THE LIFE SCIENCES LAW REVIEW

SEVENTH EDITION

Editor
Richard Kingham

THE LAWREVIEWS

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PREFACE

The seventh edition of *The Life Sciences Law Review* covers a total of 34 jurisdictions, providing an overview of legal requirements of interest to pharmaceutical, biotechnology and medical device companies. The chapters are arranged so as to describe requirements throughout the life cycle of a regulated product, from discovery to clinical trials, the marketing authorisation process and post-approval controls. Certain other legal matters of special interest to manufacturers of medical products – including administrative remedies, pricing and reimbursement, competition law, special liability regimes and commercial transactions – are also covered. Finally, there is a special chapter on international harmonisation, which is of increasing importance in many of the regulatory systems that are described in the national chapters.

The past year has seen a number of significant developments. After many years of negotiations and false starts, the United States and EU have finally begun to implement a programme of mutual recognition of inspections of drug manufacturing establishments, thus simplifying the shipment of drug products between the jurisdictions and freeing resources to carry out more inspections in third countries. In the meantime, the United States continues to debate whether to repeal the comprehensive medical care legislation enacted during the Obama administration, and is now considering measures to improve the transparency of pricing for prescription drugs. The United Kingdom is addressing changes to drug regulatory systems that must accompany the country's planned withdrawal from the EU, and drug and device manufacturers are actively planning for the effects of Brexit on their supply chains. The governments in India and China continue to consider changes in their regulatory systems for drugs and medical devices.

It is vitally important that lawyers who advise companies in the life sciences sector and the business executives whom they serve have a working knowledge of the regulations and policies that govern drugs, biologics and medical devices. It is equally important to keep up to date with developments in the regulatory systems, which govern access to the market, pricing and reimbursement, advertising and promotion, and numerous other matters that are essential to success. It is our hope that this annual publication will be helpful in this respect.

All of the chapters have been written by leading experts within the relevant jurisdiction. They are an impressive group, and it is a pleasure to be associated with them in the preparation of this publication.

Richard Kingham
Covington & Burling LLP
Washington, DC
March 2019

Chapter 12

FRANCE

Sophie Pelé[1]

I INTRODUCTION

The French regulatory framework for life sciences products is regarded as highly sophisticated and was one of the pillars for the creation of the EU regulatory framework. However, the EU framework has developed significantly and now the French and EU regulations do not always correspond to each other. An example of this is the French concept of *exploitant* (a licensed company authorised to market pharmaceutical products, which may differ from the marketing authorisation holder), which has no equivalent in the EU regulations.

Despite these discrepancies, the French regulations broadly reflect the EU regulations regarding the manufacture and marketing of pharmaceutical products and medical devices, with the exception of the pricing and reimbursement schemes, which remain national in nature. Manufacture and marketing matters are governed by the French Public Health Code.[2] Pricing and reimbursement matters are covered by the Social Security Code.[3] In addition, 'soft law regulation' tends to play an important role, not only through good practices harmonised across Europe, but also from a medico-economic standpoint.

This dual system is also reflected in the organisation of competent national authorities. The French National Agency for the Safety of Medicines and Health Products (ANSM) is in charge of the health and safety aspects of both medicines and medical devices, including:

a the approval of clinical trials;
b the granting of marketing authorisations;
c the issuance of 'dear healthcare professional' letters;
d the authorisation of advertising; and
e inspections of manufacturing premises.

The National Authority for Health (HAS) is responsible for medico-economic aspects, notably the publication of guidelines recommending therapeutic strategies for the treatment of certain diseases and the assessment of the therapeutic and medico-economic benefit for reimbursement purposes through its Transparency Committee (for medicines) and its National Commission for Medical Devices and Health Technologies Assessment (for medical devices). Finally, the Ministry of Health, which includes the Pricing Committee (CEPS), oversees the pricing of reimbursed products.

1 Sophie Pelé is a national partner at Dechert LLP.

2 www.legifrance.gouv.fr/affichCode.do?cidTexte=LEGITEXT000006072665&dateTexte=20140107.

3 www.legifrance.gouv.fr/affichCode.do?cidTexte=LEGITEXT000006073189&dateTexte=20140107.

II THE REGULATORY REGIME

Despite their supervision by the same national health agencies, medicines and medical devices are subject to two separate legal regimes. Medicines are governed by the provisions transposing the EU code relating to medicinal products for human use and cannot be tested, marketed or promoted without prior approval. Medical devices are subject to the provisions transposing into French law the CE marking requirement regime applicable throughout Europe, and harmonisation will be fostered by the direct application of Regulation (EU) 2017/745 of the European Parliament and of the Council on medical devices, and Regulation (EU) 2017/746 on *in vitro* diagnostic medical devices, both adopted on 5 April 2017, which will apply as from 26 May 2020 and 22 May 2022 respectively.

