The Life Sciences Law Review

Editor
Richard Kingham

Law Business Research

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EDITOR'S PREFACE

It is a pleasure to serve as the editor of the first edition of *The Life Sciences Law Review*, which aims to provide an overview of legal issues of special interest to pharmaceutical, biotechnology and medical device companies in 27 jurisdictions. The life sciences sector is of vital importance to the health and well-being of persons around the world. Innovative manufacturers play a key role in the discovery and development of new therapies, while generic manufacturers serve an equally important function by ensuring availability of inexpensive products once patents and regulatory exclusivity periods expire. Throughout the lifespan of a drug or device – from the earliest discovery stage, through non-clinical tests and clinical trials, the governmental approval process, and after entry to the market – lawyers play a central role as advisers to the industry.

We have sought to organise the regulatory discussion in each national entry to correspond roughly to the key stages of product development: the regulatory classification of the product, which determines requirements for approval; non-clinical studies and clinical trials; compassionate use prior to approval; product pre-clearance; regulatory incentives for investment in drug development; post-approval controls; manufacturing; promotion; distribution; legal status; imports and exports; special rules on controlled substances; and enforcement.

In addition to product pre-clearance procedures, many jurisdictions impose requirements for approval of pricing or reimbursement of pharmaceuticals and, to a lesser extent, devices. These are addressed in the entry for each country. We also set out basic information on administrative and judicial remedies, controls on financial relationships with prescribers and payors, special liability systems, and transactional and competition issues that are specific to pharmaceuticals and medical devices.

Finally, each chapter identifies issues of current interest in the jurisdiction. These include, for example, plans to increase transparency in the regulatory process without undermining protection of intellectual and industry property; efforts to adapt traditional regulatory systems to new and emerging technologies, such as companion diagnostics, gene therapy and cell processing; and implementation of regulatory pathways for

'biosimilars' as patents expire for the first generation of biotechnology-derived medicinal properties. As these and other issues develop, we expect to devote additional attention to them in future editions.

I wish to thank all of the contributors who have made this publication possible. They are an impressive group, and it is a privilege to be associated with them in this enterprise.

Richard Kingham

Covington & Burling LLP
Washington, DC
March 2013

Chapter 7

DENMARK

Mikkel Vittrup and Mette Hygum Clausen[1]

I INTRODUCTION

Denmark has a large life science sector, including a number of biotech and pharmaceutical companies and research activities. The sector is highly regulated and covered by extensive and complicated statutory requirements, executive orders and ethical standards. Denmark has incorporated most of the EU regulation and Danish law is thus to a large extent in conformity with the general EU regulation and practice of, for example, the European Medicines Agency ('EMA'). However, there are exceptions, including the Danish price and reimbursement system, please see paragraph III.

The national competent authorities are the Danish Health and Medicines Authority ('DHMA') and the Danish Ministry of Health. The legislative basis for oversight and enforcement may be found in the Danish Medicines Act ('the Medicines Act'), the Danish Pharmacy Act, the Danish Health Act and the Act concerning Medical Devices and the underlying executive orders.

II THE REGULATORY REGIME

i Classification

The definitions of and the distinctions between medicines, medical devices and other regulated products are to a large extent based on EU regulation. Medicines are defined in the Medicines Act, Section 2, as:

> *any product that (i) is presented as a suitable product for the treatment or prevention of disease in human beings or animals, or (ii) may be used in or administered to humans or animals to restore, change or modify physiological functions by having a pharmacological, immunological or metabolic effect or to make a medical diagnosis.*

1 Mikkel Vittrup is a partner and Mette Hygum Clausen is an associate at Plesner Law Firm.

Thus, medicines are defined by two independent definitions, based on either the designation or the function of the product. The definition is in accordance with Directive 2001/82/EC[2] and Directive 2001/83.[3] The definition of medical devices corresponds to the definition in Directive 1990/385/EEC, Article 1(2)(a),[4] which states that a 'medical device' means any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means. Likewise, the definition of cosmetic products[5] and food supplements[6] corresponds to the definition in the relevant directives. The DHMA determines whether a product can be considered to be a medicine or a medical device. The rules concerning cosmetics and food are administrated by other authorities.

ii Non-clinical studies

Conducting toxicological and pharmacological trials (non-clinical trials) with a view to assessing the safety of medicinal products for the purposes of applying for clinical trials, applying for marketing authorisation or maintaining the marketing authorisation may take place only following the authorisation of the DHMA, see Section 85 of the Medicines Act. Studies on animals must also be approved by the Animal Experiments Inspectorate if they are expected to cause pain, suffering, distress or lasting harm to the animals. Studies on animals are governed by the Act on Animal Testing administered by the Ministry of Justice. The DHMA performs inspections in order to ensure that non-clinical studies are performed in compliance with the OECD Principles of Good Laboratory Practice ('GLP').

