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National Agency for Medicines and Medical Devices

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THE MINISTRY OF HEALTH

ORDER
on approval of the List of International Non-proprietary Names of medicinal products at high unavailability risk, as provided to insurants in the health insurance system and agreement on a measure to secure their market availability in Romania

(Published in the Official Gazette of Romania, Part I, no. 197 of 08/04/2013)

On seeing Approval Report no. EN 3.260 of 1 April 2013 of the Pharmaceutical Directorate of the Ministry of Health,

Taking into account provisions of:

- Art. 695 (17) and Art. 792 of Law 95/2006 on healthcare reform, as amended;
- Art. 7 (4) of Government Decision no. 144/2010 on the organisation and operation of the Ministry of Health, as amended,

the Minister of Health hereby issues the following Order:

Art. 1. - (1) The List of International Non-proprietary Names of medicinal products at high unavailability risk, as provided to insurants in the health insurance system and agreement on a measure to secure their market availability in Romania, is hereby approved.

(2) Distribution outside Romania of medicinal products included in the List specified in (1) is temporarily suspended as of the date of this Order coming into force to 31 December 2013.

Art. 2. – Non-compliance with provisions of this Order will be sanctioned in accordance with provisions of Law 95/2006 on healthcare reform, as amended.

Art. 3. – This Order is to be published in the Official Gazette of Romania, Part I.

Minister of health,
Gheorghe-Eugen Nicolăescu

Bucharest, 2 April 2013.
No. 456.

ANNEX

Crt. No.	International Non-proprietary Name
1.	ASPARAGINAZUM
2.	BLEOMYCINUM SULFAS
3.	BUSULFANUM
4.	CARMUSTINA
5.	CHLORAMBUCILUM
6.	CISPLATINUM
7.	CYCLOPHOSPHAMIDUM
8.	CYTARABINUM
9.	DACARBAZINUM
10.	DACTINOMICINUM
11.	DAUNORUBICINUM
12.	DEXAMETHASONUM
13.	ETOPOSIDE
14.	FLUOROURACILUM
15.	LOMUSTINUM
16.	MELPHALANUM
17.	MERCAPTOPURINUM
18.	METHOTREXATUM
19.	PROCARBAZINA
20.	TENIPOSIDE
21.	TIOGUANINA
22.	VINBLASTINUM

ORDER
on approval of mandatory monthly reporting of placement on the market in Romania and of sales of medicinal products for human use, respectively, by authorised wholesale distributors/importers/manufacturers

(Published in the Official Gazette of Romania, Part I, no. 210 of 13/04/2013)

On seeing Approval Report no. EN 3.787 of 11 April 2013 of the Pharmaceutical Directorate of the Ministry of Health,

Taking into account provisions of:

- Law 95/2006 on healthcare reform, Title XVII – The medicinal product, as amended;

- Government Decision no. 734/2010 on the organisation and operation of the National Agency for Medicines and Medical Devices, as amended,

based on Art. 7 (4) of Government Decision no. 144/2010 on the organisation and functioning of the Minister of Health, as amended,

the Minister of Health hereby issues the following Order:

Art. 1. - (1) On this Order coming into force, at the end of each month, wholesale distribution units of medicinal products, authorised importers and manufacturers shall submit to the National Agency for Medicines and Medical Devices a report on trade operations performed, *parallel import* included, respectively on distribution of medicinal products outside Romania, in other EEA member states, performed with medicinal products in their portfolio.

(2) The final purpose of reporting is to ensure traceability of medicinal products throughout the distribution chain, from manufacturing and/or distribution to the level of community pharmacy, hospital pharmacy, drugstore, to assess the propriety of on-prescription/off-prescription medicinal product release, to detect falsified products and prevent their entry into the authorised distribution network, to combat illegal parallel circuits for medicinal product sale, and respectively warrant rapid recall of non-compliant product batches or in case of health emergencies.

Art. 2. – The report submitted to the National Agency for Medicines and Medical Devices – the Pharmaceutical Inspection Department contains the following, as required:

a) The List of medicinal products for human use entered in /exited from stocks of wholesale importers/distributors authorised in accordance with Order of the Minister of Health no. 312/2009 on approval of Regulations for manufacturing/importation authorisation of manufacturers and importers of medicinal products for human use, including investigational medicinal products and grant of the

good manufacturing practice certificate to manufacturers of medicinal products for human use and/or active substances, as amended, and with Order of the Minister of Public Health no. 1964/2008 on approval of the Norms on the set up, organisation and operation of wholesale distribution units of medicinal products for human use, for various types of import/wholesale distribution activities stating the amounts, manufacturing batches, supplier(s) and recipient(s) of medicinal products, as well as the identification data of respective fiscal documents (number, batch, date of the invoice and/or of delivery notification);

b) The List of medicinal products for human use exited from the inventory of Romanian manufacturers authorised in accordance with Order of the Minister of Health No. 312/2009, as amended, stating the amounts, manufacturing batches, recipient(s) of the respective products, as well as the identification data of respective fiscal documents (number, batch, date of invoice and/or delivery notification).

Art. 3. - (1) The report is forwarded in electronic format, accompanied by the statutory declaration of the legal representative of the reporting company on conformity of submitted data.

(2) The first reporting necessarily contains the Romanian distributor/importer/manufacturer's product stock at the time of report drafting.

(3) The tabulated form and the Guideline for its filling in (also specifying the e-mail address for submission of the report) are part of the Annex which is integral part of this Order.

Art. 4. – Non-compliance with provisions of this Order are sanctioned in accordance with provisions of Law 95/2006 on healthcare reform, as amended.

Art. 5. – This Order is to be published in the Official Gazette of Romania, Part I.

Minister of Health,
Gheorghe-Eugen Nicolăescu

Bucharest, 11 April 2013.
No. 502.

ANNEX

GUIDELINE
on filling on the table concerning monthly electronic reporting of medicinal products distributed by wholesale distributors/importers/manufacturers

For more efficient reporting and data processing, the following recommendations concerning the manner of filling in the table of medicinal products distributed must be taken into account.

Manner of reporting:

- the report is submitted on CD to the following e-mail address: raportaremedicamente@anm.ro; the CD is accompanied by a statutory declaration of the reporting company's legal representative , in compliance with the conformity of data submitted;
- the report is only submitted in .xls format;
- only standard Latin script is used, font: Times New Roman, size 10;
- consistency of the filling in manner throughout the report is taken into account (for example, the same name of the distributor/manufacturer/importer is used throughout the report);
- separately from the table, contact data of the person who has filled in each report is provided (name, telephone number, e-mail address);
- each report includes all medicinal products in the reporting company's own portfolio, provided,in two separate tables, one for OTC products and the other for on-prescription products; in case of one product elimination from the portfolio, this is reported until the remaining stock is used up;
- the monthly report is submitted until the 25th day of the following month and replaces the previously required biannual reporting.

Manner of table columns completion is as follows:

- Name of distributor/importer/manufacturer: the type of unit to be selected from the filter provided; the name does not include the acronym related to legal trade form. i.e. "SRL", "SA", or "SC" mention.
- The trade name of the product: to be filled in with the exact name as per the NAMMD Index of medicinal products (http://www.anm.ro/app/nom1/anm_list.asp).
- Pharmaceutical form: to be filled in with the exact name as per the NAMMD Index of medicinal products (http://www.anm.ro/app/nom1/anm_list.asp).
- Strength: to be filled in with the exact name as per the NAMMD Index of medicinal products (http://www.anm.ro/app/nom1/anm_list.asp).
- Type of packaging: to be filled in under "number and type of primary packaging in a secondary packaging x number of units or amount per unit" (e.g. 5 vials x 10 ml, 3 blisters x 20 tablets, 1 tube x 10 g, 2 pre-filled syringes x 2 ml).
- Marketing Authorisation Holder: to be filled in the exact name as per the NAMMD Index of medicinal products (http://www.anm.ro/app/nom1/anm_list.asp).
- Stock available on 01.MM.2013: the stock of product is declared for each batch, each time providing the product identification data (name of the distributor/importer/manufacturer, trade name of the product, pharmaceutical form, strength, packaging type, Marketing Authorisation Holder, batch, supplier).
- Batch: each cell comprises one single batch. The next line is filled in for a different batch, each time specifying the product identification data (name of the distributor/importer/ manufacturer, trade name of the product, pharmaceutical form, strength, packaging type, Marketing Authorisation Holder).

- Supplier: does not include acronym related to legal trade form. i.e. "SRL", "SA", or "SC" mention..

- Entered amount in: digits only.

- Series and number of purchase invoice: one single invoice to be filled in, as "series/number".

- Date of purchase invoice: the date to be provided as "dd.mm.yyyy".

- Exited amount out: digits only.

- Recipient: does not include acronym related to legal trade form. i.e. "SRL", "SA", or "SC" mention.

