
THE LIFE SCIENCES LAW REVIEW

FOURTH EDITION

EDITOR
RICHARD KINGHAM

LAW BUSINESS RESEARCH

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EDITOR'S PREFACE

The fourth edition of *The Life Sciences Law Review* provides an overview of legal issues of interest to pharmaceutical, biotechnology and medical device companies in more than 30 jurisdictions. As before, each chapter contains information on legal requirements relating to the key stages in the life cycle of a regulated product, from discovery, through the clinical development process, registration, manufacturing and promotion, plus other issues of special interest, such as pricing and reimbursement, special liability regimes, competition and commercial transactions in the context of the medical products business. Each of the chapters has been prepared by a recognised expert in the relevant jurisdiction, and the resulting work product will assist industry lawyers, regulatory affairs staff and others who need to have an understanding of the issues in each major market.

There is also a chapter on international harmonisation, which plays an increasingly important role in the regulation of pharmaceuticals and medical devices. In particular, the guidelines adopted by the International Conference on Harmonisation have been incorporated into the national requirements for pharmaceuticals in the European Union, United States, Japan and most other developed countries, and are increasingly influential in developing countries. Readers may find it useful to review this chapter before consulting the national chapters, because it is often key to understanding many local requirements.

Once again, I wish to thank all of the lawyers who contributed to this reference work. It is a pleasure to be associated with them.

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Washington, DC
March 2016

Chapter 18

ITALY

*Giovanni Galimberti, Massimiliano Mostardini,
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I INTRODUCTION

i Competent authorities

The Italian Ministry of Health (MoH) is responsible for all aspects of public health in Italy, including medicinal products and medical devices as well as other products such as food, food supplements and cosmetics.

The Italian Medicines Agency (AIFA) is responsible, *inter alia*, for the authorisation of medicinal products; guaranteeing access to medicinal products and their appropriate and safe use; ensuring uniformity at national level; controlling national pharmaceutical expenditure; ensuring innovation, efficiency and simplification of administrative procedures concerning the marketing authorisation of medicinal products; and strengthening relationships with the agencies of the other EU Member States.

ii Regulatory framework

The legislative framework applicable to medicinal products in Italy is essentially the following:

- a* Regulation (EC) No. 726/2004 concerning medical products authorised centrally by the European Commission following a positive opinion from the European Medicines Agency; and
- b* Italian Legislative Decree 219 of 24 April 2006 and subsequent amendments and integration, which implements in Italy Directive 2001/83/EC, Directive 2003/94/EC and Directive 2001/62/EU amending Directive 2001/83/EC.

¹ Giovanni Galimberti is managing partner, Massimiliano Mostardini is partner, Mauro Turrini is a senior associate and Evelina Marchesoni is an associate at Studio Legale Bird & Bird.

The current² legislative framework applicable to medical devices in Italy is essentially found in Italian Legislative Decree 46/1997, which implements in Italy Directive 93/42/ECC on class medical devices, Italian Legislative Decree 332/2000, which implements Directive 98/79/EEC on in vitro diagnostic medical devices and Italian Legislative Decree 507/1992, which implements Directive 90/385/EEC on active implantable medical devices.

II THE REGULATORY REGIME

i Classification

To classify a product from a regulatory perspective it is necessary to proceed as follows:

- a to look first at the specific characteristics of a particular product with regard to its intended use, and second at the definitions provided by the law, which usually apply to medicinal products, medical devices, food supplements and cosmetics, depending on the individual case;
- b to look at the guidelines on borderline products; and
- c to adopt a precautionary approach, as indicated by the law.³

All borderline issues are assessed on a case-by-case basis by the MoH (sometimes following the advice of the Superior Council of Health)⁴ in collaboration with AIFA.

For this purpose these authorities also refers to the guidance provided by the Manual on Borderline and Classification in the Community Regulatory Framework for Medical Devices, and other EU guidance documents (e.g., MEDDEV).

ii Non-clinical studies

Pre-clinical studies in vitro and in vivo (i.e., in animal models) to be used for the development, *inter alia*, of medicinal products can be performed only in centres that operate in compliance with the applicable good laboratory practice (GLP). Compliance with GLP is certified by the MoH following an inspection.

In addition to the foregoing, centres that perform studies in vivo should also obtain prior authorisation from the MoH, to be granted in accordance with Italian

2 On 26 September 2012, the European Commission adopted a Proposal for a Regulation of the European Parliament and of the Council on: (1) medical devices; and (2) in vitro diagnostic (IVD) medical devices. These regulations, once adopted, will replace the existing three medical devices directives and consequently all relevant national implementing legislation.