The adoption of these Regulations reinforces the trend towards increased similarity between both categories of products. In France, for instance, advertising material for medical devices has been mostly aligned with the prior-approval regime applicable to medicines. In addition, medicines and medical devices are subject to very similar processes in terms of pricing and reimbursement.

i Classification

Rules and principles governing the classification of health products are broadly based on EU case law. For instance, the Administrative Supreme Court referred to the European Court of Justice the regulatory status of software assisting in the prescription of pharmaceutical products,[4] which have been qualified as medical devices because of their aim.[5] At the same time, French case law continues to broaden the scope of products falling within the definition of pharmaceutical products. This is the case for various food supplements claiming to have therapeutic effects or containing substances with therapeutic properties,[6] and tiger balsam, the status of which is still not settled.[7]

More recently, the Finance Bill for 2019 introduced the new category of hybrid medicines into the French regime. Like generics, hybrid medicines may be substituted for a reference medicine, but they are not similar to the originator product in terms of indications, dosage, pharmaceutical form or route of administration. The applicable conditions for substitution are therefore still pending, and these will be determined by a ministerial order. Hybrid status might notably concern medicinal products with a different form or packaging from the originator product.

ii Non-clinical studies

The status of non-interventional studies conducted on human beings has been aligned with rules applicable to clinical trials, with some specificities. For instance, the ethics committee can give its opinion with only four members present, and the approval from the ANSM is not required.

4 Administrative Supreme Court, 8 June 2016, No. 387156.

5 CJEU, 7 December 2017, C-329/16, Preliminary ruling from France about the qualification of prescription assistance software.

6 Criminal Supreme Court, 12 July 2016, No. 15-82873, unpublished; Criminal Supreme Court, 30 January 2018, No. 16-86.702, unpublished; Criminal Supreme Court, 23 October 2018, No. 17-84.098, unpublished.

7 Criminal Supreme Court, 8 July 2015, No. 14-83.624.

iii Clinical trials

Clinical trials for medicines and medical devices conducted in France must receive a prior opinion from an ethics committee and prior approval by the ANSM. In some cases, the ANSM can refuse to grant the approval. In a judgment dated 3 April 2015, an administrative court upheld one such refusal.[8]

Decree No. 2016-1537 of 16 November 2016 significantly amended the regime applicable to clinical trials. Private sponsors must supply all the tested products free of charge to the healthcare centres hosting the healthcare professionals (HCPs) appointed as investigators and compensate for the costs and extra costs incurred in conducting the trial. For transparency reasons (particularly to avoid conflicts of interest that could arise between the ethics committees (ECs) and healthcare institutions) and to allow an appropriate assessment of the projects, the competent ECs are now designated on a lottery basis, from among those available and whose members have necessary skills in the project field under consideration. In addition, the requirements regarding reporting of adverse or unexpected events have been significantly strengthened, and can lead to the provisional suspension of the administration of the tested product in Phase I.

The ANSM initiated a pilot phase during which, on a voluntary basis, ECs, subject to the sponsor's acceptance, can implement EU Regulation No. 536/2014 on clinical trials. Following two years of implementation, the time frame for the review of applications is, on average, 68.9 days. In addition, to improve access to innovative therapies, and in anticipation of upcoming EU regulation of clinical trials, the ANSM set up, on an experimental basis, fast-track authorisations of clinical trials, which are likely to apply to both advanced therapies and new trial on known substances. Starting from 15 October 2018, this new experiment applies to all phases of clinical trials and aims to reduce the application review period from 60 to 25 days for clinical trials on known substances, and to 40 days for innovative treatments.

In 2014, the French government issued harmonised template agreements with the aim of accelerating the implementation of trials within French public hospitals.[9] Decree No. 2016-1538 of 16 November 2016 broadens their application to any type of privately sponsored trial. The harmonised agreement is exclusive of any other agreement entered into in the framework of the same trial. It must therefore include the negotiations with the investigators, associations participating in the trial, etc. Moreover, when a trial involves several centres, the negotiation of financial aspects takes place between a single hospital and the sponsor; other centres will be bound by the same financial provisions. The aim is to be able to negotiate with the coordinating centre within a 45-day period. Hospitals receive financial incentives from public funds if they successfully implement the template. Moreover, sponsors might also provide for counterparts in return for the quality of the data collected, which correspond to former financial incentives related to the inclusion of patients. In 2015, 2,135 agreements had been entered into through this route with 91 healthcare institutions, whereas there were 3,117 agreements with 112 establishments in 2016.

8 Paris Administrative Tribunal, 3 March 2015, No. 1401975/6-1, *AB Science*.

9 Instruction No. DGOS/PF4/2014/195 of 17 June 2014 relating to the implementation of a template agreement for biomedical research with a private sponsor in public hospitals.

iv Named-patient and compassionate-use procedures

Named-patient and compassionate use procedures were significantly updated and strengthened by the Bertrand Law of 29 December 2011.[10] A temporary authorisation for use (ATU) may be granted to treat severe or rare diseases for which no treatment has been authorised, if and when the treatment cannot be delayed.