- Unit type: one of the following is selected: Wholesale distributor, Open pharmacy, In-house pharmacy, Drugstore, Other persons authorised for medicinal product release to the public (e.g. medical clinics, dialysis centres etc.).

- Country of recipient residence: full name of recipient country of residence to be filled, no abbreviations allowed.

- Series and number of delivery invoice: identification data to be provided for one single invoice, as "series/number".

- Date of delivery invoice: the date to be provided as "dd.mm.yyyy".

- Stock on exit date: digits to be used only; stock available at the end of the month corresponding to each medicinal product batch becomes initial stock for the next month.

Product identification data								Input				Output						
Distributor	Medicinal product trade name	Pharm. form	Strength	Packaging type	Marketing Authorisation Holder	Stock available on 01.MM.2013	Batch	Supplier	Amount entered	Series and number of purchase invoice	Date of purchase invoice	Amount exited	Recipient	Unit type	Country of recipient residence	Batch and number of delivery invoice	Date of delivery invoice	Stock on exit date

DECISION

No. 9/10.07.2012

on approval of the mandatory monthly reporting of placement on the market in Romania, respectively of sales of medicinal products for human use by authorised wholesale distributors/importers/manufacturers

The Scientific Council of the National Agency for Medicines and Medical Devices (NAMMD), established based on Minister of Health Order no. 1123/18.08.2010, in accordance with Art. 8 (1) of the Regulation on organisation and operation of the NAMMD Scientific Council, hereby adopts the following through written procedure

DECISION

Art. 1. - (1) Mandatory monthly reporting by wholesale distribution units of trade operations, including *parallel import* and *parallel trade*, respectively, concerning medicinal products for human in their own portfolio is hereby approved; the report is submitted to the NAMMD, at the end of each month

(2) In accordance with provisions of the *Guideline on parallel imports of proprietary medicinal products for which marketing authorisations have already been granted*, approved through Scientific Council Decision (SCD) no. 1/09.03.2007:

- ”*Parallel import* of a medicinal product represents a legal form of trade within the Internal Market, based on Art. 28 of the EC Treaty and under the waivers mentioned in Article 30 of the EC Treaty.”

- **“***Parallel trade* is a legal form of trade in goods between Member States of the European Union.”

(3) The final purpose of reporting is to ensure traceability of medicinal products throughout the distribution chain, from manufacturing and/or distribution to the level of community pharmacy, hospital pharmacy, drugstore, to assess the propriety of on-prescription/off-prescription medicinal product release, to detect falsified products and prevent their entry into the authorised distribution network, to combat illegal parallel circuits for medicinal product sale and respectively warrant rapid recall of non-compliant product batches or in case of health emergencies.

Art. 2. – As required, the report submitted to the National Agency for Medicines and Medical Devices – the Pharmaceutical Inspection Department contains:

(a) The List of medicinal products for human use entered in /exited from stocks of wholesale importers/distributors authorised in accordance with Order of the Minister of Health no. 312/2009, as amended, and with Order of the Minister of Public Health no. 1964/2008, respectively, on various types of wholesale import/distribution activities stating the amounts, manufacturing batches,

supplier(s), beneficiary(ies) of medicinal products, as well as identification data for the respective fiscal documents (number, batch, date of invoice and/or delivery notification).

b) The List of medicinal products for human use exited from the inventory of Romanian manufacturers authorised in accordance with Order of the Minister of Health No. 312/2009, as amended, stating the amounts, manufacturing batches, recipient(s) of the respective products, as well as identification data of respective fiscal documents (number, batch, date of invoice and/or delivery notification).

Art. 3. – (1) The report is forwarded in electronic format, accompanied by the statutory declaration of the reporting company's legal representative on conformity of submitted data.

(2) The first reporting necessarily contains the Romanian distributor/importer/manufacturer's product stock at the time of report drafting.

(3) The tabulated form and the Guideline for its filling in (also specifying the e-mail address for submission of the report) are posted on the NAMMD website (www.anm.ro/anmdm/med.html, under "*Important notifications*").

Art. 4. – Non-compliance with provisions of this Decision is a breach of Order of the Minister of Health no. 1963/02.12.2008 on approval of the Guideline on Good Distribution Practice of Wholesale Medicinal Products and is sanctioned in accordance with provisions of Law 95/2006 on healthcare reform, as amended.

Art. 5. – This Decision is approved through Order of the Minister of Health.

Art. 6. – SCD no. 5/22.02.2011 on mandatory monthly reporting of placement on the market in Romania, and of sales of medicinal products for human use, respectively, by authorised wholesale distributors and SCD no. 17/6.07.2011 on extension of the deadline provided in Article 4 of NAMMD Scientific Council Decision No.5/22.02.2011 on mandatory monthly reporting of placement on the market in Romania, and of sales of medicinal products for human use, respectively, by authorised wholesale distributors is repealed on the coming into force of the Order of the Minister of Health approving this Decision.

PRESIDENT
of the Scientific Council
of the National Agency for Medicines and Medical Devices,

Acad. Prof. Dr. Leonida Gherasim

DECISION

No. 1/22.04.2013

on approval of the organisational strategy of the National Agency for Medicines and Medical Devices

2013 - 2015

The Scientific Council of the National Agency for Medicines and Medical Devices (NAMMD), established based on Order of the Minister of Health no. 158/18.02.2013, reunited on summons of the President of the National Agency for Medicines and Medical Devices in the ordinary meeting of 22.04.2013, in accordance with Article 12(5) of Government Decision no. 734/2010 on establishment, organisation and operation of the National Agency for Medicines and Medical Devices, as amended, adopts the following

DECISION

Sole article. – The organisational strategy of the National Agency for Medicines and Medical Devices 2013-2015 is approved, in accordance with the Annex which is integral part of this Decision.

PRESIDENT
of the Scientific Council
of the National Agency for Medicines and Medical Devices,

Acad. Prof. Dr. Leonida Gherasim

ANNEX
to SCD no. 1/22.04.2013

ORGANISATIONAL STRATEGY OF THE NATIONAL AGENCY FOR MEDICINES AND MEDICAL DEVICES 2013 - 2015

The National Agency for Medicines and Medical Devices (NAMMD) is a public institution operating under the Ministry of Health, set up through Emergency Government Ordinance no. 72 of 30 June 2010 on reorganisation of healthcare facilities and amendment of public health legislation, as a result of the merger of the National Agency for Medicines and Medical Devices with the Technical Office for Medical Devices. NAMMD organisation and operation have been approved through Romanian Government Decision no. 734 of 21 July 2010.

The NAMMD is the Romanian competent authority in the field of medicinal products for human use, ensuring marketing authorisation, surveillance of the safety of medicinal products in therapeutic use, authorisation of clinical trials and issuance of regulations in the field of the medicinal product, approved by the Ministry of Health.

In the field of medical devices, the responsibility of the NAMMD lies in control of performance and safety of medical devices in use as well as assessment of capability of the organisations providing services in this domain.

This organisational strategy is set up and updated in the context of the legal framework establishing the relation between the NAMMD and the Ministry of Health, as well as with its stakeholders. It covers the period 2013 – 2015 and allows update depending on the overall and pharmaceutical legal framework.

Additional details and information on NAMMD work can be found on its website, at www.anmdm.ro.

MISSION, VISION AND STRATEGIC OBJECTIVES OF THE NAMMD

The *Mission* and *Vision* of an organisation are a set of well individualised values to be adopted and applied in the organisation's life, strongly reflecting and being reflected in the content of the management culture.

They are an expression of the represent the course and possibilities for development.

The features of strong *Mission and Vision* are as follows:

• suitability – they are appropriate for the respective organisations, in the given context, matching the history and values of the organisation, with its performance and achievements and provide an assessment of desired situations possible to reach if specific pathways are taken;

• defining character of the organisation's purpose – they confer the actual meaning and significance to the life of the organisation and to the role of its employees;

• ability to initiate and support encouraging messages to employees for full intellectual and emotional involvement in the development of organisation activities;

• capacity to convey messages in an easily accessible manner, so as to be able to guide decisions and actions of those called upon to implement them;

• capacity to stimulate employees towards transcending their own limits in order to ensure attainment of strategic goals of the organisation;

• singularity at national level, in the community context of distinct competencies in the field of medicinal products for human use.

Mission of the NAMMD:

- **Evaluation at the highest scientific competence** of documentation for authorisation in view of marketing high quality, safe and effective medicinal products for human use;
- **Surveillance of the safety of medicinal products for human use** in therapeutic use by means of inspection and pharmacovigilance activities;
- **Maintenance of a high level of performance and safety of medical devices in use throughout healthcare networks in the country, irrespective of ownership;**
- **Most demanding assessment of technical-medical units providing services in the field of medical devices, for optimum delivery of competent and quality prosthetic and repair-maintenance services;**
- **Ensuring access for patients and healthcare professionals** to useful and accurate information on medicinal products for human use authorised for marketing in Romania;
- **Ensuring institutional administrative effectiveness, efficiency** and transparency of practices and procedures in use.

