usufruct structure enabling them to profit from the rights of others. If a parent company is sold, the remaining value (if any) of the IP may be low and so limit the tax due on exit.

Belgium also provides incentives to establish centralized structures for R&D. IP may also be retained within holding companies, in part by splitting the economic and legal ownership of the IP (in other words, the PID may apply to more than one economic owner or licensee). Trademarks and other IP rights which do not qualify for a PID can also be held in different ways.

Denmark

The entrepreneurial culture

In Denmark, start-up companies receive public funding of up to DKK750,000 (approx. €100,000) if certain conditions are met. But the amount is not considered sufficiently attractive for companies in biotechnology. The association of biotechnology companies in Denmark, Dansk Biotek, is focusing much on the general conditions of the industry in Denmark and is keenly engaged in the debate around the development of the industry. Many of the Danish biotech entrepreneurs are engaged in the association and in the debate on how to improve conditions for the industry constantly. The biotechnology industry in Denmark has benefited from having a number of pharmaceutical companies headquartered in Denmark, such as Novo Nordisk, Leo Pharma and Lundbeck, securing a base of expertise and knowledge within the industry.

Taxation

Corporate tax

In general, the amount of tax paid by a biotech company follows the usual rules under tax law. However, there are exceptions for research and development (R&D), which apply to different European projects if certain criteria are met and if the projects were approved before the end of 1989 and 1995 respectively. However, a draft bill limiting the utilization of tax loss carryforwards has been published. If enacted in the current wording, taxable income exceeding DKK1m may only be reduced by 60% by utilization of tax loss carryforwards.

Under Danish law, losses may be carried forward indefinitely, but not backwards. Losses may not be offset against interest and

other capital income, net of interest paid, if more than 50% of the shares in the company have changed ownership since the beginning of the year in which the loss was incurred. In addition, tax losses are lost entirely if a change of ownership occurs at a time when the company is without business activities.

Furthermore, in Denmark, there are three rules limiting interest. All three should be examined since they focus on different bases unless a company's net expenses are below DKK21.3m. In such circumstances, they would always be deductible unless the company is deemed to be thinly capitalized (i.e., has more debt than equity). In such circumstances, the rules restrict interest and capital gains on controlled debt where the interest ceiling and the limit on earnings before interest and taxation (EBIT) limit a company's net financial expenses. So, first make the calculation for thin capitalization because, if it applies, interest is excluded from the net financial expenses - which are limited in relation to the interest ceiling and the rule covering EBIT.

For thinly capitalized companies, a debt-to-equity ratio of 4:1 must be observed. The ratio is calculated at each year-end and is generally based on fair market values (not on book values). The equity is made up of the assets minus the liabilities. Controlled debt is debt that is provided by group entities or external debt secured by such entities.

For the interest ceiling, only net financial expenses not exceeding the taxable value of the company's assets, multiplied by a fixed interest rate of 3.5% for the income year starting in 2012, are deductible. However, an amount of DKK21.3m can be deducted, subject, of course, to the rules on thin capitalization.

Tax credit of

DKK1.25m

Funding of up to

DKK750,000

Under the EBIT rule, a company's taxable income can be reduced by 80% as a consequence of net financial expenses. However, an amount of DKK21.3m is deductible (subject again to the rules on thin capitalization and the interest ceiling).

Tax incentives

In general, Denmark has not had incentives open to biotech companies. The country allows for 100% deduction of expenses to R&D activities in the year they are incurred, or for them to be divided between this year and the subsequent four years. However, as of the income year 2012, tax credits have been introduced. The new rules regarding tax credit provide that companies can choose to receive a payment of negative tax of 25% of the tax losses for R&D cost. However, a company can receive a maximum DKK1.25m which represents 25% of R&D cost of DKK5m annually. Please note that, for jointly taxed entities, the tax credits are applied at joint-taxation level.

Tax landscape for investors

As noted above, there are no specific concessions on tax for those investing in biotech in Denmark. However, structures in which at least 10% of the shares are owned by corporate investors are commonly used for holding investments. This is because, when sold, such shares are exempt from tax (provided no companies are considered to be intermediary holding companies according to

special anti-avoidance rules). Furthermore, dividends paid to shareholders attract no tax for shareholders with more than 10% of the capital.

Tax landscape for entrepreneurs

In general, entrepreneurs receive no concessions under Denmark's tax rules. However, new rules may be introduced for shareholdings of less than 10% in new legislation under the country's Capital Gains Tax Act (which has yet to be enacted).

If they come into force, the new rules will exempt from tax capital gains entrepreneurs' shares held for at least three years. There are, of course, a number of tests to determine if such equity is classified as entrepreneurial.

Finance

Availability of capital

In Denmark, funding for biotech companies is tight. Investors are cautious and averse to risk. This, in turn, implies that such companies have difficulty funding R&D and other development at an early stage.

Structuring for the future

Protection for intellectual property (IP) within Denmark is largely the same as in other parts of the EU. Nor, so far, does the country boast a tax regime that favors IP (such as the system of Patent Boxes in the Netherlands).

France

The entrepreneurial culture

There are already more than 23,000 foreign companies doing business in France. In 2010, there were almost 400 biotechnology businesses in the country, together employing around 6,000 people, over half of whom work in research and development (R&D).

All told, there are 71 clusters of innovation in France, including partnerships between private businesses, public sector research laboratories, universities and academic institutes. Of these, eight focus on biotechnology or health. The clusters are what are known as “business ecosystems,” which already boast around 60 foreign businesses among their members.

Between 2006 and 2008, the clusters received €1.5b in funding from the state and are set to receive a similar amount to support their R&D between 2009 and 2011, thanks mainly to a special fund which is also open to foreign companies. Also, in line with last year’s “Etats Generaux de l’Industrie,” an industry conference, France’s already attractive regime on intellectual property (IP) was enhanced and extended.

The Invest in France Agency (IFA), which was created in 2001, is a public-private body responsible for promoting, prospecting and facilitating international investment in France. The agency works in partnership with regional development agencies to offer international investors opportunities and customized services. More details are available from www.invest-in-france.org.

Taxation

Corporate tax

The standard rate of corporate income tax in France is 33.33%. A social security surtax of 3.3% is assessed on the portion exceeding

€763,000, resulting in a marginal effective rate of 34.43%. Furthermore, for financial years ending between 31 December 2011 and 30 December 2013, companies with a turnover exceeding €250m will be subject to a 5% surcharge on their corporate income tax due. Therefore, for such taxpayers, the maximum standard rate is 36.1%.

There is a reduced rate of 15% (15.5% with the 3.3% social security surcharge and even 16.2% for companies with a turnover exceeding €250m in financial years that end between 31 December 2011 and 30 December 2013) applied to incomes or gains derived from the licensing or sale of patents, patentable rights and related know-how, as well as, for fiscal years beginning on or after 1 January 2011, for improvements to patents or patentable rights, provided that the IP rights qualify as fixed assets.

As a matter of principle, royalty payments are deductible in full as expenses. However, depending on the terms of the agreement that grants to the licensee the right to exploit some patents’ rights and know-how, royalty payments could be treated as the acquisition cost of an intangible asset and thus as capital expenditure, which may be eligible for depreciation and amortization.

The tax treatment of non-refundable signing fees and up-front fees, and milestones payments, mainly depend on whether the related outcome is uncertain. Depending on the circumstances, they can be treated as either deductible expenses or capital expenditure, possibly eligible for amortization and depreciation.

Intangible rights that benefit from a limited legal protection, or whose exploitation will terminate at a specific date, may be amortized for tax purposes. Under the parent-subsidiary regime, dividends are 95% exempt from corporate income tax.

400

Biotechnology companies
operating in France

Losses can be carried forward indefinitely, but can only be used during the following years within an annual limit of €1m, plus 60% of the profit of the year exceeding this limit. Losses can also be carried back against the profits of the previous fiscal year, but only up to €1m.

Under France's rules on thin capitalization, the deductibility of interest paid to related parties is limited when the debt-to-equity ratio exceeds 1.5:1. This is also the case when the interest expenses paid to related parties exceed 25% of adjusted earnings before interest, tax, depreciation and amortization or the interest received from related parties.

Dividends are subject to a domestic withholding tax of 30% (with exemptions within the EU under certain conditions). Royalties are subject to a domestic rate of 33.33% (with exemptions within the EU under limited conditions). There is no withholding tax on interest (unless it is to an uncooperative country). Rates for withholding tax may be reduced under tax treaties. For groups of companies, the rules on tax consolidation allow a French parent company to be liable for the corporate income tax for the entire consolidated group.

Indirect taxation

In France, the standard rate of VAT is 19.6%. However, various reduced rates apply to certain products or services. For instance, drugs are subject to reduced rates of either 2.1% or 7%.

Incentives

In France, there are no specific tax incentives exclusively tailored to biotechnology companies, but they are eligible for incentives offered to other companies in other industries. Biotechnology companies

generally look for one or more of the following incentives:

1) R&D tax credits

France's tax credit for R&D is the most advantageous in the world. It represents 30% (40% and 35% respectively for the first and second years) of eligible R&D expenses borne by a company in France and in other EU countries. It covers human and material resources dedicated to eligible R&D activities, subcontracted R&D, technological watch, patenting or patent protection etc. There is a cap of €2m for expenses contracted out to related parties, and a limit of three times the company's expenses.

To be eligible, the activity must (i) be part of a recognized R&D process (i.e., fundamental, applied or experimental research); and (ii) outrun general practices used in the field of application and must rely on advanced professional skills from scientists and engineers, distinct from the know-how commonly used in the profession. Consequently, companies cannot rely on the design and implementation of conventional solutions. The activity must also be commercially relevant: the simple fact that the activity is new or innovative is not enough to make it eligible for the tax credit.

The tax credit may be offset against the amount of corporate income tax due for the current financial year and to the three subsequent years. The remaining credit may be refunded after three years. Note that a ruling may be obtained from the French tax authorities in order to secure the benefit of the tax credit before R&D expenditure is borne.

2) Intellectual property

Under France's regime on IP, amortization allowances and financing costs can be

deducted at the standard rate of 33.33%. A rate of 15% applies to income derived by a French corporation from the licensing or sale of patents or patentable rights, subject to certain conditions (i.e., the character of the fixed assets and a two-year holding period for acquired IP). Investors also receive support in France. It depends on the type of investment project (i.e., whether it is a productive investment, R&D, innovation or training); the location of the project (whether, for example, it is in a priority zone for development); and on the type of company (i.e., large or an SME).

The French authorities support projects that entail investment and job creation by large companies in economically disadvantaged regions and those undergoing industrial redevelopment (according to the EU's Regional Aid Zones map). The scheme covers businesses involved in R&D, professional training for employees, job creation for defined populations, investment and the creation of jobs by SMEs in all parts of the country, as well as certain schemes to protect the environment.

State aid is available from the national government or regional and local authorities, particularly in the form of subsidies, tax exemptions and tax credits. There is a maximum limit for applicants who receive assistance from several different sources. EU law requires support to act as an incentive, so applications must be made before the project gets under way.

Tax landscape for investors

There are also benefits for investors. For eight years after their inception, small and medium-sized companies can elect to be part of the Young Innovative Enterprise (YIE) regime if (i) half of their shares are directly or indirectly held by individuals or certain types of companies in venture capital, registered

public associations or organizations, public research institutions, or another YIE; and (ii) if 15% of their total annual tax deductible expenditure goes on R&D.

The main benefit of this regime is total exemption from corporate income tax for the first three profitable years and 50% relief for the following two years up to €100,000. (Note that the exemption does not apply to certain types of income such as dividends, grants and debt forgiveness.) Companies can also claim for the immediate refund of any unused tax credits relating to R&D.

Those within the YIE also enjoy, among others, a total and uncapped exemption from social security for all employees and for legal representatives involved in R&D projects, as well as a full and uncapped exemption from local business tax for seven years (providing that a company's local authority has been consulted). Note, too, that the YIE can benefit from the tax credits on R&D.

Individuals holding shares of a Young Innovative Company can elect, before the end of the year during which they sold their shares, to benefit from a full and uncapped capital gain tax exemption if they (i) held the shares for at least three years during which the company qualified as a YIC; (ii) had the full property of the shares; or (iii) did not hold (with their families, directly or indirectly) more than 25% of the shares of the company.

Tax landscape for entrepreneurs

Expatriates employed in France benefit from one of the most advantageous tax regimes in Europe. They enjoy an exemption from tax on income earned abroad. Employees can opt for exemption from income tax on up to 50% of their total income (through an expatriation bonus plus a proportion of the remuneration received for work carried out abroad). Expatriates are exempt from wealth

tax on assets or estates held outside France for five years. There is also an exemption of 50% on income from "passive" sources, such as dividends, interests and fees, and on capital gains on equity transfers from foreign sources. And expatriates are exempt from paying retirement premiums for up to six years, granted to employees who have not previously contributed to a social security scheme within the EU.

Regulatory environment

France has a variety of legal provisions covering biotechnology. Laws regulate, among others, therapeutic products, reproductive and transplant medicine (for research on humans), genetic engineering, agriculture, the protection of the environment and food. French law also provides for an effective protection of IP rights, such as patents and trademarks, as well as copyrights and related protection rights. Biotechnology enterprises may thus seek to protect their innovations and turn their ideas into industrial property. The competent authority for registering and protecting IP rights is the National Intellectual Property Institute (www.inpi.fr).



30%

Tax credit on eligible R&D expenditure

Germany

Germany has a history of encouraging new ideas and new biotechnology companies. There are a number of agencies and initiatives - such as the BioEconomy Research and Technology Council (www.biooekonomierat.de), Go-Bio (www.go-bio.de), High-Tech Grunderfonds (www.high-tech-grunderfonds.de) and Health Research, part of Research in Germany (www.high-tech-strategie.de) - which provide support and funding for companies in the industry.

Advice is also available through the Federal Research Ministry (www.bmbf.de) and the federal Ministry of Economics (www.bmwi.de). Germany Trade and Investment (www.gtai.com) is the foreign trade and inward investment agency and provides up-to-date information to German companies seeking to expand their businesses abroad and supports companies looking to enter Germany with expert advice. This German economic development agency - cooperates closely with the funding authorities.

There are also funding programs and initiatives in the various federal states. The BioRegions of Germany - the regional initiatives for the advancement of economic application of modern biotechnology - can act as go-between and first contact.

Taxation

The German governing parties have initiated a reform of the taxation of business in Germany which was published within a working paper, *Twelve point plan*, in

February 2012. It, among others, includes some far-reaching measures affecting the current German tax grouping concept, tax loss utilization, interest expense limitations and cross-border transfer of assets. This initiative is in its very first phase and there is no draft legislation yet nor a time frame for the amendments. However, potentially any of the amendments could be introduced before the end of 2012. Potential amendments from such reform are not considered in the comments below.

Corporate tax and trade tax

Corporations, such as stock corporations (Aktiengesellschaft, or AG) and limited liability companies (Gesellschaft mit beschränkter Haftung, or GmbH), that have either their statutory seat or their place of management in Germany (resident companies), are subject to corporate income tax (Körperschaftsteuer) and trade tax (Gewerbesteuer) on their worldwide income as far as it is not covered by tax treaties. Foreign-sourced income may be tax-exempt under a German tax treaty.

Corporate income tax is levied at a rate of 15% on taxable income, regardless of whether the income is distributed or retained. A 5.5% surcharge is imposed on corporate income tax, resulting in an effective tax rate of 15.825%. Trade tax on income is imposed by the municipalities where the company has got business presence(s) to the extent that taxable income is allocable to the respective municipality. Different municipalities impose different rates generally varying between

0%

Dividend withholding tax may be reduced to zero for certain non-resident corporate shareholders

60%

Percentage of taxable income exceeding €1m that can be offset against losses

approx. 7% and 18%. For the determination of taxable income for trade tax purposes, certain adjustments are made. Primarily, these adjustments include a 25% add-back of interest on debt; a 6.25% add-back for license payments; a 5% add-back of lease payments for movable assets; and a 12.5% add-back of lease payments for immovable assets.

Tax losses may be carried forward indefinitely. Taxable income of up to €1m can be fully offset against losses carried forward from prior years. Only 60% of taxable income exceeding €1m can be offset against such losses. As a result, 40% of the excess always triggers tax (minimum taxation). This rule on minimum taxation applies to both corporate income tax and trade tax on income. For the purposes of corporate tax, but not for trade tax on income, losses can and must first be carried back into the preceding business year up to an amount of €511,500.

Tax losses expire proportionally if, within a five-year period, more than 25% of the shares of a loss-making entity are directly or indirectly transferred to one acquirer or entities related to such an acquirer or a group of acquirers pursuing the same interest. If, within the five years, more than 50% of the shares are transferred, the entire remaining loss expires. For share transfers after 31 December 2009, under a built-in gain exception, a loss carryforward survives the harmful change in ownership in an amount equal to the built-in gains of the loss company. When calculating the built-in gains, the only assets included are assets whose disposition would trigger German taxable gain in the hands of the loss entity. Under a group restructuring exemption, a transfer of shares may not be considered harmful if after a direct or indirect share transfer "the same person" still owns directly or indirectly 100% of the transferor and the transferee. For ownership changes made before

1 January 2008, different rules under the previous regime continue to apply as well. If a company with tax losses is merged into another company, its remaining tax losses generally expire and are not transferred to the surviving company under the Reorganization Tax Act.

The interest limitation rule disallows "excess net interest expense," which is defined as the excess of interest expense over interest income if such excess exceeds 30% of the taxable earnings before (net) interest, tax, depreciation and amortization (EBITDA). Unused EBITDA can be carried forward five years and excess net interest expense disallowed under the interest limitation rule can be carried forward into subsequent years for deduction. Unused carryforwards are affected by reorganizations such as business disposals, mergers or share transfers and may then fully expire.

The limitation rule does not apply if any of the following conditions are satisfied:

- ▶ The annual net interest expense is less than €3m
- ▶ The company is not a member of a consolidated group, i.e., a group of companies that can be consolidated under International Financial Reporting Standards ("group clause" - this may not apply to companies that receive loans from a direct or indirect more than 25% shareholder, a party related to such shareholder or a third party having recourse to such shareholder or related party)
- ▶ Or the equity ratio of the German subgroup is no more than 2% lower than the equity ratio for the group as a whole, as shown on the balance sheet of the preceding fiscal year (escape clause)

Incentives

There are a variety of programs available designed to fit the needs of the biotechnology industry at different stages of the investment process. Support ranges from cash incentives for investment projects to labor-related projects, as well as incentives for R&D. Germany Trade & Investment, a government agency charged with economic development, often acts as go-between.

For R&D activities in general, there are no tax incentives in Germany. Financial support for R&D is based on grants and incentives for innovative projects. Eligible costs are generally related to a specific project and include personnel costs and those for materials, subcontractors, amortization and overheads.

Tax landscape for investors

In Germany, it is generally possible for the user but not the investor to receive grants for investments. However, Germany offers numerous other incentives for investors.

Germany has a wide network of tax treaties. Most confer the right to tax a gain from a sale of the shares in a German corporation (AG or GmbH) to the state of residence of the foreign resident investor. For foreign corporate investors that are resident and hold a minimum participation in a German corporation, dividend withholding tax may be reduced to zero (compared with a domestic rate of 26.375%).

Dividend income received by a German corporate entity from its German and foreign subsidiaries is basically exempt from corporation income tax. German corporate tax law requires neither a minimum shareholding nor a minimum holding period for this participation exemption. For trade tax on income, the exemption requires a 15% minimum shareholding and is tied to some further prerequisites. Five percent of the

€8b

Funding made available to the biotechnology sector under relevant Federal Government programs

tax-exempt dividend income is treated as a non-deductible expense, while the expenses actually incurred in connection with such dividends are deductible. Consequently, only 95% of the dividend received by a corporation is effectively exempt from tax.

For individuals, different rules apply and there are no special tax incentives for individuals resident in Germany with investments in biotech companies.

Finance

Availability of capital

The National Research Strategy BioEconomy 2030 and the Health Research Framework Program, both started by the German Federal Government at the end of 2010, are also providing sustained political support for the German biotechnology sector. Funding of around €8b has been made available in the context of these initiatives.¹

Regulatory environment

Rules and regulations

To participate in R&D programs, companies must define a project with clear objectives and a fixed time line. The application should highlight the innovative character of the project and the technological risks involved.

An application for R&D funding also has to set out a plan, detailing how the results of the research will be turned into products, processes or services that generate additional turnover and/or employment in the region where the project is to take place.

The total incentives that a project may receive depends on the size of the company

(small, medium-sized or large), whether the project is conducted in cooperation with other companies or research institutes, and the type of research. Depending on the specific program and on the applicability of the products the funding quota ranges between 25% and 75% of the eligible costs. Note, too, that there are specific programs to support market access. The requirements for intellectual property can also vary.

Structuring for the future

Tax-efficient structures

If the corporate seller is resident outside Germany in a country with which Germany has a tax treaty, the right to tax such a gain is conferred in most cases to the state of residence of the investor.

Depending on the country of residence of the investor or investors, there may be ways to structure the investment so that a tax-efficient disposal can be achieved. There may be opportunities to design a tax-efficient disposal tailored to the circumstances of the investment.

The regulation of intellectual property depends on the funding in question. Generally, the terms are made clear in the approval letter of the funding authority.

Biotech is certainly one of the focal points for funding in Germany. Within the next four years, the Health Research Program is to be extended to a total of €5.5b. The Bio-economy Research and Technology Council is also to receive more support. License income from licensees resident in another state is normally taxable in Germany. R&D costs incurred are tax deductible; nor do they have to be capitalized and depreciated over time.

Hungary

The entrepreneurial culture

Hungary's Government and tax regime provide several opportunities to support new investment. There are a number of programs under the National Development Agency (www.nfu.hu), which are co-financed by the European Union.

The Nemzeti Külgazdasági Hivatal (Hungarian Investment and Trade Agency, or HITA; www.hita.hu) began operating at the beginning of 2011. Its task is to encourage foreign companies to invest in Hungary and to support foreign trade by small and medium-sized enterprises. HITA works under the direction of the Ministry for National Economy.