iii Clinical trials

Clinical trials concerning medicinal products must be notified to and prior approvals must be obtained from the DHMA and an ethics committee by the person or group that takes the overall responsibility for the trial (the sponsor), see Section 88 of the Medicines Act. There is a slight difference in the definition of the 'sponsor' in the Medicines Act compared to EU regulation, since the company financing the clinical trial – normally the pharmaceutical company – is not as such covered by the definition, unless the same company has the overall (not the practical) responsibility for the trial. A doctor or dentist (the investigator) must always participate in the conduct of the trial. The DHMA evaluates both the quality of the investigation and the patient safety of clinical trials. Furthermore, the DHMA performs inspections to ensure that clinical trials are performed in compliance with the international standards of good clinical practice ('GCP'). The research ethics committee performs an overall assessment of the trial's ethical aspects. All clinical trials and their effects are reported to the EudraCT. Furthermore, side effects must be reported to the DHMA and the EudraCT.

2 Directive 2001/82/EC of the European Parliament and the Council of 6 November 2001.

3 Directive 2001/83/EC of the European Parliament and the Council of 6 November 2001.

4 Council Directive 90/385/EEC of 20 June 1990.

5 Council Directive 76/768/EØF of 27 July 1976, Article 1(1).

6 Directive 2002/46/EC of the European parliament and the council of 10 June 2002

Participants in a clinical trial must receive both written and oral information about the trial and must give an informed consent before the trial starts. Furthermore, it is important to note that clinical trials must be conducted in accordance with the Danish Data Protection Act (i.e., the agreement between the sponsor or chief research officer and the investigator must include specific provisions concerning data protection, and non-intervention trials must also be notified to the Danish Data Protection Agency. Clinical trials will also normally include cooperation between health-care professionals ('HCPs') and the pharmaceutical company. Such cooperation shall be conducted in accordance with the regulation concerning HCPs and the principles of independence in the cooperation agreement between HCPs and pharmaceutical companies; see Section V. Furthermore, establishment of insurance and compensation regime for the participants is a requirement. The research ethics committee ensures that such requirements are fulfilled. In this regard, it should be noted that all areas in the Danish health sector and all authorised HCPs are covered by a publicly funded compensation scheme. Participants in clinical trials are covered by this scheme, which also covers pharmaceutical injuries. However, this does not exclude the need for the sponsor to have insurance coverage, see Section VI.

Clinical investigations of medical devices to be used on humans (but not on animals) require authorisation from the DHMA. The investigation may only be initiated when the DHMA has granted authorisation and an ethical committee has approved the investigation. The requirement to apply for authorisation for the conduct of clinical investigation applies to clinical investigation of non CE-marked devices and CE-marked devices, if the objective of the investigation is the application of the device for an intended use for which the device is not CE-marked. The DHMA performs inspections, which include inspection of the qualifications of the employees involved and the monitoring and reporting of serious incidents to the DHMA.

iv Named-patient and compassionate use procedures

The DHMA may in specific cases, upon application, permit the sale or delivery of a limited amount of medicines not covered by a marketing authorisation or not marketed in Denmark; see Section 29 of the Medicines Act (the compassionate use rule). It is possible to apply for a compassionate use permit regarding a specific treatment for an individual patient (single authorisation) or for use in the case of a specified indication at, for example, a hospital or practice (general authorisation). The DHMA may require documentation for the manufacturing of the product, composition, durability, packaging and the efficacy of the proposed indication and information on the approval situation in other countries, particularly the EU.

Compassionate use permits for experimental treatment with medicinal products require further documentation.[7] The rule has primarily been used in relation to patients who have a life-threatening disease such as cancer. The doctor treating them must submit

7 The required information includes a description of the treatment including the expected duration of treatment, scientific literature or other information about effects, adverse reactions etc. to the widest extent possible, copy of medical records and information about planned monitoring of course of disease.

an application to the DHMA for a compassionate use permit regarding a specific treatment for an individual patient. The DHMA's decision on whether a compassionate use permit should be granted is made following an assessment based on the criteria mentioned in Section 26 of the Executive Order on Rights for Hospital Treatment and Obstetric Aid etc.[8] The patients must be informed in accordance with the Executive Order on Information and Consent and about Disclosure of Health Information etc.[9]