Vision of the NAMMD:

- **Strengthening of its status as reference national authority** in the field of the medicinal product for human use and control of the performance and safety of medical devices in use;
- **Strengthening of its status as expert and reliable source of accurate information and timely information** in the field of medicinal products for human use, provided to stakeholders.

Strategic objectives of the NAMMD are as follows:

- **Protection and promotion of public health**, by accomplishment of the NAMMD primary role, namely warranty of compliance of authorised medicinal products with the required standards, their efficacy and their acceptable level of safety;
- **Protection and promotion of public health**, by accomplishment of the NAMMD primary role, namely warranty of compliance of medical devices with the required standards, their intended purpose and acceptable level of safety;
- **Fulfilment of the NAMMD role as a communicator**, as an expert and reliable source of accurate and timely information, by providing clear and timely information to healthcare professionals, patients and the general public;
- **Contribution to the shaping of the future legal frame** in the field of medicinal products for human use, through promotion of NAMMD efficient European and international relations;
- **Contribution to the shaping of secondary legislation** in the field of medicinal products for human use and medical devices.
- **Coordination of an organisation** endowed with quality and adequately qualified workforce, **able to cope with future challenges**.

Table of contents:

1. Introduction

1.1. – Medicinal products for human use

Since its set up in 1999, in its various stages of development, the Agency has witnessed significant developments in the legal field, both nationally (by harmonisation of national and European legislation), and on European level (European legislation which the agency sought harmonisation with was itself undergoing major changes), such as:

• Gradual replacement of former national legislation with harmonised European legislation;

• Major revision of the EU body of medicinal product legislation (amendment of Directive 2001/83/EC);

• Introduction of regulatory provisions for harmonisation of authorisation procedures and conduct of clinical trials throughout the EU (Good Clinical Practice directives);

• Introduction of regulatory provisions meant to increase availability of authorised medicinal products, particularly for the treatment of children (the Paediatric Regulation);

• Introduction of regulatory provisions in the field of traditional herbal medicinal products (by supplementation of Directive 2001/83/EC);

• Introduction of a new regulatory system concerning safety and quality of homeopathic medicinal products (by supplementation of Directive 2001/83/EC).

• Introduction of legislation in the field of tissue engineering medicinal products and their use (Regulation on advanced therapies);

• Introduction of new regulatory pharmacovigilance provisions (by Regulation and Directive for amendment of Directive 2001/83/EC);

• Introduction of new regulations for preventing the entry into the legal supply chain of falsified medicinal products (by Directive 2001/62/EU of the European Parliament and of the Council for amendment of Directive 2001/83/EC).

Medical devices

Since its set up in 2005, by reorganisation of the SVIAM, the Technical Office for Medical Devices (TOMD), currently part of the NAMMD, the organisation has actively participated in generation of national regulatory documents in the field of medical devices, by:

• set up and revision of the legal framework for conduct of control by periodic check of medical devices;

• set up and revision in compliance with European legislation of the legal framework for assessment of service providers in the area of medical devices;

• set up and revision of the legal framework for ascertaining and sanctioning the violations in the field of medical devices;

1.2. - The NAMMD has implemented a number of important specific initiatives meant to improve performance of its basic activities, extend its role through appropriation of new fields of activity and improved communication with healthcare professionals and the general public, as well as the latter's improved communication with the Agency, through:

• Enforcement of a major restructuring of medicinal product operational departments, which has led to a more consistent surveillance of medicinal products throughout their lifecycle;

• Major reorganisation of operational departments in the field of medical devices, leading to more efficient use of staff;

• Introduction of a new and important information system in support of the decision-making process and work in agency-level electronic format;

• Appointment of the largest possible number of NAMMD experts for participation in committees and working groups of European medicinal product institutions, ensuring NAMMD ability to continue its active contribution to the EU legal and decision-making process;

• Participation with NAMMD experts in ASRO committees in the field of medical devices, ensuring NAMMD capacity further make an active contribution to the standardisation process;

• Improvement of the information flow provided to healthcare professionals;

• Improvement of NAMMD profile as a communicator.

1.3. – This organisational strategy takes into account the viewpoints expressed by stakeholders and outlines the principles and main directions of NAMMD interests and activities for the next 3 years.

2. Protection and promotion of public health

2.1. - Protection and promotion of public health is the NAMMD general objective, as well as the core of its activity throughout the process related to surveillance of the development and control of the use of medical devices.

The NAMMD performs assessment at the highest level of scientific competence of documentation for marketing authorisation of quality, safe and effective medicinal products for human use.

The NAMMD carries out inspections of all aspects concerning medicinal product development and manufacturing process, taking measures against the companies or persons who fail to comply with their obligations.

The NAMMD authorises conduct of clinical trials with medicinal products in various stages of development and seeks, by intervention of specialised inspectors, implementation of Good Clinical Practice rules.

The NAMMD monitors safe use of medicinal products for human use throughout their lifecycle, by means of a well-developed adverse reaction reporting system, so as to ensure maintenance of an acceptable risk/benefit balance for the respective products, as well as careful information in that respect of relevant interested parties, patients and healthcare professionals.

The NAMMD assesses all aspects related to service delivery in the field of medical devices. The NAMMD ascertains violations of the law and takes measures against companies or individuals failing to comply with their duties pursuant to Law 176/2000 on medical devices, as amended.

2.2. - Significant improvement of the NAMMD safety monitoring systems and their underlying legislation as well as increased NAMMD efforts for better patient and public understanding of the benefits and risks associated with medicinal product use have been apparent in late years.

In Romania, pharmacovigilance work is based on European regulatory grounds, transposed and implemented into national legislation.

In accordance with public documents of the European Commission, pharmacovigilance can be defined as "the science relating to the detection, assessment and prevention of occurrence of adverse effects to medicinal products and all related activities".

The National Pharmacovigilance Centre functions within the NAMMD.

Among others, NAMMD pharmacovigilance activity includes assessment and transmission of adverse reactions into the EudraVigilance system (the European data-processing network and database management system), assessment of Periodic Safety Update Reports

(PSURs), of pharmacovigilance systems of marketing authorisation holding companies, assessment of Risk Management Plans, harmonisation of Summaries of Product Characteristics (SmPCs) by implementation of the decisions of the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) in sections dealing with medicinal product safety.

Since 1976, the NAMMD has been a member of the World Health Organisation (WHO) Collaborating Centre for international monitoring of medicinal product safety.

The WHO has played an important role in development of pharmacovigilance by means of its monitoring centre in Uppsala (Sweden), handling an international database of adverse reactions to medicinal products. The number of national centres - active members of the WHO scheme for international monitoring of the medicinal product has now reached 98, while the number of adverse reactions in the database has grown to over 5 million.

Starting with 2012, the new Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010 has come into force, amending, in terms of pharmacovigilance, Directive 2001/83/EC on the Community Code relating to medicinal products for human use, transposed through Emergency Ordinance 35/2012. This Directive has brought changed and added to the legal pharmacovigilance assignments of Member States.

It is the NAMMD intention to develop the national pharmacovigilance system in accordance with provisions of the new directive and pay particular attention to its collaboration with European bodies and competent authorities as far as medicinal products are concerned.

The NAMMD seeks to further highlight the value of reports received by providing prompt feedback to reporters and continued development of public and patient level of understanding of decisions concerning the risk/benefit balance of medicinal products for human use available on the Romanian pharmaceutical market.

At the same time, the NAMMD is intent on furthering its efforts towards guidance and encouragement of healthcare professionals for adverse reaction reporting.

Over the past years, significant improvement has been apparent of NAMMD systems for control of medical devices in use and monitoring of service providers in the same field, of legislation underlying this control activity as well as enhanced Agency efforts for better patient and user understanding of the benefits and risks associated with the use of medical devices.

For the years to come, the NAMMD envisages continued development of its working system, so as to ensure that throughout Romania medical devices are used in accordance with the law, and that prosthetic works of any kind, maintenance and repair of medical devices are performed in line with the highest quality standards.

The NAMMD seeks to pursue its efforts to educate healthcare professionals and encourage their reporting of incidents with use of medical devices.

2.3. - At the same time, the NMA plans on active involvement in development of the European community system for monitoring of medicinal product safety, which, through combined information from the 27 Member States included in the EudraVigilance database, will further strengthen the elements underlying decision-making in safety matters.

EudraVigilance is one of the basic components of the *European Risk Management Strategy* related to medicinal products.

Risk Management represents the joint action of the European Medicines Agency and of national competent authorities in the EU for strengthened pharmacovigilance activity.

Furthermore, the NAMMD plans to get actively involved in implementation of the European Risk Management Strategy related to medicinal products, whose primary actions are as follows:

a) implementation of European community legislation;

b) taking complementary initiatives for establishing an improved medicinal product monitoring system as regards:

- communication of risks and initiatives in insufficiently developed pharmacovigilance areas (vaccines and paediatrics)
- risk detection, assessment and minimisation;

c) additional consolidation of the European pharmacovigilance system;

d) initiation of a Management plan of incidents within the EU regulatory system, meant to handle medicinal product crisis situations in the EU, regardless of the procedure for their authorisation;

e) implementation of the project concerning a ENCePP-European Network of Centres for Pharmacoepidemiology and Pharmacovigilance, coordinated by the European Medicines Agency.