Taxation

Corporate tax

As a general rule, the liability for corporate income tax is 19% of the taxable base. Nevertheless, a preferential rate of 10% can be applied to the first HUF500m (€1.7m) of the taxable base.

A company's profit before tax can be modified in several ways. For example:

- ▶ Carry forward: tax losses can be carried forward from previous tax years and taken into consideration as a decreasing item in subsequent years up to 50% of the tax base in the current tax year. This means that the corporate income tax base, calculated from the pre-tax profit after taking into consideration all tax base adjustments other than the tax loss itself (e.g., R&D costs, depreciation, non-deductible costs) can be decreased by up to 50% only by applying tax losses. In other words, if a company utilizes tax losses to offset its taxable profit, it will always have to pay corporate income tax on at least 50% of its tax base.
- ▶ Royalty income: if the taxpayer collects royalties in Hungary, it may be entitled to deduct 50% of the income from pre-

tax profit when calculating the base for corporate income tax while still being able to deduct related costs, such as amortization of intellectual property. This deduction is capped at 50% of the pre-tax profit.

- ▶ Thin capitalization: if the daily average amount of debt exceeds three times the daily average of the taxpayer's equity, the interest expense on the excess debt cannot be deducted for the purposes of corporate income tax (i.e., the debt-to-equity ratio must be 3:1). Rules on thin capitalization also apply to interest expenses incurred on the pooling of cash.
- ▶ Transfer pricing: if, in transactions between related parties, a higher or a lower consideration is applied than that which would arise between independent parties in comparable circumstances, a taxpayer may need to modify its pre-tax profit by the difference between the market price and that used.

Incentives

A company's pre-tax profit can be reduced by direct costs associated with research and development (R&D) or by the depreciation of the capitalized costs for R&D. Both relate to R&D activities carried out within the scope of the taxpayer's own activity. As a result, the R&D costs or the depreciation for capitalized costs for R&D can be deducted twice (first as recognized expenses and secondly as a deduction against the base for corporate income tax).

In addition, if R&D activities are jointly performed with universities or an academy as part of a written agreement, the base for corporate income tax can be reduced by three times the amount of the R&D, with a cap of HUF50m (€170,000). The rule does not apply either to R&D costs financed from subsidies or to those purchased from Hungarian taxpayers (with certain exceptions).

10%

Corporate tax rate

70%

Percentage of FDI into Hungary from the EU

Development tax allowance

A development allowance can also be applied in certain circumstances. The allowance may reach 50% of the eligible costs for R&D. The value of the investment should reach HUF100m (€350,000). The allowance, which must be used within 10 years, reduces the company's annual liability for corporate income tax by a maximum of 80% of the tax payable.

Local business tax

The direct costs of the R&D activities can also reduce the base for local business tax.

Tax landscape for investors

The Hungarian tax system has been focusing on attracting inbound investments in regional activities, such as holding and licensing, and local manufacturing. In order to achieve this, Hungary has historically had a low corporate income tax rate (between 10% and 19%) and has offered a number of tax holidays and special tax incentives on collecting dividend and royalty income. In addition, attractive incentives and cash grants are available both for greenfield investments and developing existing establishments. Hungary has also constantly made efforts to reduce both employment burdens and administration on employees.

Tax landscape for entrepreneurs

Hungary levies no withholding tax on dividend, interest and royalty payments made to companies, while tax treaties may reduce tax rates applicable to these payments made to individuals.

Capital gains deriving from the sale of certain investments (reported shares) are exempt from corporate income tax.

Under certain circumstances, capital gains realized by a non-resident shareholder of a company holding real estate are taxed at 19%.

Finance

As a member of the European Union, Hungary can offer a broad range of subsidies. An investment of an enterprise - depending on the location - may be entitled to receive state subsidies of up to 50% of the investment costs.

The available subsidies for companies operating in the biotechnology industry are as follows:

VIP cash grant:

- ▶ The most beneficial cash grant opportunity currently available for large investors deemed strategic by the Hungarian Government
- ▶ Supports asset investments, job creation, established of shared service centers and R&D projects
- ▶ The investment value should reach €10m

Development tax allowances:

- ▶ Support asset investment or job creation
- ▶ There are several types of the allowances with various criteria

EU cash grant programs:

- ▶ Support large asset investment with complex technology development and employment creation:
 - ▶ The cash grant amount is a maximum of 35% of the eligible investment costs capped at HUF1b (€3.4m)
- ▶ Support R&D investments (basic research, applied research and experimental research):
 - ▶ Maximum 45% of the eligible R&D investment costs capped at HUF500m (€1.7m)

Availability of capital

Hungary pays special attention to investments in certain industries deemed important for its economy. It focuses, for

example, on the health industry, the green economy as well as the areas of engineering, medical, agricultural and natural sciences.

In the frame of the "JEREMIE" program, private investment funds specifically finance SME investments. The preferred industries are IT, telecommunication, biotechnology and energy.

In addition, in the frame of Széchenyi Plan programs, SMEs could apply for loans and guarantees.

According to the the Ministry for National Economy, the total cumulative value of foreign direct investments (FDI) in Hungary is €63.6b (as of January 2012) . In 2010, FDI into Hungary was €1,795m, some €300m more than the previous year. The Government hopes the figure for 2011 will reach €3b. Most of the investment has flowed into services and industries associated with vehicles and electrical machinery. Around 70% of it comes from the EU and just under 22% from Germany alone.

Structuring for the future

Hungary has a wide network of tax treaties with other countries, which can benefit investors seeking to reduce their liability for tax. Successful companies engaged in biotechnology may be able to use a holding company based in the country. In this way, investors can take advantage of exemptions from tax for income derived from royalties as well as capital gains.

Tax-efficient structures

Tax legislation in Hungary grants a number of opportunities to support a centralized structure for R&D. These include a 50% dispensation for royalty income as well as allowances for the cost of development in connection with R&D activities. There are also EU grants to encourage R&D available for relevant activities undertaken in Hungary.

12.5%

Ireland's corporate tax rate

Ireland

The entrepreneurial culture

Ireland has a respected regulatory regime with a thriving sector specializing in research, development and innovation. With strong support from the government, there is productive collaboration between industry and academia.

Ireland also enjoys easy access to the rest of Europe and the Middle East and Africa. The country has clusters of leading global companies in life sciences. During the past three years, Ireland's competitiveness has improved significantly, with a striking reduction in business costs, such as those for payroll, energy, office rents and services.

There are a number of government agencies, led by Enterprise Ireland, which help entrepreneurial activities. There are also county and city enterprise boards, totaling 35, which support small business. In addition, BASIS (Business Access to State Information and Services) provides businesses with a single access point to government (www.djei.ie). The maximum grant payable is 50% of the investment or €150,000, whichever is the lesser, provided certain conditions are met.

The National Institute of Bioprocessing and Training (NIBRT) is located in a new facility in Dublin. NIBRT is based on collaboration between University College Dublin, Trinity College Dublin, Dublin City University and the Institute of Technology in Sligo. It offers facilities of an international standard (www.nibrit.ie).

Taxation

Corporate tax

One of the key features of Ireland's tax regime is a three-year exemption from

corporation tax for start-ups, provided certain conditions are met. The maximum annual tax liabilities for which shelter is available under this scheme is €40,000 but is dependent on the amount of employer's pay-related social insurance (PRSI) paid and the number of employees.

The country has a corporate tax rate of 12.5% for active business. Trading losses can be offset against profits, with relief at the group level and the ability to carry them forward. In addition, there is a tax credit of 25% for research and development (R&D), which may be refunded over a period of three years. Effectively a 37.5% deduction for R&D expenditure can be achieved. The tax regime also provides a write-off for broadly defined acquisitions of intellectual property (IP). And holding companies are exempt from capital gains tax on disposals of shares in subsidiaries.

There is an effective exemption through a tax rate of 12.5% for qualifying foreign dividends with a flexible, onshore pooling of foreign tax credits. There is also an extensive network of tax treaties with other nations, together with access, as expected, to other members of the European Union. The country's domestic law provides for many exemptions from withholding tax. And, in certain circumstances, companies may obtain what is known as VAT 13A authorization, which allows a zero rating on purchases of goods and services, where a company is mainly manufacturing.

Incentives

Ireland has had a scheme offering tax credits for R&D since 2004. Qualifying expenditure generates a 25% tax credit to offset against corporate taxes in addition to a deduction at a rate of 12.5%. The purpose of the scheme is to encourage both foreign and indigenous

25%

R&D tax credit, giving an effective deduction in Ireland of 37.5%

companies to undertake new or additional R&D in Ireland. The tax credit is available to Irish resident companies and branches on the extra cost of in-house R&D undertaken within the European Economic Area (EEA), provided such expenditure is not otherwise eligible for tax benefits elsewhere within the EEA. Incremental spend is calculated in comparison to a base year of 2003 for R&D expenditure in excess of €100,000. So, for new entrants to R&D, the credit is essentially based on the volume of work undertaken.

To qualify for the tax credit, applicants must seek to achieve a scientific or technical advancement. The work must also help to resolve scientific or technological uncertainty. Both revenue and capital expenditure may qualify. In practice, this includes wages, related overheads, the cost of plant and machinery and buildings.

The credit regime also provides for outsourcing so that up to 5% of the expenditure on R&D can be passed on to European universities, including Irish ones. In addition, 10% of the expenditure can be subcontracted to other unconnected parties (i.e., giving a total of 15%), or €100,000, whichever is the greater amount. The tax credit can be refunded over three years where there is insufficient corporate tax liability to utilize the full credit in a particular year, or otherwise can be carried forward.

Tax landscape for investors

In certain circumstances, interest paid on loans used to invest in a partnership in which the borrower is an active partner, may be allowed in whole or in part as a deduction from total income. However, a similar allowance for investment in companies was abolished at the end of 2010.

Tax landscape for entrepreneurs

The Business Expansion Scheme (BES) is an incentive which provides tax relief for investment by entrepreneurs and others in certain corporate trades. The scheme allows an individual investor to obtain income tax relief on investments up to a maximum of €150,000 per annum in each tax year up to 2013. Relief is available at the investor's highest rate of income tax. Investors who cannot obtain relief on all their investment in a year of assessment, either because the investment exceeds the maximum amount or because their income in that year is insufficient to absorb all of it, can carry forward the unrelieved amount to following years up to and including 2013. Such rules are subject to the normal limit of €150,000 on the amount of investment that can be relieved in any one year.

In order to qualify for the relief, investments must be made in companies engaged in certain areas of manufacturing, services, tourism, R&D, plant cultivation, the construction and leasing of advance factories or in certain areas of music recording. The investee companies must be unquoted, i.e., they must not be on the official list of a stock exchange.

A further relief for seed capital provides that individuals who leave employment to start up their own businesses may claim a refund of tax on previous income for up to six years in respect of the investment in the new business. Individuals can select the tax years for which they may claim refunds from any or all of the six years prior to the year of investment. The maximum relief is €100,000 per annum at the individual's top rate of tax.

Finance

A range of services and incentives, including funding and grants, are available to those considering foreign direct investment in Ireland. These are offered to both new and existing clients by IDA Ireland, an agency which promotes inward investment.

IDA assists in the process via a range of services which include information and statistics on business sectors and locations within Ireland; assisting in setting up a business; and introducing potential investors to industry in Ireland, to government representatives and those providing services and research. Where required, the agency may also offer advice on property for international investors (<http://www.idaireland.com>).

Enterprise Ireland (EI) is the state agency responsible for supporting the development of manufacturing and international service companies. The agency provides funding and support to everybody from entrepreneurs with plans for a start-up to large companies planning to expand their activities or seeking to grow their exports. There are a number of schemes available, for example a large company undertaking a large R&D project could receive €650,000. EI (www.enterprise-ireland.com) also provides funding and support for college-based researchers to assist in the development, protection and transfer of technologies to industry via licensing or through spin-out companies. Science Foundation Ireland (SFI; www.sfi.ie) invests in academic researchers and teams likely to generate new knowledge, technologies and competitive enterprises in science and engineering. It also aims to encourage a culture of entrepreneurialism and promote partnerships (www.sfi.ie).

Availability of capital

Despite the economic difficulties in Europe, capital is still available for start-ups and other enterprises from state agencies such as IDA and Enterprise Ireland, as well as investors, venture capitalists and banking institutions.

Regulatory environment and incentives

Under European and Irish legislation, all medicinal products must be authorized by the Irish Medicines Board (IMB; www.imb.ie) before being marketed in Ireland.

Authorization to market a product or service produced through biotechnology may be obtained by taking one of several routes.

First, there is a direct approach to the IMB. This should be used only to market the product in Ireland and not in any other Member State of the European Union, or as the basis for a future application for mutual recognition to other Member States.

Second is what are known as mutual-recognition and decentralized procedures. Both aim to facilitate access to a single market by relying on the principle of mutual recognition.

Third is a centralized procedure. The European Medicines Agency (EMA) is responsible for the scientific evaluation of applications made in this way. Companies are required to submit a single application for authorization to the EMA.

Structuring for the future

Thanks to its attractive tax rate and the regime for holding companies described above, Ireland's status as a world-class location for international business is well established. Also helping, of course, are the country's regulatory and legal regimes, combined with its open and accommodating attitude to business. In recent years, too, Ireland has emerged as a favored onshore location for multinational corporations seeking to establish regional or global headquarters to manage their profits, international functions and shareholdings associated with their businesses.

Tax-efficient structuring

As such, Ireland also provides an efficient base from which to manage the disposal of businesses. Another benefit is the exemption from capital gains tax for holding companies. An exception to this rule covers gains made on the sale of patents. The exemption from capital gains tax for such sales was removed in 2011.

The support offered by the country's tax policy, and the tax credits on research and IP, also encourage companies to use Ireland as a focal point for R&D in general. Indeed, the strong regulation and a clear legal framework for protecting and exploiting IP make Ireland a preferred location for many companies looking to centralize their R&D (<http://www.patentsoffice.ie>).

€650,000

Potential grants available

Italy

The entrepreneurial culture

Notwithstanding the lack of dedicated incentives to the biotech industry, based on publicly available data, Italy boasts the third-largest number of biotechnology companies and is the country with the highest rate of growth in pure biotechnology.

The development of biotechnology industries is a priority for some of the Italian regions, which not only has the effect of grouping existing biotechnology operators in certain localities but also helps to attract new ones. As in other countries in Europe, biotechnology in Italy is often carried out by small and medium-sized enterprises, partly because such activities do not require a great deal of start-up capital.

Indeed, since it began in the 1990s, Italy's biotechnology industry has grown steadily. In fact, at the end of 2010, there were a total of 221 companies operating as "pure biotechnology" companies. Of the total, 141 firms operate in the human health sector (red biotechnology). Around 75% of all companies in the sector are "micro" (i.e., they have fewer than 10 employees) or are described as "small" (with less than 50 employees).

Those seeking guidance when setting up a new biotechnology business in Italy, as with entrepreneurs in other sectors of industry, may turn to Invitalia, a reference point for companies seeking advice on investing in Italy (www.invitalia.it). Entrepreneurs needing advice on setting up locally should contact Camera di Commercio (www.camcom.gov.it). Foreign entrepreneurs interested in entering the Italian market can also contact the Italian Trade Commission (i.e., ICE: www.ice.it), which offers insights into the country and facilitates scientific

projects. There are also two private organizations which, depending on the nature of the business, help those starting up new enterprises: IBAN (Italian Business Angel Network: www.iban.it) and AIFI (Italian Private Equity and Venture Capital Association: www.aifi.it). Finally, specific information about Italy's biotechnology industry may be obtained from the Italian biotechnology companies' association, Assobiotec (www.assobiotec.it).

Taxation

Corporate tax

Italy's tax regime does not provide specific incentives for biotech companies. Indeed, other than those granted through tax credits, biotech companies are subject to corporate tax under the same rules as all other companies.

Assuming that a biotechnology company would expect to make losses during its early years and would also need debt financing, the fact that tax losses (NOLs) and interest expenses may be deducted against tax may be of interest to them. It should also be noted that, in order to help companies facing difficult economic and financial times, the rules have been changed: taxable losses incurred by a company may be carried forward with no time limits and may be used to offset up to 80% of future taxable income. However, NOLs incurred in the first three years (start-up losses) may still be carried forward with no time limits and may be used to offset future taxable income, irrespective of the 80% limit.

It must be noted, however, that the new rules on carrying losses forward do not apply to Italian partnerships, which are still subject to the old regime. Under this, NOLs may be

3%

Notional return on equity increases from FY 2011 available as a deduction

carried forward for five years, unless they were incurred in the first three tax years, which are known as evergreen NOLs and may be carried forward with no time limit.

As with the rules covering the deduction of interest expenses, starting from 2008, the thin-cap rule was replaced by a 30% threshold for earnings before interest, tax, depreciation and amortization (EBITDA). This means that Italian companies are now entitled to deduct interest expenses (net of interest income) up to the 30% threshold for EBITDA. Interest expenses exceeding the threshold may still be carried forward with no time limit and may be deducted in any future tax year in which the 30% threshold exceeds the interest expenses incurred in the same fiscal year.

Moreover, earnings up to the threshold not fully absorbed by the interest expenses in a given year may be carried forward with no time limit and used to deduct future interest expenses that exceed the annual amount. Again, however, this does not apply to Italian partnerships, which in principle are entitled to deduct all interest expenses incurred in the fiscal year, regardless of their EBITDA.

It is proposed that, starting from FY 2011, Italian companies (and commercial entities) can deduct from their corporate income tax base an amount of notional interest (i.e., a yield fixed for years 2011-13 at 3%) calculated on their equity increases compared to the equity in their balance sheet as at 31 December 2010.

The measure is aimed at reducing the cost disadvantage of equity in the capital structure of Italian businesses and it is also applicable to Italian branches of foreign subjects. Measures to fully implement this regime and associated anti-avoidance provisions are in awaiting approval.

Incentives

Incentives are available to companies that increase their investments in research and development (R&D) during 2011 and 2012. The comparison is with the average for the period from 2008 to 2010. The tax credit is equal to 90% of the amount of investment in R&D exceeding the average between 2008 and 2010; tax credits accrued in each of the years 2011 and 2012 may be used in three tranches to offset other taxes due from the company. Note, however, that only R&D investments commissioned to external entities will be eligible for tax credits (i.e., the company must entrust universities or other research entities to carry on the work).

In addition to those for R&D, other tax credits may be available either for certain investments made or in return for hiring disadvantaged employees in Italy's southern regions.

Tax landscape for investors

A domestic provision, introduced in 2008 yet so far little used, provides an incentive for investors selling their shareholding in one company while investing in another operating in the same sector. It works by exempting any capital gain realized through the initial disposal. There may also be ways to structure holdings in a tax-efficient way (e.g., through corporate tax fiscal unity, VAT tax grouping, branches acting as holding entities and partnerships).

Tax landscape for entrepreneurs

Entrepreneurs' income is subject to tax (either individually at progressive rates or at a corporate rate of 27.5%); in addition, entrepreneurs are liable for a regional tax (IRAP), which is levied at 3.9% on the

value added, which is roughly equal to the earnings before interest and taxation. (The actual rate of tax may vary according to the region in which the firm operates and on the nature of the business.) Other direct taxes may apply depending on the assets held by the entrepreneur (such as municipality tax ranging from 0.4% to 0.7% charged on the properties' value).

Overall, tax on entrepreneurs in Italy can be burdensome. Not only is the system complicated, the tax authorities are also focusing on business in general in a renewed attempt to tackle evasion and tax abuse.

Finance

Grants and other support

Most of Italy's biotech companies fund their business in one of three main ways:

1. Debt
2. Grants (national and regional as well as those available through European and international sources)
3. Venture capital and private equity funds

As funding through grants decreases, more and more biotech companies are resorting to venture capital or private equity firms for funding. That said, the most popular option is debt. An increasing number of firms are also considering a public issue of shares on a stock exchange.

Companies specializing in red biotech often receive grants or other forms of funding from a combination of official sources: the Italian Ministry of Education, University and Research (MIUR); the Ministry of Health (MDS); and the Italian Ministry for Economic Development (MSE). A big role is

played by the regional governments, which are autonomous in deciding on policies to encourage biotech incentives.

Availability of capital

National support for the industry through MIUR for 2012 has yet to be decided. However, under EU Decision no. 1982/2006, the Seventh Framework Program (in force from 2007 to 2013), a total of €1,935m was earmarked to support new biotech ventures across Europe.

Regulatory environment and incentives

Intellectual property (IP) rights on biotech inventions are ruled by Law no. 78, dating back to 2006, which enacted the Directive 98/44/CE. However, many, including Assobiotech, believe rights to IP on biotech products and processes should be increased and improved. One of the main hurdles is the difficulty in transferring technology from universities or research centers to companies. The costs of depositing and registering patents are, in Assobiotech’s opinion, still too high, especially for small and medium-sized companies.

Structuring for the future

Tax-efficient structures

One of the main choices facing entrepreneurs setting up biotech businesses is the vehicle through which the operation is established in Italy (e.g., a company, partnership, permanent establishment, holding company and so on). How a company is financed is also important. MNEs, in particular, should plan their transfer pricing policies (e.g.,

royalties for the right to use intangibles) and bear in mind that, under Italy’s tax rules, the deduction of expenses incurred by black-listed entities may be challenged. (Note that, as far as the Italian authorities are concerned, some Swiss companies may be black-listed entities.)

When disposing of a business, owners may usually save on tax if they sell shares rather than assets directly. Provided that the investment in the Italian company shares has been held for at least 12 months and other conditions are met, the capital gain realized by an Italian holding company through the sale of a participation may be up to 95% exempt from corporate tax (IRES). Nor would it be subject to IRAP on benefiting.

Capital gains realized on the disposal of a going concern are usually subject to a rate of 27.5% IRES. The disposal of operations through a merger or contributions is tax neutral.

In principle, Italy’s regulators support the idea of a centralized structure for R&D so that rights to IP can be placed under one roof. Yet, unlike other jurisdictions, income derived from the licensing of IP is usually subject to nominal rates of tax under IRES and IRAP. In addition, any remuneration for the licensing of IP rights to related foreign parties may be subject to an arm’s length principle under Italy’s transfer pricing rule.

