Italy

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A. DISTRIBUTION

1. PRECONDITIONS FOR DISTRIBUTION

1.1 What are the legal preconditions for a drug to be distributed within the jurisdiction? Does the drug need to be licensed (authorised) for distribution? Are there exceptions or different categories such as compassionate use?

Drugs can be distributed in Italy provided that they are:

- licensed by the Italian Medicine Agency (*Agenzia Italiana del Farmaco*, AIFA) (national procedure) as provided in Directive 2001/83/EC (implemented in Italy by Article 8 of the Legislative Decree No. 219/2006); or
- licensed pursuant to EC Regulation No. 726/2004 and 1394/2007 (mutual recognition procedure and decentralised procedure): all the procedural requirements listed in Article 28 of Directive 2001/83/EC (implemented in Italy by Articles 41–49 of the Legislative Decree No. 219/2006) apply; or
- licensed by the Italian Medicine Agency (*Agenzia Italiana del Farmaco*, AIFA) as parallel imported drugs pursuant to Ministerial Decree dated 29 August 1997 (see question 1.4).

1.2 Are any kinds of named patient and/or compassionate use programmes in place? If so, what are the requirements for pre-launch access? (For EU countries only: has Article 5 (1) of Directive 2001/83/EC been transposed by your national legislator?)

Therapeutic use of unlicensed drugs can be authorised only upon specific request from the doctor who has the patient in his own care and provided: (i) that the required drug is considered to be absolutely necessary for the treatment; and (ii) there is no equivalent licensed product in the Italian market.

A doctor must apply for authorisation for the unlicensed use by submitting an application to the Italian Ministry of Health providing: (i) details of the healthcare centre where he/she works; (ii) details of the custom office territorially competent for the importation; (iii) details of the foreign pharmaceutical company; (iv) details of the drug (name, active principle, dosage, etc.); (v) confirmation that the drug is duly authorised in the country of origin; (vi) confirmation that it cannot be replaced in the therapy by a drug licensed in Italy, and (vii) the volume needed.

The doctor also has to undertake that the drug shall only be given to a

limited number of patients under his/her own responsibility and that he/she gives his/her informed consent to the therapy on the condition that the therapy does not last longer than 90 days for each patient. Once the Ministry of Health has provided its authorisation, the drugs can then be imported.

Unlicensed drugs might also be used following the end of a clinical trial in order to continue to provide the trial drug (still unlicensed) to trial participants upon the specific request of the doctor provided that: (i) the trial drug has been or will be included in phase III clinical trials, or, in case of terminally ill patients, the drug has been induced in phase II clinical trials; and (ii) results of the required trials show efficacy and tolerability of the trial drugs.

Such use is permitted both for participants of the clinical trials and new patients.

1.3 What is the structure of the procedure regarding licensing a drug for distribution? Which national body (agency) is responsible for licensing?

The national body responsible for licensing new drugs or varying granted licenses is the Italian Medicine Agency (AIFA) (the Agency). The procedures followed are those set out in the EU section.

The technical and scientific assessment is completed with the assistance of the Technical Scientific Commission (CTS), with the co-operation of experts belonging to the National Institute of Health (ISS) and of other experts of well-known experience belonging to the Italian academic and health community.

1.4 Is there a simplified licence procedure or are there relaxed licensing for drugs which have already been licensed for distribution in another jurisdiction? What about parallel imports, is there a simplified procedure for these?

The mutual recognition or centralised procedures apply in the EU (see EU laws section). The procedures set forth under Article 28 of Directive 2001/83/EC (implemented in Italy by Articles 41–49 of the Legislative Decree No.219/2006) shall apply, depending on whether Italy acts as a reference member state or not.

The above procedures apply even in the case of parallel imports/exports. Within those activities concerning the parallel export of drugs licensed according to the mutual recognition procedure, the Agency provides the requesting regulatory authorities of the other Member states with information regarding some of the identification elements of the drugs licensed in Italy.

Indeed, in case of parallel import of drugs already licensed in Italy, the procedure set forth in the Ministerial Decree dated 29th August 1997 shall apply: the importer shall apply for authorisation by submitting an application to the Agency providing: (i) details of the importer and the relevant Member State; (ii) name of the drugs to be imported; (iii) qualitative and quantitative composition; (iv) therapeutic specifications, contraindications and side-effects; (v) dosage, medication, etc.; and (vi) summary of the product'

specifications and handout of the packaging both translated into Italian. The Agency shall provide its authorisation or not within 45 days from the date when the application was submitted.