When requested by the pharmaceutical company intending to market the product, an ATU will be granted if safety and efficacy are presumed and if a marketing authorisation has or will be applied for within a given time frame. When requested by a physician on a named-patient basis, an ATU will be granted if safety and efficacy are presumed, if the patient cannot be treated through a clinical trial, and if the product is either subject to a clinical trial or an application for marketing authorisation (even temporary), at least in a request form. The last of these conditions may be bypassed in a few specific cases, such as where there is a high probability of severe consequences for the patient without treatment. The Finance Bill for 2019 has opened up the possibility of obtaining an ATU for medicines that are already authorised for another indication where previously only medicines that had not been authorised were likely to be granted an ATU, for their first indication. Moreover, the Bill also provides that medicinal products authorised without a previous ATU but meeting the ATU criteria may be subject to a temporary reimbursement on that basis until final agreement on their reimbursement price, under conditions including the obligation to keep the product on the market for a certain length of time and at a price that may be set unilaterally by the CEPS.

Alongside these ATUs, the Bertrand Law has created a regulated scheme for off-label use, called temporary recommendation for use (RTU). A product may be prescribed off-label without any marketing authorisation or ATU, either because it is indispensable to the treatment of a patient, in light of the existing state of the art, or because it is permitted by an RTU issued by the ANSM. The conditions for granting RTUs are similar to those for ATUs, except that they are imposed on pharmaceutical companies by the authorities. In addition, the law amending social security funding for 2014[11] broadened the RTU regime to include cases where therapeutic alternatives might be available but not with the same active substance, dosage or pharmaceutical form. On 29 June 2016, the Administrative Supreme Court upheld this broadening of the RTU regime to cases where therapeutic alternatives are available, which had been challenged on the basis of, among other things, violation of Article 5 of Directive 2001/83/EC.

RTUs tend to get closer to standard marketing authorisations in several ways: first, they are issued for up to three years but can be indefinitely renewed (for example, an RTU was adopted for the medicinal product Avastin in 2015 and this was renewed for a new three-year period in September 2018); second, the Social Security Bill for 2018 has mirrored the pricing negotiation regime for the indications covered by an RTU, for which a distinct price can be agreed with the Pricing Committee (CEPS). The objective is clearly to encourage the use of the RTUs, despite the fact that they are deemed to cover exceptional circumstances.

10 Law No. 2011-2012 of 29 December 2011 relating to Increasing the Safety of Medicines and Health Products.

11 Law No. 2014-892 of 8 August 2014 on Amendments to Social Security Funding for 2014.

v Pre-market clearance

The procedures for the approval of commercial distribution of medicines and medical devices stem from EU regulations. There is a peculiarity in France arising from the concept of an *exploitant* of medicines. In addition to the requirement of a marketing authorisation, a medicine may only be marketed by an authorised marketing company, whose premises and operation have been inspected and authorised by the ANSM. The *exploitant* must either be the marketing authorisation holder, a third party appointed by the latter, or both. He or she must carry out the pharmaceutical activities connected with the sale, promotion and monitoring of the products, and only pharmacovigilance activities can be subcontracted as such. A head pharmacist is responsible for the control of all the pharmaceutical activities, such as pharmacovigilance processes and the compliance of promotional material with relevant laws.

Medical devices can be marketed in France provided they carry a CE marking. However, in addition, manufacturers located in France must notify the ANSM of the first marketing of their devices, as well as any commercialisation in France of implantable and Class III medical devices on French territory (pursuant to the classification of the Council Directive 93/42/EEC of 14 June 1993 concerning medical devices), and provide a copy of the instruction leaflet.

vi Regulatory incentives

Data and market exclusivity rules in France follow EU regulations. However, there are some national peculiarities concerning the preservation of originators' intellectual property rights. First, originator companies must notify their rights to the ANSM for publication purposes. Second, such rights can also be notified to the CEPS, which undertakes, in principle, not to issue any reimbursement decision for generic products more than six months before the expiration of the originator's intellectual property rights. The CEPS cannot, however, prevent an at-risk launch scenario.