The Netherlands

The entrepreneurial culture

The Netherlands has a number of strengths, not least its infrastructure of telecommunications and transport. Several years ago, the Government introduced an attractive facility for foreign companies investing in innovation. Surprisingly, some 20% of those participating were found to be unaware of the existence of the "Innovation Box." Yet the facility proved to be a deciding factor for a similar number of companies that chose in favor of the Netherlands.

NFIA

The Netherlands Foreign Investment Agency (NFIA) is part of the Dutch Ministry of Economic Affairs, Agriculture and Innovation. The agency provides advice, information and assistance with establishing a business in the country (<http://www.nfia.nl>).

NL Agency

NL Agency consists of five divisions: NL Energy and Climate Change; 1110NL EVD International; NL Innovation; NL Environment; and NL Patent Office. The agency focuses on sustainability, innovation, international business and cooperation. It also works closely with Syntens, a network for entrepreneurs. NL Agency is the main point of contact for businesses, knowledge institutions and government bodies. Answers for Business (Antwoord voor bedrijven) is also part of NL Agency (<http://www.agentschapnl.nl>).

Taxation

Corporate tax

Corporate income tax is levied on resident and non-resident companies. Resident companies are those incorporated under Dutch civil law, including subsidiaries of foreign companies, European companies (Societas Europaea, or SEs) and European Cooperative Societies (Societas Cooperativa Europaea, or SCEs), which are established in the Netherlands, even if their management and statutory seat is abroad. In addition, companies are resident if they are incorporated under foreign civil law, but effectively managed and controlled in the Netherlands.

Resident companies are subject to tax on their worldwide income. Non-resident companies, primarily branch offices of foreign companies doing business in the Netherlands, are taxable only on specific income items, such as real estate and business profits in the Netherlands.

For 2011, the standard rate of corporate tax was 25%. A tax rate of 20% applies to the first €200,000 of taxable income. An effective tax rate of 5% is available for income related to certain intellectual property (IP).

Rulings are agreements concluded with the tax authorities on the (future) consequences of transactions or situations involving Dutch taxpayers. For certainty in advance on transfer pricing, an advance pricing agreement (APA) can be concluded with the

5%

Corporate tax rate applied to income under the Innovation Box regime

tax authorities. APAs provide taxpayers with certainty about the arm's length nature of transfer prices. For almost all other matters, such as the applicability of the participation exemption, the tax consequences of hybrid finance structures or permanent establishment in the Netherlands, an advance tax ruling (ATR) can be concluded.

The period to which a ruling applies depends on the type of ruling. Some apply to a specific case and therefore, in principle, apply indefinitely. However, in general, ATRs are concluded for a period of four to five years. If the facts on which the APA or ATR was based do not change then, in principle, the APA or ATR can be renewed indefinitely.

No distinction is made in the Netherlands between capital gains and other income. In certain cases, capital gains are exempt or a rollover is available based on case law or under the reinvestment reserve.

The standard rate of withholding tax on dividends is 15%. However, several exemptions and reductions, as described below, may apply. Under the participation exemption, dividends paid by resident companies to other resident companies are usually tax free.

Dividend withholding tax is not imposed on dividends distributed from a Dutch company to a qualifying entity in another EU Member State that owns at least 5% of the nominal paid-up share capital of the payer. The qualifying entities are specified in the EU Parent-Subsidiary Directive. The threshold of 5% may be lower in certain circumstances. Under an extensive network of Dutch treaties,

the rate of dividend withholding tax rate is typically reduced to a rate as low as 0%.

All corporations located in the Netherlands (except qualified investment companies that are subject to a rate of corporate income tax of 0%), including holding companies, are, in principle, exempt from Dutch corporation tax on all benefits connected with certain qualifying shareholdings (participations).

Benefits include cash dividends, dividends in kind, bonus shares, "hidden" profit distributions and capital gains realized on the disposal of the shareholding. A capital loss that might result from the disposal of the shareholding is similarly non-deductible (but a liquidation loss of a subsidiary company is, in principle, deductible).

The participation exemption applies to all holdings of 5% or more of the nominal paid-up capital of the subsidiary, unless the participation is a "portfolio participation."

In principle, depreciation is based on historical cost, the service life of the asset and the residual value. From January 2007, depreciation is limited on buildings, goodwill and other assets. Despite those restrictions, a write-down to a lower market value remains possible.

Goodwill must be depreciated over a period of at least 10 years. As a result, the maximum annual depreciation rate is 10%. If the goodwill is useful for a longer period, this period must be taken into account. For other assets such as inventory, cars and computers, the depreciation is limited to an annual rate of 20% of historical cost, unless

the accelerated tax depreciation mentioned above is applied.

Incentives

In the Netherlands, a taxpayer may deduct immediately from taxable income, subject to the regular rate of corporate income tax, the costs of developing intangible assets. As a result, such costs do not need to be capitalized.

In addition, if certain conditions are met, a taxpayer can elect to apply the Innovation Box. The aim of this box is to encourage innovation and investment in research and development (R&D), including that of software. The Innovation Box is the successor to the Patent Box, which applied from January 2007, and was converted into the Innovation Box, as of 1 January 2010.

In the Innovation Box, net income from qualifying IP is effectively taxed at a rate of 5% by reducing the tax base by about 80%. The 5% rate applies only to the extent that the net earnings derived from the self-developed intangible assets exceed the development costs. The development costs are deductible at the standard rate of tax and form the threshold. If the Innovation Box regime is adopted for a particular intangible asset, the other intangibles are not required to be allocated to the box. The Innovation Box, unlike the Patent Box, does not impose a limit on the amount of income from intangible assets that can be taxed at the reduced rate.

An important condition of the Innovation Box is that the taxpayer must have been granted

a patent. In order to apply for the Innovation Box, applicants must meet the following requirements:

1. An intangible asset has to be owned and developed by (i) the Dutch taxpayer, (ii) through contract research or (iii) through a cost contribution arrangement
- 2a. The development of the intangible asset for which a patent has been granted, has to be finished after 31 December 2006. This includes plant variety rights
- 2b. Or the development of the intangible asset for which an R&D declaration (from the Ministry of Economic Affairs) has been granted, has to be finished after 31 December 2007
3. Expected profits must originate for an important part from the patent or R&D declaration

Trademarks, logos and similar assets do not qualify. Contracted R&D for qualifying intangible assets is allowed. ATRs and APAs are also available.

Where there is a treaty, withholding tax on foreign royalties can normally be credited

against Dutch corporate income tax, but the amount of the credit is limited to the Dutch corporate income tax attributable to the relevant income on royalties.

Tax credits on R&D (WBSO) provide a tax facility for companies, research centers and self-employed persons who perform R&D work. Under the scheme, there is a contribution toward the wage costs of employees directly involved in R&D. The facility involves a reduction in the total deduction of tax on wages and social security contributions by the R&D institute, subject to compulsory deductions. The reduction amounts to 50% of the first €220,000 of the total wage costs for R&D and 18% of the remainder. In 2012, the amount changes to €110,000 at 14%.

From 2012, the R&D declaration could also give access to a new tax incentive, the Research & Development Deduction (RDA). Under the RDA, entrepreneurs will become entitled to a deduction of 40% of their profits. Consequently, companies that are subject to corporate income tax at the rate of 25% will obtain a benefit of 10%.

At the moment, it is only a proposal to amend the legislation on corporate income tax, but it is expected that this additional incentive will come into effect from 2012. The objective of the RDA is to facilitate costs - but not those on labor - and investments in R&D. The third incentive aims to provide an incentive for innovation in addition to the Innovation Box and the tax credit on R&D. The new incentive fits in with the policy to replace subsidies by incentives to bolster innovation and to attract more venture capital for new companies and entrepreneurs.

Tax landscape for investors

Foreign investors, including big pharma and biotech, have chosen the Netherlands for foreign direct investment but also to organize, fund, own and grow their overseas companies and businesses. Investment companies (Fiscale Beleggingsinstelling or FBI) enjoy a beneficial tax regime if certain requirements are met. Under this, profits are not subject to tax provided the net investment income is distributed within eight months of the following financial year.



Dutch withholding tax on interest and royalties

There is a commonly used structure, which is tax effective, for holding investments, where the interest on a loan, contracted due to a takeover purchase of the company, is deductible. From 2012, this structure will be discouraged and not all the interest may be deductible. However, it seems that there will remain opportunities to lower the effective tax rate by deductions of interest.

Tax landscape for entrepreneur

There are many reasons for setting up as an entrepreneur in the Netherlands. Among the main ones are:

- ▶ A 25% rate of corporate income tax
- ▶ No taxation of dividends and capital gains from qualifying subsidiaries (participation exemption)
- ▶ No Dutch withholding tax on interest and royalties
- ▶ No Dutch withholding tax on dividends when using a Dutch cooperative
- ▶ No capital tax or stamp duty
- ▶ An extensive network of tax treaties as well as access to EU directives

As a result, companies pay a low foreign withholding tax on distributions from investments and have favorable tax treatment for foreign employees. Companies may receive accelerated and random depreciation of business assets to stimulate their investments. Companies may also be able to use hybrid loan structures. There is also a practice of ATRs and APAs, which provide certainty on international tax structures. In addition, companies can carry forward tax losses for nine years as well as carry them back.

Not only is there certainty up-front from the Dutch tax authorities by way of a formal

agreement, there is a tried-and-tested structuring for multinational companies, private equity and investment funds. What is more, Dutch corporate income tax returns can be filed in another currency as a functional currency.

Finance

Local authorities may be willing to provide additional incentives and to facilitate (large-scale) investment projects.

International innovation

The program stimulates innovations that take place within an international consortium. The maximum grant is €750,000 per project. There are no specific technology areas defined. The main criteria are innovation, collaboration, economical impact and market potential. Eligible R&D projects should be carried out in a consortium, but only costs for the Dutch participants are eligible for funding.

The consortium should consist of at least one company established in the Netherlands and one company established in an emerging market (Brazil, China, India, Indonesia, Malaysia, Thailand, South Africa, South Korea, Taiwan); an industrialized country (Canada, Japan, Singapore, the US) or a country that participates in the EUREKA program (European countries).

Energy Research Grants (EOS)

The Dutch Government intends gradually to move toward an economy that is no longer based on oil and other fossil fuels but on clean, affordable and reliable sources of energy. The Energy Research Programme aims to initiate and support innovation and research in the fields of energy efficiency and sustainable energy. In all, the program

encompasses about 20 fields of research. Eligible projects include innovative early-stage ideas, long-term research, collaborative and demonstration projects. The maximum amount of subsidy is €1m per project.

Regulatory environment and incentives

The Netherlands is party to all major treaties and conventions for protecting and registering IP. It has a strong and efficient infrastructure to register patents and trademarks, with international protection.

Structuring for the future

Tax-efficient structures

The Netherlands also has advantages when it comes to disposing of businesses. There is an exemption under which benefits such as dividends and capital gains derived from a qualifying participation are exempt from corporation tax. The exemption generally applies if the parent company holds at least 5% of the shares in the subsidiary, and this subsidiary is not considered a "low taxed passive investment subsidiary." Capital gains from the sale of a qualifying participation are also exempt from corporate taxation. Capital gains realized upon mergers and split-offs may be rolled over under special provisions. Capital gains realized on the disposal of business assets may, under certain circumstances, be placed in a reinvestment reserve or low taxed, provided the income qualifies for the Innovation Box.

It is possible to establish a centralized R&D structure in another country and license the IP through the Netherlands to a third country. This is a tax-effective structure. The IP, other than the legal ownership of patents, may also be in the Netherlands.

Norway

The entrepreneurial culture

Innovation Norway may, upon application, assist with start-up finance (www.innovasjon Norge.no).

Taxation

Corporate tax

The general corporate tax rate is 28% flat. Losses may be carried forward indefinitely.

Apart from the general "Skattefunn" research and development (R&D) incentive (explained below) which is limited to a specified amount that may be granted to each company, there are no particular incentive tax regimes for biotechnology start-ups.

There is, on the other hand, some uncertainty related to whether R&D costs may be expensed on a current basis or capitalized for tax purposes. Furthermore, there is also great uncertainty related to from when, and for which period, the R&D capitalized asset may be depreciated for tax purposes.

As a starting point, costs incurred in order to acquire, maintain or safeguard taxable income is deductible for tax purposes. However, business assets with a useful life of at least three years and a cost price of more than NOK15,000 must be capitalized for tax purposes.

Cost incurred pursuant to self-performed R&D that is related to a specific project and that may, or has become, a business asset, must be capitalized for tax purposes. Accordingly, if it is more likely than not that a project may become a business asset, cost incurred in relation to the R&D project must be capitalized for tax purposes, i.e., above 50% technical, commercial and economical probability.

The tax authorities commonly question the tax treatment of R&D costs during tax audits.

Incentives

According to the "Skattefunn" tax incentive regime, a company that has incurred R&D costs may apply for a tax relief (a tax credit) in addition to the ordinary deductions. A condition for receiving this tax deduction is that the project is accepted in advance from the Research Counsel of Norway (NFR).

For the tax year 2011, the maximum tax relief available amounts to 18% (or 20% if the taxpayer is a small or medium-sized company) of R&D cost, not exceeding NOK5.5m for own R&D costs, or NOK11m for pre-approved R&D projects. Therefore, the tax credit maximum is effectively NOK2.2m a year.

A company entitled to relief that is not in a tax paying position will receive the same amount as a governmental contribution.

Tax landscape for investors

There are no specific incentives or tax concessions available for investors.

However, in general, there is no Norwegian tax on capital gains on shares in a Norwegian company accruing to a non-Norwegian tax resident investor.

Furthermore, dividends accruing to a corporate shareholder resident within the EU or EEA are not subject to withholding tax (WHT) provided that certain requirements are met. For example, the EU or EEA resident company must actually be established (i.e., have real substance) and be engaged in genuine economic activity. However, if the shares are effectively connected to a permanent establishment (PE) situated in Norway, 3% of the dividend income is subject to tax at a rate of 28%, giving an effective tax rate of 0.84%.

Also, dividends accruing to a Norwegian company on shares in a Norwegian company or a company established within the EU or EEA are, as a starting point, subject to 28%

tax on 3% of the dividend income, giving an effective tax rate of 0.84%.

However, if a Norwegian holding company holds more than 90% of the share capital and corresponding voting power in the above-mentioned companies, the dividends are entirely tax exempt.

Dividends accruing from a company outside of the EU or EEA to a Norwegian holding company are 97% tax exempt as well, provided that the distributing company is not resident in a low tax jurisdiction and the Norwegian holding company has held at least 10% of the share capital and corresponding voting power for at least two years.

Capital gains on shares accruing to Norwegian corporate shareholders are, as a starting point, subject to 28% tax. However, provided that certain requirements are met, capital gains on shares accruing to Norwegian corporate shareholders are either 100% or 97% tax exempted.

Arm's length interest expenses are in general deductible, provided there is no thin capitalization issue. There is no WHT on interest income accruing to non-resident creditors.

Finance

There is no specific support for biotechnology, yet agencies such as Innovation Norway, the Research Council of Norway and the Industrial Development Corporation of Norway offer advice and incentives. Innovation Norway (www.innovasjon Norge.no) may help with start-up finance.

Availability of capital

Its underlying economic strength has meant that Norway has not been particularly affected by the current situation in the financial markets. However, the banks are becoming increasingly reluctant to fund high-risk projects.

Structuring for the future

A common way of setting up a Norwegian business is to incorporate it in a limited liability company, which is held directly by an EU or EEA resident company, or by an intermediate Norwegian holding company.

To make sure that dividends are not subject to WHT, the first tier non-resident holding company should be tax resident within the EU or EEA and have a substantial stakeholding (e.g., offices, employees) in that country.

Alternatively, if the substance criterion is not possible to meet, this holding company should be tax resident in a country with which Norway does not levy WHT according to a tax treaty (and this country has a beneficial tax treaty network with third countries).

An arm's length debt finance should render the interest deductible in Norway. Furthermore, no WHT is levied in Norway on the interest.

Tax-efficient structures

There is no capital gains tax on the disposal of shares made by a non-resident with no PE situated in Norway.

Careful consideration should be given to selecting a Norwegian company to hold ownership of intellectual property (IP). Such ownership may be better located in an alternative EU or EEA country that has a more favorable IP tax regime. The trend is to emigrate IP from Norway and continue production activities in the country as a contract manufacturer.

That said, in Norway, it is also possible to set up a centralized structure that owns IP and which can be licensed to users outside the country.

NOK2.2m

Maximum additional R&D tax credit available per annum under "Skattefunn" tax incentive regime

14

Number of special economic zones where exemptions from corporate income tax are available

Poland

The entrepreneurial culture

The Polish Government provides a form of cash grant called the Multi-Annual Support Programme (MASP). It is designed mainly for large investments, which are considered crucial to the country's economy. The level of support is based on the number of newly created jobs; it ranges from PLN3,200 to PLN15,600 per job created. There are no application rounds; motions for support may be filed throughout the year. In order to benefit from this form of aid, a company should first talk to the Polish Information and Foreign Investment Agency (PAIIZ) and with the Ministry of Economy (MoE). Grants are made in cash, based on a bilateral agreement between the MoE and the investor. Under MASP, the support granted to companies or entrepreneurs planning an investment is greater in "priority sectors." Either way, grants last for no longer than five years.

So, for example, the Government would look favorably on an application from a biotechnology company spending a minimum of PLN40m over two years, while creating no fewer than 250 jobs. Similarly, a center for research and development (R&D), which intended to invest at least PLN3m while creating 35 jobs for highly educated researchers, would also be likely to win favor, as would an investor planning to spend, say, PLN160m to create at least 50 jobs.

Also available for SMEs are cash grants called technology credits from the European Union. This type of grant aims to support projects leading to a "technological bonus." Under the scheme, up to PLN4m is available for each project. However, the technological bonus cannot exceed the limits imposed under regional aid. Again, much depends on where the investment is made. For instance, those in and around Warsaw attract only 30%, whereas those in areas away from the capital may be worth 50%. Applications are limited to specific rounds: the next one is likely to be during the second quarter of 2012.

The aim is to support investments linked to the production of new or significantly improved products, processes or services. When implemented, the technology must be in the form of industrial property rights or the results of R&D or unpatented technical knowledge. The applicant must be a micro, small or medium-sized enterprise; it must also be able to obtain credit on commercial terms.



Maximum support level:

- 50%*
- 40%*
- 30%*

* Potentially the aid intensity may be increased by:
- 20 p.p. for small enterprises
- 10 p.p. for medium-sized enterprises

Another program, called Innotech, is divided into two parts: In-tech (which supports cooperation between scientists and business) and Hi-tech (which provides backing for advanced industrial technology).

Another EU grant scheme supports investments leading to the creation or expansion of shared service centers or centers for information technology, which create at least 100 new jobs. Also covered are investments relating to the launch or expansion of R&D with expenditure of at

PLN4m

Maximum cash grant available for SMEs as technology credits

The Innotech program

In-tech	HI-tech																																																								
<ul style="list-style-type: none"> ▶ Support is granted in a form of a cash grant for projects including: <ul style="list-style-type: none"> ▶ R&D works ▶ Help with preparation such as documentation, tests, the protection of industrial rights, certifications, market research etc. 	<ul style="list-style-type: none"> ▶ Support is provided in the form of a cash grant for projects including R&D or preparation such as purchasing consulting services connected with innovation 																																																								
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least PLN2m while generating 10 new jobs or more. The maximum amount of state aid granted for such a project may amount to 30% of the total or, in the case of R&D, between 30% and 50% (depending on the location) of the eligible investment costs or employment costs for a period of two years. Investment costs may include the land or the cost of renting premises, together with the fixed assets needed for the business.

Among the criteria is that the percentage of new employees with higher levels of education should exceed 50% of the total and that the company must commercialize the results of its research. The project must also lead to competitive products and technologies being introduced to the market. However, the availability of funds under this scheme is currently limited.

The purpose of yet another EU grant scheme is to encourage entrepreneurs to contribute to innovation. There are two types of projects funded: planned research or investigation aimed at developing knowledge and skills to develop new products, processes or services, or for bringing about a significant improvement in existing products, processes or services. Then there is the development work to bring these to a commercial reality.

Under the program, the total value of a project cannot exceed the equivalent of €50m. The maximum support for R&D is €7.5m. In the case of projects located in the Lodz Voivodeship, Mazowieckie, Lubelskie, Podlaskie, Warmia and Mazury, Kujawsko-

Pomorskie or Podkarpackie, the value of eligible expenditure within the R&D phase of the project must exceed PLN400,000. For other locations there is no minimum specified.

Taxation

Corporate law

Under Polish law, an exemption from corporate income tax can be granted only on the basis of a permit for running a business in one or more of the special economic zones issued by the Ministry of Economy. At present, there are 14 such zones in Poland. An investor may choose either to enter an existing zone or to apply for one to be extended to private land.

The holder of a permit not only avoids corporate income tax at a rate of 19%. The amount of the exemption can be used for as long as the zone exists (provisionally until 2020, although extension beyond 2020 is now available). A permit for a zone can usually be obtained within six to eight weeks. Investors apply for the permit individually as there is no formal call for applications. It may take up to 12 months to extend a special economic zone to private land.

Under yet another scheme, called Research and Development Center Status, applicants may create an "innovation fund." Contributions may be up to 20% of a company's monthly revenues, which are then deductible for the purposes of corporate

income tax. The main requirement is the contributions must cover expenses linked to R&D. Other benefits include exemptions from real estate tax, forest and agricultural taxes. The total exemption can amount to €200,000 over three consecutive years.

The main provisions of the scheme are that an R&D center must generate net revenues on the sale of goods and products and on its financial operations of at least €1.2m, with a minimum of 20% generated on sales of its own R&D (in the year prior to the one in which the application is filed). Applicants must also have no outstanding liabilities for tax or social security.

Tax landscape for entrepreneurs

Poland has 16 different regional operational programs aimed at entrepreneurs, one for each voivodeship. They are intended to boost regional economies, enhancing their technical infrastructure, as well as increasing their human capital. Some such measures are also aimed at increasing a region's R&D potential. For example, in Mazowieckie voivodeship, there is support for developing links between scientists and the real economy.