1.5 Is it possible to distribute drugs 'virtually' from your jurisdiction (i.e., the physical products never enter the country but are distributed using the authorisation obtained in your country).

No, there is no provision permitting the above.

1.6 Is there a legal remedy (appeal) against licensing decisions?

Should the license application be refused, the Agency shall notify the applicant of this decision who is then entitled to submit an opposition to the Agency. This opposition shall be decided within 90 days.

Appeals against Agency decisions are to be made to the Regional Administrative Courts (*Tribunale Amministrativo Regionale*, TAR) within 60 days of the receipt of the decision..

1.7 What are the costs of obtaining a licence?

Cost of obtaining a license in Italy run from EUR 55.680 for new marketing authorisation supported by a full dossier to EUR 21,600 or EUR 36,000 for new marketing authorisation not supported by a full dossier.

2. DISTRIBUTION TO CONSUMERS

2.1 What are the different categories of drugs for distribution?

The different categories of drugs for distribution can be summarised as follows:

- prescription drugs;
- renewable delivery prescription drugs;
- special prescription drugs;
- restricted prescription drugs:
    - drugs distributable to consumers only upon prescription of healthcare structures;
    - drugs usable only within healthcare structures; and
    - drugs usable only by specialists;

non-prescription drugs:

- OTC drugs;
- all other drugs that do not require a medical prescription.

2.2 Who is entitled to distribute prescription drugs to consumers? What authorisation do they require?

Pharmacists are entitled to distribute prescription drugs to consumers. In order to act as pharmacist a specific qualification and the relevant enrolment with the public register shall be obtained. Individuals might then obtain a licence to a physical premises after a competitive state examinations and by virtue of acquisition or succession.

2.3 Who is entitled to distribute over-the-counter drugs to consumers?

OTC drugs can be distributed to consumers within pharmacies or supermarkets and other commercial shops. In these latter two cases, the presence of a pharmacist is always required during store hours.

2.4 Which drugs may be distributed by the attending physician, and under what circumstances?

Any attending physicians are not authorised to distribute drugs.

2.5 Who may prescribe prescription drugs to consumers?

Doctors are entitled to prescribe drugs to consumers. As are dentists graduated earlier than 1985 as they are doctors specialised in dentistry, whilst dentists graduated later, in the specific faculty of dentistry, are entitled only to prescribe drugs connected with their profession.

2.6 Is direct mailing/distance selling of drugs permitted? Under what conditions, by whom, and to whom? Might sales be made beyond the borders of your country?

There are no further provisions on this point, aside from what has been stated above relating to parallel import/export.

2.7 Which body (agency) is responsible for supervising distribution activities regarding consumers? How is supervision implemented? Is there a legal remedy (appeal) against decisions?

The Local Health Authorities (*Aziende Sanitarie Locali*, ASL) are responsible for supervising the distribution and prescription of drugs to consumers.

In case of non-compliance, the ASLs report to the Ministry of Health and to the Agency. Penalties up to EUR 3,000 can be imposed as well as the closing of the pharmacy/commercial shop for a period of up to 30 days.

Appeals against the decisions made by the authorities can be made before the Regional Administrative Courts (*Tribunale Amministrativo Regionale*, TAR) within 60 days of the date when the decision has been notified to the interested party or the latter has become aware of it.

2.8 What are the legal consequences in case of non-compliance?

Please refer to question 2.7.

3. WHOLESALE DISTRIBUTION

3.1 What is the legal regime regarding wholesale of drugs? Under what conditions, by whom, and to whom is wholesale of drugs permitted?

The wholesale distribution of drugs under Italian law is provided for in Articles 79 and 80 of Directive 2001/83/EC (implemented in Italy by Articles 101–104 of Legislative Decree No.219/2006). The wholesale distributor is required to keep a record of all drugs that are distributed.