3 That is, ‘in case of doubt whether a product, considering all its characteristics, can fit within the definition of “medicinal product” and within the definition of another product regulated by community law, the provision of Legislative Decree 219/2006 will apply’, see Article 2 of Italian Legislative Decree 219/2006.

4 The general technical advisory body of the MoH that assists at national level.

Legislative Decree 26/2014, which implements in Italy Directive 2010/63/EU. For the purpose of the granting of this authorisation, applications must demonstrate, *inter alia*, compliance with the applicable requirements for the protection of animal welfare.

iii Clinical trials

Legislative framework

Key provisions relating to interventional clinical trials in Italy are contained in the following laws:

- a* Regulation (UE) No. 536/2014, which entered into force on 2014 and that will be effective no earlier than as 28 May 2016 as per Article 99(2) thereof;
- b* Italian Legislative Decree 211/2003, which implements Directive 2001/20/EC in Italy; and
- c* Italian Legislative Decree 200/2007, which implements Directive 2005/28/EC in Italy, laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products.

The key provisions relating to non-interventional clinical studies (or ‘observational studies’) in Italy are contained in AIFA’s decision of 20 March 2008, concerning the guidelines for the conduct of observational studies.

Procedure

A sponsor, which must be established in the EU or have appointed a legal representative for the EU,⁵ can start a clinical trial for a medicinal product in Italy only after having obtained a prior positive opinion from the competent ethics committee (normally issued within 60 days of receipt of a valid application) and provided that the competent authority has not raised any motivated objection within 60 days of receipt of the relevant application.

A sponsor must obtain prior written approval from the competent authority in the event that the following are included in a list adopted by the MoH: (1) medicinal products that do not have marketing authorisation; (2) other medicinal products with specific characteristics (medicinal products whose active substance is of biological origin or containing biological components or the manufacture of which requires such components); and (3) medicinal products for gene therapy, somatic cell therapy, including xenogeneic cell therapy, as well as all medicinal products containing genetically modified organisms.

AIFA is the competent authority for all clinical trials.

Insurance policy

Italian Legislative Decree 14 July 2009 sets ‘minimum requirements for insurance policies that safeguard participants to clinical trials of medicinal products’. This decree

5 See Article 20 of Italian Legislative Decree 211/2003.

regulates, *inter alia*, the scope of the insurance policy (i.e., the damages to be covered) and the duration. The insurance policy is one of the aspects that must be checked by the ethic committees for the purpose of issuing their opinion.

Informed consent

Informed consent (about the nature, importance, scope and risks connected to the study) is one of the pre-requisites for carrying out a clinical trial and it must be given by the study subject him or herself or, in the case of minors or people who cannot express their own consent, by their legal representative.

Safety reporting

The law imposes an obligation on investigators to immediately notify the sponsor of any serious adverse event (with the sole exception of those excluded from immediate notification pursuant to the relevant protocol), and also information relating to suspected serious and unattended adverse reactions leading to the death or threatening the life of the study subjects.

The sponsor must guarantee that all information concerning such serious unexpected adverse reactions is registered and notified to the competent authority and also the relevant ethics committee promptly and, in any case, within seven calendar days of knowledge from the sponsor, and that all relevant information is communicated within eight days of the initial notification.

Non-profit investigator-initiated studies

Non-profit investigator-initiated studies are regulated in Italy by Decree 17 December 2004.

iv Named-patient and compassionate use procedures

In principle, no medicinal product may be placed on the market in Italy unless a marketing authorisation has been issued by AIFA or by the European Commission. There are, however, some exceptions to this general principle, specifically:

- a* medicinal products prepared in a pharmacy ('magistral formula' and 'official formula') pursuant to Article 3(a) and (b) of Legislative Decree 219/2006;
- b* advanced therapy medicinal products prepared in hospitals pursuant to Article 3(f) of Legislative Decree 219/2006;
- c* medicinal products industrially manufactured pursuant to Article 5 of Legislative Decree 219/2006;
- d* medicinal products not authorised in Italy but in another EU Member State and imported into Italy pursuant to Decree of the MoH of 11 February 1997;
- e* medicinal products or therapeutic indications not authorised in Italy and reimbursed by the national health-care system (NHS) pursuant to Law No. 648/1996; and
- f* medicinal products for compassionate use pursuant to Decree of the MoH of 8 May 2003.