The DHMA ensures that the requirements in the Medicines Act on quality and safety are fulfilled. Companies and laboratories producing or in other ways handling medicinal products must be authorised by the DHMA according to Section 8 of the Medicines Act. Adverse reactions related to medicinal products must be reported to the DHMA according to the same procedures as authorised medicines.

v Pre-market clearance

Prior to the sale of a pharmaceutical product in Denmark, a marketing authorisation must be obtained from the DHMA or EMA for that specific product, see Section 7 of the Medicines Act, and Directive 2001/82/EC,[10] Directive 2001/83[11] and Regulation No. 726/2004.[12] The applicant for and holder of a marketing authorisation must be established in an EU or EEA country. The holder of a marketing authorisation may appoint a representative. An authorisation may be obtained according to the centralised procedure, the decentralised procedure or the mutual recognition procedure. The authorisation is conditional on proof of efficacy and safety. The basic rule found in Section 8 of the Medicines Act states that the granting of a marketing authorisation presupposes that the benefits and risks are considered favourable. This fundamental requirement applies to all medicines, but the documentation requirements are not quite as strict for herbal medicines. Vitamin and mineral supplements are not usually classified as medicines. However, they must be approved as medicines if they contain vitamins or minerals exceeding the recommended daily dosage.

The principles for approval and the presentation of documentation are stated in the Notice to Applicants.[13] If a marketing authorisation is not used within a period of three years, it will be withdrawn unless specific conditions are stated, see Section 28 (the sunset clause). The fees in relation to an application for a marketing authorisation are listed in the Executive Order on Fees Payable for Medicinal Products.[14] When the pharmaceutical company has obtained a marketing authorisation, the medicine may be marketed, presupposing that the price has been registered with the DHMA; please see Section III

8 Executive order No. 1439 of 23/12/2012.

9 Executive order No. 665 of 14/09/1998.

10 Directive 2001/82/EC of the European Parliament and the Council of 6 November 2001.

11 Ibid.

12 Regulation (EC) No. 726/2004 of the European Parliament and of the Council of 31 March 2004.

13 Notice to applicants and regulatory guidelines medicinal products for human use prepared by the European Commission in consultation with the competent authorities of the Member States and the EMA.

14 Executive Order No. 1407 of 20 December 2012

below. Imported medicines may be sold in Denmark if these are approved by the EMA according to the centralised procedure. The owner of the marketing authorisation must be located within the EU. Other foreign companies must appoint a Danish representative.

Generic products may be authorised according to the abridged application procedure. The authorities impose a number of general and specific requirements on the results of bioequivalence studies that generic companies must submit as part of an application for generic medicines. These general and specific requirements may be found in the EMA's Guideline on the Investigation of Bioequivalence.

As mentioned in Section II, v, the DHMA may in specific cases, upon application, permit the sale or delivery of medicines not covered by a marketing authorisation.

The manufacturer of medical devices is responsible for the safety of the product when it is marketed. The authorities do not grant an approval of the medical devices. However, medical devices must be CE-marked and must fulfill the requirements in this regard. Danish manufacturers and authorised representatives placing new Class I devices and systems and procedure packs on the market as of 1 May 2011 shall register the devices with the DHMA.

vi Regulatory incentives

The marketing authorisation process and the patent system are separate according to Danish law, and the DHMA does not take the patent situation into consideration in relation to an application for marketing authorisation (i.e., there is no patent linkage in Denmark).

However, the rules concerning orphan drugs do have some similarities with patent linkage. Companies that are able to obtain an orphan designation for a medicinal product benefit from incentives such as protocol assistance, 10-year marketing exclusivity, fee reductions or exemptions, and national incentives detailed in an inventory made available by the European Commission. The criteria for designating a medicinal product as an orphan medicinal product can be found in Regulation No. 141/2000. The criteria include that it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting no more than five in 10,000 persons in the EU, or a seriously debilitating or a serious and chronic condition, where it is unlikely that expected sales of the medicinal product would cover the investment in its development. Of crucial importance in relation to orphan drugs is the 10-year market exclusivity. According to Article 8(1) of Regulation No. 141/2000, the Community and the Member States shall not, for a period of 10 years, grant a marketing authorisation or accept an application to extend an existing marketing authorisation for the same therapeutic indication in respect of a similar medicinal product.