The wholesale distributor is required to employ a Qualified Person

as provided for by Article 79(b) of the Directive 2001/83/EC who shall be a graduate of Pharmaceuticals, Chemistry, Industrial Chemistry or Pharmaceutical and Chemical Technologies. This person is required to have a clean criminal record and should not be linked to the unlawful trade of pharmaceutical products. Should a whole distributor own more than one wholesale outlet, he/she is not required to employ more than one responsible person provided that the appointed responsible person is able to fulfil his/her tasks within reasonable working hours.

The competent authorities responsible for granting the wholesale distribution authorisation are the regions or the autonomous provinces, where the wholesale activity will be carried out. In the case of wholesale distribution in more than one region, a wholesale distribution authorisation for each region is required. The wholesale distribution authorisation is required to be granted within 90 days of receipt of the application, although time to grant varies depending on the region. Each region is entitled to ask for certain documents and certifications with the application, however the following documents are required as standard:

- fitness for use of the buildings issued by the territorially competent municipality;
- enrolment on the Companies' Register;
- prevention of fire; and
- wiring system compliant with law (and other connected certifications such as atmospherics and grounding safety certifications).

The submission of internal procedures concerning points 2, 3, 4, 5, and 6 of the GDP are also required. It is important to bear in mind that authorisation requirements will differ from region to region.

3.2 Which body (agency) is responsible for supervising wholesale distribution activities? How is supervision implemented? Is there a legal remedy (appeal) against decisions?

In addition to the territorially competent region, both the Ministry of Health and the Agency are entitled to undertake inspections of the wholesale distributors' premises. In case of non-compliance, penalties up to EUR 18,000 can be imposed on the wholesale distributors. Appeals against decisions made by the authorities can be made before the Regional Administrative Courts (*Tribunale Amministrativo Regionale*, TAR) within 60 days of the date when the decision has been notified to the interested party or the date the latter has become aware of it.

3.3 What are the legal consequences for non-compliance?

Please refer to question 3.2.

B. MARKETING

4. PROMOTION (MARKETING)

4.1 What is the general legal regime regarding marketing of drugs (overview)? What are the general limits on marketing activities?

Briefly, drugs which have been duly licensed either pursuant to the national procedure or to the mutual recognition and the decentralised procedures can be marketed.

The promotional information must always be truthful to the exact nature of the drug and shall: (i) aim to encourage the rational use of the drug, presenting it in an objective way and without exaggerating its properties, and (ii) not be misleading.

The marketing authorisation holders must establish a scientific service within their company which will be responsible for coordinating the information about the drugs. This information shall in turn be managed by a responsible person who is a graduate of medicine, pharmaceuticals or chemistry.

Through the above service, the license holder shall comply with all of the following obligations: (i) ensuring that the promotion of drugs is compliant with the regulations, (ii) verifying that pharmaceutical sales representatives employed by the company have been adequately trained and act in compliance with the regulations, and (iii) providing assistance to the Authorities and complying with their rules. The above-mentioned obligations will be adhered to by all members of the promotional party.

When advertising to consumers and Healthcare Professionals (HCPs), there are special restrictions on the promotional activities possible. (See sections 5 and 6)

4.2 Besides the legal regime, are there other codes of conduct, e.g. from professional or industry organisations? How are they implemented? What is the relationship between the industry code (if any) and the legal regime?

In addition to the legal regime and apart from the codes of conduct implemented by each company, guidelines concerning, among others, the promotion of drugs are set forth in the *Farmindustria Ethic Code*. *Farmindustria* is the Italian pharmaceutical companies' trade association. The Code represents the commitment of the industry not only to abide by specific laws in force but also to operate on the basis of transparent standards of conduct that regulate the various circumstances in which corporate activities take place. The Code is a voluntary agreement entered into by the pharmaceutical companies belonging to *Farmindustria*, and is designed to regulate relations not only between companies but also between companies and the health industry.

All members of *Farmindustria* are required to accept and comply with the provisions of the Code. The Code is considered to be a reference guideline for companies that are not necessarily members of *Farmindustria*.

5. MARKETING TO CONSUMERS

5.1 What is the legal regime with respect to marketing to consumers (overview)? Which products might/might not be advertised to consumers?

Promotion of drugs to consumers is only permitted if the drugs are non-prescription or do not need the intervention of a doctor for diagnostic purposes.