2.4. – Starting with 2013, the new Directive 2011/62/EU as regards prevention of the entry into the legal supply chain of falsified medicinal products, amending Directive 2001/83/EC on the Community Code relating to medicinal products for human use, has been implemented into Member States national legislations. This Directive has made essential additions to legal assignments of competent authorities, as well as to manufacturers, importers and distributors in their fight against falsified medicinal products.

For best implementation of the new Directive, the NAMMD will set up a specialised structure within the Pharmaceutical Inspection Department, meant to handle and monitor complex issues related to prevention of entry of falsified medicinal products into the legal supply chain.

In the current context of falsified medicinal products becoming increasingly stronger reason for concern for regulatory authorities and the public, the NAMMD has initiated and continued cooperation with national institutions involved in fight against sale of falsified medicinal products, particularly over the internet, as well as with correspondent institutions in EU or non-EU member states, to establish new permanent connection points, meant to limit such criminal phenomena.

Thus, one of its main objectives has been to establish an overall frame for bilateral cooperation and exchange of information related to falsified medicinal products for human use with the General Inspectorate of the Romanian Police.

The main directions of NAMMD cooperation with the General Inspectorate of the Romanian Police are as follows:

- Compliance with legislation concerning medicinal products for human use;
- Exchange of information, to meet their legal assignments;
- Conduct of market studies and analyses, for most accurate knowledge of the Romanian market of medicinal products for human use, particularly as regards manufacturing, import and distribution;
- Surveillance of the operation of markets to identify non-compliances with national and/or community law for falsified medicinal products and legal provisions for medicinal products for human use, for measures to be taken by the two authorities as required, according to their respective competencies and their correlation;
- Communication and information of the public and economic agents active on markets of medicinal products for human use concerning measures taken in case of violation of national and/or community legislation relating to falsified medicinal products;
- Mutual support to ensure efficient operation of and safety in the medicinal products for human use sector, required legal changes included.

2.5. - For the following 3 years, the NAMMD envisages the following:

• Insurance of authorised medicinal products compliance with the adequate quality, safety, efficacy standards and authorisation in the shortest time possible;

• Authorising changes/variations to the marketing authorisations of medicinal products for human use (for new strengths or pharmaceutical forms etc.) in the shortest time possible, while safeguarding public health;

• Further authorisation of clinical trials and investigations only providing adequate warranty for patients, in accordance with harmonised community regulations;

• Further development of the National Pharmacovigilance Centre operating within the NAMMD and improvement of the adverse reactions/events reporting system, so that collection

of information is allowed from the most comprehensive sources, reporting is undertaken in the simplest manner and feedback is quickly delivered to encourage participation;

• Increased transparency and improved communication in the field of medicinal product safety;

• Performance of actions to ensure efficient surveillance of medicinal products for human use throughout Romania;

• Insurance of full NAMMD undertaking of its role in implementation of EU legislation for increased number of medicinal products particularly authorised for the treatment of children;

• Providing support to governmental initiatives in handling of severe public health risks (e.g. pandemic flu, bioterrorism) and fulfilling the NAMMD role in ensuring availability of relevant products to cover any increased demand;

• Provision to the public of adequate information/instructions on safe use of medicinal products, as well as warnings concerning their use under risk situations, when needed, for both on-prescription and over-the-counter (OTC) medicinal products;

• Maximum use of available instruments in support and consolidation of monitoring the safety of medicinal products for human use;

• Promotion of a risk-based approach in inspection activities, in line with NAMMD public health responsibilities and optimal use of resources;

• Taking efficient and prompt measures to prevent the entry of falsified medicinal products into the legal supply chain, in the context of NAMMD legal assignments as derived from provisions of Emergency Ordinance no. 91/2012, transposing Directive 2011/62/EU as regards prevention of the entry into the legal supply chain of falsified medicinal products.

• Developing cooperation with other institutions and bodies involved in this activity and increasing public awareness of falsified medicinal products hazards.

• Review of regulatory documents governing control activity through periodic check-ups of medical devices, so that the list of controlled medical devices and the regularity of check-ups are compliant with the degree of device risk;

• Continued improvement of procedures for assessment and surveillance of organisations seeking to service medical devices and assertion of establishment of labour conditions at European level;

• Investigation of all incidents involving medical devices together with in conjunction with habilitated institutions, in view of determining and minimising the causes.

3. Information and communication

3.1. - Most regulatory activities result in communication of updated information on medicinal products for human use as new knowledge thereof emerges during their use. This is usually undertaken as either provision of information to healthcare professionals or revised versions of the Patient leaflet. The quality of the information provided by the NAMMD is thus essential in fulfilling its role to protect public health.

The ever increasing degree of in-use knowledge of medicinal products for human use and their manner of regulation will also contribute to media and public understanding of the safety issues and the exceptional circumstances requiring product recall from the market.

3.2. - Healthcare professionals as well need clear information and recommendations to rely on when discussing options of treatment with their patients, whereas patients and the public look for access to information on medicinal products they use in their own care, related to their mode of action, the benefits which may be expected, the risks associated with their use, as well as better understanding of the manner in which the benefit/risk balance is established.

3.3. - The NAMMD has elaborated a Communication Strategy (2013 – 2015), describing the frame for internal and external communication throughout this period and establishing the key actions required for communication development. The communication strategy can be updated depending on the overall and pharmaceutical legal framework.

The main objective of the NAMMD communication strategy will be achievement of a higher degree of understanding of the risk/benefit balance assessment and of the manner of NAMMD decision-making for performance of its assignments as well as stimulation of adverse reactions/events reporting.

To be able to attain the most important strategic objective concerning protection and promotion of public health, the Agency must be able to constantly describe the content of its work.

The NAMMD communication strategy has established the core messages defining the Agency's activity and representing the key messages at the highest level has been conveying in order to meet the objectives this strategy provides for.

3.4. - The NAMMD is seeking that the public fully trust the medicinal product regulatory system, acting towards their best interest, by applying an approach best described by openness and transparency.

Much has been accomplished to this end over the past years and the NAMMD will further improve the transparency of its own activities and their accessibility to the public. The NAMMD will also promote transparency in the activity of the industry under its regulatory scope.

3.5. - Among the NAMMD strategic priorities mention should be made of the need for, closer and more effective engagement with patient associations and the general public, as well as identification of general ways of bringing patient perspective in its work. This activity has been initiated previously and will be continued and developed.

The NAMMD will continue to:

• Take action in view of strengthening its status as an expert and reliable source for the most recent information concerning medicinal products for human use on the market, by implementation of the NAMMD Communication Strategy;

• Make sure that the information accompanying medicinal products are easy to use, through full compliance with requirements established for user testing of the leaflets;

• Establish ways to enhance transparency throughout the decision making process, on both NAMMD and industrial level under its regulatory scope;

• Address healthcare professionals with targeted information, for improved adverse reactions/events reporting and promotion of safe use of human medicinal products (e.g. by adequate description, search and request of adequate information from the NAMMD);

• Make targeted information available to the public, in view of better adverse reaction reporting by the patient, promotion of better informed patient decision concerning the use of medicinal products for human use;

• Further develop its own website so as to be acknowledged as an expert and reliable source of the latest information on medicinal products for human use;

• Contribute to better understanding by the public and/or healthcare professionals of the benefit/risk balance of medicinal products for human use;

• Cooperate with professional bodies, academic staff and others, in order to ensure an adequate content of training programmes for healthcare professionals, in such issues as safety and risk in prescription and use of medicinal products for human use;

• Devise and implement new ways of increasing patient and public involvement in NAMMD activity and optimal utilisation of their contribution to the decision making process.

4. Shaping of a balanced legal framework

On European level

4.1. - The NAMMD will continue in its role as the Romanian and EU competent authority in the medicinal product field, fully integrated in the operations of EU competent

authorities as well as in the work of medicinal product committees and working groups of European bodies.

As of 2008, the NAMMD also acts as Reference Member State in the coordination of assessments of marketing authorisation applications submitted for authorisation through European procedures, particularly through the decentralised procedure, thus proving its expertise in the ongoing development of the Agency's assessors.

Following ratification of the Convention for the European Pharmacopoeia, within the Council of Europe, Romania has become a full member as of 2003. As member of the European Pharmacopoeia Commission, the NAMMD assigned representative actively participates in its working sessions.

The Agency aims at maintaining its very important contribution to the activity of the European network of competent authorities in the field of the medicinal product as well as to the activity of the Official Medicines Control Laboratories (OMCL) network.

