ARTICLE

GOVERNMENT REGULATORY NEWSFLASH

European Law Environmental Law Public Law and Public Procurement Law | 19/01/12 | Hélène Billery

News in the health sector: a new Act for the improvement of medicinal and health product safety

The aim of Act no. 2011-2012 of December 29, 2011 for the improvement of medicinal and health product safety (the "Act") is to restore trust in the system that seeks to ensure the safety of health products, and, in particular, medicinal products. This Act follows on from the events which have marked the headlines since 2009 and highlighted the problems and perfectible practices in the previous system. Besides implementing Directive 2010/84/EU of 15 December 2010 on pharmacovigilance and Directive 2011/62/EU of 8 June 2011 as regards the prevention of the entry into the legal supply chain of falsified medicinal products, the Act profoundly modifies the French Public Health Code (French acronym: "CSP") and the French Social Security Code (French acronym: "CSS"), in particular:

- Replacement of the Agence française de sécurité sanitaire des produits de santé (AFSSAPS – French Agency for Health Product Safety) by the Agence nationale de sécurité du médicament et des produits de santé (ANSM – National Agency for Medicinal and Health Product Safety);
- Strengthening of ethics rules and obligations;
- Modification of the system of marketing authorisations ("MA") for medicinal products;
- Reorganisation of the pharmacovigilance system.

The main key points of the reform having a considerable impact on health professionals are described below.

From AFSSAPS to ANSM

AFSSAPS disappears to be replaced by ANSM which has been vested with new powers. From a date due to be set by decree no later than August 1, 2012, ANSM will exercise all of AFSSAPS' rights and obligations. Until such decree is passed, the Act of December 29, 2011 vests AFSSAPS with the same powers and remit as ANSM.
The composition of ANSM's board of directors has been adjusted to overcome the dysfunctions in AFSSAPS. Previously, besides the chairman, half of the board's members were State representatives and the other half were qualified persons selected on the basis of their skills in the fields falling within the scope of the Agency's remit and staff representatives. From now on, greater importance is given to health professionals and users. The board of directors will therefore be composed of State representatives (three MPs and three senators), representatives of the mandatory basic health insurance schemes, representatives of health professionals authorised to prescribe and dispense certain products, representatives of approved associations, qualified persons, staff representatives and its chairman (Art. L.5322-1 CSP). The State representatives continue to hold half of the votes. With this new organisation, the board of directors is opened up to citizen control.

A broad remit

ANSM has been conceived as an expert agency with powers to evaluate health products. In this respect, its main missions relate to the assessment, re-assessment and monitoring of the benefits and risks of health products intended for human use and of products intended for cosmetic use (Art. L.5311-1 et seq. CSP). The Act heightens the assessments conducted by the Agency and improves its response capabilities in case of a danger for public health. ANSM has therefore been vested with powers to request clinical trials on medicinal products in the form of active comparator studies and placebo-controlled studies. Producers or operators of medicinal products are required to substantiate any opposition they may make to an active comparator study.
Moreover, registering a medicinal product on the list of refundable medicinal products is now contingent on conducting comparative studies, i.e., therapeutic strategy studies, when they exist (Art. L.162-17 CSS).
Also, the MA can now be suspended, withdrawn or modified on a variety of other grounds than were allowed previously, and without reference to "normal conditions of use": therefore, the MA may be withdrawn even if the side effect results from the patient's use of the medicinal product in a manner that does not follow the prescription (Art. L.5121-9 CSP).
ANSM is authorised, for the same reasons and in the interest of public health, to ban, for all or only some batches, the prescription and dispensing of a pharmaceutical specialty and withdraw it from the market (Art. L.5121-14-2 CSP).
Obligations are also placed on MA holders. Indeed, after the MA has been granted, the holder may be required to provide, at ANSM's request and in the timeframe specified by it (Art. L.5121-8-1 CSP):
- Post-authorisation safety or efficacy studies carried out under conditions that are as close as possible to actual treatment conditions, i.e., in comparison with the available originator treatments (if any) and not only in comparison with placebos;
- A specific monitoring of risks, complications and medical-social care and support, through a register of affected patients, when the medicinal product is likely to have a serious adverse effect despite having been withdrawn.