Increasingly, regulatory incentives tend to be developed at the pricing and reimbursement stage. Indeed, framework agreements entered into by the CEPS and the pharmaceutical and medical devices companies provide for pricing incentives or conditional pricing, subject to the conduct of additional studies to monitor the safety and efficacy of their products.[12] The framework agreement between the CEPS and the pharmaceutical companies covering the period 2016–2019 also confirms the ability to agree on pay-for-performance schemes, but only in situations where the application of the usual pricing provision is not adequate. Moreover, the ministries supervising the CEPS stated that they intended pay-for-performance agreements to be limited to cases where the social security would not bear any risk, which *de facto* reduces the number of such innovative agreements.[13]

In addition, the framework agreement speeds up the process for the determination of the price for the most innovative products, and provides for the discharge of mandatory rebates to innovative, orphan and paediatric drugs. Also, various provisions favour innovative

12 See https://solidarites-sante.gouv.fr/archives/archives-presse/archives-communiques-de-presse/article/signature-d-un-nouvel-accord-cadre-entre-le-comite-economique-des-produits-de for medicines and its amendment dated 7 December 2018 available on https://solidarites-sante.gouv.fr/IMG/pdf/avenant_a_l_accord_cadre_du_31-12-2015_entre_le_ceps_et_le_leem_20181207.pdf, and www.sante.gouv.fr/IMG/pdf/accord_cadre_dispositifs_medicaux.pdf for medical devices.

13 Ministerial Orientation, 17 August 2016.

paediatric indications, which are granted a one-year extension of guaranteed pricing (six years instead of five), as well as a guaranteed daily treatment cost not lower than for the adult dosage or the possibility of agreeing on a capped total turnover.

On another front, prescription of biosimilar medicines delivered in community pharmacies is incentivised by various means. First, healthcare institutions that have entered into an agreement with a Regional Health Agency will get an incentive corresponding to 20 per cent of the price difference between the biosimilar and the reference medicine in proportion to the biosimilar prescription rate. Moreover, since October 2018, certain healthcare institutions have been selected to trial alternative means of increasing the use of biosimilars alongside an increased incentive of up to 30 per cent.

vii Post-approval controls

Following the French scandal concerning Poly Implant Prothèse (a company that produced breast prostheses), post-approval controls have been increased for medical devices. The ANSM can launch unannounced inspections to detect deviations from applicable technical standards, and impose fines or suspend the marketing of non-compliant products.

In the same way, post-approval controls over pharmaceutical products have improved quite significantly with the right of the ANSM to deliver marketing authorisations on a conditional basis, provided that the holder carries out safety or efficacy studies in real treatment conditions and in comparison with existing therapies within a given time frame. However, this route is very rarely used.

The inspection means should be optimised thanks to the agreement on mutual recognition on good manufacturing practice inspections entered into between the European Union and the United States; this agreement has become effective following the 1 March 2017 decision[14] but remains in the transition phase until July 2019. EU Member States will now be able to use data from inspections carried out by the US Food and Drug Administration (FDA) and vice versa (France is one of the first of 20 EU Member States whose inspection methodology has been recognised as acceptable by the FDA).

Pharmacovigilance reporting obligations have also been broadened. For example, pharmaceutical companies must report to the European database EudraVigilance all suspected adverse effects within 15 days of obtaining knowledge any serious side effects and within 90 days of others. Moreover, as specified in the marketing authorisation, periodic safety update reports must be transmitted regularly to the European Medicines Agency.

viii Manufacturing controls

Recurrent issues relating to the shortage of certain medicines, including those of high therapeutic value or without therapeutic equivalent, have given rise to several changes in the regulations.

Decree No. 2016-993 of 20 July 2016 obliges companies themselves to identify medicines with high therapeutic value, for which they must elaborate detailed alternative supply plans and organise emergency call centres to dispatch products in the event of an actual shortage. Any suspected shortage must be notified to the ANSM. In addition,

14 Decision No. 1/2017 of 1 March 2017 of the Joint Committee established under Article 14 of the Agreement on Mutual Recognition between the European Community and the United States of America, amending the Sectoral Annex for Pharmaceutical Good Manufacturing Practices [2017/382].

pharmacists are allowed to import alternative products in the event of a shortage. Despite these measures, the ANSM registered 405 shortages in 2016. The French Senate published a report recommending implementing a new set of measures, including the creation of a national shortage management unit under the authority of the Prime Minister, or the purchase of medicine reserves for some patient populations.

ix Advertising and promotion

Following the Bertrand Law of 29 December 2011 relating to the strengthening of the safety of medicines and health products, any kind of advertising and promotion of medicines and certain medical devices now requires prior approval from the ANSM.

Advertising and promotional materials for medicines must be submitted to the ANSM following a specific timetable determined by the ANSM: quarterly for advertising to HCPs, and during one of the eight weeks stipulated by the Director General of the ANSM for 2019 for advertising to the public. In the absence of a negative answer from the ANSM two months after the expiry date of each period determined by the ANSM for the receipt of proposed advertising, the advertising is deemed approved and will be valid for two years.

The approval process is the same for advertising and promotional materials for medical devices, except that submissions are not bound by the trimestral timetable.