Denmark has also incorporated EC Regulation 469/2009 on supplementary protection certificates ('SPCs'). SPCs prolong the protection of the patent for one specific product by up to five years. An application for an SPC should be filed with the DHMA. Article 36 of Regulation 1901/2006 provides for a further six-month extension of the SPC. Such extension is available only under certain conditions, the most notable being the requirement for the submission of a new application for marketing authorisation containing data from all trials conducted in accordance with an agreed paediatric investigation plan. An extension of an SPC can only be awarded if there is an SPC to extend, but it is possible to obtain a negative-term SPC, which does not prolong the protection period in itself, but

may form the basis of a paediatric extension. Application for a paediatric extension should also be filed with the DHMA.

Furthermore, the pharmaceutical company may benefit from the rules on data exclusivity in relation to the data submitted by the company in connection with the marketing authorisation. The period of protection is eight years from the first marketing authorisation in the EEA, see the Executive Order on Marketing Authorisation etc.,[15] Section 9, corresponding to Article 10 in Directive 2004/27/EC,[16] but the marketing authorisation based on the data may only be used after 10 years. If there are new indications, the period may be extended to 11 years.

vii Post-approval controls

In July 2012 new pharmacovigilance legislation came into effect across the EU. The new legislation aims to strengthen patient safety by improving the present system used for monitoring the safety of medicines in the EU. The new legislation transposes changes set out in Directive 2010/84/EU and Regulation No. 1235/2010. The rules of the new legislation are underpinned by a number of guideline modules (good vigilance practice – 'GVP' modules), each addressing different major elements in the new legislation.

Sections 53–56(a) of the Danish Medicines Act stipulate the holder of the marketing authorisation's obligation to use a pharmacovigilance system[17] and the requirements in relation to reports of adverse effects.

Articles 22a and 104a of Directive 2010/84 are implemented in Section 9 of the Danish Medicines Act stating that the DHMA may attach terms to the marketing authorisation when it is granted. Article 22a concerns the conduct of a safety study if there are concerns about the risks of an approved medicine or an efficacy evaluation, if the understanding of the disease or the clinical methodology indicates that previous efficacy evaluations might be revised significantly. Article 104a concerns risk management systems if there are concerns about the risk-benefit balance of the medicinal products authorised before 21 July 2012. For products authorised after 21 July 2012, it is mandatory to have a risk management system in accordance with Article 104(3)(c).

Sections 53–56(a) of the Danish Medicines Act state the situations in which the DHMA may change, suspend or withdraw a marketing authorisation including, but not limited to, if the risk-benefit balance of the medical product is not favourable, the terms attached to the marketing authorisation in accordance with Section 9 are not met or changes are made in the summary of product characteristics without the authorisation of the DHMA, see also the Danish Medicines Act, Section 26(1) and Regulation No. 1234/2008.[18]

A new product code must be sought if the marketing authorisation is transferred to a new holder. Product codes may be obtained from the Danish Drug Information A/S (a company owned by the Danish Association of the Pharmaceutical Industry).

15 Executive Order No. 1239 of 12 December 2005.

16 Directive 2004/27/EC of the European Parliament and the Council of 31 March 2004.

17 The rules correspond to the regulation in Directive 2001/83/EU.

18 Commission Regulation (EC) No. 1234/2008 of 24 November 2008.

viii Manufacturing controls

Companies manufacturing medicinal products and intermediate products must have an authorisation from the DHMA, please see Section 39 of the Danish Medicines Act. An authorisation for manufacturing medicinal products and intermediate products will only be granted if the services of at least one named qualified person are available. Furthermore, the companies must act in accordance with good manufacturing practice ('GMP').[19] Companies authorised to manufacture medicines are supervised regularly by the DHMA.

Manufacturers and authorised representatives based in Denmark placing custom-made medical devices, systems and procedure packs in Class I on the market are required to register with the DHMA providing details of themselves and the medical devices. This also applies to sterilisers of systems and procedure packs or other CE-marked medical devices designed by the manufacturer to be sterilised before use. Manufacturers and authorised representatives based in Denmark placing *in vitro* diagnostic medical devices on the market are required to notify the DHMA with details of the company and the product they are placing on the market.

ix Advertising and promotion

The advertising of pharmaceuticals is regulated by the detailed provisions in Chapter 7 in the Danish Medicines Act. The purpose of the regulation is to secure that the public has 'access to objective and adequate information about medicinal products', and that the public is 'protected against misleading advertising and other illegal marketing of medicinal products', see Section 1 of the Medicines Act. One of the most important rules is the absolute ban on advertising in Section 66. According to this provision, advertising to the general public shall not be allowed in the case of medicinal products that are:

a available only on prescription;
b inappropriate for use unless the patient has first consulted a doctor with a view to diagnosis or monitoring of the treatment; or
c included in the Act on Euphoriant Substances.