Portugal

The entrepreneurial culture

Aicep Portugal Global, which was created in 2007, is the agency in charge of supporting entrepreneurial activity in Portugal, particularly foreign investment into the country. The agency aims to encourage the best foreign companies to invest in Portugal and to contribute to the success of local companies abroad, either in the drive to become international or in boosting their exports.

In biotechnology alone, there are more than 40 companies, most of them created between 2001 and 2006, which attract international attention. With a focus on research and development (R&D), most of the work of these companies is directed at health care and medical areas, as well as agro-food and environmental biotechnology.

Much of the R&D depends on the work of Portuguese scientists. Many are internationally recognized because of their achievements both at foreign universities and in the field of biotechnology.

Taxation

Corporate tax

In Portugal, corporate income tax (IRC) is levied on resident and non-resident entities. Entities whose principal activity is commercial, industrial or agricultural are subject to IRC of 25% on worldwide profits, but a foreign tax credit may reduce the

amount payable: direct foreign tax may be credited against the liability for Portuguese tax up to the amount of IRC attributable to the net income from foreign sources.

Companies or other entities that operate in Portugal through a permanent establishment are subject to IRC of 25% on the profits attributable to the permanent establishment. Companies or other entities without a permanent establishment in the country are subject to IRC on income that is deemed to be derived in Portugal.

A reduced IRC rate of 10% or 15% applies to activities carried out in parts of the country specified by the Government (for example, undeveloped regions). Such taxes are subject to an additional municipal surcharge of 1.5%, with some exceptions. A state surcharge of 2.5% is levied on the taxable profit determined for IRC purposes that exceeds €2m.

Double tax treaties may further limit the scope of a permanent establishment in Portugal. From 2010, tax losses can be carried forward for four years, provided that certain conditions are met.

Incentives

Biotechnology companies may benefit from a variety of incentives, including the following:

- ▶ SIFIDE (a tax incentive system for corporate R&D), which aims to provide companies in Portugal with tax benefits that promote R&D, with the accent on boosting productivity, economic

32.5%

SIFIDE tax credit of R&D expenses performed

20%

RFAI tax credit of relevant investment performed

development and the qualifications of the workforce. Expenses on R&D may lead to a tax credit, which is made up of two components: a base rate of 32.5% of expenses during the current tax year; and an incremental rate of 50% on expenses incurred during the period and an incremental rate of 50% of the incremental expenses of the period, in comparison to the simple average of the two previous tax years, with a limit of €1.5m.

- ▶ RFAI is a tax credit of 20% (on up to €5m of relevant investment) and 10% (with respect to relevant investment above €5m), of amounts invested in land, plant, equipment and certain intangibles. In addition, RFAI provides an exemption from, or a reduction of, the municipal holding tax for buildings used in the project as well as an exemption from, or a reduction of, the property transfer tax and a similar dispensation from stamp duty for contracts necessary to complete the project, including financing agreements. Note that this incentive refers to sectors such as agriculture, forestry, agro-industrial use, energy, manufacturing and extractive businesses.

Contractual incentives are also available for qualifying new investment projects established before 31 December 2020. To qualify, the project must have a value exceeding €5m, develop sectors considered to be of strategic importance to the Portuguese economy, be designed to reduce regional economic imbalances, create jobs and stimulate technological innovation and scientific research in Portugal. The incentives may comprise a tax credit of 10% to 20% of the eligible investments made (which is deducted against the taxable profit of the project); an exemption from, or a

reduction of, the municipal holding tax for buildings used in the project; an exemption from, or a reduction of, the property transfer tax for buildings used in the project; and an exemption from, or a reduction of, the stamp duty for acts and contracts necessary to complete the project, including financing.

Tax landscape for investors

Investors may benefit from an exemption to domestic capital gains on the disposal of shares held by foreign investments (provided certain conditions are met).

Investors may also gain from double taxation treaties signed by Portugal with more than 60 other countries. Also available is an exemption from withholding tax on dividends paid to EU shareholders eligible under the Parent-Subsidiary Directive (provided again that certain conditions are met). Investors should consider using a holding company based in the European Union (EU) in order to benefit from exemptions from withholding tax as well as other reliefs.

In addition, there are benefits for those who are not permanent residents of Portugal. These apply to non-residents for the previous five years who decide to become resident (and so taxed) there. This involves a special flat tax rate of 20% applicable to net income derived from activities that qualify as "high added value" of a scientific, artistic or technical nature. Also covered are exemptions for income from foreign sources, provided certain requirements are met. Employment income derived from high added-value activities earned abroad may benefit from an exemption if they are subject to effective taxation abroad. Dividends, interest, rental income and capital gains may also benefit from an exemption, provided

they are subject to taxation in the country of source under the double tax treaties.

Finance

There is a range of support under the EU's structural funds program (from 2007 to 2013) as part of the National Strategic Reference Framework (NSRF). National or foreign companies that intend to invest in Portugal can apply for incentives in areas as diverse as industry, trade (generally only for small and medium-sized enterprises (SMEs)), services, tourism, energy (production only), transport and logistics. There are three main avenues:

- ▶ SI&DT is an incentive system that supports research and technological development (R&TD) and other such projects. The system may also be used to create and boost internal skills and to value R&TD. Under certain conditions, the incentive may reach 75% of the global investment, not subject to reimbursement.
- ▶ SI Inovação is a scheme that supports innovation fostered by one or more companies in cooperation. The objectives are (i) to foster innovation in business by producing new goods, services and processes that provide progress along the value chain, (ii) to reinforce interest in international markets and (iii) to stimulate entrepreneurialism and investment in potential growth areas. SI Inovação may finance up to 55% of an applicant's global investment, subject to reimbursement. However, 75% of the grant conceded might be requalified as a non-reimburse incentive, depending on the performance evaluation of the project.
- ▶ SI Qualificação PME is a way to foster investment by one or more

SMEs in cooperation. Its aim is to foster innovation, modernization and internationalization. Note that support in sectors subject to specific EU restrictions on state aid must comply with the relevant EU framework. In each sector, the incentives also take into account the Business Activity Classification (CAE) within which the projects are eligible.

Companies can also apply for support for vocational training. Projects under the SI Inovação scheme may include a training component. The incentive granted is equivalent to a percentage of the actual investment that is deemed eligible in accordance with the law, while the eligible expenses vary according to the nature of the project.

Both SIFIDE and RFAI are up and running, despite the difficulties facing the economy. Indeed, the Government increased some rates and raised caps in 2010 compared with 2009.

Structuring for the future

Structures that provide a tax-efficient base for successful operations include the tax-free zone of Madeira, a Portuguese archipelago. Portugal offers benefits if investment is made through the tax-free zone of Madeira. The zone offers a reduced rate of corporate income tax of 4% (for the financial year 2012) and 5% (for the years 2013 to 2020). This applies to foreign income (i.e., that which has no Portuguese source) that is derived from a licensed activity.

The reduced rates are limited to ceilings of taxable income, which are associated with the number of existing jobs. However, an administrative order was enacted by the Madeira Autonomous Region, granting more flexibility on the definition of a job.

If an EU holding structure is put in place, investors may get an exemption of withholding tax paid on dividends distributed; an exemption from or a reduction in withholding tax on interest payments. Also applicable are relief on capital gains on the disposal of shares in a Portuguese company, and relief on stamp duty paid on financing.

Investors can also benefit from setting up a special purpose vehicle (SPV), which is financed by debt to acquire a Portuguese target company where both entities form a tax consolidation in Portugal. Setting up an SPV that is financed by debt to acquire a Portuguese target, which is followed by either a merger either upstream or downstream, can also bring relief.



75%

SI&DT - rate that may be attainable on relevant global investment

Spain

The entrepreneurial culture

Despite the economic hardships felt in Spain during the 2009 recession, the national biotechnology sector continued to expand, with sector growth rates outperforming those of the previous years.

In 2009, the Spanish biotechnology sector comprised 1,095 companies that carry out biotechnology activities and 399 companies focused primarily or exclusively on biotechnology. A total of 148,648 professionals work in the sector, which generates revenue of €53,152m. Biotechnology companies (those whose principal activity is biotechnology) invoiced €7,711m, 15% of the sector total.

Despite the economic recession, the sector continued to grow in size, at rates similar to the previous years: 16.2% in the case of companies using biotechnology and 30.8% in the case of biotechnology companies. This consolidates the extremely high accumulated annual growth rates recorded since 2005 (23% and 35%, respectively).

This growth can be partially explained by the transversal nature of biotechnology: companies in different sectors are increasingly incorporating more biotechnology activities in their products and services. This type of growth naturally arises when new emerging technologies become regular features in the productive system.

The most salient indicators include the almost 7% rise in the number of biotechnology R&D personnel employed and the over 5% growth in private R&D expenditure. In addition, companies carrying out biotechnology R&D grew 12%. Other output indicators are also noteworthy, such as the number of patent applications, which virtually doubled (up 85% in the past year). These indicators confirm

the efficiency and strength of the national bioindustry sector.

The sector structure remains stable. Ninety-three percent of the companies using biotechnology had less than 250 employees, a figure which rose to 95% in the case of biotechnology companies. The INE survey also revealed that biotechnology companies account for 25% of sector employment and 15% of the total revenue generated.

In 2009, private internal R&D expenditure in biotechnology exceeded €485m, up 5.4% on the previous year. The bulk of these funds were received from Spanish sources (89.5%). Specifically, activities were financed using companies' own funds (67.8%) and, to a lesser degree, funds from public administrations (24.8%). Other companies (6.3%) also account for some funding, as do private non-profit institutions and universities (both with 1%).

Useful links:

- ▶ www.asebio.com
- ▶ www.mineco.es
- ▶ www.gen-es.org

Taxation

Corporate tax

Corporate tax is imposed on the income of resident companies and non-residents that conduct business activities in Spain through a permanent establishment at the rate of 30%. Small and medium-sized enterprises are taxed at a rate of 25% on profits up to €120,202.41 and at the general rate of 30% on the tax base exceeding this amount.

Taxable base is the company's income for the year determined from the annual financial statements prepared under Spanish GAAP

¹ Information obtained from 2010 ASEBIO ANNUAL REPORT.

and adjusted for certain statutory tax provisions.

Tax losses may be carried forward and offset against future taxable income for a period of 18 years. For newly established enterprises, the 15-year period begins in their first profitable year for tax purposes.

Incentives

There are no specific tax incentives for biotechnological SMEs, other than general R&D incentives.

In Spain, there is an association of business angels named ESBAN which is making efforts to promote investments on business start-ups and other SMEs by “angel finance.” However, nationwide, the Government has not established any kind of income tax facility in this matter. Only regionally, the regions of Cataluña and Madrid have taken measures of this kind. This income tax facility consists of the possibility of applying a 20% Personal Income tax “PIT” quote deduction if certain requirements are met. In any case, there is an annual deduction limit of €4,000 for this purpose.

Other than those for R&D in general, Spain’s central government provides no tax incentives for SMEs engaged in biotechnology. Start-up finance is available through ESBAN, an association of business angels. But it is the regions that have taken the biggest steps to encourage investment. The governments of both Cataluña and Madrid have introduced measures of late. In each case, the facility consists of a deduction in income tax of 20% if certain requirements are met. Even so, the incentive is subject to an annual deduction of €4,000.

According to Spanish CIT regulations, R&D activities have the right to apply a tax credit on the expenses and certain investments made on R&D during the year. Spanish legislation distinguishes between R&D projects and Technologic Innovation (IT) projects. In view of the different applicable rates, the qualification of a project as R&D or IT has a very relevant impact on the amount of the potential tax credit.

To determine whether the activities carried out by the company qualify for the purpose of the R&D or IT tax credits, an in-depth technical analysis that requires knowledge of the business and products should be made by experts. The Spanish legislation provides the possibility of requesting a certificate to certain authorized organisms about the qualification of the activities carried out by the company as R&D or IT for these purposes.

R&D tax credit is calculated by the application of a fixed percentage on the R&D expenses of the year. The general applicable rate is 25%, but if the yearly expenses exceed the average expense of the preceding two years, 42% will be applicable to such excess. An additional 17% credit is available for personnel expenses corresponding with qualified researchers and 8% for investment in assets (excluding real estate) exclusively affected by R&D.

The tax credit base is made up of the amount of R&D expenses and, if applicable, investments in tangible fixed and intangible assets, excluding real estate and land. Expenses, including the depreciation of the assets used in the R&D activities, shall be deemed to be R&D expenses if they are directly related to, and are actually applied, the pursuit of those activities, and are separately registered by project.

The IT tax credit is also calculated by the application of a fixed percentage (12%) on the IT expenses.

The tax credits base shall be reduced by 65% of the subsidies received for those activities which are attributable as income in the tax period.

In the past, R&D and IT expenses relating to activities pursued abroad only qualified for the tax credit if the main activity was carried out in Spain under certain circumstances. However, for financial years starting after January 2008, this limitation does not apply for EU Member States.

Amounts paid to carry out activities in Spain at the request of the company, either individually or jointly with other entities, shall also be deemed to be R&D expenses.

The amount of the tax credit may not exceed in aggregate (R&D and IT) 35% of the gross tax due, net of domestic and international double taxation tax credits and of tax reductions. However, this limit would be increased to 50%, if the tax credit corresponding to expenses incurred and investments made in the tax period exceeds 10% of gross tax due, net of domestic and international double taxation tax credits and of tax reductions.

The excess can be carried forward for 15 years. For newly incorporated companies the 15-year period computation will not start until the first year of profits.

Patent Boxes

Law 16/2007 introduced a patent box type of incentive regime into the Spanish tax system. This regime was conditioned to its express conformity with the EU provisions, but, on 13 February 2008, the European Commission announced that the regime is compatible with EU state aid rules and, consequently, the regime entered into force retroactively for tax years starting from January 2008.

Under the new regime, regulated by article 23 of the CIT Law, 50% of incomes arising from the transfer of the right to use certain qualifying intangible property (IP) rights are tax exempt, with a limit of six times the cost of the asset which generates the right of applying this regime. This 50% exemption applies on gross income, so expenses incurred in the development of these rights are fully deductible.

Qualifying assets include patents, designs or models, plans, or information concerning industrial, commercial or scientific experience (know-how).

This regime is applicable within tax groups formed by companies and it is compatible with R&D tax credits.

Finance and incentives

Biotech industry aid is mainly grants, credits and zero interest rate advances. These types of aid can either come from Europe or the Spanish Central Government (as well as the regional entities). In the European sphere, the Seventh Framework Program (FP7) is the main instrument for funding investigation projects and technological development on the EU for the years 2007-13. With a budget

of €50,521m, the Program is structured into four more specific programs.

It is the cooperation program of great interest to biotechnology industry.

Nationwide, the varied public support depends on specific programs approved and the investment activities; for example: the following can be mentioned:

- ▶ Proyectos de investigación y desarrollo (PID): based on zero interest rate credits given to multi-year projects with a budget of at least €240,000
- ▶ Línea banca-CDTI para financiación tecnológica: subsidized interest rate financing offered to innovative physical capital that improves competitiveness, as long as the technology built is considered to be "emerging" in the sector
- ▶ Iniciativa NEOTEC para la creación y consolidación de empresas de base tecnológica: subsidizes necessary expenses for the company incurred for implementation, except from land purchase and civil construction

0%

Tax on unlisted participation held by companies

Sweden

The entrepreneurial culture

There are several private actors that can help facilitate new investments and start-ups in Sweden.

ALMI Företagspartner can provide complementary funding if a company does not have sufficient funding or cannot obtain a bank loan for the full amount. ALMI is a state-owned company that helps companies with capital and advice. The aim is to promote the development of competitive small and medium-sized enterprises (SMEs), as well as to stimulate new enterprises. Companies can apply for a loan with ALMI of up to SEK250,000 without security. However, please note that a higher interest is charged for these types of loans than average bank rates. The loan amount is not limited, but for loans exceeding SEK250,000 an additional financier and security is generally required. ALMI can also offer specific loans for innovation and export companies.

Read more at www.almi.se. Also visit: www.verksamt.se for general information about starting a business in Sweden.

VINNOVA is the Swedish Governmental Agency for Innovation Systems. It invests in research and strengthens Sweden's capacity for competitiveness, sustainable development and growth.

VINNOVA's efforts range from programs for R&D projects in small companies and at universities, to long-term development of strong research and innovation environments that attract R&D investment and expertise from around the world. VINNOVA's efforts are based on cooperation and co-financing with industry, academia and the public sector. For more information, visit: www.vinnova.se.

Innovationsbron focuses on turning research and innovation into business. Its vision is for Sweden to become an international

leader in commercializing research-related business ideas. Innovationsbron combines early-stage financing with support to develop companies to stages where they can attract commercial funding, partners and customers. Innovationsbron helps researchers, innovators and entrepreneurs to translate their ideas into business. Its efforts are focused on projects and companies in the early stages of development, helping overcome the initial difficulties and risks associated with developing business ideas before commercial players, such as private equity companies, come on board. Innovationsbron's business development work combines seed-funding with intensive efforts to develop the business concept and answer questions about business models, technology, markets and economic potential.

It also runs a national program for incubators, or entrepreneurial environments, where new start-ups can receive support. Seed-funding is supplemented with coaching in areas such as customer contacts and team enhancement that promote faster growth. Once companies are equipped to meet the commercial market, Innovationsbron plays an active role in engaging subsequent investors. This reduces the gap to the next financier and enables the company to focus on developing its operation. Visit www.innovationsbron.se.

Industrifonden offers venture capital, competence and a network of contacts to SMEs with international growth potential. The focus is on creating value in the portfolio companies. All investments are made on commercial terms agreed by entrepreneurs and co-investors. Industrifonden is an independent ever-green fund founded by the Swedish Government in 1979. It operates on a commercial basis and receives no government funding. Revenues are returned to the business for new investments. Visit www.industrifonden.se.

Taxation

Corporate tax

There are no corporate tax regulations in Sweden that apply specifically to biotech companies, either in the start-up phase or for existing businesses. A limited company established in Sweden pays business tax of 26.3% on the profit the business had during the year.

Tax losses are carried forward and can be offset toward future taxable income without time limitations. The unlimited carryforward period of tax losses is an advantage compared with other countries, as it is common for time limitations to apply to the utilization of losses carried forward. Moreover, current year tax losses can generally be offset against group profits through group contributions from Swedish group companies (limitations can apply after change of control). Group contributions are tax deductible for the paying company and taxable income for the receiving company.

Unlike several other jurisdictions, there are no thin capitalization rules in Sweden. However, certain restrictions apply on interest deductions on intercompany loans as a result of an internal restructuring. General restrictions on the deduction of interest are expected for 2013.

Incentives

Costs for R&D are deductible for tax purposes according to a specific regulation in the Swedish Tax Act. This includes research performed in the taxpayer's own business, as well as contributions paid to another company that performs research activities, on the condition that the research performed by the latter company is of reasonable interest for the contributor's business. The term "reasonable" was added to the wording of this section from 1 January 2012 in order to broaden the scope of the rule.

There are currently no tax incentives specifically aimed at biotech companies in Sweden.

There is no established monetary limit on contributions from one company to another company performing the R&D activity. Moreover, in 2011, the Government appointed a committee to examine Swedish corporate taxation. The corporate tax investigation aims to among other things present suggestions for tax incentives regarding R&D costs.

Tax incentives in the form of expert tax relief is generally granted in Sweden for foreign experts, researchers and key personnel under certain prerequisites (such as that the individual intends to work in Sweden for no longer than five years and that the individual

is a non-resident and non-citizen of Sweden). An application must be filed within three months of the employee's arrival in Sweden. If approved, 25% of the compensation is exempt from Swedish employer social security contributions as well as personal income tax. Moreover, the following benefits can be provided tax free: moving expenses to Sweden and back home; two home trips for the whole family per year; and school fees for children. The actual tax relief is granted for the first three years of the employment period.

Employees with a monthly salary of SEK88,000 or more are always eligible for expert tax. If the salary is lower, the employee must meet one of the following requirements:

- ▶ Work with special tasks with a high degree of competence which is highly difficult to find in Sweden
- ▶ Undertake qualified research or development projects with a specific competence or at a specific competency level which is difficult to find in Sweden
- ▶ Work at the top management level or conduct similar tasks that ensure a key position in the company

Under Swedish law, compensation should normally be paid by a Swedish payer. Compensation paid from a foreign payer can, under certain circumstances, be subject to expert tax.

SEK250,000

Security free loan available to SMEs from
ALMI Företagspartner

Tax landscape for investors

Unlisted participations held by corporations are normally exempt from tax under the Swedish participation exemption, which creates an effective tax environment for holding structures. However, please also note that capital losses and write-downs on such participations are correspondingly not deductible.

Individuals are normally taxed 25% on dividends or capital gains from shares in unlisted companies. For listed shares, the tax rate is 30%. Please note, however, that very special rules apply for owners who are operative in closely held companies (see below).

In 2011, the Government announced a review of corporate taxation. Among the issues under review is how to reduce the current asymmetrical treatment of equity compared to loan financing. The Corporate Taxation Committee (Sw. Företagsskattekommittén) submitted its first progress report, "Tax incentives for venture capital," in January. The report proposes two alternative tax incentives for venture capital related to new capital invested in a company, either at establishment or in connection with a new share issue. One proposal, venture capital deduction, is directed at individuals. The second, emission credits, is aimed at companies (Sw. Emissionskredit). The report proposes that the provisions come into force on 1 January 2013.

Tax landscape for entrepreneurs

The taxation of individuals depends on how individuals choose to establish their business (sole proprietorship, partnership, limited liability company etc.). The owner of a limited

liability company is taxed on salary for work done or dividends on shares. A progressive tax rate between approximately 30% and 58% applies to income from employment.

However, very special taxation rules apply to owners who are operative in closely held companies in Sweden. These are taxed for dividend or capital gains on the shares in part as capital income and in part as employment income. Tax rates vary between 20% and 58%. A closely held company is defined as four or fewer people together owning at least 50% of the shares of the voting power in a company. If the owners are operative in the company's business, these specific rules could be applicable on their shareholdings. Note that the rules are very detailed and complex, and are continuously subject to amendments. For example, family members are, in this regard, treated as one person. The same goes for operative owners.