The following kinds or drugs are not to be promoted to consumers at all: drugs which are available on medical prescription only;

- drugs which contain psychotropic or narcotic substances; and
- drugs which are totally or partially reimbursed by the National Health System.

A specific application for each single advert, even if the same advert is released through several different media, shall be submitted to the Ministry of Health for an authorisation to market drugs to consumers. Should the Ministry of Health not provide this authorisation within 45 days of the date of the application, it is deemed to have been granted. The authorisation lasts for 24 months.

The authorisation is not required when: (i) the promotional message is included in newspapers or periodical press and reproduces in full the information provided in the patient information leaflet, or (ii) it consists of a picture of the package put on price tags.

5.2 What kinds of marketing activities are permitted with regard to consumers and the products which might be advertised to them?

Italian regulations require that promotion to consumers:

- are clear that the message is a promotion and about a drug;
- include the following minimum information:
    - the name of the drug as well as the name of the active ingredient (the latter only if the drug contains only one active ingredient);
    - the information necessary for correct use of the drug;
    - an express and legible invitation to read carefully the instruction on the package leaflet or on the outer packaging. In case of promotional messages included in newspapers or periodical press, such an invitation must be in font size nine.

5.3 Is it permitted to provide consumers with free samples? Are there particular restrictions on special offers e.g., 'buy one get one free'?

No, it is not permitted to give consumers free samples or to give them promotional offers on drugs.

5.4 Are there particular rules/codes of practice on the use of the internet/social media in respect of drugs and their advertising?

No specific legal provisions are set forth on the use of the internet in respect of advertising drugs; the general principles concerning marketing to consumers apply, including the authorisation procedure for advertising. The only specific provision is provided for in the *Farmindustria Ethic Code*. this

requires that internet websites opened by an Italian company or a company operating in Italy which is addressed either to consumers or to HCPs shall always guarantee that the company on whose behalf the advertising is placed, the source of all information set forth in the site, the designated recipients of such information and the objectives of the site are all clearly identified and/or specified. In all cases access to sections providing promotional information on the company's products shall be exclusively reserved to HCPs in the case of products which are not permitted to be advertised to consumers or for which the authorisation to be advertised has not been granted yet. .

5.5 Which body (agency) is responsible for supervising marketing activities to consumers? How is supervision implemented? Is there a legal remedy (appeal) against decisions?

The Ministry of Health is the authority responsible for supervising marketing activities to consumers. In case of non-compliance, the Ministry of Health is entitled to order the immediate termination of the promotional activities as well as the circulation of a retraction press release. As a general rule, fines from EUR 2,600 to EUR15,600 can be imposed. Higher amounts are imposed in cases of infringement of the prohibition to show a drug in a non-advertising contest such to indirectly promote its use (fines from EUR10,000 to EUR60,000) for example if the drug is shown during movies or TV shows.

5.6 What are the legal consequences for non-compliance?

Please refer to question 5.5.

6. MARKETING TO PROFESSIONALS

6.1 What kinds of marketing activities are permitted with regard to professionals?

Marketing activities can only be directed to HCPs who are authorised to prescribe or supply the relevant drugs. Marketing material shall firstly be submitted to the Agency and, ten days after the submission, it can be delivered to the HCPs. No actual authorisation is required, there is a only a duty to submit it with the Agency. It cannot be used only if the Agency prohibits it..

Marketing statements must always be substantiated by documented and verifiable evidence. Exaggerated statements, universal and exaggerated claims and comparisons without any objective basis are inadmissible. Use of email, automated calling systems and other electronic communication aiming at divulging promotional material regularly approved by the Agency is prohibited, unless the company holds a prior written and informed consent from the HCPs to whom the material is addressed.

In general terms the following kinds of marketing activities (some of which will be better examined in the following questions) are permitted with regard to HCPs, provided that the relevant material meets the above mentioned requirements:

- verbal information;
- delivery of promotional material;

- free samples;
- scientific congresses and conventions;
- refresher courses;
- visits to companies' laboratories;
- investigators' meetings;
- scholarships and scientific consultancy.

6.2 Are there particular types of marketing activities which are not permitted with respect to professionals (e.g. provision of reprints, non-interventional studies, provision of and type of gifts/ educational items)?