The term 'the general public' includes any person who is not a doctor, dentist, veterinarian, pharmacist, veterinary nurse, pharmacologist or a student training to become one of the these. The definition and ban are stipulated in Directive 2001/83/EC and the special rules on advertising for medicines are thus predominantly EU consistent. However, the DHMA applies a very strict interpretation of the regulation. The regulation is enforced by the DHMA, which may refer the case to the police.

Advertising for medical devices is only lawful if it is directed towards doctors, dentists or persons buying the medical devices for commercial purposes if the medical devices are intended solely for the use of doctors and dentists.[20] Advertising for medical devices that are

19 See The Rules Governing Medicinal Products in the European Union, Volume 4, Guide to Good Manufacturing Practice for Medicinal Products.

20 Executive Order No. 695 of 28/09/1998.

not intended solely for the use of doctors and dentists are lawful if the advertisement fulfils the requirements in the Executive Order on Commercials for Medical Devices.[21]

x Distributors and wholesalers

Distributors and wholesalers of medicines must be authorised by the DHMA according to Section 39 of the Danish Medicines Act. Companies authorised to distribute medicines wholesale are supervised regularly by the DHMA. Inspections are carried out according to the good distributor practice rules ('GDP rules'). This is done in accordance with the agreed European procedures for inspectorates.

Distributors and wholesalers of medical devices do not need authorisation or registration.

xi Classification of products

The DHMA determines whether medicines should be classified as prescription-only or over-the-counter. The rules are national and there is not full consistency within the EU in relation to which medicines are prescription only. Emphasis is placed on whether the medicines – even when used correctly – may constitute a health hazard, if utilised without medical supervision; whether they present a health hazard because they are frequently and widely used incorrectly; whether they contain substances or preparations whose effect or side effects are necessary to monitor; and whether they are administered parenterally (injected or the like).

In Denmark, pharmacies have exclusive rights to sell prescription-only medicines to consumers. Likewise, a great number of over-the-counter medicines are only permitted for sale in pharmacies. Over-the-counter sales outlets may sell non-prescription medicinal products suitable for sale outside pharmacies.

xii Imports and exports

Any company that handles medicines or intermediates must be authorised by the DHMA according to Section 39 of the Medicines Act. Companies producing, importing or distributing active ingredients or mediate medicines (not physically handling the medicines) must be registered with the DHMA. The DHMA only authorises and registers companies with an address in Denmark. Companies within the EU must have similar authorisations granted by the competent national authority. Companies outside the EU must have an authorised representative within the EU. Furthermore, according to Section 75 of the Medicines Act anyone who brings a medicinal product on the market and wholesale distributors of such a medicinal product are obliged to ensure appropriate and continued supplies of the product in question.

xiii Controlled substances

Import and export, sale, purchase, delivery, receipt, production, processing and possession of euphoriants are prohibited, except if authorisation is given by the health authorities. Such

21 Executive Order No. 695 of 28/09/1998.

authorisation will only be given under certain conditions, for example, if the euphoriants are used for medical purposes as part of the medical treatment of drug users.

xiv Enforcement

The DHMA monitors and enforces compliance with the requirements laid down in the Medicines Act and the rules laid down under the Act in relation to the content, quality and handling of medicines, intermediates and raw materials, see Section 44. The DHMA also monitors compliance with the requirements in relation to the Section 39-authorisation, see Section II, x and xii above. The DHMA has the authority to carry out inspection of companies that have a marketing authorisation or a Section 39-authorisation and companies producing certain raw materials without obtaining a court order. However, unannounced inspections may only be performed if they have reasonable suspicion that raw materials are not being produced in accordance with Section 44(2) of the Medicines Act. In order to carry out its duties according to Section 44, the DHMA may obtain samples of medicines and products, including their packaging and leaflet, intermediates and raw materials, free of charge. The Authority may also require all information and materials needed for the check. Finally, the DHMA may issue orders if the companies do not act in accordance with the above-mentioned rules and may seize medicines and products sold to users that are contrary to these rules, see Section 44(b)–(c).The above-mentioned check is performed in cooperation with the EMA.

The DHMA enforces the regulations for medical devices and investigates adverse or serious incident reports from manufacturers and users of medical devices.

III PRICING AND REIMBURSEMENT

The Danish health-care system is decentralised and tax financed. Reimbursable medicines are financed by national health insurance, which, despite its official name, is a tax-funded system for paying for (or paying part of the costs of) medicines, visits to physicians, etc. The price formation for medicines is a purely national matter. Most issues related to pricing and reimbursement of medicines are dealt with by the DHMA.