In addition, the distribution of samples is now restricted to new medicines or for new indications within the first two years of their launch, and only in reply to a written request placed by an HCP.

x Distributors and wholesalers

Wholesale activities have been affected by various measures aiming to address shortages of some key products. Wholesalers, who in France are entrusted with certain public service duties, must notify the ANSM of their geographical area of activity. In addition, the Public Health Code states that wholesalers must first distribute their products to meet the health needs in the notified geographical area before exporting them. As a result, pharmaceutical companies shall ensure an appropriate and continuous supply of products to any and all wholesalers, to enable them to comply with these duties.

The ANSM has audited compliance with wholesalers' requirements and has suspended several wholesale licences of distributors whose activity had deviated from the coverage of the French territory to the export of medicines.

Distribution in pharmacies has also been significantly affected by several changes, as outlined below.

First, medicines and medical devices fall within the pharmaceutical monopoly, namely only a pharmacy that has been granted an authorisation from a regional health agency (ARS), based on the number of residents within its market area, can sell those products to the public. Law No. 2014-344 of 17 March 2014 has removed contact lens solutions, pregnancy tests and ovulation predictors from the monopoly, allowing their distribution in grocery stores.

xi Online sales

The transposition into French law of Directive No. 2011/62/EU on the sale of falsified medicines was rendered difficult by the classification of pharmaceutical products. Indeed, France first restricted online sales to a subcategory of non-prescription drugs, registered on

the list of products available by direct access to the public.[15] The Administrative Supreme Court annulled this provision on the grounds of non-compliance with the EU directive that envisaged online sales of any and all over-the-counter products.[16] Consequently, all over-the-counter products are now available online.[17]

More specifically, online sales of medicines are regulated by ordinance No. 2012-1427 of 19 December 2012. The obligations imposed on the functioning of online pharmacies are quite similar to those for brick-and-mortar pharmacies. An authorisation from the ARS is required. Pure players are not allowed as online pharmacies must rely on traditional brick-and-mortar ones.[18] Two ministerial orders of 28 November 2016 set out good distribution practices for pharmacists, covering all types of situations, including online distribution, as well as the technical requirements for websites, aiming at ensuring the same level of confidentiality and safety as with physical distribution. The Administrative Supreme Court recently overruled some provisions of these two ministerial orders that were deemed a restriction on online pharmacies, in breach of EU law.[19] For instance, the Court considered it not possible to ban any kind of promotion by online pharmacies, whereas this is not the case for bricks-and-mortar pharmacies.

xii Imports and exports

Adopted on 26 January 2016 with a view to modernising the French health system, the Health Bill has introduced a prohibition on wholesalers exporting any medicine of high therapeutic value or without therapeutic equivalent. In addition, the Public Health Code states that other medicines may only be subject to export once national needs are covered; furthermore, it states that a trial or pilot scheme should be carried out whereby wholesalers would notify an independent third party of the volumes not distributed on the French territory. However, an order setting out the conditions for undertaking such a trial has never been published.

xiii Controlled substances

Controlled substances are classified into three categories (narcotics, psychotropics, and drugs on controlled substance Lists I or II), depending on their level of danger. Registration is made by a ministerial decree, following the opinion of the ANSM when the substances are medicines. Drugs can receive a categorisation different from that of one of their compounds and, in the event of doubt or multiple categorisations, the stricter category will prevail.

Controlled substances in the form of active ingredients are subject to administrative requirements of traceability to track the precise volume used.

Drugs included on Lists I or II will be subject to specific requirements in terms of storage in separate and secured premises, labelling with a symbol for death, limited volume of product delivered and, concerning narcotics, use of secured prescriptions.

15 Article L. 5125-34 of the French Public Health Code, inserted by Article 7 of Ordinance No. 2012-1427 of 19 December 2012.

16 Administrative Supreme Court, 17 July 2013, No. 365317.

17 Ordinance No. 2016-966 of 15 July 2016.

18 Article L. 5125-36 of the French Public Health Code.

19 Administrative Supreme Court, 26 March 2018, No. 407289 and 4 April 2018, No. 407292.

xiv Enforcement

The enforcement of regulations relating to health products is the responsibility of several authorities. For instance, the ANSM is the main sanctioning authority with regard to health products. The ANSM's powers and sanctions have been strengthened by Ordinance No. 2016-966 of 15 July 2016 through a simplification of the scope of its activity. The Directorate General for Competition Policy, Consumer Affairs and Fraud Control is also entitled to sanction certain behaviours, such as infringements of the anti-kickback law.

III PRICING AND REIMBURSEMENT

Pricing and reimbursement activities are governed by framework agreements entered into between the CEPS and the professional organisations representing the medical devices industry on the one hand, and medicines and drug industry on the other.[20]

The framework agreement concerning medical devices was signed for the first time on 16 December 2011. Its main aim is to define a template for each agreement on the pricing of medical devices, applicable procedure and time limits. Its duration was initially envisaged to be three years but it has not been amended since then.