However, if an external investor (not operative in the company) owns more than 30% of the voting powers of the company, these special rules are not applied. This means that dividend or capital gain on shares are normally taxed at 25% for an owner who is an individual. The lower tax rate of 20% on dividend or capital gain for individuals is the lowest rate in Sweden. Consequently, these rules can result in a very favorable tax treatment if sufficient tax planning - before start-up and continuously during the holding - is carried out.

Finance

In addition to those sources already outlined above, public support may be obtained from the European Union, e.g., the FP7 program. Swedish biotech companies have been successful in this respect.

Availability of finance

Sweden has a strong economy and profitable banks. Moreover, as described above, the Sw. Företagsskattekommittén has submitted its first progress report as part of the current corporate tax investigation. The report proposes two alternative tax incentives for venture capital related to new capital invested in a company, either at establishment or in connection with a new share issue. The proposals are designed to promote venture capital investment among Swedish individuals and companies.

Regulatory environment and incentives

There appear to be no regulatory incentives (tax or other) specifically targeted at biotech companies.

The Swedish Patent and Registration Office handles all issues relating to the registration and protection of patents, trademarks and design in Sweden. Currently, there is no mutual recognition of rights patented in Sweden. You can apply for a European patent at www.epo.org (the link is found at the Swedish Patent and Registration Office's homepage).

The Medical Products Agency is responsible for regulations governing the approval and control of technical pharmaceutical and medicine products. Swedish medicinal legislation is essentially the same as that of the rest of the EU. Please read more at: www.lakemedelsverket.se.

Compliance with the rules on chemicals is monitored by the Swedish Chemicals Agency (KemI). EC legislation is harmonized in EU Member States, including Sweden.

However, specific environmental concerns and worker protection aspects could provide scope for deviations from the requirements in European Community regulations and directives. Read more at: www.kemi.se.

Exemption for teachers

The legislation relating to the right to employee inventions (LAU 1949:345) regulate the extent to which the employer may be entitled to take over the rights of an employee's patentable inventions. Paragraph 1 states that "teachers at universities, colleges of higher education and other institutions with the right to teach" are exempt. This means that they are not considered to be employees as defined by the legislation.

In Sweden, teachers, researchers and doctoral students are exempt, which means that these groups own the right to their own patentable inventions even if they are made during working hours.

However, teachers, researchers and doctoral students may agree to give up this right, to those funding their research.

Structuring for the future

As mentioned above, Sweden has no special tax or other regulatory incentives for IP or biotech companies. However, an intense debate between industry and government is currently going on over these issues. Sweden regards itself as a "knowledge-based economy" and realizes that measures need to be taken to improve conditions for business. As mentioned elsewhere, this debate is likely to result in the implementation in the foreseeable future of new tax incentives regarding R&D activities.

However, due to the Swedish participation exemption, setting up a structure with a Swedish holding company might be suitable.

Due to the very special rules regarding closely held companies, it must, however, be examined whether the Swedish holding company should be owned by individuals if they would be taxable in Sweden for dividends or capital gains and, in that case, if these special rules are applicable. Without the correct tax planning, it could be expensive for individual owners to receive dividend or capital gains on shares in closely held Swedish companies.

Note also that, from a Swedish perspective, it is important to structure and localize the IP to the appropriate company and jurisdiction from the start. A transfer of assets from a Swedish company to a foreign associated company is taxed as if performed to market value, which could create a taxable profit in Sweden.

As regards transfer pricing, Sweden generally complies with OECD guidelines.

Tax-efficient structures

As described above, unlisted participations held by companies are normally exempt from tax under the Swedish participation exemption. Present rules allow for unlimited interest deductions on acquisition debt. The arm's length rule is applicable. This creates an effective tax environment for holding structures. The most usual structure is a Swedish holding company to which the acquisition debt is allocated, and one or more operative subsidiaries.

Sweden is usually not used for centralized R&D ownership structures. However, the ongoing debate between the industry and the Government, and the forthcoming proposals related to R&D tax incentives, will hopefully make Sweden more attractive in this respect.



25%

Of compensation and certain benefits paid to foreign experts, researchers and key personnel can be exempt from Swedish tax

10 years

Potential length of cantonal tax holidays

Switzerland

The entrepreneurial culture

Switzerland encourages entrepreneurs, including those in biotechnology. There are clusters of research and development (R&D) in the cantons of Basel/Baselland, Zurich and Geneva/Vaud. All have a high concentration of companies that invest heavily in R&D. It is also possible to team up with the universities of Basel, Zurich, Geneva and Lausanne. Indeed, with its world-class universities, Switzerland offers a pool of scientists and other personnel. The Government may also reform the country's corporate tax laws to include extended credits for R&D.

The Swiss Biotech Association is the industry's focal point (www.swissbiotech.org). In Switzerland, promoting the economy is mainly the preserve of the 26 cantons, most of which have departments responsible for doing the job.

Location Switzerland is the national agency which promotes Switzerland as a business location (www.osec.ch).

As the Confederation's innovation promotion agency, Commission for Technology and Innovation (CTI) lends support to R&D projects, to entrepreneurship as well as to the development of start-up companies. CTI helps to optimize knowledge and technology transfer through the use of thematic and regional networks and platforms.

CTI lends support to:

1. Market-oriented R&D projects
2. Creation and development of start-up companies
3. Knowledge and technology transfer

Support is generally available for R&D projects relating to scientific innovations in all

disciplines. Project proposals are submitted using the bottom-up principle and are mainly selected on the basis of their innovativeness and market potential.

CTI's Venturelab program offers made-to-measure training modules for up-and-coming entrepreneurs. These training modules provide the knowledge, skills and methodology needed to establish a new company and successfully transform their promising business ideas into marketable products and services. Young entrepreneurs can also benefit from professional coaching. New knowledge-intensive and technology-based companies with considerable market potential are eligible.

The CTI supports the transfer of knowledge and technology between higher education institutions and industry in a targeted and results-oriented manner. Professionally run R&D and Knowledge and Technology Transfer "KTT" networks offer SMEs services in terms of channeling technology know-how through higher education institutions and by providing solutions for business-specific needs. In addition, innovative Swiss businesses and researchers should have development opportunities through access to international programs and networks such as EUREKA, ERANet and FP7, or European technology platforms (ETP).

Taxation

Corporate tax

In Switzerland, net income is subject to corporate income tax at federal, cantonal and municipal levels. This results in a combined effective ordinary tax rate of between 12% and 25% depending on the location. Lower rates are available in special tax regimes, i.e.,

12%-25%

Combined effective tax rate depending on location,
without accessing preferential tax concessions

for holding, principal and mixed companies (for details on the latter two see below). Unlike anywhere else, taxes qualify as a tax deductible expense.

At the cantonal and communal level, there is an annual "capital tax." It is charged on a corporation's net equity at book value. Rates vary between 0.001% and 0.5%, depending on the canton. Some allow corporate income tax to be credited against capital tax. Value added tax (VAT) is levied at the standard rate of 8% or at a reduced rate of 2.5% for certain industries, such as pharmaceuticals, fertilizers, pesticides, seeds and so on.

Capital gains are generally taxed at the same rate as other income. However, capital gains from disposals of qualifying investments in subsidiaries are subject to participation relief (provided there is a minimum investment in the equity of 10%, which is held for a minimum of one year).

Relief is also granted with regard to taxes on dividends from qualifying participations (i.e., those with a minimum equity investment of 10% or where the investment has a fair market value of at least CHF1m). The tax liability may be reduced according to the proportion of net dividend income to total taxable income.

Loss relief is available on income during the current year and may be offset against losses incurred in the preceding seven years (i.e., under a carryforward provision). Losses cannot be carried back.

There are also federal guidelines on thin capitalization that are also applied by most cantons. Under these, a minimum capitalization is calculated based on the fair market value of the individual assets held. For each type of asset, only a specified percentage may be financed with debt

from related parties (e.g., cash: 100%; participations: 70%; intangibles: 70%).

Depreciation may be calculated using either the straight-line (SL) method or the one based on declining balance (DB). At federal level, maximum rates for intangibles are 40% (for DB) and 20% (under SL). Some cantons have favorable provisions (e.g., an immediate or one-time allowance for depreciation).

Withholding tax is levied on dividends and certain interest payments (generally on bank accounts and bonds) at a rate of 35%. No withholding tax is generally levied on interest on commercial loans. In addition, there is no withholding tax on royalties. Furthermore, it should be noted that the applicable rates may be reduced under an agreement between Switzerland and the European Union or under other similar double tax treaties.

Except for the purposes of VAT, the concept of a consolidated or group return is unknown in Swiss tax law. Each corporation is treated as a separate taxpayer and files its own return.

Incentives

Biotech companies may benefit from a range of general incentives:

1) Tax holidays

For up to a maximum of 10 years, cantons are free to grant full or partial relief from corporate income tax and capital taxes to newly established companies, those relocating a new business to Switzerland, and those contemplating a significant expansion of an existing business. In order to qualify for such relief, it is usually required to create new jobs, promote innovative economic activities or sustainably develop an economic area.

At federal level, tax incentives are limited to ventures in the "Economic Renewal Areas." In

these, companies may receive full or partial exemption from tax for up to 10 years. Tax relief is usually granted to industrial companies and production-related service firms, creating new jobs or preserving existing ones on a long-term basis. In general, tax holidays will be granted with claw-back provisions. This means the tax holiday may be revoked if the requirements for relief are not met.

2) Provisions

Federal and cantonal regulations provide that a company may record a tax-deductible reserve amounting to one-third of the value of its inventories. At the federal level and in most cantons, too, provisions for future third-party R&D costs are allowed up to 10% of taxable profit or up to a maximum of CHF1m. Provisions to cover doubtful accounts receivable and expected liabilities are generally allowed for tax purposes if they are justified commercially. Certain lump-sum provisions for accounts receivable are possible without substantiation.

3) Capitalization of R&D expenses

Under these provisions, R&D costs may be expensed or, if justified, capitalized and amortized over their useful lifetime. If the R&D expenses are capitalized, the limitation on losses carried forward for seven years can be mitigated. In that respect, it should be noted that, in general, the treatment for accounting purposes is the basis for the tax treatment.

Tax landscape for investors

In Switzerland, there is usually no withholding tax on interest on commercial loans, including those made by foreign parents to Swiss subsidiaries. In order to reduce double taxation (of corporate income as well as that from dividends), the partial taxation of

dividends was introduced for Swiss residents holding a minimum of 10% of the capital of a company. The rule applies both at the federal level and the cantonal and municipal level.

Until last year, any repayment of equity that failed to qualify as a repayment of paid-in share capital was subject to income and withholding tax (according to the principle of nominal value). As part of the latest tax reform, the capital contribution principle (CCP) was introduced at the beginning of 2011. Under this, repayments of capital contributions directly received from shareholders after 31 December 1996 and disclosed in a separate account in the balance sheet of the distributing company, are exempt from income tax (at the level of Swiss individual shareholders). They are also exempt from withholding tax.

Tax landscape for entrepreneurs

In Switzerland, tax rates vary widely because of the multilayered system. The maximum overall rate of federal income tax is 11.5%. On top of that, cantonal and municipal taxes are levied at progressive rates. The maximum combined rates (including all three levels) range from approximately 19%-45%, depending on the location. In addition, cantons and municipalities levy net wealth taxes.

For expatriates, an annual lump-sum deduction of CHF18,000 at the federal level is allowed to cover housing fees and other such expenses (e.g., moving expenses). Similar allowances may be granted at the cantonal level. Otherwise, only minor standard deductions are available.

That said, a number of mandatory contributions are fully deductible against tax. These include the Confederation's old-age and survivors' insurance with a contribution

rate of 10.3%, split in half between employee and employer. Also covered are contributions to the (mandatory) company pension fund. Rates vary according to the plan, gender and the age of the employee. The employer must bear at least half of the total contribution. Some contributions toward individual savings are also tax-deductible up to a certain level.

The cost of insurance against unemployment can also be deducted from the income, as is the family allowance, which is paid by employers at rates that vary according to the canton.

Finance

The Swiss National Science Foundation (SNSF) is Switzerland's leading provider of scientific research funding. The SNSF annually supports some 7,200 researchers, almost 80% of whom are aged 35 years or younger. With its federal mandate, it supports basic research in all disciplines, from philosophy and biology to the nanosciences and medicine.

The focus of its activities is the scientific endorsement of projects submitted by researchers. The best applicants are funded by the SNSF with an annual total amount equaling approximately CHF700m.

Established in 1952 as a foundation under private law, the SNSF has the autonomy it needs to promote independent scientific research. The SNSF is committed to promoting young scientists and works to ensure that scientific research in Switzerland has the most favorable conditions for developing internationally. It also encourages dialogue between scientists and representatives in society, politics and the economy.

Availability for capital

In general, capital is available in Switzerland, either from business angels, family offices or specialist venture capitalists. In addition, Swiss banks are - compared to some of their competitors - in good health, which may be of advantage in financing discussions. See also the data analysis presented in the Swiss reports on biotechnology (www.swissbiotechreport.ch), published annually since 2004.

Regulatory environment and incentives

There are a variety of legal provisions in Switzerland relating to biotechnology, particularly for research. Federal laws and ordinances regulate therapeutic products and medicines as well as genetic engineering, agriculture, protection of the environment and food. There are also supervising authorities. The one for human research is Swissmedic (www.swissmedic.ch).

Swiss law provides for the protection of intellectual property (IP), such as patents and trademarks as well as copyright and related protection. So enterprises may protect their innovations and turn their ideas into industrial property (www.ige.ch).

There is also support for start-ups. The Swiss National Science Foundation in Bern (www.snf.ch) is the point of contact for basic and targeted research. The Commission for Technology and Innovation deals with applied R&D (www.kti-cti.ch). Individual cantons also offer help to firms starting up.

In addition, Switzerland takes part in programs such as the European Union Framework Program for Research and Technological Development or the European Cooperation in the field of Scientific and

Technical Research (www.sbf.admin.ch;
www.euresearch.ch; www.hfsp.org).

Structuring for the future

Tax-efficient structuring

In Switzerland, there is usually no capital gains tax levied on shares held as a private asset when disposed of by individuals. At a corporate level, tax relief is granted for capital gains on investments if, as discussed already, certain requirements are met.

A securities transfer tax, if applicable, can usually be avoided if a shareholding, and its subsequent disposal, are structured correctly. Federal guidelines provide for a special tax regime for what are known as principal companies, which can apply to those specializing in biotechnology. A Swiss company within an international group may be treated as a principal company if the firm assumes risks and responsibilities for activities such as purchasing, R&D, manufacturing, marketing, distribution and logistics; if manufacturing is usually performed outside Switzerland on a contract or toll basis; and if sales are conducted outside the country through related parties that operate as commissionaires or limited risk distributors.

In such cases, taxable income may be reduced by maximum 50% at the federal level and taxation is as a mixed company at the cantonal level resulting in an overall effective tax rate between 4.5% and 9%, depending on activities and location.

Another benefit is that, subject to certain requirements (cf. above), companies may qualify for tax holidays. This may reduce the effective tax rate in the best case to zero for a period of up to 10 years.

The status of mixed company is, as discussed above, available at the cantonal and municipal level. To secure such a status, a company needs to be engaged predominantly abroad with only minor involvement in Swiss domestic market. Usually, this means having at least 80% of its income sourced from abroad and a similar percentage of expenses related to foreign activities. However, the requirements vary from canton to canton. In the best case, the status secures an effective tax rate of as low as 8%-12%, depending on the location.

A company with its statutory seat in the Canton of Nidwalden is entitled to run, within its normal business, a "license box" to which IP and R&D activities, as well as related income and royalties, can be attributed. So far, the arrangement is available only in

Nidwalden but there is talk of other cantons doing the same. The definition of royalties matches that in article 12 of the convention drawn up by the Organization of Economic Cooperation and Development. Income from both domestic and foreign sources may benefit equally from the license box. It can apply to capital gains and expenses incurred for R&D expenses are deductible, too, resulting in an effective tax rate of 8.8%.

Although some of the above tax regimes, in particular the mixed company concept, are currently under scrutiny by the EU, alternatives are sought for and should be available in time before the current regimes may be phased out.

7,200

Number of researchers supported annually by the
Swiss National Science Foundation

The United Kingdom

£10m

Lifetime limit of concessional tax relief for individuals on qualifying assets

The entrepreneurial culture

The UK Government has a single website for all aspects of trade and industry (www.bis.gov.uk). Business Link is the Government's online resource for businesses. It contains all essential information, together with details about support and services for business, whether for a large organization or one that is starting up (www.businesslink.gov.uk). StartUp Britain is a campaign by entrepreneurs for entrepreneurs, which was launched in March 2011. Designed to celebrate, inspire and accelerate enterprise in the UK, it is backed by David Cameron, the Prime Minister, George Osborne, the Chancellor of the Exchequer, and the Government as a whole (www.startupbritain.org).

The Technology Strategy Board is the UK's national agency for innovation. Its goal is to accelerate the pace of economic growth by stimulating and supporting business-led innovation. To this end, the Technology Strategy Board manages a number of publicly funded programs including Grant for R&D and Knowledge Transfer Partnerships (www.innovateuk.org).

The Regional Growth Fund operates across England. With funds of £1.4b at its disposal until 2014, the fund acts as a lever for investment from the private sector. It aims to help areas and communities dependent on the public sector to make the transition to the private sector. Among the projects it has funded is Redx Parma (Merseyside), which is to receive £5.9m.

Enterprise Zones enable areas with problems to create new businesses and jobs. Companies operating from such zones benefit from laxer planning rules. They also pay lower business rates (www.bis.gov.uk).

Taxation

Corporate tax

The UK is trying to encourage businesses to invest in the country by offering a more competitive tax regime. The rate of corporation tax is due to fall to 25% from 1 April 2012 and the Government has committed to reduce it still further, to 23%, by April 2014.

There are also separate consultations in progress with the aim of rebalancing the economies of both Northern Ireland and Scotland: there are suggestions as part of the talks to lower the rate of corporate taxes closer to that of the Republic of Ireland.

Tax losses

In the UK, there is no limit on the extent to which tax losses, including those for start-ups, can be carried forward. Nor is there a limit on how much of the loss can be utilized in any one year. The UK currently gives full relief on interest costs arising from financing structures, providing it is charged at arms length and providing it is not restricted by the worldwide regulations on debt caps. Broadly, these rules restrict interest cost where the UK net debt is greater than 75% of a group's external gross debt worldwide.

Incentives

The UK has a general scheme covering research and development (R&D) for large companies that provides for tax relief at 130% of qualifying expenditure incurred on projects that meet the definition. In addition, there is a separate scheme for small and medium-sized enterprises (SMEs), which provides for tax relief at a rate of 200%. From April 2012, the latter rises to 225%.

200%

Potential rate of tax relief for SMEs on certain R&D expenditure

There have also been several recent changes to enhance and refine the credit further to the benefit of small companies specifically.

Tax landscape for investors

The UK is increasingly a more attractive holding location for corporate investors due to:

- ▶ Low headline rate of corporation tax

The headline rate has fallen from 28% at the start of 2011 to 25% with further reductions to 23% proposed.

- ▶ The broad-based exemption from UK corporation tax on dividends received by UK companies

Under tax law that came into effect on 1 July 2009, dividend income of a UK company that comes from both UK and non-UK sources should be exempt from corporation tax if a number of qualifying conditions are met. Although it is necessary to undertake some due diligence to ensure that one of the qualifying conditions will apply, the exemption is broad based and is a full (100%) exemption, which does not contain a "minimum shareholding" test, a "period of ownership" test, or a requirement that considers the activities of the payor or how the payor is taxed. On the assumption that a UK holding company controls a group company or it holds 100% of the ordinary share capital of a group company, it should be possible for the UK holding company to qualify for this exemption, such that dividend income received from the group company should not be subject to corporation tax.

- ▶ No outbound dividend withholding tax
- ▶ An extensive treaty network

The UK has tax treaties with more than 100 jurisdictions and also benefits from access to the EU Interest and Royalties Directive and EU Parent-Subsidiary Directive.

- ▶ Generous interest deductibility rules

Traditionally, the UK has been viewed as a beneficial territory for tax-efficient financing due to its relatively generous provisions available for interest deductions, notwithstanding the anti-avoidance provisions in place to stop "excessive deductions" (thin cap, arbitrage, debt cap, unallowable purpose, etc.). This can produce a much more favorable and commercial result than the rules in territories that apply strict limitations, or mathematical formula-based approaches.

- ▶ Exemption (by election) of foreign branch profits from corporation tax

With effect from 1 January 2012, UK companies may elect to exempt from corporation tax the profits earned by their foreign branches. This exemption will be attractive to companies with branches in low tax foreign locations where additional "top up" UK corporation tax would be payable in the absence of the election.

- ▶ Controlled foreign corporation (CFC) reform

CFC reform has been on the agenda as part of the wider overhaul of the taxation of foreign profit since June 2007. There are a number of factors that have driven the need to reform the CFC regime including a stated desire to create the most competitive tax system in the G20, the need to update an old piece of legislation to reflect modern day business practice and the requirement that the regime is EU law compliant.

It is intended that the new regime will target situations that pose a high risk of artificially diverting UK profits and will ensure that if a CFC charge arises it will only be applied to the proportion of overseas profits that have been artificially diverted from the UK. The majority of the new rules are expected to be introduced in Finance Act 2012.

An important part of the current proposals is the Finance Company Partial Exemption (see "Tax-efficient structures").

- ▶ The Substantial Shareholding Exemption which exempts any gain on the disposal of a qualifying holding of shares for the requisite period

Any disposal of shares by a UK company of its shares in a group company will be regarded as a taxable disposal. A taxable gain will initially arise to the extent the consideration or market value of the shares disposed of exceeds their acquisition cost (less indexation allowance). However, this taxable gain can, under many circumstances, be exempt from UK corporation tax where the conditions of the substantial shareholdings exemption (SSE) are satisfied.

In most cases involving the disposal by trading groups of shares in companies that carry out trading activities (rather than investment activities), the SSE will typically apply.

- ▶ The proposed UK Patent Box Regime (see "Tax-efficient structures").