In all the circumstances above, the costs of medicinal products can be paid to their manufacturers (by the NHS or by the patient as applicable) with the sole exception of medicinal products provided under Decree of the MoH of 8 May 2003 on compassionate use of medicinal product, which must be provided for free by its manufacturer. Compassionate use of medicinal products should also comply with a specific protocol.

Medical devices compassionate use

Public and private health-care structures can request authorisation for the use of a medical device for which the conformity assessment procedure has not been performed or completed on a single patient in exceptional case of need and urgency, provided the responsible clinician motivates such request and that an alternative product, already marked CE, is not available on the market. In the event of compassionate use of a medical device, a responsible clinician is required to provide an adequate follow-up.

v Pre-market clearance

Procedure

The marketing authorisation procedure varies according to the registration route chosen by the applicant. Depending on the case, applicants may opt for a purely national procedure,⁶ a mutual recognition procedure or a decentralised procedure. Medicinal products authorised centrally can, of course, also be placed on the market in Italy.

Formally, an 'accelerated procedure' for the granting of a marketing authorisation does not exist; in practice, however, in the event that specific circumstances recur, AIFA may be approached to discuss a possible fast track.

Applications for marketing authorisation, which essentially differ according to the type and amount of information to be provided in the relevant registration dossier (i.e., pre-clinical and clinical data), include:

- a* a full dossier application;
- b* an informed consent application;
- c* an abridged application (generic, biosimilar and hybrid);
- d* a well-established use application;
- e* a fixed combination application; and
- f* a homeopathic application.

Some additional obligations may apply to applicants for marketing authorisations for biological medicinal products in relation to the peculiar nature of this type of product.

Specific rules also apply for the granting of a marketing authorisation for homeopathic and herbal medicines. The law essentially provides for a simplified procedure in the event that certain conditions are met.

6 The national procedure should last, in principle, for 210 days and the cost starts from about €61,000 for a basic full dossier and from about €23,000 for a basic generic application.

Medical devices

Medical devices are placed on the market or put into service only if they comply with certain essential requirements (on their design and construction) that are intended to ensure the safety of said products.

Medical devices are divided into three categories: (1) class medical devices; (2) diagnostic *in vitro*; and (3) active implantable medical devices. Class medical devices are then divided into four classes, ranging from low risk to high risk (Class I, IIa, IIb, and III).

Once compliance with the essential requirements has been verified (via a self-assessment or a notified body assessment as applicable) the CE mark, which is mandatory by law, can be placed. The CE mark provides market surveillance authorities with confirmation that the relevant medical device is marketable and fulfils the applicable provisions.

The only exceptions to the rule of CE marking are custom-made devices and devices intended for clinical investigation.

Custom-made devices are any devices specifically made in accordance with a duly qualified medical practitioner's written prescription that gives, under his or her responsibility, specific design characteristics and is intended for the sole use of a particular patient.

A medical device intended for clinical investigation means any device intended for use by a duly qualified medical practitioner when conducting clinical investigations.

In addition to the foregoing, for a medical device to be placed on the market in Italy, unless limited exceptions apply it must be registered on the Italian database of medical devices held by the MoH.

vi Regulatory incentives

Patent term extension for medicinal products is regulated by Regulation (EC) No. 469/2009. The duration of a Summary of Product Characteristics (SPC) may be prolonged for six months by a paediatric extension in compliance with Regulation (EC) No. 1901/2006. SPCs and paediatric extensions are requested from and granted by the Italian Patent and Trademark Office. Third parties may challenge patent term extensions by filing proceedings on the merits for the (at least partial) revocation of the SPC.

According to Italian law (see Article 11 of Law No. 189/2012) a generic or biosimilar medicinal product whose reference medicinal product is still under patent protection (i.e., patent or SPC) cannot be reimbursed by the Italian NHS. It is not entirely clear from the law to which type of patent or SPC the rule will apply (e.g., patents or SPCs covering a product or a process), but based on recent case law the provision should be interpreted as applying only to patents or SPCs covering the products (see Sentence of the Italian Conseil d'Etat No. 4394/2014).

Rules on data and market exclusivity for full dossier medicinal products apply in Italy in accordance with Community legislation. Thus, no additional incentive has been introduced in this country.