The framework agreement concerning medicines (which entered into force on 31 December 2015 for the period 2016–2018 and has been amended to apply until the end of 2019) provides a comprehensive framework for the determination and evolution of prices. In particular, it allows for an acceleration of the procedure applicable to determine the price of innovative products, by accepting a mechanism whereby the company declares its selling price and the CEPS accepts it within two to three weeks, as long as it is consistent with prices in Germany, Italy, Spain and the United Kingdom, and provided that the company commits to compensating sales above its forecasts for four years. As a result of Brexit, the United Kingdom will be excluded from this list and replaced by another EU reference Member State. This matter will probably be subject to negotiations between the CEPS and the French Pharmaceutical Companies Association when entering into the new framework agreement. Outside this specific scheme, the CEPS undertakes that products recognised as having an important therapeutic benefit (with an 'added clinical value' (ASMR) rating of I, II or III) will not be priced below the lowest of the prices in the aforementioned countries for a five-year period, extended by one additional year for paediatric indications. Other provisions concern paediatric and orphan drugs, including the possibility of agreeing on a provisional price, pending its confirmation following agreed studies. However, the parties did not manage to agree on rules to apply to biosimilars and their originator products; this will be one of the most important points in the new framework agreement to be negotiated during 2019 and is probably the reason why the agreement has been renewed for one more year.

Health technology assessment (HTA) procedures were implemented in France by a decree of 2 October 2012.[21] They concern the pricing and reimbursement of products (medical devices and medicines) that claim an important medical benefit (with an ASMR and 'added service value' rating of I, II or III) and that may have a significant impact on the social security budget. The latter criterion is deemed to be fulfilled if the turnover is above

20 See footnote 12.

21 Ministerial Decree No. 2012-1116 of 2 October 2012 relating to the Medico-economic Functions of the Health Authority.

€20 million as from the second full marketing year.[22] However, the HAS may also produce a medico-economic opinion on other products it deems to have a significant impact on the organisation of the healthcare system, according to the claims for the product.

The procedure is similar to the procedure relating to opinions issued by the transparency committee for the eligibility for reimbursement by social security: the HAS first issues a draft opinion and then companies can request a hearing within eight days. In guidelines issued in November 2016, the HAS clarified the methodology of HTA studies, notably the fact that the financial expectations should cover a three- to five-year term.

IV ADMINISTRATIVE AND JUDICIAL REMEDIES

The Administrative Supreme Court reviews the legality of health authority decisions that have a mandatory effect.

Recent case law has significantly increased the monitoring of the CEPS's room for manoeuvre in setting prices. The Administrative Supreme Court does not hesitate, even in summary proceedings, to request from the CEPS detailed economic justifications explaining the level of price decrease imposed. The CEPS cannot impose a price decrease simply to maintain the global increase in spending authorised by parliament; objective and transparent criteria must be met.[23] In the same way, the Administrative Supreme Court verifies the legality of the criteria used by the CEPS and does not hesitate to overrule any decision based on criteria that cannot be the sole legal ground for price decrease decisions.[24] In addition, on the basis of the Transparency Directive dated 21 December 1988,[25] the CEPS has been sanctioned for not having published the criteria followed for the refusal to reimburse a product.[26] As a consequence of this judgment, the Social Security Finance Bill for 2017 significantly amended the circumstances in which price decreases can be imposed.[27] But this was not sufficient to retroactively validate decisions refusing the reimbursement of a product adopted before that publication.[28] The Court also stressed that the CEPS should adhere to the set criteria for the determination of the price. For instance, the Court criticised the fact that it took into account only 50 per cent of the value of trademark rights, whereas its assessment was based on the total cost of the goods.[29] On the basis of the same Transparency Directive, the Court also cancelled an implicit refusal opposed by the Ministry for not having provided the reasoning behind the refusal.[30] It is interesting to note that one of the arguments is based on confirmation that the opinions of the Transparency Commission are not binding on the Ministry. As such, they cannot be directly challenged before the Court. On the other

22 Letter from HAS and CEPS of 24 September 2013, DEMESP/SEESP/CRP/IBD/AT DIR 2013_45.

23 Administrative Supreme Court, 18 April 2016, No. 397909, *Advanced Technical Fabrication*.

24 Administrative Supreme Court, 21 February 2018, No. 404964, *Crinex*; 28 November 2018, No. 413512, *Teofarma*.

25 Council Directive 89/105/EEC of 21 December 1988 relating to the transparency of measures regulating the prices of medicinal products for human use and their inclusion in the scope of national health insurance systems.