4.2. – The NAMMD will continue to:

• Ensure active participation in technical and scientific debates regarding the setup of new legal provisions in the field of medicinal products for human use;

• Ensure the most efficient possible operation of the present regulatory system in the field of medicinal products for human use and promptest implementation of future changes brought to the European regulatory framework in this field;

• Strengthen surveillance of the Romanian/European market through closer cooperation and collaboration with the other European medicines agencies;

• Provision of knowledge and expertise to other states, signatories of *the Collaboration Agreement of Drug Regulatory Authorities in European Union Associated Countries (CADREAC)]/New Collaboration Agreement between Drug Regulatory Authorities in Central and Eastern European Countries (nCADREAC).*

On an international level

4.3. – Particularly following Accession, within the European pharmaceutical regulatory system, the NAMMD cooperates with all national competent authorities in the European Union (EU) and in the European Economic Area (EEA), as well as with the European Medicines Agency (EMA).

Via the EMA, the NAMMD hopes to be able to also further develop international connections with the United States Food and Drug Administration (FDA), within the cooperation framework established between the EMA/EU and the FDA/USA.

It is the NAMMD belief that, for efficient performance of its regulatory assignments in the field of medicinal products for human use, for public health benefit, it also needs good working relationships with non-EU countries, particularly with those displaying abilities for the development of medicines, which increasingly represent a significant source of supply for the EU market.

4.4. – The NAMMD considers it advisable that regulatory authorities worldwide be able to cooperate for setup of harmonised standards, applicable to global connections to the pharmaceutical industry.

4.5. – The Agency will further:

• Develop its international and cooperative relations in the field of medicinal products for human use, in the context of a global market for medicinal products;

• Support proceedings concerning harmonisation of regulations of the International Conference on Harmonisation (ICH) in the medicinal product field;

• Develop cooperation established with competent authorities in strategically important countries, such as China, India and Korea, which will become an increasingly important source for manufacturing and development of medicinal products for human use, subject to NAMMD authorisation and surveillance.

Implications of scientific and technological progress

4.6. - The NAMMD anticipates significant scientific and technological progress with potential impact on regulation of medicinal products in the following fields:

• Biotechnology products;

• Progress in the fields of molecular biology, genomics, gene and cell therapy;

• Use of new screening technologies and mechanisms, better adapting medicinal products to patients, development of "personalised" and "niche" medicinal products and diagnostic tests, for identification of suitable patients;

• Development of products combining a medicinal product with its own release system, into a medicinal product/medical device association;

• Use of nanotechnology, biomedical science, microelectronics and computer technology;

• Tissue engineering.

4.7. – The NAMMD may contribute to the development of efficient treatments to benefit health by promoting a supportive context for conduct of clinical trials in Romania, according to European legislation in force.

The Agency will continue its collaboration with partner organisations and support European efforts for harmonised approach of the requirements for clinical trial authorisations, by diminishing inconsistencies and bureaucracy while maintaining safety measures regarding trial participants.

4.8. – The NAMMD will further:

• Ensure preservation, through contribution with adequate expertise in debates of scientific committees organised by European bodies, of the legislative ability to establish a proper balance between cautious approach of the safety issue and the freedom of innovation;

• Establish contacts with academic and professional centres of renown in the field of medical, pharmaceutical and legislative sciences, for ensured NAMMD capacity to rely on optimal abilities and knowledge in preservation of its own expertise;

• Promote an optimal internal context for clinical research and cooperation with EU bodies for harmonisation of regulations on clinical trial authorisation.

Towards Better Medicinal Product Regulation

4.9.1. – The NAMMD Scientific Council establishes the Agency's scientific policy, in accordance with its assignments.

Meetings of the Scientific Council discuss and approve, as Scientific Council Decisions, regulations in the medicinal product field, as well as regulations concerning the professional activity of the Agency..

NAMMD Scientific Council decisions of ruling character are approved by the Minister of Health and are published as Minister Orders in the Official Gazette of Romania, Part I.

4.9.2. – It is the NAMMD duty to ensure that medicinal product regulatory activity is proportionate with and adequately reflects the current level of knowledge regarding benefits and risks.

This amounts to NAMMD ongoing self-assessment and insurance that it adequately reflects the needs of stakeholders, provision of an effective regulatory service and direction of activities towards compliance with the Agency's main objective of protecting public health.

Considering the lack of specialised personnel, the NAMMD is unable to engage in scientific advisory activities; however, it frequently gives advice on regulatory issues.

4.10. - The NAMMD intends to carry on its risk-based approach in the inspection field, allowing focus on issues of potential concern, to fully capitalize on its inspection resources.

The Agency undertakes to further explore the scope of a risk-based approach of the NAMMD regulatory functions and search for fields providing room for regulatory practice improvement, compliant with both the law and the NAMMD role in protecting public health.

4.11. - The NAMMD is also aware of the need to ensure concise and unambiguous legal provisions underlying any of its regulatory activities.

National legislation in the field of medicinal products for human use has undergone significant changes over the years, but as of entry into force of Law 95/2006, Title XVII – The medicinal product, it has been fully harmonised with European legislation and amended in accordance with emerging European regulations.

4.12. – The NAMMD will continue to:

• Develop its risk-based inspection and search for other opportunities for reducing unnecessary legal obligations, as well as find areas allowing for attainment of the Agency's objective concerning substantiation of regulations on risk and proportionality;

• Support the European Commission's initiative for better regulation and continued contribution to this issue on national and European level;

• Strengthen and rationalize the law in the field of medicinal products for human use.

5. Leadership of a successful organisation

5.1. - Given the dynamic context for its operation, the NAMMD needs to preserve its influence in its own field, as well as its flexibility and ability to respond to changes.

The coming into force of the new European legislation has generated significant changes in workload, therefore enabling the Agency to anticipate the further development of specific EU aspects, whereas others may remain constant or even diminish.

The NAMMD will take the necessary measures to maintain its flexibility and ability to adapt to a fluctuating workload, namely to increased/decreased demand, which would be an advantage for both the Agency and the industry.

5.2. – The NAMMD needs good working relationships with the industry under its regulatory scope, created through efficient dialogue with the leading manufacturers' associations and marketing associations in the field of the medicinal product for human use, as well as with healthcare professionals and patients taking these medicinal products.

Good cooperative relations need to be preserved with other governmental bodies, whose activity is closely related to NAMMD work.

5.3. – The Agency will further:

• Make investments and develop efficient information management systems in support of its own activity and undertake an active role in the context of the EU debate on elaboration and enforcement of adequate and consistent systems;

• Ensure that its own work reflects the needs of interested parties, thus meeting its main objective of protecting public health;

• Maintain efficient relations with other governmental bodies;

• Maintain and improve collaboration and cooperation with the pharmaceutical industry and maintain adequate contacts with leading manufacturers' associations and marketing associations in the field of medicinal products for human use.

• Maintain and improve collaboration and cooperation with the medical devices industry as well as appropriate connections with the ASRO, RENAR and the national health insurance houses.

Agency staff

5.4. – Its own staff is the Agency's chief resource. Enforcement of efficient regulation to protect public health involves **maintenance of highly qualified and motivated workforce**.

This goal is particularly difficult to achieve under the present circumstances when current public system possibilities to reward its employees can hardly compete with opportunities on the private market, that have attracted specialists whose expertise is due to their work in the Agency.

The NAMMD will have to further its efforts to preserve its currently available staff with regulatory and scientific expertise, providing at least motivation through adequate assessment of performance and acknowledgment of professional competence, respectively, until creation of a favourable legislative context allowing for appropriate financial motivation for reward of special professional merits.

5.5. – Depending on progress of the current economic crisis, the NAMMD seeks to:

• Undertake efficient recruitment and selection of new staff, particularly from among new graduates of medical-pharmaceutical higher education.

• Implement promotion policies to ensure the human resources in the NAMMD, mainly in areas where analysis reveals deficits of personnel of higher education;

• Provide staff with a wide range of professional training and opportunities for improvement, for developed human resources..

Financing of Agency operation

5.6. – At the end of 2009, **the Agency was reorganised as a public institution wholly financed from the state budget**, in accordance with Law 329/2009 on reorganisation of certain authorities and public authorities, rationalisation of public expenditure, support to business and compliance with the framework agreements with the European Commission and the International Monetary Fund.

Considering that the Agency used to be self-financed before 2009,, subsequent fiscal-financial measures have had a major negative impact on human resources management and implicitly on financing of the Agency's entire work.

The NAMMD seeks to at least maintain its financial stability through a balanced budgetary exercise, within the allocated budget, an in observance of legislation in force.

5.7. – The NAMMD periodically updates its tariffs depending on changes in its activities.

The NAMMD aims at further finding activities able to enhance its income, such as organising conferences, training sessions etc.

Conclusions

The NAMMD is a mature institution, fully able to manage the activities arising from its status as an EU competent authority.

This is also the case in European context, where the NAMMD is met with recognition and appreciation as Romania's competent authority in the field of medicinal products for human use.