Provisions have been adopted to facilitate access for patients to medicinal products indicated for rare diseases (e.g., reimbursement and exemption from regional

taxes, fast-track for reimbursement, exemption from clawback system) and innovative medicines (e.g. a specific fund for expenses borne by the NHS for the purpose of the purchasing of these medicines).

vii Post-approval controls

Requirements for infrastructure and staffing

A marketing authorisation holder must establish, within its undertaking, a scientific service in charge of information about the medicinal products that it places on the market independently from the marketing department and also have permanently and continuously at its disposal an appropriately qualified person responsible for pharmacovigilance (see below).

Pharmacovigilance

Pharmacovigilance is currently regulated in Italy by the provisions contained in Legislative Decree 42/2014 and the Decree of the Italian MoH of 30 April 2015, which implements Directive 2012/26/EU in Italy.

The rule on pharmacovigilance under Italian law is substantially similar to the one provided by Community legislation.

Post-approval obligations

A marketing authorisation can be granted under ‘exceptional circumstances’, provided the applicant complies with certain obligations.⁷ Validity of such an authorisation shall be reviewed on an annual basis.

Device vigilance

The MoH is responsible for monitoring and assessing possible incidents concerning medical devices. In particular, health-care professionals are responsible for notifying to the manufacturer or its legal representative, as applicable, all incidents concerning a medical device, while the manufacturer or its legal representative must notify them to the MoH.

Validity, revocation, suspension, variation

A marketing authorisation for a medicinal product lasts, in principle⁸, five years from the date of publication of the relevant AIFA decision in the Italian Official Journal, following which it can be renewed and considered valid for an unlimited period of time or subject to a further five-year renewal.

7 Relating to, for example, the safety of the product, the notification to AIFA of any adverse event connected with the use of the product and the adoption of specific measures.

8 An authorisation may be also granted subject to the compliance of specific conditions. In this case, the validity of the marketing authorisation must be reassessed on an annual basis (see Article 33 of Italian Legislative Decree 219/2006).

A marketing authorisation may be revoked or suspended by AIFA in circumstances affecting the quality, safety or efficacy of the product (see Article 141 of Italian Legislative Decree 219/2006).

A marketing authorisation may also cease to be valid in cases where the medicinal product concerned is not placed on the market within three years of issuance of the authorisation, or in cases where the medicinal product initially placed on the market is subsequently no longer marketed for three consecutive years (a 'sunset clause').

A marketing authorisation may be varied by AIFA pursuant to Regulation (EC) No. 1234/2008. The procedure may vary, essentially based on the impact of any modifications to the safety or efficacy of the medicinal product.

For a type IA variation a 'do and tell' procedure applies; for a type IB variation and a type II variation, a 'tell and do' procedure applies.

Transfer of marketing authorisations

A marketing authorisation can be transferred following a 90-day procedure.

Such an application must include a written undertaking from the authorised manufacturer and a qualified person in favour of the transferee to continue manufacturing.

viii Manufacturing controls

No company can manufacture a medicinal product in Italy (and per thereof) until it has obtained prior authorisation from AIFA. A relevant application must specify: (1) the medicinal product and the pharmaceutical forms that are intended to be manufactured; (2) the place, equipment and instrumentation to be used; and (3) the qualified person responsible for manufacturing.

The relevant procedure should, in principle, last no more than 90 days, but in practice it normally takes over six months. Variations to an existing manufacturing authorisation can be implemented only following the prior authorisation of AIFA unless they are considered non-essential variations pursuant to the relevant guideline adopted by AIFA.

Transfer of ownership of a manufacturing authorisation is possible and the relevant procedure should last no more than 30 days.

ix Advertising and promotion

Advertising to health-care professionals is limited to those health-care professionals who may prescribe or sell medicinal products. Advertising to health-care professionals during visits of sales representatives must, in principle, always include presentation of the most recently authorised SPC, supply classification and public price.

In principle, advertising of medicinal products to health-care professionals needs the prior authorisation of AIFA (a 10-day tacit consent procedure).

Advertising to the general public is limited to medicinal products that do not require the help of a medical doctor for a diagnosis, or for the prescription and monitoring of their use. Medicinal products under prescription, medicinal products containing narcotics and psychotropics, medicinal products reimbursed by the Italian NHS, pharmacy (galenic) and industrial formulation and investigational medicinal products cannot be advertised to the general public.

In principle, advertising of medicinal products to the general public needs the prior authorisation of the MoH (i.e., a 45-day tacit consent procedure).