Assuming that all the above-mentioned marketing activities are compliant and honour the *Farmindustria Ethic Code*, no gifts, pecuniary advantages or benefit in kind can be directly or indirectly supplied, offered or promised to HCPs, unless they are inexpensive and relevant to the practice of medicine or pharmacy.

6.3 Are there restrictions on how, when, where or how often professionals might be targeted by sales representatives?

There are no particular restrictions on this save that sales representatives must always provide the HCPs with a summary of the product's characteristics, information on the selling price as well as the conditions under which it can be reimbursed by the national health system. This is not necessary if the HCPs already have publications which include the most recent version of this information.

6.4 What are the restrictions on meetings with groups of professionals and the provision of hospitality?

Direct organisation of, and/or providing financial support to meetings, conventions, congresses, educational conferences and similar events which are held, in Italy or abroad, to discuss matters related to the use of drugs and that consist of an occasion for pharmaceutical companies to meet HCPs shall be notified to the Agency at least 60 days before the commencement date. The following information must be provided to the Agency: (i) details of the pharmaceutical company, (ii) location and date of the event, (iii) the matters to be discussed during the event, (iv) the possible attendees, (v) speakers' qualifications, and (vi) a detailed estimate of the costs. Any positive opinion from the Agency will be issued within 45 days.

Should the event be held abroad or involve costs higher than EUR 25,800, a specific authorisation shall be granted by the Agency for events in Italy or involving Italian HCPs before the commencement date as well as the payment of a rate equal to EUR 1,859.24.

During the events, no kind of display and/or distribution of samples for promotional purposes is permitted with the exception of leaflets and other information-bearing conference materials.

As far as hospitality is concerned, pharmaceutical companies may only offer economy-class air travel to Italian HCPs invited to conference events

in Italy or abroad, while the category of hotel accommodation must not exceed four stars. In addition, the same HCP cannot be invited by the same pharmaceutical company more than twice a year. This restriction does not apply to speakers or moderators.

No events may be directly or indirectly organised by a pharmaceutical company outside Italy if it is to be mainly attended by Italian HCPs.

The duration and the venue of the event are also subject to specific conditions. Events shall be held in places and venues chosen for logistical, scientific and organisational reasons, which excludes restaurant facilities. If the conference is to be held in a location popular with tourists, the following restrictions apply: no conferences are to be held at seaside resorts during 1 June–30 September and no conferences are to be held in mountain resorts during 1 December–1 March and 1 July–31 August.

The hospitality offered to the participants cannot exceed a 12-hour time period prior to and immediately after the event and such hospitality must be secondary to the technical and/or scientific content of the event. No hospitality of any kind or form can be offered to guests of the invited HCPs.

6.5 What information is legally required to be included in advertising?

The minimum particulars to be included in all advertising are (i) the information listed in the summary of the product characteristics, (ii) the supply category of the drug, and (iii) the selling price and the conditions under which it can be reimbursed by the national health system. The promotional material may also include the name of the drug, the name of the active ingredient, together with the name of the license holder and of the co-promoter, if any.

6.6 Are there rules on comparisons with other products that are particularly applicable to drugs?

There are no specific rules concerning comparative promotions applicable solely to drugs.

6.7 Are discounts permitted? If they are, under what conditions, by whom, and to whom?

No discounts from the selling prize are permitted. Promotion to HCPs shall be carried out by pharmaceutical sales representatives who belong to the scientific service of the company which shall be independent of the marketing service of the company.

6.8 Is it permitted to provide professionals with free samples?

Free samples of drugs can only be supplied to HCPs qualified to prescribe them and then only exclusively by pharmaceutical sales representatives (*informatori scientifici del farmaco*). HCPs are required to keep the samples according to the instructions put on the packaging or in the patient information leaflet.

The following strict criteria shall be adhered to:

- any supply of samples shall be in response to a written request, signed, stamped and dated by the HCP;
- in the first 18 months after the first marketing of the drugs, only two samples for each drug can be supplied to one HCP during each visit and in no case no more than eight samples per year;
- after the above time period, only four samples for each drug can be supplied to each HCP during each visit and in no case more than ten samples per year;
- each sample shall be equal to or less than the smallest packaging put on the market provided that this is expressly stated on the sample's label;
- each sample shall always be supplied together with the summary of the products' characteristics;
- each sample shall be marked with 'free sample – not for sale' (*campione gratuito – vietata la vendita*) or with other similar wording;
- no samples of drugs containing psychotropic or narcotic substances can be supplied.