In principle, pricing is free and approval by the DHMA is not needed, but the pharmaceutical company must provide a list price for sale to the pharmacies to the DHMA 14 days before the product is marketed, see Section 77 of the Medicines Act. The price will be fixed for 14 days. The price registration is a condition for selling the product, and in order to maintain the price registration the pharmaceutical company must be able to fulfil the pharmacies' need for medicines, see Section 75. The pharmaceutical company will receive prior warning if the DHMA intends to delete the registration. Prices are published on www.medicinpriser.dk.

The rules concerning substitution are very important. The pharmacies can and shall distribute a 'synonymous medicine', which may be parallel-imported medicine or a generic version of the medicine if this is cheaper than the prescribed medicine, unless the physician has stated that there should be no substitution, or the patient wishes to have the original product and pay the difference in price. Thus, in practice the cheapest medicine will 'win' the market very quickly. Whether a medicine is 'synonymous' is determined by the DHMA.

Due to the Danish pricing system, where the price in the pharmacies is fixed, discounts or rebates on prices are considered an illegal economic advantage to the purchaser. Therefore, such discounts cannot be given to pharmacies, except:

a for rebates strictly related to cost savings obtained by the supplier as a direct consequence of the procurement patterns of the recipient, see Chapter 9 in the Danish Order on Advertising; and

b discounts to hospitals and discounts given in connection with tenders invited by the regions' pharmaceutical organisation, Amgros.

For such hospitals, the pricing system is quite different. Pharmaceutical companies are not prohibited from offering the hospital pharmacies lower prices than the list price, and discounts are normally obtained through tendering and bulk purchasing by Amgros, which handles 99 per cent of the purchases of medicines used in public hospitals in Denmark. The rules concerning the tenders are determined in an EU Directive[22] and Danish tender legislation.

Reimbursement is a national matter and determined by DHMA on the basis of recommendation of the Reimbursement Committee. The rules concerning reimbursement are very important for the pharmaceutical companies. The pharmaceutical company must apply for and give reasons for the request for reimbursement. The difference in the Danish rules compared to other EU countries is a consequence of the free pricing of medicine in Denmark and the fact that no negotiation or approval of prices takes place. There are two types of reimbursement:

a general reimbursement (including general restricted reimbursement) meaning unconditional reimbursement for a given medicine or a specific patient group; and

b single reimbursement based on an application from the patient's physician on behalf of individual patients.

The criteria for granting general reimbursement are set out in the Executive Order on Reimbursement.[23] The reimbursement status is re-evaluated on a continual basis. The re-evaluation includes the development on the market, including patent expiry in relation to other products.

22 Directive 2004/18/EC of the European Parliament and the Council of 31 March 2004.

23 The criteria include (1) whether the medicine has a secure and valuable therapeutic effect on a well-defined indication; and (2) whether the price of the medicine is proportionate to its therapeutic value. The criteria are listed in Executive Order No. 180 of 17 March 2005 on reimbursement. The criteria are setting the stage for a medical as well as a health economic evaluation. Economic evaluations on a voluntary basis can be filed with the application in order to provide documentation of a reasonable relationship between price and therapeutic effects by the pharmaceutical company. The European Commission proposed on 1 March 2012 a revision of the EU Transparency Directive, in which it is amongst others clarified that elements already assessed in the framework of the marketing authorisation process (quality, safety and efficacy, including bioequivalence) may not be reassessed in the framework of pricing and reimbursement procedures.

The Danish Centre for Health Technology Assessment, an entity within the DHMA, carries out health technology assessments ('HTAs') with the aim of improving quality, standards and value for money and aims to integrate HTA principles into the running and planning of the public health service at all levels.

IV ADMINISTRATIVE AND JUDICIAL REMEDIES

An administrative decision may be appealed by a company, provided the company in question is able to demonstrate legal standing, which is given to companies with a substantial, individual interest in the matter. Applicants of a marketing authorisation always have legal standing.

Decisions of the DHMA can be appealed to the Ministry of Health, whose decision may in turn, if it goes against the company filing the complaint, be appealed to the Parliamentary Ombudsman. There is no deadline for filing a complaint to the Ministry, but an appeal to the Ombudsman must be filed within one year of the decision in question. In addition to the right to complain, legal standing also grants an extended right of access to documents in the case file. The Ministry of Health will review the decision of the DHMA in its entirety, but the Ministry will, however, be less inclined to reverse it to the extent the decision is based on a medical assessment, since the Ministry does not generally possess the same medical expertise as the DHMA. If the Ministry's decision goes against the appealing company, the company may complain to the Ombudsman. However, as the Ombudsman usually focuses on the legal aspects of the matter including, in particular, whether the relevant case processing rules have been observed, he or she will most likely be even less minded to reverse a decision based on a medical assessment.