The context for NAMMD operation has been subject to numerous changes, which it has strived to understand and adapt to requirements of the process related to the shaping of developments and the enforcement of new policies

Relying on its long and efficient activity, the NAMMD, will have to prepare to cope with any challenges future may bring.

DECISION

No. 2/22.04.2013

on approval of the Communication Strategy of the National Agency for Medicines and Medical Devices (2013-2015)

The Scientific Council of the National Agency for Medicines and Medical Devices (NAMMD), established based on Order of the Minister of Health no. 158/18.02.2013, reunited on summons of the President of the National Agency for Medicines and Medical Devices in the ordinary meeting of 22.04.2013, in accordance with Article 12(5) of Government Decision no. 734/2010 on establishment, organisation and operation of the National Agency for Medicines and Medical Devices, as amended, adopts the following

DECISION

Sole article. – The Communication Strategy of the National Agency for Medicines and Medical Devices (2013-2015) is approved, in accordance with the Annex which is integral part of this Decision.

PRESIDENT
of the Scientific Council
of the National Agency for Medicines and Medical Devices,

Acad. Prof. Dr. Leonida Gherasim

ANNEX
to SCD no. 2/22.04.2013

Communication strategy
of the National Agency for Medicines and Medical Devices
(2013-2015)

The drafting and implementation of the Communication Strategy of the National Agency for Medicines and Medical Devices (NAMMD) are an essential prerequisite for strengthening the status as European institution in the medicinal product field, a model of efficient and transparent performance.

I. INTRODUCTION

1. The overall context of the strategy

Romania's accession to the European Union (EU) has created the particularly favourable context for development of the communication policy of the National Agency for Medicines and Medical Devices (NAMMD). Approach of an adequate communication strategy allows the NAMMD to strengthen its credibility with its partners and may become an actual protector and promoter of public health in Romania.

For competent authorities throughout the EU in the field of medicinal products for human use, one of the most important objectives is setup of an efficient connection with all stakeholders, namely healthcare professionals and professionals in fields such as research and industry, patients and the general public, the media.

The most important strategic objective of the NAMMD is promotion and protection of public health, by accomplishment of the NAMMD primary role, namely warranty of compliance of authorised medicinal products with the required standards and intended purpose as well as of their acceptable level of safety. For successful attainment of this goal, the NAMMD will further strengthen its status as expert and reliable source of accurate and timely information in the field of medicinal products for human use, provided to its most important stakeholders, who have to turn into actual and active communication partners.

2. Scope and purpose

The Communication strategy outlines the frame for internal and external communication activities performed by the NAMMD, by establishing key actions necessary for developing Agency communication, as national regulatory and control authority in the field of the medicinal products for human use.

The Communication strategy is devised, set up and implemented by the Communication, institutional relations and pharmacopoeia service within the Department for policies and strategies, but implementation of its objectives cannot be acheived without support and cooperation of the entire Agency personnel.

The entire Agency staff, be they specialists such as pharmacists, physicians, or biologists involved in activities related to assessment of authorisation dossiers, control and/or inspection thus contribute to implementation of the Communication strategy. Therefore, it is mandatory that professionals in the Agency be actively involved in the draft of responses requested by the mass-media and/or any stakeholder, in conveying specialised information to all its partners and, last but not least, to the general public, in the development of the NAMMD website, in identification of stakeholders' emerging needs, in organising meetings and actual participation. The NAMMD needs to manifest increased openness for more efficient communication with all partners in the

field; in that respect, the NAMMD has organized and plans on further setting up meetings with Marketing Authorisation Holders (MAHs), with Romanian and international associations of manufacturers of medicinal products and of patients, with associations of companies coordinating clinical trial conduct and associations of medicinal product distributors.

The NAMMD finds it necessary to continue organisation and provision of professional training courses on topics subjects of major significance to its partners (legislation, good manufacturing and control practices), whose final goal is to facilitate communication between the NAMMD as national regulatory and control competent authority and the stakeholders.

Ensuring effective communication with all European bodies in the field (the European Medicines Agency, the Heads of Medicines Agencies, the Council of the European Union, the European Directorate for the Quality of Medicines and Healthcare, the European Commission etc.) is in itself an additional application and purpose as such communication strategy.

II. OVERVIEW

1. General objective of the Communication strategy

The general objective of the Communication strategy is achievement of a higher level of understanding of risk/benefit assessment and NAMMD decision–making for performance of its duties as well as stimulation of adverse reactions/events reporting by healthcare professionals (physicians, medical examiner, pharmacists, medical assistants, midwives) and patients.

2. Specific objectives of the Communication strategy

The NAMMD Communication strategy has the following specific objectives:

- To improve the ability of Agency specialists to analyse, debate, suggest, update and convey regulations in the field of medicinal products for human use in full compliance with European legislation and standards in force;
- To develop communication activities through improvement and development of its infrastructure;
- To reinforce procedures and processes in order to clarify the roles and responsibilities in the context of the NAMMD mission;
- To attain increased visibility among other bodies, i.e. recognition of NAMMD status as expert and reliable source of accurate information in the medicinal product field;
- To strengthen the impact of communication upon NAMMD partners by ensuring ample and immediate availability of information;
- To insure bilateral, quality communication with the various stakeholders (by means of message exchanges, questions and answers);
- maintaining NAMMD perception as trustworthy source through continued and constant attainment of all objectives established, irrespective of difficulties encountered in resolution of emerging problems;

As a live document, endowed with sufficiently flexible objectives to respond to the continually changing external context, once drafted and implemented, the Communication strategy will remain under permanent NAMMD leadership assessment, undergoing updates as required by the rapid dynamic of the pharmaceutical field, so as to insure its permanent adaptation to emerging changes.

3. Content

This document analyses the various aspects of NAMMD activity, the Agency's relationship with its partners, stakeholders' expectations, thus establishing a Communication strategy.

The strategy has been issued following wide research for material, by study of other corresponding European Agencies' Communication strategies, by reference to national and European realities

In order to meet the top strategic objective, namely protection and promotion of public health, the Agency must be able to constantly describe the content of its work. to this end.

The following key messages outline the activity of the Agency and represent key **messages** at the highest level, which the NAMMD will further convey through implementation of this communication strategy:

- There is no adverse reaction-free medicinal product, the essential being a positive risk-benefit balance;
- The NAMMD is responsible for insurance of authorised medicinal products compliance with required standards as well as efficacy of medicinal products for human use and their acceptable safety;
- The European Union has introduced a new medicinal product labelling process subject to particularly close monitoring by regulatory authorities in the field of the medicinal products for human use. Such products will be provided with a black triangle printed on the leaflet and on the Summary of Product Characteristics, as additional protection and information for patients and healthcare professionals.
- The NAMMD performs surveillance of in-use medicinal products for human use through inspection and pharmacovigilance activities, however there are products subject to more careful monitoring. The black symbol shows that there is less information available on such products, due to their "novel product" status or to limited data concerning their long-term use.
- The NAMMD promptly adopts appropriate decisions for public health protection whenever needed.
- The NAMMD encourages patients to report any suspected adverse reactions directly to the authority and discuss any medicinal product related unclear issues or concerns with their physicians.
- The NAMMD seeks to ensure, as much as possible, public access to information.
- The NAMMD pursues to ensure transparency of practices and procedures employed in the institution.

The above key messages in fact correspond to elements of the NAMMD mission, expressing objectives pursued by the Agency in clear and accessible terms. Implementation of this strategy will mean NAMMD continued communication and support of key messages, whenever necessary, while at the same time ensuring through self-assessment their uninterrupted impact on the target audience of the institution.

4. Solutions, valorisation

- Continued support of the NAMMD mission of promoting and protecting public health through timely provision of the latest and most accurate information on medicinal products for human use;
- Insuring a high level of accessibility to information;
- Finding ways to insure the highest degree possible of transparency in decision-making on the level of both the NAMMD and the industry under its regulatory scope;
- Finding appropriate methods to appeal to healthcare professionals for improved reporting of adverse reactions and events;
- Adequate information of healthcare professionals to promote safe use of medicinal products for human use (for instance, by means of suitable prescription, search and request for adequate information from the NAMMD);
- Pursuance of thorough observance of requirements established for improved readability and understanding of patient leaflet information and labelling and user testing;

- Making information available to the general public to be able to first initiate and then develop the process of adverse reaction reporting by the patient directly not only to the physician but also to the competent authority, in light of the new approach of pharmacovigilance in the EU, aiming to gain patients'trust;
- Making information available to the general public to promote a better informed decision of the patient regarding the use of medicinal products for human use;
- Harmonisation with the Communication Strategy of the European Medicines Agency (EMA) on additional monitoring of medicinal products (tagged with the black symbol and the associated warning text under Product-related information) by launching its own campaign addressing patients and healthcare professionals until March 2014;
- Development and permanent update of the NAMMD website for strengthened status as reliable source for the latest information on medicinal products for human use;
- Promotion of risk understanding and directing public attention towards the danger of purchase of medicinal products over the internet;
- Promotion of risk understanding and directing public attention towards the danger of encouraging self-medication through inappropriate advertisement of medicinal products for human use;
- Contribution to better understanding by healthcare professionals and the general public of the fact that, although there are no risk-free medicinal products, their benefits for the patient and the public fully justify the risks as long as the risk/benefit ratio remains positive;
- NAMMD collaboration with professional bodies and academic staff etc. in the field, so as to insure appropriate content for healthcare professionals' training and education in matters of risk and safety in prescribing and use of medicinal products for human use, Good Clinical Practice rules etc.;
- Insuring recognition of NAMMD status as a competent authority through understanding the manner for NAMMD actual regulation of the medicinal product field;
- Design and implementation of new ways to improve patient and general public involvement in NAMMD work and maximum valorisation of their contribution to the decision-making process.