For the purpose of on-going assessment, the Agency may request the MA holder to provide data demonstrating a

continually positive risks-to-benefits ratio.
Industrials may therefore be required to carry out additional studies after the grant of the MA. These will need to be integrated into their development plans.

Ethics & preventing conflicts of interest

Before the Act was passed, provisions on ethics were dispersed throughout the CSP depending on the health authorities concerned. This dispersion prevented any coherent overall approach. Henceforth, section V of book IV in the first part of the CSP deals with the common rules of ethics.
In addition, to resolve conflicts of interest, the rules on the public statement of interests have been heightened and unified. The managers, officials and experts of health authorities identified in the CSP will be required to make a public statement of interests (French acronym: "DPI") upon taking office, and subsequently update it, reporting their ties with the pharmaceuticals industry during the past five years (Art. L.1451-1 et seq. CSP). This reform is particularly significant as it provides a broad interpretation of conflicts of interest.
Such conflicts of interest consist in "all types of direct or indirect ties that the declarant has or has had during the five years prior to his/her taking office, with undertakings, institutions or bodies whose activities, techniques and products fall within the remit of the health authority where he/she performs his/her duties or the advisory body of which he/she is a member, and with the consultancy firms or bodies operating in the same sectors" (Art. L.1451-1 CSP).
Although the Senate had proposed an outright ban on all ties, the National Assembly did not follow the Senate's proposal and preferred to opt for a reporting system. The legal DPI system is nevertheless severe as decisions taken with the participation of a person having declared or undeclared ties are considered illegal. The persons concerned cannot take part in the works, deliberations or votes of such bodies if they have a direct or indirect interest in the matter under review, subject to criminal penalties (Art. 432-12 of the French Criminal Code on the illegal acquisition of interests). A penalty has been added to this legal regime, as knowingly omitting to issue or modify a DPI in order to update the information therein or making a misrepresentation is now punishable by a EUR 30,000 fine (Art. L.1454-2 CSP).
Companies will need to bear such DPIs in mind when they call upon the services of experts.
Furthermore, agreements entered into between pharmaceutical companies and professionals in the health sector (experts, learned societies, patients associations, specialist press bodies, etc.) also require publication (Art. L.1453-1 et seq. CSP). This obligation is placed upon the company and not the health professional. Therefore, companies will need to set up internal systems adapted to the company's size in order to ensure the publication of such agreements, especially as the companies concerned are liable to a EUR 45,000 fine should they knowingly omit to publish the existence of such agreements and the advantages they procure (Art. L.1454-3 CSP).

Strengthening of pharmacovigilance

The aim of pharmacovigilance is to monitor, assess, prevent and manage the risk of adverse effects related to the use of medicinal products for humans (Art. L.5121-22 CSP).
Responsibility for pharmacovigilance lies with the Agency (Art. L.5121-23) and with any company or body exploiting a medicinal or health product (Art. L.5121-24).
The need to improve the circuit for collecting information was highlighted by several working groups. For example, the collection of information, kept by ANSM, will cover all listed adverse effects and not only serious and unexpected side effects.
The Act also requires companies or bodies exploiting a health product to immediately inform the Agency of any ban or restriction imposed by the authority in a Member State where the drug is marketed, and of any new information that might influence the assessment of the benefits and risks of the product concerned (Art. L.5121-9-2 CSP). A marketing authorisation holder which stops marketing a drug in another State than France is also required to immediately inform the Agency indicating the reasons for discontinuing the marketing (Art. L.5121-9-4 CSP).
Moreover, in liaison with the Haute Autorité de Santé, the Union nationale des caisses d'assurance maladie and under the supervision of the Health Ministry, ANSM shall set up a public database storing administrative and scientific data on diseases, their treatments and good use of health products. Based on its data, ANSM will define the alert thresholds necessary for triggering an investigation (Art. L.161-40-1 CSS). The data may be consulted and downloaded free of charge on the Health Ministry's website.
ANSM will therefore be in charge of implementing the pharmacovigilance system in order to conduct scientific assessments of information, examine the options to prevent risks or reduce them and take necessary measures (Art. L.5121-23 CSP). It also encourages research, conducts patient management studies and provides the scientific and technical support necessary to draw up and implement public health plans (Art. L.5311-2 CSP).