In addition to the administrative complaint system, at any point in the process an action (declaratory action) before the civil courts against a decision of a public authority can be filed. However, the courts will also be less inclined to reverse or annul a decision of a public authority if the decision is based on an expert's opinion, for example, following a medical assessment.

V FINANCIAL RELATIONSHIPS WITH PRESCRIBERS AND PAYORS

Interactions with health-care professionals ('HCPs') with respect to marketed medicinal products and related pre-launch activities are highly regulated to ensure that cooperation takes place in an ethically responsible manner with professionalism and patient safety as the focus point. Parts of the pharmaceutical industry have decided to go one step further and complement legislation with a number of voluntary rules. The EFPIA Code and the Danish Ethical Rules for the Promotion of Medicinal Products to HCPs strive to ensure that pharmaceutical companies' interactions with HCPs serve to benefit patients and enhance the practice of medicine. The Ethical Committee for the Pharmaceutical Industry in Denmark ('ENLI') serves as a voluntary complement to the control carried out by the DHMA. The regulatory basis of ENLI includes regulation that in some cases goes significantly beyond Danish law.

The Danish Trade Association represents producers of medical devices and has issued a set of ethical guidelines in Danish. The guidelines are identical to Eucomed's 'Guidelines on interactions with Healthcare Professionals' of September 2008. Furthermore, the area is the object of considerable political attention, and the introduction of national legislation (probably inspired by the rules on medicinal products) is currently being considered.

HCPs are defined in Section 1(3) of the Executive Order on Advertising as 'doctors, dentists, veterinarians, pharmacists, nurses, pharmaconomists and students in these disciplines'. Legal advertising towards HCPs must meet a number of requirements set out in Articles 91 and 92 of Directive 2001/83/EC and in Chapter 4 of the Executive Order on Advertising. In addition, the advertisement shall be adequate and objective and must not be misleading or exaggerate the properties of the medicine, see Section 66 of the Medicines Act, which corresponds to Article 87(3) in Directive 2001/83/EC. Similar rules apply to advertising directed at HCPs in relation to medical devices.

The financial relationships between companies that market medicines and medical devices and HCPs or persons who make decisions concerning utilisation or reimbursement for such products is also affected by the rules on bribery. Section 122 of the Danish Penal Code stipulates that it is illegal to provide financial benefit to public officials who have the authority to give or deny benefits, authorisations, etc. Kickbacks are covered by Section 299. The special regulation concerning medicines and medical devices is stricter on bribery than in the normal sense.

To ensure independence, the Pharmacies' Act and Veterinary Act prohibits a doctor, dentist or veterinarian from operating or being affiliated with a pharmaceutical company without the DHMA's consent. The ban is primarily motivated by a general desire to maintain independence. Affiliation is not defined only as ownership but includes any strong affiliation. If consent is given, the affiliation will be published on the DHMA's website. It is the doctor who is the addressee of the approval, but the pharmaceutical company must notify the affiliation as well.

VI SPECIAL LIABILITY OR COMPENSATION SYSTEMS

All patients in Denmark are covered by a publicly funded compensation scheme. The compensation scheme covers injuries occurring in connection with treatments in the public and private health-care system and injuries caused by pharmaceuticals. The right to compensation is regulated by the Danish Act on the Right to Complain and Receive Compensation within the Health Service. According to this Act compensation paid pursuant to the publicly funded compensation scheme is the primary compensation. Consequently, a patient or his or her surviving relatives are prevented from claiming compensation pursuant to other Danish laws on damages if the publicly funded compensation scheme covers the claim. However, it is important to note that the Danish Patient Insurance Association might have a recourse claim against the pharmaceutical company, manufacturers of the medical devices etc.

The rules on product liability apply if the patient's injury can be classified as an injury caused by a defective product, (i.e., a result of defective medicines or faulty medical devices). The Danish Product Liability Act contains two kinds of product liability, product liability based on EU Directive 374/1985 EC on the approximation of the laws, regulations

and administrative provisions of the Member States concerning liability for defective products, and product liability based on case law.

When claiming damages according to the Danish Act on the Right to Complain and Receive Compensation within the Health Service the patient will have to register his or her claim with the Danish Patient Insurance Association. Registration and any further administrative procedures are free of charge. The Danish Patient Insurance Association determines whether a patient shall be compensated. In the event a patient is awarded damages according to the Danish Act on the Right to Complain and Receive Compensation within the Health Service the patient is not allowed to claim additional damages pursuant to the Danish Product Liability Act and *vice versa*.