For individual investors, entrepreneur's relief now provides for a tax rate of 10% (compared with the normal rate of tax on capital gains of 28%) for lifetime gains of up to £10m on qualifying assets. This includes a qualifying hold on shares in a personal company (up to

£5m to £10m

The recent increase in the lifetime limit for entrepreneurs' relief on tax

5%) in which the individual is an employee or an officer and which is held for the qualifying period.

Enterprise Investment Schemes and Venture Capital Trusts also offer tax incentives to stimulate personal investment. These schemes were recently further extended.

Tax landscape for entrepreneurs

The recent increase in the lifetime limit for entrepreneurs' relief on tax from £5m to £10m, as mentioned above, has made the UK more favorable compared with competitors.

Finance

As with other industries in UK, companies may seek guidance from the following website on whether there are grants available for their industry. The site also gives details of trade organizations and other such bodies, which may help those looking for advice (www.businesslink.gov.uk/finance).

Local Enterprise Partnerships are between local authorities and businesses that play a role in determining the priorities facing a community. Not only are they a means of spurring decentralization, they are also a way for local authorities and businesses to work together in order to quicken the pace of economic recovery (www.communiites.gov.uk).

Other useful websites include:

- ▶ www.fundmap.co.uk/bio
- ▶ www.bis.gov.uk/RGF
- ▶ www.innovateuk.org

Regulatory environment and incentives

As well as offering incentives for R&D as described above, the UK's tax regime also provides for relief on the amortization of intangible assets, such as patents, trademarks and other forms of intellectual property.

Recent changes to the UK's regulatory system could also be seen as advantageous to companies looking to operate here. However, they are at an early stage. The changes include switching to a single regulator for research and a streamlined process of approval at a local level.

The Government has established the National Office for Coordination of Research Infrastructure (NOCRI; www.nihr.ac.uk). The new body has been set up to help public, as well as those in charities and industry, work in partnership with government.

NOCRI supports partners by research signposting - e.g., helping them to navigate clinical research and find experts as well as facilities and technologies. NOCRI also helps to develop collaborative research partnerships. A model agreement has been developed to streamline contracting for partnerships involving those within pharmaceuticals and biotechnology, as well as universities and organizations within the National Health Service.

Structuring for the future

From the perspective of an individual shareholder, the key to setting up new

ventures in biotechnology is to structure shareholdings correctly from the outset. This may help an applicant not only to qualify for entrepreneurs' relief, it will also help to incentivize management, so that the company is able to manage its affairs for the medium and long term.

Tax-efficient structures

In the UK, there are structures that provide for the sale of operations free of tax for corporate holders disposing of shares in a biotechnology company. Similarly, there are structures that enable investors to take advantage of entrepreneurs' relief for individual shareholders in such companies.

Finance Company Partial Exemption (FCPE)

The FCPE which forms part of the overhaul of the CFC regime generates an opportunity to establish a low tax platform for non-UK lending with limited tax risk. Where the exemption is available, it will, in most situations, give rise to an effective 5.75% corporation tax rate on profits from overseas intergroup finance income by the year 2014. There are also limited situations where a full exemption is achievable.

UK Patent Box

As part of the Government's growth agenda and its stated aim to create the most competitive tax regime in the G20, the Patent Box is being introduced to provide an additional incentive to develop, commercialize and retain innovative patented technology in the UK.

The regime is due to be introduced in April 2013 and is potentially far more generous than originally anticipated which, unlike other IP regimes that look to tax only profits attributable to the IP at a lower rate, there is potential for the vast majority of some business's profits to fall within the UK regime. A business can lower its UK and global effective tax rate as well as its cash outlay, by considering how to obtain the greatest benefit from the Patent Box regime.

The potential benefit that can be obtained is to a large extent dependent on the business's global operating structure and wider intellectual property (IP) strategy. The regime requires a detailed knowledge of how patents are owned and exploited by the business to generate income. Businesses should look to understand the regime's impact including how it interacts with the supply chain, R&D and other aspects of UK tax and how best to approach it in order to obtain the maximum benefit in the context of their global operations. This may require careful structuring to yield long-term benefits and may make the UK more favorable as a central operating location.

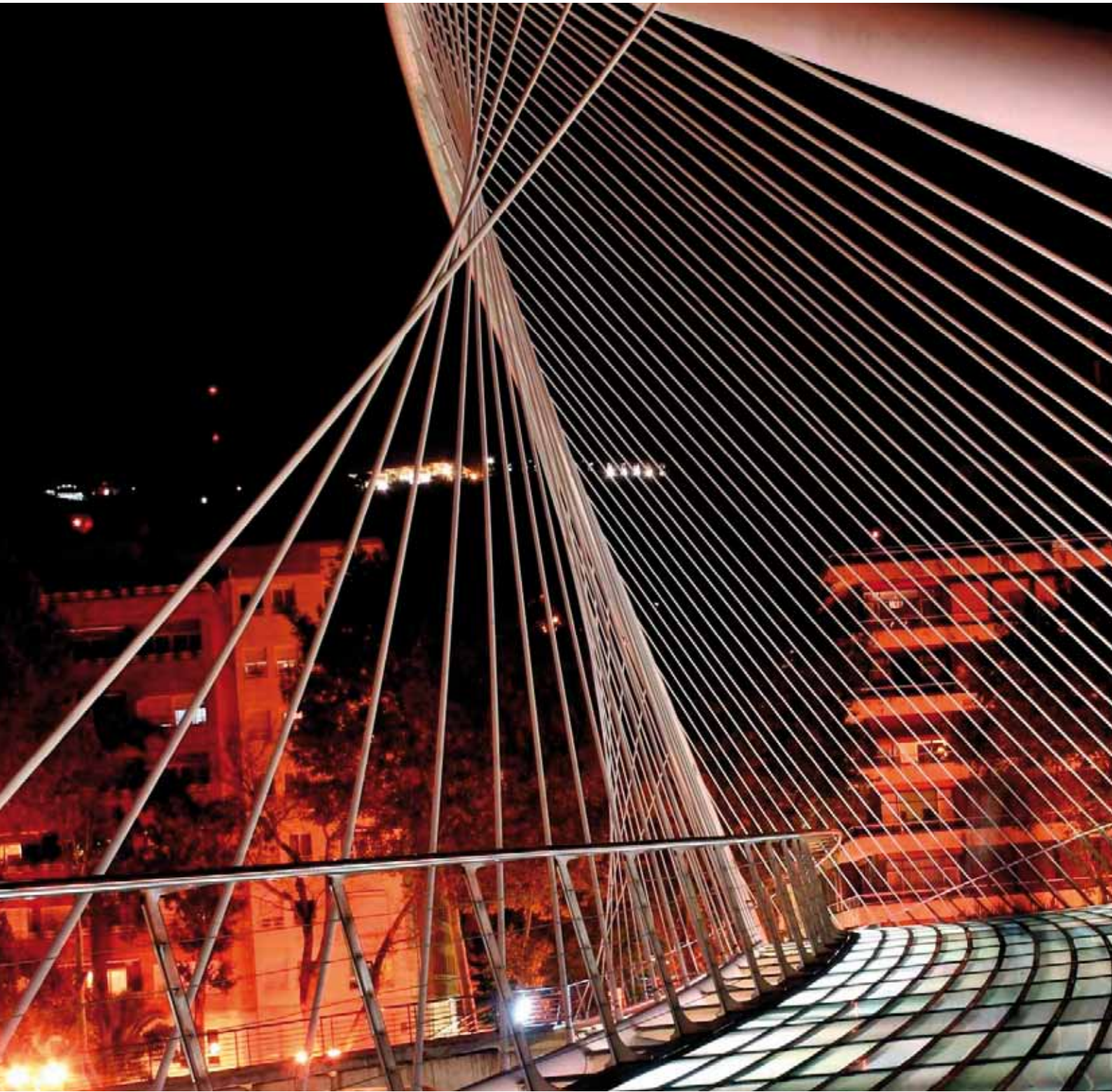
To qualify for the regime, a business must own or exclusively license UK IPO or EPO registered patents or limited similar IP. The rules work at a very basic level by taking Patent Box profits and taxing at 10%. The 10% rate applies from 2017 with benefits to be phased in from 2013.



10%

The tax rate, applicable from 2017,
on the Patent Box profits







Part B:

Key tax considerations
through the
biotechnology
life cycle

Importance of understanding customs and international trade considerations for carrying out clinical trials on a global basis

Clinical trials are a set of procedures in medical research and drug development that are conducted to allow safety and efficacy data to be collected for new products. These trials can take place only after satisfactory information has been gathered on the quality of the non-clinical safety, and health authority approval has been granted in the country where the trial program is taking place.

In recent years, there has been an ever-increasing spread of clinical trials to emerging markets. The reasons for this expansion range from significantly lower per-patient cost, to wider patient pools and more “treatment-naïve” patients, i.e., those who have never previously taken drugs for treatment. However, while embracing the benefits of such markets, companies often forget to budget for the hidden import duty and VAT costs that arise from moving the necessary dosage and supporting materials into the markets in question.

Unlike Europe and the US, dosage-form clinical trial materials are subject to import duty in many of the favored emerging market trial locations, such as India, China, Russia and Brazil. The duty rates in question range from 3%-27%. When you add on an import VAT, which applies in over 100 countries worldwide and is often irrecoverable, the total hidden cost can be 20%-30% of the value of the materials. VAT is mostly irrecoverable in the case of clinical trial materials because the materials are not sold on as part of normal commercial business, which in emerging markets is a key criteria for VAT recovery. While different companies adopt different valuation methodologies for their trial materials, ranging from variations

of cost-plus to resale-minus, import values often run into millions of dollars and must be capable of being justified to the local customs authorities.

Often, these import taxes are not taken into account in budgeting the per-patient costs of the trials. This can result not only in significant additional trial costs, but also in significant delays at importation, as the local customs authorities will not release the materials until the import taxes have been paid.

Many global pharmaceutical and biotech companies have woken up to this significant potential cost and risk, and are now adopting strategies to deal with it. These strategies include strategically assessing the sourcing of dosage materials at the outset; planning trial timescales, which allow the company to take advantage of existing specific local reliefs or regimes which can eliminate these costs; and working with the authorities to secure further such opportunities.

One of the key areas requiring particular attention is the question of customs valuation of the product. This is the value that determines the amount on which import taxes are charged. While customs valuation rules are consistent around the world, as always, it's the small things that can cause problems and different countries will adopt different approaches.

Background on key customs and international trade considerations

All clinical trial materials (CTMs) entering a country must be declared at the border in accordance with the national customs legislation. All nations have rules for submitting customs declarations. Failure to follow these rules can result in fines, penalties and even criminal punishment for the company and its employees, as well as

seizure of the goods in question. All of these sanctions would have an adverse impact on clinical trial timelines.

Fines, penalties and forfeitures can arise from any kind of customs error. Errors in customs declarations (such as origin, tariff classification, valuation and quantity declarations), in the use of special trade programs or of free trade agreements, and even post-entry submissions (such as end-use statements), can all be the basis for a penalty.

Customs can impose penalties on an importer even if the customs broker made the error. Additionally, if a third party (such as a customs broker, air freight courier or customer) enters goods in the name of the importer and they suffer a penalty because the declaration is found to be incorrect, they may be able to seek redress from the importer if the cause of the error was their reliance on specific information provided by the importer. Similarly, the customs officials will usually have the power to seize the goods in question - in this case, their trial materials.

Penalties for customs offenses can either be civil or criminal. Civil penalties are usually issued for accidental errors (those due to carelessness or honest mistakes). Criminal penalties are usually issued for intentional violations and are inevitably much more serious.

Focus on: customs valuation

The value of the goods to be imported is an issue of particular resonance for the customs and international trade environment, particularly when one is considering “non-commercialized” shipments, such as those at issue with movements of CTMs.

Determining an acceptable customs value for CTMs is one of the key challenges facing R&D groups.

Despite the fact that the materials are not being imported for commercial resale, the customs declaration and assessment rules apply, i.e., a value must be determined and any duties and taxes paid. If the customs authorities challenge the declared value, this can lead to the R&D team having to balance the risk of cost escalation against the risk of delay or cancellation of the proposed trials.

The challenges of customs valuation have long been recognized as being critical to international commerce generally, and the World Trade Organization (WTO) requires all its members to apply the same rules for determination of customs value. These rules define six methods that are required to be applied sequentially (only if Method 1 is inapplicable can the importer resort to Method 2 and so on). But these rules do not provide a method of valuing materials that can be readily applied in an R&D clinical trial context.

The six methods set out in the WTO Valuation Agreement are as follows:

- ▶ Method 1: “Transaction value” based on the sale of the goods that are being imported (so typically, this cannot be applied in a clinical trials situation as there is no sale)
- ▶ Method 2: Value based on sales of “identical goods” that were actually imported into the same country (so while, for example, this method might be applied to comparator drug products, it would not likely be relevant to the investigative drug product)
- ▶ Method 3: Value based on sales of “similar goods” - again not likely to be applicable to CTMs
- ▶ Method 4: “Computed value” taking account of all costs, including

development and an amount for profit and general expense (P&GE). Some companies have successfully developed customs value methodologies using this valuation, even though it can be difficult to track and allocate costs in real time and there is uncertainty over what P&GE should be applied

- ▶ Method 5: “Deductive value” based on the resale of goods after importation. Here, again, this is not relevant in a clinical trials situation
- ▶ Method 6: This is often referred to as the “fallback method” and is based on a more flexible application of the methods outlined above

Ideally, companies should resolve in advance the technical basis on which they determine the values and how they will be declared to customs (e.g., by the carrier or CRO). Such a valuation must be carried out in close conjunction with tax and transfer pricing colleagues, as well as market access and pricing and reimbursement specialists in the company to ensure consistency.

This way, the risk of any contention over the value can be resolved quickly and without additional cost. It is particularly important that companies do not allow use of “notional” or “nominal” values, as these are not provided for in the rules and their use can have very serious consequences. This is especially true if it results in the material not being declared to customs, as this can be treated by customs as either smuggling, evasion of duties and taxes, or both.

Key messages

Structuring clinical trials globally is a key element of the life cycle of a biotech (and indeed pharmaceutical company). There are many key commercial issues in this

process requiring great care and attention, and tax and customs issues are not always front-of-mind.

However, key to getting trial materials, comparator drugs and placebo into a market for trials is transporting them across the border safely and securely without undue delay. To do this correctly, and with minimum cost, there are three key steps:

- ▶ **Value:** ensure you have a proper valuation policy for clinical trial materials and that it can be supported
- ▶ **Identify and minimize:** identify all import taxes that will be due in the key trials markets in advance and ensure that you can avail of any possible exemptions, while ensuring budget availability to fund remaining taxes
- ▶ **Recover:** where possible, maximize recovery of the import taxes that have to be paid

Summary of major tax considerations for exploitation of intellectual property

Once intellectual property (IP) has been developed, it's essential to consider the options available for exploitation of this asset, as well as the corporate structures to achieve other relevant aims. It may take the form of an outright sale of the IP to a third party, or the biotech start-up may decide to go it alone with a marketing strategy and so sell directly to the market. This latter option will preserve shareholder value. In this section we examine the considerations for international tax and transfer pricing when the start-up decides to exploit the IP directly.

First, we consider what happens when the start-up retains the IP and exploits it directly.

Capital is required to complete the R&D, obtain regulatory approval and build out infrastructure such as a manufacturing footprint and a sales and marketing force. In these challenging times, it is difficult to access capital directly.

At the same time the industry is undergoing significant change due to the impending "patent cliff" of drugs whose patents are due to expire. This is due to poor R&D pipelines, caused in part by increased costs and pricing pressures.

These trends have resulted in more collaborative agreements between biotech start-ups and "big pharma," especially where there is a desire to enter overseas markets. The ability to access a larger number of markets, and to do so quickly, is among the

benefits of collaborations of this nature. Also, the stage at which big pharma gets involved in a collaboration is important because the earlier it does so at the clinical phases, the better the opportunity for it to fund the remainder of the R&D. The timing needs to be considered carefully, however, since a disadvantage of earlier involvement by big pharma is that shareholder value is eroded.

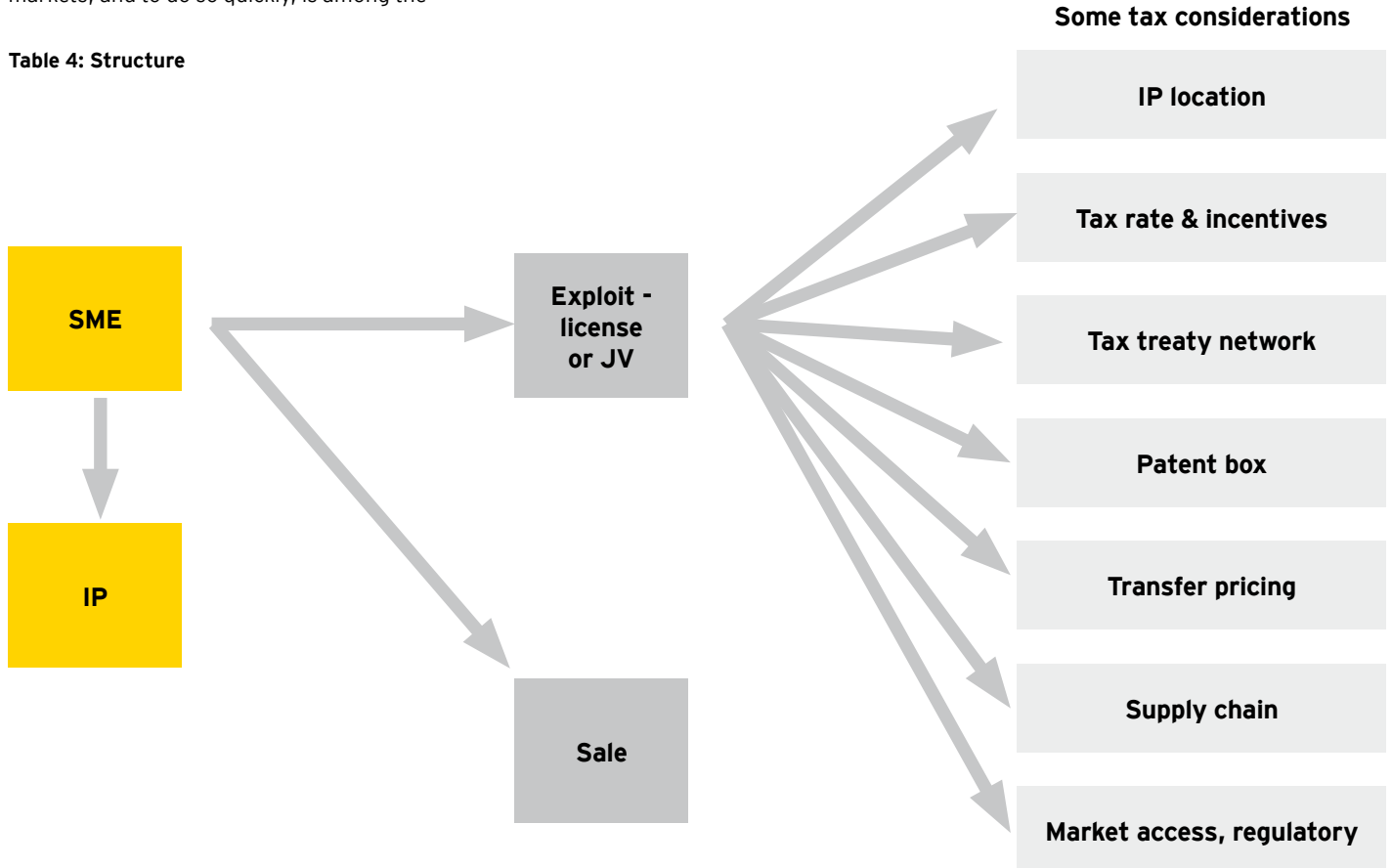
Other key questions to consider

How should you identify the right strategic partner and fit, as well as funding, and what synergies can be achieved? With collaboration, control is an issue: how should you balance the additional resources while retaining control of the direction of the development?

There are various types of collaborations, each involving different deal structures which can become quite complex. Some of the most common include:

1. License the technology to big pharma, which manufactures, or controls manufacturing; has a sales and marketing force in place, especially overseas; and pays a royalty to the biotech start-up.
2. Form a partnership or joint venture (JV). At what stage do you involve a partner or consider a collaboration?
3. Enter a limited agreement on sharing profits and losses on commercialization, or form a co-marketing or co-promotion agreement.

Table 4: Structure



The recent Ernst & Young 2010 Global Transfer Pricing Survey identified the following trends:

- ▶ Transfer pricing is one of the key tax issues today: it is more important than it was two years ago.
- ▶ Audits are increasing in significance, intrusiveness and scope.
- ▶ Litigation remains infrequent but it is on the rise. Meanwhile, the use of and degree of comfort with advanced pricing agreements is increasing, while experience with new arbitration processes remains extremely limited.
- ▶ Enforcement actions are placing greater emphasis on intercompany financing transactions and service transactions.
- ▶ Taxpayers are taking a more coordinated and globalized approach to the documentation for transfer pricing.
- ▶ Tax considerations relating to business restructuring are expected to become more important in the coming years.

Whether the biotech start-up goes it alone or collaborates with big pharma, there is an opportunity to plan tax around the ownership of the IP.

International tax

Biotech start-ups tend to begin operating in one jurisdiction, and will usually have generated tax losses on R&D by then. As biotech companies grow and expand into overseas markets, managers and investors should consider the implications for tax. It is important to understand the risks and how circumstances may have an impact on the effective tax rates. Companies also need to consider the political and economic stability of the countries where they may base their facilities, as well as the availability of a skilled workforce.

There are opportunities to minimize tax rates by proactively managing the ownership and development of the rights to IP worldwide. An important element of effective tax planning is aligning tax strategies with the company's business activities and objectives. Many of these strategies take time to mature as IP is developed. Therefore, it is important that, at an early stage in their development, biotech companies consider tax planning. Planning needs to start long before a product is ready for commercialization.

One of the challenges around IP planning is how to fund product development and ensure that the risk is shouldered by a low-tax or tax-efficient jurisdiction.

For the few successes that are accompanied by the appropriate amount of planning, the

prize can be big: there may be significant profits in a tax-efficient location.