Information and advertising of medicinal products for human use

Up until now, there was only a limited, Community-based, regulation of advertising for medical devices. The Act sets forth a comprehensive set of rules on advertising.
Regarding vaccines, Article L.5122-6 simply specified before the reform that "public advertising campaigns for vaccines are not permitted unless they contain the mandatory minimum information, which should be clearly identifiable."
The Act limits which vaccines may be advertised, in accordance with vaccination policy, the aim of this being to give the

public clear and consistent information.
Regarding the “advertising of medicinal products to the members of the health professions”, Article L.5122-9 required ex post checks where the advertisement had to be registered with AFSSAPS within 8 days of its dissemination.
From now on, advertising will be regulated more strictly. In this respect, the advertising of medicinal products to members of the health professions authorised to prescribe, dispense or use them during the performance of their profession is subject to ANSM’s prior authorisation, known as an “advertising clearance” (Art. L.5122-9). The clearance is granted for a period that cannot exceed the validity period of the MA for the medicinal product. The advertising of certain medical devices presenting a major health risk is also subject to prior authorisation granted by the Agency for a renewable period of 5 years (Art. L.5213-4 CSP).
By undergoing such prior checks, industrials will have to wait until ANSM’s decision before disseminating their advertisement.
Violations of the advertising regulations are subject to the penalties set forth in Articles L.5421-8 and L.5421-9 CSP (see below).

Transparency rules

The December 2011 reform is also intended to clarify ANSM’s role and make it more transparent. In this respect, it is provided that ANSM will publish the agenda and minutes (along with details and explanations of the votes) of commission and committee meetings and meetings of collegial bodies of experts whose opinions form a basis for an administrative decision (Art. L.5324-1). In doing so, the new Act goes further than the practice which AFSSAPS had already set up (publication of the verbatim report of MA committees, etc.).
Non-compliance with these publication obligations is liable to constitute grounds for the revocation of ANSM’s decisions resulting therefrom.
Also, each year, a report will be published containing an annual review of the re-assessment of the risk-to-benefit ratio of the drugs for human use mentioned in Article L.5121-8 CSP.

Administrative penalties

As part of the Agency’s health policing powers, the Act strengthens the possibility of ordering administrative penalties and institutes financial penalties (Art. L.5312-4-1; Art. L.5421-8 et seq. CSP). The Agency may order administrative fines along with daily penalties against individuals or legal entities producing or marketing the products mentioned in Article L.5311-1 CSP or providing services related to such products. The fines levied by the Agency cannot exceed the amounts set in Article L.5421-9 CSP (administrative fine of no more than 10% of turnover, up to a maximum of one million euros, against the perpetrator of a violation + a daily penalty of no more than €2,500 per day).
The Articles on the penalties and fines levied by ANSM will enter into force on July 21, 2012.
The National Assembly did not follow the Senate’s proposal of including the possibility for victims of harmful drugs to initiate class actions.

To conclude, the Act of December 29, 2011 renovates the health safety system for health and medicinal products. Its practical implementation will require industrials to adapt to the reform. Although it has only just been passed, voices have already been heard, particularly in the Parliament, emphasising the shortcomings of the reform. It will be important to remain vigilant in this area, as further changes may soon see the light of day.

Christian Pierret- Partner

Dominique de Combles de Nayves- Partner

Hélène Billery- Senior Associate