VII TRANSACTIONAL AND COMPETITION ISSUES

i Competition law

Danish competition law is generally very similar to EU competition law. There are no differences in regulation, enforcement or case law of special significance to the life sciences sector.

However, it is worth noting that the Danish competition authorities have expressed concerns regarding the Danish regulation of the pharmacy sector on a number of occasions. Most recently, the Danish Competition Council recommended a significant deregulation of the sector in June 2012, including, notably, an abolition of:

a the requirement that owners of pharmacies hold an MSc degree in pharmacy;
b the limitation on the number of pharmacies in Denmark; and
c the fixed-price system for retail sale of certain pharmaceuticals.

Partly in response to these recommendations, the Danish government has commissioned a working group that is to consider the possibility of modernising the Danish pharmacy sector, including the recommendations of the Danish Competition Council set out above. It is expected that a modernisation initiative based on the recommendations of the working group will be presented in the course of 2013.

ii Transactional issues

Transactions within the Danish life sciences industry are not considerably different from those in other European jurisdictions. One could argue that there is greater focus on securing representations and warranties in the transaction documentation, as they affect rights that, if not properly secured, are associated with an economic risk higher than normal. Consequently, due diligence exercises accompanying many of the transactions are quite complex exercises. Valuation is always a big issue in life sciences transactions and a strong focus on the drafting of complex consideration scenarios is therefore often preferred.

The life sciences industry is associated with considerable research costs and consequently the continual need for the procurement of capital, in a situation where the future of the business is very uncertain. Thus, there is often a focus on more complex equity contributions, including a number of warrant and convertible loan programmes, multiple share classes and (compared to the size of the companies) quite extensive and complex shareholders' agreements.

Because of the larger capital needs and the greater risks involved, the Danish life sciences business has also experienced a fair amount of stock market activity, believed to be larger (compared to the industry's share of the overall business market) than in other jurisdictions.

VIII CURRENT DEVELOPMENTS

The life sciences industry has, like most sectors, been very affected by the financial crisis. The public health-care budget has been under a lot of pressure in recent years, which has had a very high impact on the price of reimbursable prescription medicines sold by the Danish pharmacies. In 2009 the Danish Association of the Pharmaceutical Industry and the Ministry of Health agreed on a cap and a price reduction on the price of reimbursable prescription medicines sold by the Danish pharmacies. On 18 December 2012 the agreement was extended until 31 December 2015, and new price reductions were agreed as a result of the prices expected in the rest of Europe. The pressure on the budget has also affected the reimbursement system, and the DHMA is now re-evaluating the reimbursement status on continual basis.

Furthermore, the medical device area is subject to considerable political attention at the moment, especially due to an increasing concern about the safety of medical devices. The Minister of Health has recently put forward a proposal for new national legislation that aims to improve patient safety, including for the use of implants and medical devices. The proposal may enter into force on 1 July 2013.

The Medicines Act has also been amended in order to be in accordance with Directive 2011/62 to prevent the entry of falsified medicinal products into the legal supply chain. Previously, Section 39(b) of the Danish Medicines Act entitled the DHMA to shut down websites dealing with illegal medicines. This provision has as of 1 January 2013 been 'replaced by' Section 41, requiring the holder of an authorisation under Section 39(1) who, within the scope of such authorisation intends to sell medicinal products online, to notify the DHMA thereof no later than simultaneously with the beginning of the online sale.

Appendix 1

ABOUT THE AUTHORS

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Mikkel Vittrup is partner in the IP department at Plesner Law Firm – one of the leading Danish law firms. Mikkel Vittrup provides advice on IP law, focusing in particular on the legal enforcement of intellectual property rights (patents, copyrights, trademarks and design rights etc.) through legal proceedings, including injunctions and preservation of evidence. Mikkel Vittrup has specific experience in the area of life sciences and advises on, for example, regulatory issues in respect of medicinal products, medical devices and foodstuffs, as well as on the conclusion of agreements on the development and commercialisation of technology such as licence agreements, research and development agreements, clinical trial agreements etc. Mikkel Vittrup also provides advice in respect of competition law and European Union law, in particular on the interface between competition law, European Union law and IP law.

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Mette Hygum Clausen is an associate in the IP department at Plesner Law Firm – one of the leading Danish law firms. Mette Hygum Clausen provides advice on IP law, focusing in particular on the legal enforcement of patent rights through legal proceedings, including injunctions and the preservation of evidence. Mette Hygum Clausen also provides advice on IP and life sciences contracts and regulatory issues in respect of medicinal products and medical devices.

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