Advertising of medical devices in Italy is regulated by Italian Legislative Decree 46/1997. Advertising to the general public of medical devices to be supplied on prescription only or to be used only with the assistance of health-care professionals is prohibited. In principle, the advertising of medical devices to the general public needs the prior authorisation of the MoH (i.e., a 45-day tacit consent procedure).

The advertisement of medical devices to health-care professionals is not expressly regulated by law, but such advertising to health-care professionals must also comply with relevant product information and is to be disseminated via adequate and selected channels (e.g., specialist magazines).

Provisions concerning the advertisement of medicinal products and medical devices to health-care professionals are also contained in industry association codes of conduct and in the guidelines of the State–Regions Conference⁹ on the advertising of medicinal products to health-care professionals (which some Italian regions have also voluntarily made applicable to medical devices).

x Distributors and wholesalers

In principle, wholesale distribution of medicinal products requires a prior authorisation from the region in which the relevant warehouse is located, which is granted following a positive inspection performed by the local health-care authority (ASL).

xi Classification of products

A medicinal product can be classified by AIFA as under prescription (subcategories apply) or under no prescription pursuant to Article 87 of Legislative Decree 219/2006.

According to the type of classification, different rules apply with regard to the advertising of such medicinal products, to the reimbursement and to the distribution channel (pharmacy only or para-pharmacy).

Medicinal products under prescription, medicinal products containing narcotics and psychotropics, medicinal products reimbursed by the NHS, galenic formulation and investigational medicinal products cannot be advertised to the general public and can be sold only by pharmacies.

Medicinal products not under prescription such as OTC medicinal products can be advertised to the general public and can also be purchased in para-pharmacies.

xii Imports and exports

Import of medicinal products requires a manufacturing authorisation to be issued by AIFA that may be limited to batch release activities.

⁹ The State–Regions Conference is where representatives of the central government and regions meet to discuss and agree on, *inter alia*, public health matters that must be dealt with at national and regional level to ensure coordination and cooperation.

Export of medicinal products may require a prior manufacturing authorisation (where the exporter is also the manufacturer of the product) or a prior wholesale distribution authorisation.

Recently, a modification in the law empowered AIFA to restrict the export of certain medicinal products, to be identified from time to time by AIFA, in the event of their shortage.

AIFA can issue, upon request, a certificate stating that a certain medicinal product has been manufactured in Italy in compliance with the applicable GMP.

Import and export of medical devices

Import of medical devices requires the prior issuing of an entry clearance notice to be issued by the border authority provided the medical devices is marked CE, the labelling in compliance with the requirements of the law, the medical devices has been registered within the database held by the MoH, where applicable, or the importer has formally undertaken not to place into service the medical devices until such registration has taken place.

The MoH can issue, on request of a manufacturer or its representative in the EU established in Italy, a certificate of free sale for export outside the EU.

xiii Controlled substances

The import, export and commercial sale of controlled substances, such as narcotics and psychotropics, and constituents thereof, such as precursors, are regulated in Italy by Decree of the President of the Republic (DPR) 309/1990.

The administrative requirements for use (e.g., import, export, storage, manufacturing, transformation or distribution) of said controlled substances may vary. In particular, use of controlled substances is, in principle, allowed only once the relevant authorisation has been granted by the MoH, while use of precursors of said controlled substances may be subject – depending on the actual precursor (which DPR 309/1990 divides into four different categories) – to a straightforward notification or to an express authorisation (in some cases to be renewed every three years).

xiv Enforcement

Medicines

Competent authorities can perform inspection at any time, expected or unexpected. Inspections may concern compliance with GLP (MoH) GMP, GCP or pharmacovigilance (AIFA). Inspection can also be carried out by the anti-adulteration unit (NAS), a specialist part of the Italian military with specific competences in the sanitary sector. Following an inspection, in the event of non-compliance, AIFA can impose sanctions that may vary in accordance with the type and degree of the violation. Violation may, of course, depending on the case, also be sanctioned under Italian criminal law, as is the case, for example, in case of performance of an activity without the requisite administrative authorisation.

Medical devices

The MoH can also carry out inspections at any time, expected or unexpected, in relation to medical devices. Inspections can also be performed by local health authorities, the Maritime, Aviation and Border Health Office (comprising sanitary offices placed at the borders – airports and harbours) or by the NAS.

Industry associations (e.g., Farmindustria for medicines and Assobiomedica for medical devices) can impose sanctions on members that have been adjudged responsible for violating the relevant codes.