Some key pointers for companies to consider as their operations start to expand:

- ▶ Permanent establishment exposures: where is your distributor located?
- ▶ Moving IP: at what stage should it be done, and what tax may it trigger?
- ▶ Access to new markets: the ramifications of emerging markets and other such developments.

Transfer pricing

As the company grows internationally, functions are commonly performed across a number of jurisdictions by a number of entities in the group. These functions typically include R&D, regulatory, finance and operations, supply chain and IP management. These multinational groups have significant intergroup arrangements and cross-border activity and subsequently dedicate significant resource, in the form of management time and in-house tax personnel, to ensuring the pricing in relation to these transactions is compliant with transfer pricing legislation in the relevant jurisdictions of operations.

In recent years, a significant number of pharmaceutical groups seeking to increase their global footprint have implemented new operational models to optimize business performance, while enabling the realization of the tax benefit associated with the new structure. The companies have implemented transfer pricing design projects to align the economic substance of operations and

transactions with the newly adopted business models.

Most of the strategies relate to a business decision as to the location of various functions of the supply chain (manufacturing, commercialization) coupled with the ownership and funding, as well as the development or exploitation of IP.

There has been a trend in recent years for tax authorities to focus more on the pharmaceutical industry after some high profile tax adjustments. This, together with the global economic down turn, is resulting in more transfer pricing audit activity and ever-greater demands on the requirement for documentation to support positions taken by companies on their pricing strategy. The OECD is also updating key elements of its transfer pricing guidance.

A cost benefit analysis is key to transfer pricing planning. In structuring transfer pricing models the significant costs in R&D need to be considered, especially given the high probability these costs may prove to be abortive resulting in no new product, and the fact that the lead time from development to commercial exploitation can be significant (8-10 years). Also, the considerable costs to bring the few successes to market and patent protection can be just as significant as the R&D cost and also need to be factored into planning. Such expenditures in low tax jurisdictions may not always be deductible or are deductible against income that will be taxed at a negligible tax rate.

Part C:

An industry study
and the outlook
for biotechnology
in Europe



Pharma - the current cornerstone of biotechnology in Europe

Although the European Commission and the governments of many Member States are keen to promote not only all applications of biotechnology generally, but diversity within the sector, currently a large portion of the biotechnology companies in Europe are biopharmaceuticals.

The pipeline for biopharmaceuticals

The sustainability of biopharmaceutical companies depends largely on the flow of new start-ups, which both feed the pipelines of big pharmaceutical companies and create a new generation of emerging companies with middle capitalizations. These mid-cap companies can then feed into big biopharma players through mergers and acquisitions.¹

However, this idea has been called into question because of a dwindling number of small-, mid- and large-cap companies. For example, in 2005, there were 329 pharmaceutical and biopharmaceutical companies with capitalizations varying from US\$50m to US\$200b. Today, there are only 240 companies worth more than US\$50m. That equates to a 27% reduction over five years.²

Some reasons for the shrinkage are that there are not enough companies maturing into public companies; too few new biopharma companies are being started; and too many smaller companies disappear through mergers.³ In future, the pharmaceutical industry will need to pay more attention to this trend, since it could make it harder for it to grow.

Aside from this, biopharmaceuticals are witnessing an increase in pipeline for medicines and vaccines from biotechnology. According to the Pharmaceutical Research and Manufacturers of America Foundation, biotechnology can offer patients and their doctors more choice. Such biotechnologies are innovative therapies, which offer enormous potential to address needs that have previously gone unmet. Biotechnology could also help the pharmaceutical industry to meet the rising cost of health care by ensuring that the most effective care is used.⁴

Contract research organizations (CROs) on the rise

An increasing number of drug makers are outsourcing trials to CROs. As prices continue to rise in the pharma industry, with large and mid-sized firms seeing fewer and fewer price decreases, CROs are becoming even more important in the effort to keep costs and prices under control.⁵

This reliance on CROs is phasing out the traditional model of start-up pharmaceutical and biotechnology companies licensing out products after phases I and II. They now retain more compounds within their pipelines and take them closer to market through CROs. This new trend is increasing both the value of the product and that of the company.⁶

The role of social media

The Wall Street Journal reported last year that roughly half of all Americans do not stick to their medicine regimes. This includes between 20% and 30% of prescriptions written by doctors never being presented,

medications not being taken as directed, as well as a lack of prescription refills. This lack of involvement is not only harmful to the patient, since such actions could be detrimental to one's health, but in some cases can increase expenditure because of hospitalization. It also affects pharma companies because they lose out on potential sales.

In the hope of persuading patients to follow advice that is related to prescriptions, many drug makers and pharmacies are looking to social networking and mass media to get their message across.

It has also been reported that 26% of US adults access health information through their mobile phones, up from a reported 12% in 2010, as reported by Manhattan Research.⁷

Despite the increase in the use of this type of technology by patients, some argue that pharma companies do not leverage the internet to the best of their ability.⁸ In future, the pharmaceutical industry will rely more on media channels such as the internet in the hope of communicating more effectively with patients.

Looking to emerging markets

With IMS Health predicting that expenditure on prescription in the US and Europe will shrink significantly by 2015, there is pressure on the pharmaceutical and biotechnology industries to look elsewhere for growth and opportunities. A recent study points out that, while emerging markets generated US\$154b in revenue last year, amounting to 18% of global sales, they are expected to reach US\$487b, or 37% of total sales, by 2020.⁹

¹ "Our Shrinking Biopharma Ecosystem," Life Sciences Daily News, 9 September 2011.

² Ibid.

³ Ibid.

⁴ Ibid.

⁵ "Why Contract Research Organizations are Hot," Pharmed, 4 October 2011.

⁶ "US CRO Market 'to exceed \$20 billion by 2017,'" PharmaTimes, 17 October 2011.

⁷ "Study: 26 percent are mobile health users," MobiHealthNews, 19 October 2011.

⁸ "Pharma needs to leverage the internet, says Google," PharmaTimes, 21 October 2011.

⁹ "Will Emerging Markets Really Save Pharma?" Pharmed, 20 October 2011.

Manufacturers of pharmaceuticals are increasing their focus on emerging markets because such nations will boast not just growing populations but a faster pace of economic growth. Some economists believe that, by 2015, emerging markets will account for 40% of the world's gross domestic product.¹⁰ Emerging markets may contribute up to 90% of the growth of the pharmaceutical industry by 2020.

Indeed, health care information provider IMS Health has described 16 developing nations as "pharmerging" countries. They are China, Brazil, India, Russia, Turkey, Poland, Venezuela, Argentina, Indonesia, South Africa, Thailand, Romania, Egypt, Ukraine, Pakistan and Vietnam.

Based on such forecasts, these markets will together have a compound annual growth rate (CAGR) of between 13% and 16% by 2015.

They were also expected to produce half of the growth in demand for pharmaceuticals during 2011.¹¹

Table 1: Key indicators of growth in primary emerging markets¹²

Emerging market	Key findings	Reasons for growth
Brazil	<ul style="list-style-type: none"> ▶ World's fifth-largest population ▶ Pharmaceutical market valued at US\$20.18b in 2010 	<ul style="list-style-type: none"> ▶ Strengthened economy ▶ Growing population ▶ Public insurance covers 90% of the population
Russia	<ul style="list-style-type: none"> ▶ World's ninth-largest population ▶ Pharmaceutical market expected to expand to US\$18.6b in 2011 	<ul style="list-style-type: none"> ▶ Increased government spending on health care ▶ Expansion of private health insurance sector ▶ Increasingly health-conscious population
India	<ul style="list-style-type: none"> ▶ World's second-largest population ▶ 10% of the population covered by health insurance 	<ul style="list-style-type: none"> ▶ Rising middle class ▶ Expansion of private medical insurance sector ▶ Favorable government health care policies
China	<ul style="list-style-type: none"> ▶ Largest emerging market ▶ World's largest population ▶ Third-largest economy ▶ Projected drug sales >25% in 2011 	<ul style="list-style-type: none"> ▶ Rising standard of living ▶ Expanding middle class ▶ Government health care stimulus package ▶ Rapid urbanization

A focus on health outcomes

As pharmaceutical expenditures continue to rise, there has been an increase in the number of regulated health care systems using formal cost-effectiveness analysis (CEA) research to assess a drug's value. Health care system regulators make informed decisions about pricing, reimbursement and use within their health care system based on CEA research.¹³

Under the CEA approach, drugs are assessed for use and reimbursement price by evaluating incremental health-related effects, as well as costs relative to existing treatments. The first jurisdiction to adopt a CEA policy was Australia in 1993, followed by

New Zealand and several Canadian provinces. The UK established the National Institute for Health and Clinical Excellence (NICE) in 1999 to review the efficacy and cost of technologies that had health or budgetary impacts - using cost per quality adjusted life year (QALY) - and to establish guidance on the use of these technologies in the National Health Service (NHS) in England and Wales. In Sweden, the Dental and Pharmaceutical Benefits Agency (TLV) utilizes CEA to make decisions regarding the reimbursement of drugs. Other European countries that also request economic submissions for new medicines include Belgium, Finland, Ireland, Norway, the Netherlands, Portugal and Germany. In addition, some countries in

¹⁰ Standard & Poor's, "Industry Survey Healthcare: Pharmaceuticals," 2 June 2011, p. 13.

¹¹ Ibid.

¹² Ibid., pp. 14-15.

¹³ "Measuring Value: Pharmacoeconomics in Theory and Practice," Office of Health Economics, Towse, Drummon, Sorenson, 21 May 2011, p. 5.

Eastern Europe, Asia and Latin America have adopted similar policies.¹⁴

CEA is less established within the US. However, over the past few years, there has been an increasing interest in establishing a more formalized process for conducting comparative effectiveness research (CER). In fact, comparative effectiveness has been specifically incorporated into at least 10 bills over the past few years. For instance, the American Recovery and Reinvestment Act of 2009 authorized US\$1.1b for CER.¹⁵

CER is designed to provide evidence related to the effectiveness, benefits and harms of different treatment options. Research studies generate evidence, and there are two ways that this evidence is found. First, there are research reviews that consider all of the available evidence about the benefits and risks of each choice for various groups of people from existing clinical trials. Second, there are studies conducted that generate new evidence of the comparative effectiveness of a drug.¹⁶

CEA addresses the principal concept of whether the technology is worthwhile, given a number of competing factors. There are five primary elements to the CEA inquiry:¹⁷

- ▶ Is the technology effective and what benefits does it provide?
- ▶ For whom does the technology work?
- ▶ What costs are entailed in its use?
- ▶ How does the technology compare with available treatment alternatives?

- ▶ Given the answers to the above questions, is the technology worth using in the health care system for some or all of those who would benefit?

A primary reason for the use of CEA is to improve resource allocation in health care. CEA also has the effect of regulating drug prices indirectly through an analysis of cost-effectiveness. CEA supports the notion that higher prices can be charged for the more effective and safer drugs, and they can still be cost-effective compared with less effective and less safe drugs. Thus, it provides efficient incentives for R&D. Furthermore, by using the CEA approach, the indications in which the use of a drug would be efficient can also be identified, thus encouraging a more cost-effective use of the drug in the health care system.¹⁸

Manufacturing and supply chains

The “patent cliff” is lowering sales projections. In response, pharmaceutical companies are cutting their manufacturing costs and closing sites to reduce their manufacturing footprint. Companies have also reduced excess capacity, closing products with low profitability, and increased their use of contract manufacturing to reduce their costs. In 2001, US-based Johnson & Johnson shut down two factories and cut 1,000 jobs related to the production of Cypher stents.¹⁹ In 2011, Merck, the US drug company, said it would shed up to 14% of its workforce and close several manufacturing facilities.²⁰ Switzerland’s Novartis has cut

2,500 jobs at sites across the world in an effort to reduce costs.²¹ The cuts included the closure of a factory in the UK, which brought the loss of 500 jobs.²² Dendreon, another US biotechnology company, laid off 25% of its workforce, with many manufacturing positions lost.²³

Pharmaceutical companies are also streamlining their supply chains and being more flexible in how they manufacture. According to a study by consultants Accenture, the industry holds as much as €35b in excess inventories.²⁴ Companies have increased their use of modeling and analytics to improve their manufacturing and supply chains. UK-headquartered GlaxoSmithKline (GSK), for example, entered into a five-year alliance with McLaren, a Formula 1 racing team. The two companies will establish a £20m research facility to make use of McLaren’s technology. GSK hopes that its production efficiency can be improved by applying McLaren’s capabilities in engineering, analytics and modeling.²⁵

The industry has turned to contract manufacturing to reduce costs and improve its flexibility as companies shut down some of their facilities and trim their excess capacity. Germany’s Bayer announced in 2011 that it was to close a manufacturing facility in California that produced a drug to treat multiple sclerosis. Bayer decided to transfer production to the contract manufacturing division of fellow pharma company Boehringer Ingelheim.²⁶ Bayer cited flexibility as a main reason for the closure of

¹⁴ Ibid.

¹⁵ “Comparative Effectiveness Regulations and Pharmaceutical Innovation,” *PharmacoEconomics*, Vernon, Golec, and Stevens, Volume 28, No.10, 1 October 2010.

¹⁶ “What is Comparative Effectiveness Research?” US Department of Health & Human Services, Agency for Healthcare Research and Quality.

¹⁷ “Measuring Value: Pharmacoeconomics in Theory and Practice,” Office of Health Economics, Towse, Drummon, Sorenson, 21 May 2011, p. 8.

¹⁸ Ibid., p. 9.

¹⁹ “J&J to Exit Stents, Cut 1,000 Jobs,” *FiercePharma*, Tracy Staton, 16 June 2011, accessed at: <http://www.fiercepharma.com/story/jj-exit-stents-cut-1000-jobs/2011-06-16>

²⁰ “Stent Pioneer J&J to Exit Business,” *The Wall Street Journal*, Jonathon Rockoff, 16 June 2011, accessed at: <http://online.wsj.com/article/SB10001424052702304186404576387420811221538.html>

²¹ “Corrected - Novartis Cut 2,500 Jobs Globally - Paper,” Reuters, Catherine Bosley, 25 September 2011, accessed at: <http://www.reuters.com/article/2011/09/25/novartis-idUSL5E7K002X20110925idUSL5E7K002X20110925>

²² “Swiss Paper Totes Up Novartis Layoff Count: 2,500,” *FiercePharma*, Tracy Staton, 26 September 2011, accessed at: <http://www.fiercepharma.com/story/swiss-paper-totes-novartis-layoff-count-2500/2011-09-26>

²³ “Dendreon to Cut 500 Jobs in Restructuring,” Reuters, Bill Berkrot, 8 September 2011, accessed at: <http://www.reuters.com/article/2011/09/08/dendreon-plan-idUSN1E7871TG20110908>

²⁴ “Why Streamlining Pharma Supply Chain is Essential,” *European Pharmaceutical Law*, GDS International, accessed at: <http://www.europeanpharmaceuticalreview.com/7159/news/industry-news/why-streamlining-pharma-supply-chain-is-essential/>

²⁵ “McLaren Alliance to Turbocharge GSK Research,” *InPharm*, Phil Taylor, 16 September 2011, accessed at: <http://www.inpharm.com/news/167317/glaxosmithkline-mclaren-research-alliance>

²⁶ “Bayer to Cut Roughly 540 Jobs in CA,” *FiercePharma*, Liz Jones Hollis, 27 May 2011, accessed at: <http://www.fiercepharma.com/story/bayer-cut-roughly-540-jobs-ca/2011-05-27>

the facility.²⁷ In 2010, contract manufacturing of drugs was worth US\$48.6m.²⁸ Marketresearch.com, a provider of market intelligence, predicts that the industry will grow to US\$86.3b by 2016, a CAGR of 10%.²⁹ Such rates of growth highlight the industry's reliance on contract manufacturers to help reduce costs and improve flexibility.

Pharmaceutical companies may face higher costs on compliance and risk management when outsourcing to contract manufacturers. Last year, the US Food and Drug Administration (FDA) issued a warning and import alert to Yag Mag, an active pharmaceutical ingredient (API) supplier in India. It also issued import alerts for 30 different medications manufactured by Ranbaxy.³⁰ The FDA inspects and investigates manufacturing facilities, including those located outside of the US. The FDA may issue a warning with recommended action after a plant inspection. If there are severe problems, the FDA may issue an alert that bans the import of the drug to the US until action has been taken.

A shift in marketing and selling

Throughout the 1990s and early 2000s, pharmaceutical companies expanded their sales forces in an effort to reach physicians and realize value on their blockbuster drugs. Between 1996 and 2005, the number of US sales representatives almost doubled to a total of 100,000. During the same period, the number of practicing physicians increased by only 26%. Recent developments, such as the impending patent cliff, increased scrutiny of payments to doctors. Tighter pricing and reimbursement controls have forced pharmaceutical companies to reduce their sales forces and shift their marketing efforts.

Pharmaceutical companies began laying off sales representatives in 2006. Over the past five years, most major drug makers have made sizable cuts. New York headquartered Pfizer cut 20% of its US sales force in 2006. In 2008, Merck reduced its sales force by 14%, the US's Schering-Plough cut 10% and Wyeth (which was taken over by Pfizer in 2009) shed 1,200 sales representatives. More recently, Pfizer announced an 11% reduction in Spain and laid off 500 employees in Germany. In both instances, the announcements were made after the respective governments said they would introduce more restrictive pricing for drugs. The new policy in Spain will require doctors to write prescriptions using a drug's generic name, further eroding post-patent sales of branded drugs, such as Lipitor. ZS Associates, a US consulting firm, estimates that, by 2012, only 75,000 representatives will be selling pharmaceuticals products in the US market, 26% fewer than in 2007.

After recent legislation and other outside pressure forced them to disclose their spending, pharmaceutical companies are also reducing their payments to doctors. US-based Cephalon, for example, cut spending from US\$9.3m in 2009 to US\$5m in 2010. Eight of the major pharmaceutical companies spent more than US\$220m in 2010 on promotional speakers for their products, according to news outlet ProPublica. Pfizer spent roughly US\$34.4m on speakers in 2010, and was ranked third among the top eight companies. Payments to one doctor amounted to US\$318,250 over an 18-month period.

The industry has also reduced its support for medical education because of the increased scrutiny of payments to doctors and speakers. It currently supports between 37%

and 60% of accredited medical education, but that percentage is likely to drop. Support has already fallen from US\$1.2b in 2007 to US\$830.8m in 2010, according to the Accreditation Council for Continuing Medical Education.³¹

These cost-cutting measures highlight a change in the marketing and sales strategies of large, vertically integrated pharmaceutical companies. Such companies have begun to concentrate on developing clinical evidence and educating opinion leaders, while shifting their focus away from visits by sales representatives.

The companies have begun to run additional trials and use analytical tools to help organize the clinical data. Eight of the top 15 pharmaceutical companies, measured by market capitalization, now utilize Doctor Evidence, a software platform that helps to organize clinical data and develop guidelines for managing care, assessing efficacy and identifying safety concerns. Clinical evidence not only helps to encourage doctors to try new treatments. It also helps to convince those in health care to pay for the nascent treatments. Pharmaceutical companies are starting to dedicate more resources to educating those in health care, such as insurance companies and even governments, of the benefits of a new drug. Health care payers are also having an influence on a patient's prescribed treatment and therapy. Pharmaceutical companies have begun to hire more economists and management specialists who can prove the economic utility of the new treatments.

Companies have begun to change their training and incentives for representatives too. The sales staff who survived the cuts have a better understanding of the diseases

²⁷ Ibid.

²⁸ "Contract Pharmaceutical Manufacturing, Research and Packaging: Global Markets," Market Research, 1 September 2011, accessed at: <http://www.marketresearch.com/BCC-Research-v374/Contract-Pharmaceutical-Manufacturing-Research-Packaging-6556362/>

²⁹ Ibid.

³⁰ Daiichi-Sankyo gained majority control of Ranbaxy in June 2008.

³¹ "Commercial Support For CME Funding Dives," *Pharmalot*, Ed Silverman, 12 September 2011, accessed at: <http://www.pharmalot.com/2011/09/commercial-support-for-cme-funding-dives/>

and new treatments. They now focus more on ensuring that physicians understand the efficacy and safety aspects of new compounds. Representatives must provide information to doctors on insurance and reimbursement, as well as educating them about new treatments. Sales representatives can add value by briefing doctors, who have little time to stay abreast of the changes in health care policy. The companies, through their medical affairs organizations, concentrate on educating opinion leaders about the efficacy and safety concerns of new treatments. Such people are doctors who are leaders in their fields and widely respected in their area of practice. Recommendations or disapproval from these individuals can contribute to the success of a drug.

Pressures on pricing and reimbursement

The provision of health care and its costs differ widely in the US and Europe. Given the high costs of pricing and reimbursement to public budgets, and the differences in resources in each country, pricing and reimbursement are treated differently across geographies. Pricing dynamics in Europe are primarily dictated by government regulations, rather than free-market economics. In the US, a significant portion of health care is provided by private companies, with 55% of total health care expenses being borne by the private sector.³²

About 59% of US workers had health insurance provided by their employers in 2009.³³ Of those with health insurance, 98% were covered under managed care plans, with traditional fee-for-service coverage. Of those in managed care plans, 60% were in programs provided by what are known as

preferred provider organizations (PPO); 20% were enrolled in more rigid but less costly health maintenance organizations (HMOs); 10% were in point-of-service (POS) plans; and the remainder were in other types of plans. Patients in PPOs can select providers from the insurer's broad network, or pay more to go outside of the network. HMOs' participants must use network providers, who are paid a set monthly fee per patient.³⁴

Meanwhile, European countries rely on universal systems largely controlled by government agencies and funded by the public purse. Many European governments regulate pharmaceutical prices, as a means of making pharmaceutical products available to more consumers. These price ceilings lead either to certain companies removing themselves from countries altogether, or companies accepting the price ceiling and stringent reimbursement mechanisms, which results in lower product prices.