III. ANALYSIS OF THE CURRENT SITUATION

1. Period of pre-accession to the European Union: challenge and opportunity

During pre-accession to the European Union, the National Medicines Agency's communication activity of that time was the same with the aspiration for EU accession, aiming to become the first public voice in the field of medicinal products for human use to guide this process due to its ability to perform national scale communication on accession requirements and expected outcomes. At the time, the key preoccupation of the Agency's communication strategy was to increase reliability of its structures, able to perform their regulatory and control function and to successfully implement the objective of EU accession.

2. SWOT analysis

Strengths:
- National competent authority in the field of human medicinal products
- Considerable appreciation at EU level
- Communication service able to communicate efficiently

Weaknesses:
- Lack of funding for appropriate financing of communication activities
- Lack of staff trained for communication

- Lack of adequate procedures to facilitate communication with all stakeholders

Opportunities:

- Reinforcement of the medicinal product legislative context by establishing partner relationships with civil society and the media, based on communication and transparency
- Involvement of NAMMD partners in the Agency's activity reinforces public support
- Healthcare professionals, the media, patients and the general public willing to receive more information about medicinal products
- Availability of a relatively small number of employees able to facilitate communication between the NAMMD and stakeholders' representatives
- Participation in meetings at European level of the working groups on communication
- Demonstration of conjugated operation of the European medicinal product regulatory network (EMA, EC and national competent authorities).

Threats:

- Low level of public confidence and credibility
- Lack of a consolidated relationship with part of the media
- The Communication strategy may become unproductive in want of real partnership with the media, which may possibly turn into a patient and public manipulation factor through conduct of a campaign for defamation of community competent authorities and of the national medicinal product competent authority
- The communication strategy cannot meet its objectives outside a real partnership with civil society.

3. Strategic priorities

Currently, 6 years after Accession, the Agency's mission and strategic objectives follow the same evolutionary path as any of other EU competent authorities. The credibility of the Agency's message is currently supported by its structures' capacity to demonstrate harmonisation with European values and standards, setup and maintenance of consistent cooperation with European competent institutions, bodies and authorities in this field.

The Communication strategy hereby expresses the strategic priorities for attainment of the NAMMD mission in the field of medicinal products for human use, to contribute to protection and promotion of public health through:

- Evaluation at the highest scientific level of authorisation dossiers for the marketing of safe, quality and effective medicinal products;
- Surveillance of the safety of medicinal products for human use in therapeutic use (while placing emphasis on additional monitoring of medicinal products whose leaflet and SmPC are inscribed with the black symbol), by means of inspections and pharmacovigilance activities;
- Provision of access to healthcare professionals, pharmaceutical industry, patients and public to useful and accurate information on medicinal products authorised for marketing in Romania;
- Insurance of Agency's administrative effectiveness and efficiency and transparency of its practices and procedures.

The NAMMD seeks to continue approach of the above strategic priorities for development of communication activities, such as:

3a. *Improved flow of information to healthcare professionals*

The NAMMD is aware that the first contact of most patients and the general public is public healthcare services and treating healthcare professionals, respectively. Therefore,

healthcare professionals should be timely provided with accurate high quality information able to aid them in advising their patients on utilisation of medicinal products for human use.

Hence, the Agency has focussed on continued efficient provision of key information for healthcare professionals in that respect, in order to adequately support their or other people's patient care.

In this respect, the NAMMD will pursue:

- Review and update of its website for better accessibility of information for all stakeholders, healthcare professionals included;
- Assessment of communication channels currently used in relation to healthcare professionals: rapid alerts, current pharmacovigilance issues (direct communications to healthcare professionals, EMA press releases concerning efficacy and safety issues, notifications to medical practitioners ads, pharmacovigilance regulations, submission of Summaries of Product Characteristics, patients leaflets etc.)

***3b**. Improved NAMMD profile as a communicator*

The NAMMD fully assumes responsibility for communicating with the media relationship, in a context of increased demand for printed press and television interviews, thus continuing to promote a fair and efficient relationship with the press, given the increasing societal role of the media in recent years. Accurate, rapid and impactful information conveyed in appropriate terms in the field of medicinal products for human use as well is a vital source for any type of decision, and the media is their main means of dissemination to the general public.

Considering that, in addition to its informative role, the mass media can also be used to shape opinion and ideas and develop attitudes, the NAMMD relationship with the press must be built in such a way as to insure accurate, clear and appropriately expressed medicines-related body of information, particularly related to safe use, in order to achieve a maximum degree of understanding by the general public. To a lesser or greater extent, this relates to the Agency's control over information on medicinal products for human use, and a good relationship with the press is mandatory to achieve this goal.

In exercise of its duty as a proactive and reactive communicator, the Agency aims at insuring a balance between its work and the issues it faces.

***3c**. Improved internal communication*

Internal communication takes place on several levels, contributing to fulfilment of the Agency's objectives. In the same was as many other organisations, the NAMMD uses the intranet and the electronic mail, for their speed and ease of use. It aims at supplementing and updating employee directed information on the Intranet, to ensure rapid quality professional information and/or proper organisational aspect.

Other internal communication alternatives are: operative meetings of the NAMMD management with the heads of the various internal structures and Agency committees, meetings on department / service / bureau level, inter-departmental meetings, internal publications on the intranet etc..

The Agency aims at:

- continuous monitoring of the development of more effective communication skills of its employees in respect of interpersonal or face-to-face communication;
- improved vertical communication mechanism ("top-down" – in line with the hierarchical organisation, and "bottom up" – from the lower to the upper hierarchical levels), in particular as regards:
  - ensured possibility for "feedback" receipt;
  - increased speed of "feedback" receipt;
  - improved communication mechanism on group level, manifest in departments, services, laboratories, offices. This level focuses on sharing of information, discussion of issues, coordination of tasks, resolution of problems and reaching consensus.

- scheduled meetings within the Agency to monitor employee awareness about the role of the communication function, the importance of ensuring good internal communication envisaging attainment of the NAMMD mission;
- collaboration with the Department for Human Resources, Payroll to develop a training program concerning better NAMMD employee communication skills;
- revaluation of existing channels of internal communication and focussing efforts towards developing of bilateral written and verbal communication.

3d. *Improved involvement in Agency work of patients and the general public*

Priority will be given by the NAMMD to continued direct communication with patients' and general public associations allowing identification of more opportunities for their involvement in agency work, such as:

- planning meetings with patient / public groups of interests for proposal of specialists to participate in their meetings;
- creating a patient / public "reference group" able to, within its collaboration with the NAMMD, contribute to improved decision making and level of understanding of safety issues and risk in prescription and use of medicinal products for human use.

3e. *Promotion of informed debates on the various aspects involved in medicinal products for human use: the benefit / risk balance, generic versus innovator medicinal products, patient role in development of readable leaflets able to ensure a high level of understanding, reporting adverse reactions to healthcare professionals, physicians, pharmacists, medical assistants) and to the NAMMD etc*.

- Debates on the issue of non-existence of risk-free medicinal products, the essential point being that a positive benefit / risk ratio would provide better understanding of the Agency's work and set an example for transparency promotion in NAMMD policy and strategy, as the national regulatory authority in the field of medicinal products for human use.
- Continued debate on generic versus innovative medicinal products.
- Initiation of debates on the involvement of healthcare professionals (physicians, medical examiners, pharmacists, medical assistants, midwives) and patients in implementation of the new Directive 2010/84/EU for amendment of Directive 2001/83/EC establishing a Community code on medicinal products for human use in terms of pharmacovigilance, transposed into national legislation through Emergency Ordinance no. 35/2012 amending Law 95/2006 in terms of the new approach of pharmacovigilance in the EU.
- Launch of a personal information campaign meant for patients and healthcare professionals, until March 2014, concerning the significance of the black symbol as a novelty on future leaflets and SmPCs of medicinal products undergoing additional monitoring of their post-authorisation safety as of July 2013.

IV. ANTICIPATED OUTCOMES

1. Ensuring communication and transparency

The NAMMD is intent on paying particular attention to ensuring effective information and communication with the media and other stakeholders in accordance with provisions of Law 544/2001 on free access to public information and Law 95/2006 on healthcare reform, Title XVII – The medicinal product, concerning transparency in competent authorities' activity in the medicinal product field in the EU.