26 Administrative Supreme Court, 27 June 2016, No. 386332, *GSK*.

27 Social Security Bill for 2017, No. 2016-1827, 23 December 2016.

28 Administrative Supreme Court, 14 June 2017, No. 400608, *Roche*.

29 Administrative Supreme Court, 13 May 2016, No. 381148, *Teofarma*.

30 Administrative Supreme Court, 17 November 2017, No. 398573, *Abbvie*.

hand, the opinion is not deemed to provide sufficient grounds for an implicit refusal, in the sense of the Transparency Directive. This ruling should significantly reduce the number of implicit refusals, which, by their nature, do not detail their reasoning.

V FINANCIAL RELATIONSHIPS WITH PRESCRIBERS AND PAYERS

The French transparency regime was established by the Bertrand Law, and amended by a decree and a governmental circular published on 21 and 29 May 2013 respectively.[31] The reforms became effective on 1 June 2013, and have been applicable to the relationships between HCPs and the health industry since 1 June 2012.

That transparency legislation aims to make public any kind of advantages, whether in cash or in kind, amounting to €10 or more for each advantage granted by any company that manufactures or markets pharmaceutical products or medical devices (regardless of their status in relation to reimbursement by social security), and any company delivering services in connection with such products, including marketing, public relations and events agencies, directly or indirectly to HCPs registered in France and their professional associations, as well as students, patient associations, foundations, healthcare centres, prescription software editors, the media and professional training institutions. In addition, pharmaceutical and medical device companies (as defined below) must also disclose the existence of any agreement entered into with HCPs. The Health Bill, as amended by Ordinance No. 2017-49 of 19 January 2017, broadened the disclosure obligations to the detailed object of the agreement, its date, the identification of the direct and final beneficiaries and the remuneration paid to HCPs above a threshold of €10.

Publication occurs biannually: on 1 October for the first half of the year, and on 1 April of the following year for the second half of the year. All data will remain available for five years, or longer if an agreement is entered into for more than five years.

The Ordinance of 19 January 2017, which entered into force on 1 July 2018, has also significantly reshaped the French anti-kickback rules. The scope is broadened regardless of the status of the products with regard to reimbursement. Any type of advantage proposed or procured is prohibited. However, it is now specified that royalties paid in connection to IP rights are not deemed an advantage. Fees paid for research or consultancy, grants, professional training and hospitality are subject to a written agreement and prior authorisation from the physicians' professional board. The maximum criminal fines have been increased to up to €150,000 for natural persons and €750,000 for legal persons. Although the implementing decree of the Ordinance is still subject to discussions, the draft decree provides that the amount beyond which agreements shall be authorised depends on the kind of benefit granted (e.g., compensation, donation).

VI SPECIAL LIABILITY OR COMPENSATION SYSTEMS

The Health Bill introduced into French law, for the first time, a class action for compensation for physical damage caused by health products. The action will be opened retroactively as well

31 Ministerial Decree No. 2013-414 of 21 May 2013 relating to Transparency of Advantages Granted by Companies Manufacturing or Marketing Health or Cosmetic Products for Human Use; Ministerial Notice for Guidance No. DGS/PP2/2013/224 of 29 May 2013 for the Application of Article 2 of Law No. 2011–2012 of 29 December 2011 relating to Increasing the Safety of Medicines and Health Products.

for damage caused by products that are no longer on the market. Actions may be brought by associations of healthcare system users and will be initiated by a single judgment on liability. Expert evidence may, however, be necessary at this early stage to establish the defect and causality in relation to damage caused and corporate responsibility. The judgment will list the damage eligible for indemnification, as well as publicity measures. Victims will have between six months and five years to opt into the action. The judgment may also, with the agreement of the parties, appoint a mediator for the determination of the indemnification level.

Importantly, the first phase of the class action procedure will suspend the time limit for individual actions.

The class action regime has been effective since the publication of Order No. 2016-1249 of 26 September 2016, but, contrary to the practice in the United States, it has not been widely used in France.

VII TRANSACTIONAL AND COMPETITION ISSUES

i Competition law

EU and French competition laws prohibit anticompetitive agreements and abuse of a dominant position. In this respect, at the national level, agreements between companies that have as their object or effect the prevention, restriction or distortion of competition within the French market are forbidden by French competition rules.[32] In the pharmaceutical sector, this may apply to price fixing, co-marketing or co-promotion agreements, which may also give rise to illegal exchanges of sensitive information insofar as they lead to a restriction of competition among the concerned companies. In addition, unilateral conduct by a dominant undertaking that acts in an abusive manner is also prohibited.[33] When there is a suspicion of such conduct – which may be brought through a claim by the victim of the conduct – the French Competition Authority (FCA) is empowered to conduct an investigation at the undertaking's premises (in practice, extensive investigative powers apply) or to send a request for information. Fines for this kind of anticompetitive behaviour can reach 10 per cent of the group's worldwide turnover.[34] The FCA may order interim measures in urgent and extreme cases.