Pharmaceutical companies must train their pharmaceutical sales representative in accordance with the above criteria as well as to keep records of the requests of free samples collected by the pharmaceutical sales representatives for an 18-month period.

6.9 Is sponsoring of professionals allowed? Under what conditions, by whom, and to whom and for what purpose(s)?

Pharmaceutical companies may work with HCPs as consultants for services such as speakers and moderators at conferences or invite them to participate in observational studies or training and education services. Based on the *Farmindustria Ethic Code*, the following criteria shall be fully complied with:

- A written agreement shall be signed between the HCP and the pharmaceutical company specifying the nature of the service. The need for the service shall be clearly identified and stated.
- The agreement shall also state that the HCP undertakes to disclose his or her relationship with the pharmaceutical company whenever he or she writes or speaks in public on the subject matter to which the cooperative relationship refers to. The same obligation also applies in the event that the pharmaceutical company employs practising HCPs on a part-time basis.
- The company is required to keep the documentation on the services provided by HCPs for at least three years.
- The fees paid by pharmaceutical companies for the provided services shall meet cost-performance criteria and reflect the market value of such services. The initiative shall guarantee coherence and appropriateness in respect of the pursued objectives and it shall be capable of being fully documented.
- Whenever journeys or any form of hospitality are provided for, the provisions set forth under question 6.4 shall apply.

6.10 Are other indirect incentives allowed? Under what conditions, by whom, and to whom?

No indirect incentives are permitted.

6.11 Which body (agency) is responsible for supervising marketing activities regarding professionals? How is supervision implemented? Is there a legal remedy (appeal) against decisions?

The Agency is the authority responsible for supervising marketing activities to HCPs. In case of non-compliance, the Agency is entitled to order the immediate termination of the promotional activities and the circulation of a retraction press release to be uploaded to the corporate website as well. Fines from EUR2,600 to EUR15,600 can be imposed. Higher amounts are set forth if free samples are marketed without the indication 'free sample – not for sale' (fines from EUR5,000 to EUR30,000).

6.12 What are the legal consequences for non-compliance?

Please refer to question 6.11.

7. ENGAGEMENT WITH PATIENT ORGANISATIONS

7.1 What kinds of activities are permitted with respect to engagement with patient organisations?

Based on the *Farmindustria Ethic Code*, any form of economic support, whether direct or indirect, by the pharmaceutical companies towards a patient organisation shall comply with the following criteria:

- a specific and preliminary agreement aimed at regulating the amount of and reasons for financing shall be reached. For this reason, each pharmaceutical company shall develop a standard internal procedure for the approval of this category of agreements;
- the public utilisation by a pharmaceutical company of the logo or material owned by a patient organisation shall be authorised in advance by the organisation. In order to get such authorisation, the objectives for, and the manner of, using the logo must be clearly defined;
- any form of sponsorship by the pharmaceutical companies towards the patient organisation shall be transparent and without promotional objectives;
- no company can request to be the sole financier of a patient organisation;
- in all the cases in which journeys or other forms of hospitality are provided for, the above-mentioned provisions, as also set forth in the *Farmindustria Ethic Code*, shall apply; and
- companies must publish on their internet sites a list of all patient organisations that are financially supported by the company in the previous year. This list must detail the monetary value of the support and must be publicly available for a period of three months coinciding with the first three months of each year.

Agreements between pharmaceutical companies and patient organisations under which they provide any type of services to companies are only allowed if such services aim at supporting healthcare activities or research. Patient

organisations may be engaged as experts and advisors for services such as participation at advisory board meetings and speaker services. A written agreement shall be executed in advance in order to specify the nature of these services as well as the basis for payment of those services. A legitimate need for the services shall be clearly identified and documented in advance of requesting them. The compensation for the services shall be reasonable and not exceed the fair market value of the services provided. Companies are also required to publish an annual list of the patient organisations that they have engaged to provide services.

7.2 What are the restrictions imposed on relationships with patient organisations?

Please refer to question 7.1.