III PRICING AND REIMBURSEMENT

i Medicinal products

For price and reimbursement purposes, medicinal products in Italy are classified essentially into three classes:

- a* Class A – medicinal products for serious, chronic or acute diseases reimbursed by the NHS;
- b* Class C – medicinal products for minor diseases not reimbursed by the NHS; and
- c* Class H – medicinal products reimbursed by the NHS that can be supplied to and administered only by hospitals.

The prices of Class A and H medicinal products are negotiated with AIFA pursuant to CIPE Decision No. 3/2001. In principle, except for when exceptions apply, the relevant procedure should last no more than 180 days, but in practice, in most cases it takes longer. Prices so agreed cannot be freely modified by a company. The profit margins of each of the participants in the supply chain of medicinal products reimbursed by the NHS (manufacturers, wholesale distributors and pharmacies) are calculated as a percentage of said price, fixed by law.

AIFA performs a health technology assessment for the evaluation of the clinical effectiveness and budgetary impact of new and existing medicinal products.

The price of Class C medicinal products is freely determined by manufacturers and can be lowered at any time, but may only be increased during January of odd-numbered years.

ii Medical devices

Medical devices are not subject to a prior procedure to be reimbursed by the NHS. Costs for medical devices are, *de facto*, borne by the NHS in the event they are purchased by structures belonging to the Italian NHS via, for example, public tender procedures and used therein, or where they fall within the scope of the designated essential levels of care.¹⁰

10 *Livelli Essenziali di Assistenza (LEA)*.

IV ADMINISTRATIVE AND JUDICIAL REMEDIES

Final administrative acts that have a direct effect on identified or identifiable natural entities or legal entities may be challenged before the same administrative body that adopted the act in question or before the relevant administrative court, respectively within 30 and 60 days of its notification or otherwise knowledge of the act.

Specifically, an administrative act can be challenged by filing a claim before the competent administrative regional tribunal. An appeal to a first-instance decision can be filed before the *Consiglio di Stato* (the Italian supreme administrative court). An administrative act can alternatively be challenged by filing a claim before the President of Italy within 120 days of notification or of knowledge of the act.

The subject challenging an administrative act must have an actual and direct¹¹ interest in the administrative act being annulled or otherwise adequately modified. The legal grounds for challenging an administrative act are 'lack of competence', 'violation of law' or 'misuse of power'.

V FINANCIAL RELATIONSHIPS WITH PRESCRIBERS AND PAYORS

Financial relationships (such as paid consultancies) between companies that market medicines and medical devices and health-care professionals or persons who make decisions concerning utilisation or reimbursement for such products in principle are not allowed; whereas, provided certain conditions are met, financial relationships between companies that market medicines and medical devices and health-care professionals or persons who do not make decisions concerning utilisation or reimbursement for such products are allowed in principle.

Indeed, according to the code of conduct of public employees, a public employee cannot accept assignments from natural or legal entities that have or have had, during the past two years, an economic interest in the decision or activities of the office in which the public employee operates.

Moreover, Article 53–16-ter of Italian Legislative Decree 165/2001 provides that public employees that exercised, during the past three years of service decision-making or negotiation powers on behalf of the public administration, cannot work, during the three years following the termination of said public employment, for the subjects who have been addressed by said decision-making or negotiation powers.

Gifts are, in principle, allowed provided certain conditions are met.¹²

Financial relationships intended to obtain an unlawful advantage (such as increasing prescriptions or sales) may be sanctioned pursuant to the Italian Criminal

11 Subjects owning a collective interest (e.g., associations) can also in principle start an action before an administrative regional tribunal.

12 They are of negligible value and, in the case of health-care professionals, they are also consistent with the activity performed by the recipient.

Code (crimes of corruption or *comparaggio*, the latter being a sort of bribery applicable only to the sanitary sector) and also under Legislative Decree 231/2001, concerning administrative liability of legal entities for crimes committed by their employees.

VI SPECIAL LIABILITY OR COMPENSATION SYSTEMS

Under Italian law there is no special system intended to compensate persons injured by medicines or medical devices. Certain provisions have been adopted by the Italian government, however, to deal with specific circumstances that have occurred in the past such as damages resulting from transfusions with infected blood or from mandatory vaccinations, or from transplants with defective prostheses.

VII TRANSACTIONAL AND COMPETITION ISSUES

i Competition law

Currently, there is no case law involving pay-for-delay agreements in Italy.