The pricing of new pharmaceuticals is determined by various factors. These include the relative efficacy and safety profile of a drug compared with its competition; the size of the market and its level of competition; and the drug's development costs. Drug pricing also varies among different kinds of payers. Generally, large-scale payers, such as hospitals and institutional customers, pay well below list prices because they negotiate large discounts with their volume purchases. Government organizations and programs tend to receive some of the largest discounts for drugs. In contrast, wholesale distributors and pharmacy chains for the retail market pay higher drug prices.³⁵

In Europe, where countries have been affected by constrained government budgets and concerns over sovereign debts, there have been unilateral reductions

in pharmaceutical pricing and use. The reductions have been fairly widespread, with cuts permeating almost all major EU countries across both branded and generic sectors. Many European countries have cut prices by 3%-5%, with deeper reductions in countries with serious budgetary concerns.³⁶

In an effort to control costs, various controls are used across countries and markets.³⁷ These include:

- ▶ Profit controls
- ▶ Reference pricing
- ▶ Price cuts, freezes and ceilings
- ▶ Discounts and rebates
- ▶ Pricing negotiations

In addition, payers have implemented various controls on reimbursement to manage pharmaceutical spending. These reimbursement controls include:

- ▶ Patient co-pays
- ▶ Formulary positive/negative lists
- ▶ Volume limitations
- ▶ Pharmacoeconomics
- ▶ Risk-sharing
- ▶ OTC switching
- ▶ Pharmacist/automatic substitution
- ▶ Budget caps
- ▶ Generic-name prescribing

Governments in many countries throughout the EU, as well as in Australia and Japan, are implementing cuts in the prices of drugs and restrictions on reimbursements in an effort to reduce their health care expenditure. Figure 1 below depicts a range of pressures that are hurting the pharmaceutical industry.

³² "Europe and the US: Whose Healthcare is more socialist?" International Economics, Jacob Funk Kirkegaard and Peterson, 6 April 2009.

³³ "Employer Health Benefits," 2010 Annual Survey, Henry J. Kaiser Family Foundation, p. 4.

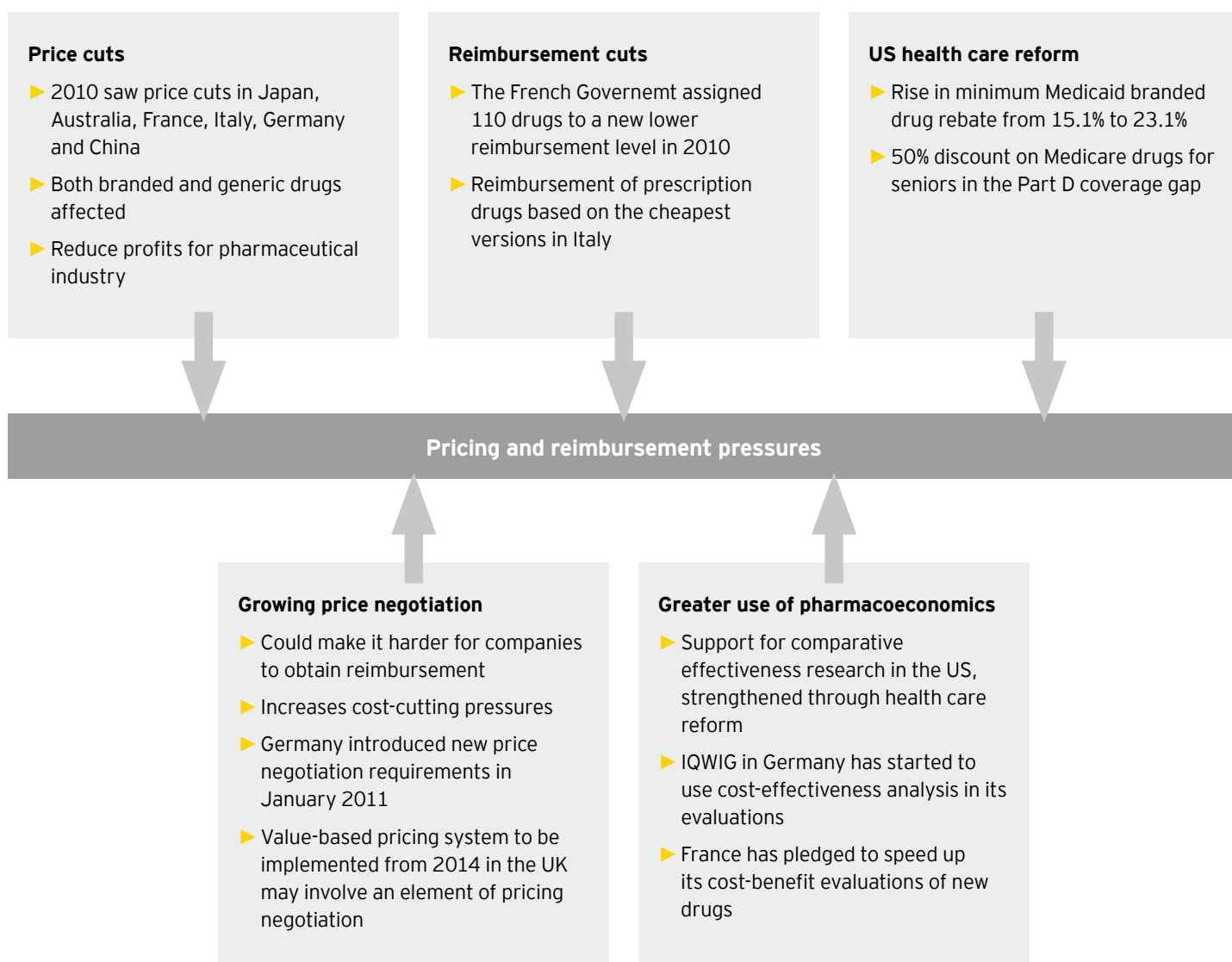
³⁴ Standard & Poor's, "Industry Survey Healthcare: Pharmaceuticals," 3 June 2010, pp. 18-19.

³⁵ Standard & Poor's, "Industry Survey Healthcare: Pharmaceuticals," 2 June 2011, p. 28.

³⁶ Ibid., p. 12.

³⁷ Datamonitor, "Pharmaceutical Key Trends 2011 - Healthcare System and Drug Regulatory Overview," March 2011, p. 58.

Figure 1: Pricing and reimbursement pressures³⁸



³⁸ Ibid., p. 59.

Reimbursement is crucial for the commercial success of a product. Both private and public payers are taking increasingly stringent positions in evaluating the cost-effectiveness of recently approved drugs. In Europe, several governments have established semi-independent organizations to make recommendations on whether a new drug should be reimbursed and, in some controversial cases, they have argued against coverage.³⁹ This has resulted in the rejection of more drugs and pricing proposals, resulting in lost revenue and substantial reimbursement variances for companies. The US has not taken this approach, although it is considering the establishment of an organization to evaluate reimbursement. US payers increasingly differentiate drugs within the same class and place them in separate tiers, with varying contributions from patients. This is aimed at incentivizing patients to use certain drugs.⁴⁰

The growing presence of managed care continues to be a strong trend in the US pharmaceutical industry. The following provides examples demonstrating how the managed care system influences the cost of drugs and the types of drugs to which physicians and patients have access:

- ▶ The size of the system of managed care affects drug prices because of the system's ability to negotiate large discounts with suppliers. Pharmaceutical benefit managers (PBMs) are the third-party negotiators of many of the insurer-based discounts and rebates offered. As part of their response to the threat to managed care in the early 1990s, many pharmaceutical companies acquired PBMs, with the aim of switching prescriptions to their own products. The Government introduced regulations requiring that PBMs' decisions be kept independent of the parent drug company.

- ▶ Health insurers have introduced such strategies as cost sharing, drug formularies and utilization reviews to contain costs. Cost-sharing provisions influence patients' demand for health services and medications, while formularies constrain physicians' ability to prescribe drugs by restricting reimbursement to a select list of approved drugs that are viewed as cost-effective. The bureaucratic difficulty in having non-formulary drugs reimbursed implicitly discourages their prescription.

Prices for new drugs are increasingly related to the effectiveness of the products and many plans perform an explicit CEA on each new product. FDA approval is not enough to obtain equitable reimbursement rates from insurers. A pharmaceutical company must show that its products have pharmacoeconomic benefits, such as reducing hospitalization or surgery costs, or providing the most cost-effective treatment option available.⁴¹ In Europe and other markets, drug companies must provide cost-benefit studies of new drugs in order to get approval from government regulators.

The trend toward managed care affects nearly all aspects of pharmaceutical companies' business, especially R&D and marketing. For example, products that are unlikely to offer clear therapeutic advantages over existing products are less likely to be developed, unless they can be profitably marketed at a low price. The restriction of drug choice has the potential to result in products that are less effective, less convenient and have worse side effects.

³⁹ Standard & Poor's, "Industry Survey Healthcare: Pharmaceuticals," 3 June 2010, p. 32.

⁴⁰ Ibid.

⁴¹ "Health-Care Investor Watches US Policy," *The Wall Street Journal*, 7 February 2002.

Outlook for the biotechnology industry in Europe

From this report, we can conclude that Europe indeed has the potential to be a world leader in the field of biotechnology. Already there are many tax, financial and regulatory incentives for established companies, as well as start-ups operating in Europe. The excellent research base and skilled labor force on offer throughout many EU Member States is also of great benefit to the biotechnology sector. However more needs to be done by industry and regulatory authorities alike.

We hope that this report can be used as an exchange of best practice between Member States and their associated regulatory authorities, so that a holistic approach to policy is developed and Europe's vast potential for innovation is exploited.

In reality, it is not enough to have a good tax or finance system in place. The right policies and incentives for R&D development are also essential to growth in this industry. There is currently a three-speed Europe for the biotechnology industry, with each of the three applications - health care, agricultural and industrial - all operating under different regulatory and approval processes.

Health care biotechnology

Currently, 50% of all medicines in the global pipeline are derived from biotechnology. It is important to note that more than 70% of these companies in the EU employ fewer than 50 people. These companies face a complex regulatory and financial system; however, 2012 will be an important year for health care biotechnology policy in Europe. Access to innovative medicine for patients and competitiveness of the industry is top of the agenda for all stakeholders. Both

the Transparency Directive and the Public Procurement Directive will be going through legislative processes at the European Parliament and the Council of the European Union over the course of the year. In addition, Vice-President Tajani's Initiative regarding the Process on Corporate Responsibility in the Field of Pharmaceuticals will deliver its conclusions and recommendations on a number of key issues for the sector. These include orphan medicinal products, biosimilars and access to medicines in small markets.

"Clinical trials legislation" is also under review in 2012. A simplified and efficient regulatory framework for clinical trials is key to making Europe a more attractive place for clinical research. Such a framework will benefit all stakeholders. It will allow faster access to innovative treatments for patients, reduce the administrative burden, and cut costs for public and private sector researchers - as well as for Member States.

Moreover, in 2011, legislators decided that the EU should take a leadership role in further guaranteeing patient safety when using a product after marketing authorization. Last year's adoption of the new pharmacovigilance legislation dramatically transformed the role of the European Medicines Agency (EMA) and the approach of companies to post-marketing vigilance of their products. This transformation creates significant implementation challenges both for regulators and for the health care biotechnology sector.

Another piece of legislation, the revision of the In-Vitro Diagnostic Directive, should also provide a timely platform to discuss the regulatory challenges for companion diagnostics, a critical element in personalized medicine. Indeed, the revision offers opportunities to explore how a cohesive and appropriate regulatory framework

for companion diagnostics can be created with proper definitions, requirements, and assignment of roles and responsibilities among the different stakeholders. A robust and flexible framework is needed. This would provide a platform for companies to continue innovating, maximize patient safety and minimize bureaucracy. Any potential future legislative framework should be adapted to allow companies of all sizes to operate successfully within this framework.

Industrial biotechnology

One of the key challenges faced by industrial biotechnology companies, which are often still in the early and start-up phase, is access to finance. Industrial biotechnology is one of the fastest growing industries in Europe, and has been identified as a key enabling technology by the EU Commission in making the shift toward a greener, more sustainable, bioeconomy in the EU. The bioeconomy itself has an estimated value of €2t and employs around 22 million Europeans. It offers Europe the potential to accelerate its transition toward a new economic model, while at the same time developing a high-value, globally competitive, sector capable of generating good-quality jobs in rural as well as urban settings. However, to take advantage of the unique opportunities presented by industrial biotechnology, it is essential that the EU develops holistic and workable policy measures that support research and innovation in the bioeconomy, and that problems surrounding access to finance are solved.

A number of critical industrial biotechnology policy developments are currently under discussion. These include the recently published legal proposal on the European Union's Common Agricultural Policy (CAP) for 2013-20; the launch of the new Common Strategic Framework Program for research

and innovation funding in Europe for 2014-20, entitled "Horizon 2020," and the recently launched Bioeconomy Strategy.

At this crucial time for the industry, the right policies are needed to ensure that a supportive and predictable political, regulatory and financial framework is in place. Such a framework would lead to access to renewable feedstock; increased funding for research and innovation; and lead market initiatives for biobased products to boost the sustainable growth of the bioeconomy.

With the European Commission's adoption of its new Strategic Framework for Research and Innovation, Europe has taken a decisive step toward integrating biotechnology into its policy-making process. Biotechnology is now central to the main aims of Horizon 2020, which are to tackle societal challenges; promote industrial leadership; and boost European excellence in research, development and innovation (RDI). Horizon 2020 listed the bioeconomy as one of the grand challenges that future EU research and innovation policy should tackle. In addition, biotechnology is highlighted as one of the six enabling technologies that will be supported further by increased funding. Since the last Framework Program, the proposed budget for the bioeconomy has more than doubled, from €2b to €4.7b. Horizon 2020 also aims to create synergies between the different EU funding instruments, policies and governance structures, in an effort to meet societal challenges. In the case of industrial biotechnology, funding for pilot and demonstration plants is also crucial to bridge the gap from research to commercialization.

The good news is that the Bioeconomy Strategy, launched in February 2012, has the potential to make this happen. The new strategy should be a strong, coherent and fundamentally holistic approach that funds and supports the development of biobased products and processes, facilitates

access to feedstock and reduces funding fragmentation.

Agricultural biotechnology

The biggest regulatory challenges facing the biotechnology industry in Europe are in the area of agricultural biotechnology. In Europe, only two genetically modified (GM) crops are currently permitted for cultivation: MON810, a type of maize that helps fight off pests, and Amflora, a potato for industrial use. In comparison, there are more than 90 GM crops currently available for cultivation in the US. It is clear that Europe's competitiveness in this industry is under serious threat. In fact, the European approval process for the cultivation of new crops is so slow that the two GM crops currently being cultivated by European farmers are no longer even available for planting in the US, where newer varieties have since been developed. Science and innovation are moving forward at a fast pace. It is important that Europe is not left behind.

Europe currently imports a substantial portion of its animal feed, and a large part of this supply is GM. Around 30 million tons of grain are imported each year from third countries, including 13 million tons of maize and 2 million tons of oilseed rape. In particular, European animal farmers rely on soybean imports for animal feed. Europe imports most of the soybeans it uses, and most of those imports are from North and South America. It is clear that this situation is unsustainable if the industry in Europe is to remain competitive and grow in the long term. There are already indications that industry will pull out of Europe and move to countries where there is a more supportive regulatory environment, resulting in the substantial loss not only of excellence in science and Research development & innovation (RDI), but also of jobs.

However, there are signs of movement at an EU level in favor of the agricultural biotechnology industry. The Nationalization Proposal, which was introduced first in 2010, and saw little movement for some time, has suddenly begun to cause a stir among policy-makers. The current political block on the rate of approvals for the cultivation of new GM crops may also be softening, with two recent reports from the European Commission indicating that the current approval process is in need of speeding up.

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Glossary of terms

Accounting period

The period of time used to determine a company's or organization's taxable profit for corporation tax. The period normally matches an organization's financial year.

Bioeconomy Strategy

A strategy adopted by the Commission in 2012 to shift the European economy toward greater and more sustainable use of renewable resources. It outlines a coherent, cross-sectoral and interdisciplinary approach to the issue. The goal is a more innovative and low-emissions economy, reconciling demands for sustainable agriculture and fisheries, food security and the sustainable use of renewable biological resources for industrial purposes, while ensuring biodiversity and environmental protection.

Capital allowances

Enable a company to deduct (write-off) the cost of capital assets, such as machinery, computers, equipment or vehicles, against taxable profits for corporation tax, instead of deducting the full cost of the item as an expense from taxable profits in the year it was acquired. A portion of that cost is deducted over a period of years.

Carry on business

A company or organization that is active.

Chargeable gain

If a company or organization is liable for corporation tax, capital gains tax is not due separately on capital gains (in contrast to individuals, self-employed, sole traders or partners in partnerships). Instead, tax on chargeable gains is paid as part of corporation tax profits.

Clinical phase

Refers to the stage of the clinical trial process:

Phase 1 - the first phase of a clinical trial, which usually involves a low number of participants and has the purpose to determine the best method of delivery, best dosage and, most importantly, if the treatment is safe for humans.

Phase 2 - the second phase of a clinical trial which involves more participants than phase 1 and is carried out to determine if the treatment is effective on patients. It also provides additional safety data.

Phase 3 - the third phase of a clinical trial with the purpose of determining if the new treatment works better than the established treatment for the same disease or condition.

Common Agricultural Policy (CAP)

The EU Common Agricultural Policy is aimed at supporting farmers' incomes while also encouraging them to produce high-quality products demanded by the market and ensuring rural development in the most environmentally sustainable way. The CAP is due to be reformed by 2013 with the aim of making it a more effective policy to boost innovation, competitiveness and sustainable agriculture in rural areas.

Computation

The mathematics which shows how entries have been calculated from the figures in company accounts.

Corporation tax

A tax on the taxable profits of limited companies and some organizations, including charities, clubs, societies, associations, cooperatives and other unincorporated bodies.

Credit, tax

Tax credits reduce the amount of corporation tax paid by deducting an amount (the credit) directly from the amount of corporation tax payable. If there is no corporation tax to pay, sometimes there is a cash repayment.

Declaration

The section at the end of a company's tax return which an authorized person must read, sign and date to verify that the information is correct and complete.

Deduction

An amount deducted from taxable profit for corporation tax purposes. Tax authorities use deductions and reliefs to refer to various expenses, losses or allowances to be subtracted from profits before corporation tax is paid. This is in contrast to credits or other types of relief which are deducted directly from the amount of corporation tax payable.

Depreciating assets

Any fixed plant or machinery, not forming part of a building, or any asset that will have a life of 60 years or less in the UK from when it was acquired by a company or organization.

European Medicines Agency (EMA)

The European Medicines Agency is a decentralized agency of the European Union, located in London. The agency is responsible for the scientific evaluation of medicines developed by pharmaceutical companies for use in the European Union.

EU 2020 Initiative

Europe 2020 is the EU's growth strategy for the coming decade. Concretely, the Union has set five ambitious objectives - on employment, innovation, education, social inclusion and climate/energy - to be reached by 2020. Flagship initiatives are what underpin this strategy.

Genetically modified crops (GM crops)

Genetic modification of crops means that existing genes are modified or new genes included to give plant varieties desirable characteristics, such as resistance to certain pests or herbicides, or enhanced nutrient profiles.

Health Technology Assessment (HTA)

HTA is a research-based assessment of the medical, economic, social and ethical implications of the incremental value, diffusion and use of a medical technology in health care.

Horizon 2020

Horizon 2020 is the financial instrument implementing the Innovation Union, a Europe 2020 flagship initiative aimed at securing Europe's global competitiveness. Running from 2014 to 2020 with an €80b budget, the EU's new program for research and innovation is part of the drive to create new growth and jobs in Europe.

HTA authority

A national body tasked with carrying out health technology assessments (HTAs) for prospective new medical technologies (e.g., the UK's National Institute for Clinical Excellence or NICE).

Indication

The purpose for which a certain medical technology, such as a test, medication, procedure or surgery, is used and approved.

Intangible assets

Intangible assets include, subject to some exceptions, goodwill and intellectual property such as patents, trademarks, registered designs and copyright, together with licenses to exploit such assets and other intangible assets, such as agricultural and fishing quotas.

Market access

An opportunity for a company to enter a specific market to commercialize its products or services.

Marketing authorization application (MAA)

An application for authorization to place medicinal products on the market.

Orphan disease

A rare disease which affects a small percentage of the population.

Permanent establishment

A company that is not resident but carries on a trade from a fixed place of business (a permanent establishment) is liable for corporation tax on that activity.

Pivotal clinical trial

A trial which provides the significant evidence which enables the "cost-benefit" analysis of an authority charged with carrying out HTAs.

Pricing and reimbursement (P&R)

Pricing refers to the direct or indirect setting of pharmaceutical prices by Member States within the European Union. Reimbursement refers to the process of a state paying back (reimbursing) a patient the cost of a medicine approved for reimbursement. Systems differ between Member States with some reimbursing only to a point, while others do so fully.

Pre-clinical

The pre-clinical stage is the stage of product development when the substance has yet to be tested on humans.

Rates (of corporation tax)

There are two rates of corporation tax in the UK, depending on the company or organization's taxable profits: the lower rate - also known as the small profits rate, and the upper rate - known as the full rate or main rate. There is also a sliding scale between the lower and upper rates known as marginal relief.

Relief

An amount deducted from taxable profit for the purposes of corporation tax. The tax authorities use reliefs and deductions to refer to various expenses, losses or allowances subtracted from profits before the amount of corporation tax is calculated. This is in contrast to credits or other types of relief which are deducted directly from the amount of corporation tax payable.

Research and development (R&D)

In the context of commerce, "research and development" normally refers to future-oriented, longer-term activities in science or technology, using similar techniques to scientific research without predetermined outcomes and with broad forecasts of commercial yield.

Small and medium-sized enterprise (SME)

In the European Union, an SME is defined as a company with no more than 250 employees, annual turnover of €50m or less and a balance sheet not exceeding €43m.

Tax credit

Reduces the amount of corporation tax paid by deducting an amount (the credit) directly from the amount of corporation tax payable.

Tax liability

The amount of corporation tax owed.

Transfer pricing

Refers to the setting, analysis, documentation, and adjustment of charges made between related parties for goods, services or use of property.

Tax treaty network

Many countries have agreed with others in treaties to mitigate the effects of double taxation. The treaty may cover income tax, corporation tax, indirect tax or other taxes.





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EYG no. DL0576

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04/2012. Artwork by EMEIA MAS.

No expiry



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