In this context, the FCA issued two decisions in 2013, fining Sanofi and Merck (€40 million and €16 million respectively) for having abused their dominant position in relation to generics. On 18 October 2016, the Supreme Court validated the fine imposed on Sanofi in the *Plavix* case. More recently, the FCA fined Janssen Cilag up to €25 million on 20 December 2017 for having abused its dominant position on fentanyl transdermal patches by disparaging generics, discouraging HCPs from switching, and influencing health agencies in charge of granting generics marketing authorisations by 'illegally' or 'illegitimately' using regulatory paths.

The FCA made a specific case with respect to these pharmaceutical companies, because of the context in which they operated. Moreover, it considered that a communication about a pharmaceutical product that faces a competing generic product may constitute a quasi-automatic abuse to the extent that the communication is capable of having a negative impact on the generic product. This could happen, for example, if the originator did not

32 Article L. 420-1 of the French Commercial Code.

33 Article L. 420-2 of the French Commercial Code.

34 Article L. 464-2 of the French Commercial Code.

limit itself to pointing out the objective qualities of its own product and did not refrain from emphasising the differences between the originator product and the generic drug. Such communication is analysed both in detail and within the general context. As such, isolated elements, while in themselves not illegal, may be punished by the FCA as a global, coherent and structured communication strategy, the goal of which is considered to be preventing or limiting the entry of the generic medication onto the market.

Moreover, in a decision dated 20 November 2017, the FCA announced the opening of a wide investigation covering the pharmaceutical sector, with a focus on the pharmaceutical distribution chain and the medicines price-setting process.

This new inquiry, which follows the investigation conducted in 2013, focuses on conditions of over-the-counter medicine sales to pharmacies, but also the interplay between competition and pricing discussions with the CEPS (particularly regarding the contractual rebate mechanism), and competition in calls for tenders organised by healthcare institutions.

While the FCA was expected to issue its first recommendations regarding medicine distribution schemes and the field of medical biology in 2018, after analysis of the responses, supporting documents and interviews with various stakeholders, it recently launched a public consultation with relevant professionals (physicians, pharmacists, wholesalers, etc.) to complement its initial findings. These findings have highlighted the need to amend the current inadequate French regime in this area, and at the time of writing, the FCA's final recommendations were expected to be adopted at the beginning of 2019. The findings from the analysis of the price-setting process should be issued in summer 2019.

ii Transactional issues

Given the size of the potential combined turnover in question, mergers in the health area often give rise to an analysis from a competition law standpoint. A key element in this respect is the determination of the relevant market in respect of which the potential effects of the contemplated merger will be assessed. The case law is not fully settled in this field. Indeed, although the competition authorities consider the ATC/DDD[35] classification, at Level 3, as a starting point, the FCA may then combine various classes in light of the products' therapeutic indications or galenic form. In addition, the analysis may narrow to Level 4 or even Level 5, at the molecular level. Indeed, this was the approach taken by the FCA in a recent case, where it cleared a concentration by analysing the market shares of two companies from ATC/DDD Levels 3 to 5.[36]

VIII CURRENT DEVELOPMENTS

As an extension of the policy implemented in recent years by the French government to limit pharmaceutical companies' bargaining power regarding pricing, the Social Security Finance Bill for 2019 contains various provisions aimed at reducing Social Security expenses. For example, the price of health products used in combination may be set unilaterally by the CEPS, which will be able to impose rebates if an agreement between the manufacturers and the CEPS cannot be reached.

35 The World Health Organization's Anatomical Therapeutic Chemical Classification System with Defined Daily Doses (ATC/DDD).

36 Decision No. 13-DCC-106 of 6 August 2013 related to acquisition of sole control of Warner Chilcott Company by Actavis Inc.

Moreover, to promote the use of generics and biosimilars, which are cheaper than their originator products, this Bill regulates the use of 'non-substitutables' by physicians. A ministerial order is expected to be adopted to strictly define medical cases for which healthcare professionals are allowed to prescribe an originator product instead of a generic or a biosimilar.

Appendix 1

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Sophie Pelé is a national partner at Dechert LLP. She focuses her practice on life science regulatory matters and is experienced in competition, litigation and public law matters in a wide variety of regulated industries. Her 'strong regulatory expertise' was noted in *The Legal 500 EMEA* 2015. Ms Pelé has substantial experience in clinical trial agreements, manufacturing or promotion agreements, marketing authorisations, pricing and reimbursement with governmental authorities, distribution schemes, import–export and parallel trade, public procurement in hospitals, compliance and interaction with healthcare professionals, advertising, and substitution of generic and biosimilar products.

Ms Pelé regularly represents multinational companies before authorities in French administrative jurisdictions.

Prior to joining Dechert, Ms Pelé served as a senior associate in the competition and regulatory department of another international law firm. Her previous experience also includes working at another leading law firm in life sciences in Paris.

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