In 2014 the Italian Competition Authority sanctioned two pharmaceutical companies with fines of over than €90 million each for collusion in excluding a cheaper drug and steering consumers towards a more expensive drug by drawing an artificial distinction between the two products.

Moreover, in 2014 the Conseil D'Etat confirmed a previous decision of the Competition Authority, which fined an originator company over than €10 million for the abuse of a dominant position in preventing and delaying the launch of generic product through the misuse of the patent system.

ii Transactional issues

Asset deals

Asset deals are normally concluded by companies deciding to focus their research and development efforts in a specific area.

Where asset deals concern the sale of a business division or branch, Articles 2,555 to 2,562 of the Italian Civil Code, concerning the definition of business and its transfer, will apply. The transfer of business requires the entering into of a notary deed, which sets out the assets and liabilities to be transferred. The deed must be filed with the companies' registry.

An asset deal must clearly define its scope (i.e., the type of assets falling within the scope of the agreement and the actual rights granted on these assets).

Often, together with an asset deal, a distribution agreement is also concluded to allow the purchaser to start selling the product even if a regulatory procedure (e.g., transfer of the relevant marketing authorisation) is still pending.

Joint ventures

Joint ventures are fairly common in the life sciences sector, in particular for the purpose of conducting joint research and development programmes.

Joint ventures are neither regulated nor defined under Italian law, and are therefore considered under Italian law to be 'atypical contracts'. Consequently, the rules

applicable under Italian law to a joint venture must be identified on a case-by-case basis, according to the circumstances. In principle, the rules applicable to joint-stock or limited liability companies, or to consortia¹³ may apply in the case of a corporate joint ventures, whereas the rules applicable to contracts, and more precisely the general category of multiparty contracts in which parties pursue a common objective,¹⁴ may apply in the case of contractual joint ventures.

VIII CURRENT DEVELOPMENTS

i Supply chain

Currently, in Italy, participants in the supply chain for medicines retain a profit margin on the distributed products that is calculated as a percentage of the price to the public of the same.

This system, which has been highly criticised in the past (including by the Competition Authority), is due to be modified by 31 December 2016.¹⁵

The new remuneration system, which should encompass a fixed and a variable amount for each medicine supplied, is intended to contribute to the reduction of NHS pharmaceutical expenditure, *inter alia*, by incentives for the use of generics.

ii Measures for the containment of NHS expenditure

Clawback system

In 2007 a ‘territorial company budget’ was introduced in Italy;¹⁶ that is to say, the maximum amount that could be reimbursed by the NHS in relation to a company’s sales of medicines via pharmacies. In 2012, a ‘hospital company budget’ was also introduced in Italy.¹⁷ The two sets of rules, which are very similar, provide that in the event that the threshold of national pharmaceutical expenditure reimbursed by the NHS, which is set out each year by the law in relation to both the territorial and the hospital channel, is exceeded, the companies responsible for this over-expenditure (i.e., companies that have also exceeded their own budget) must pay back (to the region) any amount that is calculated by AIFA in proportion to their contribution to the over-expenditure (a ‘clawback system’). For the territorial channel, 100 per cent of the over-expenditure is paid back by manufacturers, wholesalers and pharmacies in a percentage established by the law. For the hospital channel, 50 per cent of the over-expenditure is paid back by manufacturers and the remaining 50 per cent by the regions that exceeded their own threshold.

13 See Article 2602 et seq. of the Italian Civil Code.

14 See Article 1420 of the Italian Civil Code.

15 Entry into force of the new remuneration system has, however, been already postponed several times.

16 See Law No. 222/2007.

17 See Law No. 135/2012.

Product cap

A 'product cap' is the maximum expenditure that can be reimbursed by the NHS in relation to a certain medicinal product, as agreed through the relevant procedure for price and reimbursement. In the event of over-expenditure, the relevant marketing authorisation holder is obliged to pay back the relevant amounts, as applicable.

Revision of the list of medicinal products reimbursed by the NHS

On 9 October 2015, AIFA published the revised list of medicinal products reimbursed by the NHS. The revision, which was based on cost-benefit criteria and on the therapeutic efficacy of the concerned products, was conducted by setting reference prices for certain homogenous therapeutic classes identified by AIFA.¹⁸

Off-label use of medicinal products

Off-label use of a non-authorised medicinal product or therapeutic indication can be authorised under Italian law and reimbursed by the NHS pursuant to Law No. 648/1996 (see Section II.vi, *supra*). In 2014, Law No. 648/1996 was amended by Legislative Decree 36/2014 and converted into Law No. 79/2014, so that where there exists a valid therapeutic alternative among authorised medicinal products, an unauthorised indication of an authorised medicinal product can also be prescribed on the NHS. For this purpose the Law requires that a positive prior assessment has been performed by AIFA, that the indication is known and compliant with studies conducted by the scientific community and that it complies with economic and appropriateness parameters. The change in the Law follows recent debate in Italy that arose in relation to a well-known case involving two pharmaceutical companies that were fined over €90 million each in 2014 by the Italian Competition Authority as a result of its findings of an anti-competitive agreement; this agreement aimed at excluding or limiting the off-label use of a cheaper product, which at the time was reimbursed by the NHS, to increase sales of a more expensive medicinal product duly authorised for the relevant therapeutic indication.

The above-mentioned recent amendments to Law No. 648/1996 have been strongly criticised by the industry, which recently started an action for infringement of Community legislation under Article 258 of the Treaty on the Functioning of the European Union.

18 See Agreement between State and Regions concerning the years 2014 to 2016 and Law No. 190/2014 –Stability Law 2015 – as well as AIFA Decision 1267/2015.

Appendix 1

ABOUT THE AUTHORS

GIOVANNI GALIMBERTI

Studio Legale Bird & Bird

Giovanni Galimberti is one of the founding partners and managing partner of the Italian office of Bird & Bird and co-head of the firm's Milan intellectual property department.

He is widely recognised across Europe for his expertise in all IP matters, including patents, trademarks, design, domain names and unfair competition, assisting clients across sectors, including pharmaceutical, mechanical, electronics, automotive and food. Mr Galimberti has handled and coordinated numerous pan-European cases for national and international clients and is known as one of the best IP litigators in Italy.

He is the author of various publications in the field of patent and trademark law for Italian and European legal magazines and he is one of the experts called upon by the Arbitration Chamber of Milan to decide proceedings concerning the reassignment of domain names.

MASSIMILIANO MOSTARDINI

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Massimiliano Mostardini is the founder of the firm's Italian practices and co-head of the firm's Milan intellectual property department.

He is also member of the international global board and international management committee.

Mr Mostardini regularly assists clients and public institutions in domestic and pan European litigations in Intellectual property (patents, trademarks, copyright, advertising, unfair competition) as well as in non-contentious IP/IT/TMT matters (licensing, R&D, MTA, clinical trials, software, maintenance, outsourcing, advertising pre clearance, management of trademarks portfolios, etc.) in the sectors of life sciences, media, IT, internet, telecommunications, food and luxury goods, including regulatory aspects and data protection.

Having graduated *cum laude* from the University of Milan, he has practised since 1990 and is lecturer at San Raffaele University. He is author of several publications concerning licensing, product liability, copyright, transfer of technology and inventors awards.

He is often invited to speak at national and international conferences in the life sciences, biotech, trade secrets, software, charities, start-ups, incubators, cloud computing and crowd-sourcing sectors.

MAURO TURRINI

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Mauro Turrini is a senior associate and member of the international intellectual property and life sciences groups, based in Milan and Rome.

He has over 10 years' experience advising clients on and life sciences (medicinal products, medical devices, food supplements) and intellectual property matters.

Before joining the firm in 2008, Mr Turrini spent a number of years working for pharmaceutical competent authorities, the Italian Medicines Agency (AIFA) and the European Medicines Agency (EMA). During his time at the EMA, he was responsible for all legal matters relating to intellectual property protection and innovation development. He provided legal support to the Paediatric Committee and the Name Review Group and also contributed to the Advanced Therapy Regulation implementation. While there, Mr Turrini was responsible for providing a full range of pharmaceuticals advice, including generics and data exclusivity issues, biosimilars, parallel import and parallel distribution issues, orphan drugs, SMEs and transparency issues. He was also a member of the EMA Innovation Task Force, a team within the European Agency specialised in pharmaceutical product classification and borderline issues.

EVELINA MARCHESONI

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Evelina Marchesoni is an associate in the firm's intellectual property group and is based in Milan. She joined the intellectual property group in 2005 and has been involved in a broad range of intellectual property work, particularly in relation to patents, trademarks, design, domain names and unfair competition, covering both contentious and non-contentious matters.

In particular, Ms Marchesoni has significant experience in pan-European patent and supplementary protection certificate litigation assisting pharmaceutical companies.

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