1a. External communication

The Agency will ensure proper and adequate notification of its partners about activities performed in all fields under its scope.

The NAMMD will continue quarterly publication on its website of the bilingual Newsletter mirroring the Agency's legislative and regulatory activity in the field of medicinal products for human use, in accordance with European legislation, as well as other priority activities. The following are posted in the Newsletters:

- Laws, ordinances, government decisions in the field of medicinal products for human use or other fields of NAMMD interest;
- Orders of the Minister of Health for approval of NAMMD Scientific Council Decisions and Orders of the Minister of Health related to NAMMD other fields of interest;
- NAMMD Scientific Council Decisions;
- NAMMD Administration Council Decisions;
- The quarterly list of marketing authorisation/renewal applications forwarded to the NAMMD;
- The quarterly list of the new EMA centrally authorised medicinal products, for which a marketing price was established in Romania;
- The quarterly list of medicinal products authorised for marketing by the NMA/NAMMD;
- The quarterly list of medicinal product batches recalled by the NAMMD because of quality non-compliances.

The NAMMD will continue to issue and post on its website the Index of medicinal products for human use, which contains all medicinal products allowed for circulation on the Romanian pharmaceutical market, as well as information about their trade name, International Non-proprietary Name (INN), Marketing Authorisation Holder, pharmaceutical form, strength, route of administration, manner of packaging, manner of release etc. The electronic versions of the Summaries of Product Characteristics (SmPCs), leaflet and labelling information will be implemented.

The NAMMD will permanently develop and update the information posted on its website. In this respect, the following information and documents will be further posted and updated on the NAMMD website:

- EMA press releases on medicinal product safety;
- NAMMD important announcements, responses to certain written press and TV issues related to the Agency's medicinal product policy, to the attention of stakeholders;
- Direct Healthcare Professional Communications;
- Notifications to the attention of Marketing Authorisation Holders (MAHs) or other stakeholders related to issues of interest;
- The List of NAMMD employees assigned as full members or alternates in the Management Board, scientific councils and working groups of the European Medicines Agency (EMA);
- The list of NAMMD appointed EMA experts.

A new section related to the national procedure has been added to the NAMMD website; just as the other two sections dedicated to the centralised and MRP-DCP procedures, this hosts information about contact persons, special warnings, SmPC, leaflets and labelling information. Moreover, the "National procedure" section of the new NAMMD website will further provide the "List of parallel import authorisations" issued by the Agency since 2009.

Because of the interest it bears with external users of the website, the sections will be updated with:

- Medicinal product legislation, structured according to the type of the regulatory document:
  - Laws, Ordinances, Government Decisions;
  - Minister of Health Orders;
  - NAMMD Scientific Council Decisions;
  - NAMMD Administration Council Decisions;
  - Index of medicinal products for human use authorised for marketing in Romania;

- Forms;
- Useful information.

The NAMMD will also continue to inform stakeholders about activities in relation with other publications, apart from its Newsletters. Thus, its website will continue to host the activity report for the previous year (in English as well).

Moreover, the NAMMD will carry on publication of articles dealing with various issues related to the Agency's activity in Romanian professional magazines ("Farmacist.ro", "Medical Business", "Viața Medicală", "Pharma Business", "Medica Academica", "Practica farmaceutică" etc.).

NAMMD representatives will further submit professional papers for various scientific events organised in Romania (and abroad) for pharmacists and physicians. Communication can thus be insured between two professions - physicians and pharmacists, both in the service of sick people.

1b. Internal communication

The NAMMD will continue supplementation and update of information available to employees on the local network (Intranet) to ensure the fastest and optimal professional and/or organisational information, such as:

- Instructions of the NAMMD president;
- NAMMD policies in the field of quality;
- NAMMD regulations;
- Glossary on quality insurance;
- Departmental activity plans;
- Useful forms;
- Information of the Pharmacopoeia Service;
- Information on training courses organised by NAMMD/specialised companies;
- Reports set up by participants in training in Romania and abroad;
- Situation of staff training;
- Outcomes of the staff motivation poll ;
- Useful information;
- Useful addresses etc.

2. Forthcoming actions, conduct of funding activities to meet proposed strategic goals

2a. Staff recruitment

Depending on the progress of the economic crisis and of the legal framework, the NAMMD intends to carry out efficient actions to maintain and recruit highly qualified and motivated staff, with communication skills necessary to attain the goals and priorities of the Agency's communication strategy.

2b. Funding of communication activities

Despite obstacles created in 2009-2010 by the unfavourable economic context, the agency is at least aiming at further maintaining its financial stability through a balanced budget year, in accordance with the laws in force.

It is worth mentioning that, for economic reasons, printed publication of both the Agency's quarterly newsletter and the NAMMD Annual Report brochure has been further cancelled, these being only posted on the Agency website. Distribution of such specific illustrative work in written format to certain interested state institutions, faculties of pharmacy and medicine abroad and at home, to certain medical and pharmaceutical personalities as well as to other national medicinal product regulatory authorities would more widely insure a successful

agency communication strategy. Therefore, the NAMMD pursues to resume printing/distribution of such publications as soon as feasible from a financial standpoint; this will ensure an opportunity for more accurate estimate by healthcare professionals, internal and external partners of constant Agency efforts towards recognition of its reinforced status as European competent authority in medicinal products for human use.

Depending on financial, material and human resources, the Agency aims at development and diversification of communication instruments, considering that an effective communication strategy combines some or all of the following tools: Internet, print publications and other printed materials, press releases, interviews, important notifications, conferences etc. The tools used depend on the strategic objectives, the profile of the target audience (healthcare professionals, research and industry, patients and the general public), the various advantages and disadvantages of each instrument and, last but not least, the communication budget.

2c. NAMMD funding through communication activities

The Agency aims at continued identification, organisation and promotion of fundraising activities based on communication, such as conferences, training sessions etc.

CONCLUSIONS

The National Agency for Medicines and Medical Devices, whose foundations were laid in 1999, is currently recognised on European and international level as an institution fully able to meet requirements imposed by consolidation of its status as regulatory authority in medicinal products for human use of an EU member state.

The most important NAMMD strategic objective is protection and promotion of public health, by accomplishment of the NAMMD primary role, namely warranty of compliance of authorised medical devices with the required standards and intended purpose as well as of their acceptable level of safety. To successfully meet this goal, the NAMMD must continue as an expert and reliable source of accurate and timely information in the field of medicinal products for human use for the most important stakeholders, including healthcare professionals, research and industry, patients and the general public.

DECISION

No. 3/10.05.2013

approval of the priority assessment of marketing authorisation applications through national procedure for International Non-proprietary Names (INNs) determined in short supply on the pharmaceutical market

The Scientific Council of the National Agency for Medicines and Medical Devices (NAMMD), established based on Order of the Minister of Health no. 158/18.02.2013, in accordance with Article 8 (1) of the Regulation on the organisation and operation of the NAMMD Scientific Council on written procedure, hereby adopts the following

DECISION

Sole article. – Priority assessment of marketing authorisation applications through national procedure for INNs determined in short supply on the pharmaceutical market is approved, under (but not limited to) the following circumstances:

- INN included in national healthcare programs and determined in short supply by the specialised commissions of the Ministry of Health;
- NAMMD identification in the Index of medicinal products for human use of maximum three medicinal products with the same pharmaceutical form for the same INN.

PRESIDENT
of the Scientific Council
of the National Agency for Medicines and Medical Devices,

Acad. Prof. Dr. Leonida Gherasim

DECISION
No. 7/22.04.2013

on approval of the templates concerning authorisations and Good Manufacturing Practice and Good Distribution Practice certificates

The Scientific Council of the National Agency for Medicines and Medical Devices (NAMMD), established based on Order of the Minister of Health no. 158/18.02.2013, reunited on summons of the President of the National Agency for Medicines and Medical Devices in the ordinary meeting of 22.04.2013, in accordance with Article 12 (5) of Government Decision no. 734/2010 on organisation and operation of the National Agency for Medicines and Medical Devices, as amended, hereby adopts the following

DECISION

Sole article. – The following templates are approved for authorisations and Good Manufacturing Practice and Good Distribution Practice certificates, in accordance with community legislation (the Compilation of Community Procedures on Inspections and Exchange of Information), in line with the Annexes which are integral part of this Decision:

- Annex A: Form - Manufacturing authorisation;
- Annex B: Form - Good Manufacturing Practice Certificate;
- Annex C: Form - Wholesale Distribution Authorisation;
- Annex D: Form - Good Distribution Practice Certificate;
- Annex E: Form - Good Distribution Practice Certificate for active substances to be used as starting materials for medicinal products for human use.

PRESIDENT
of the Scientific Council
of the National Agency for Medicines and Medical Devices,

Acad. Prof. Dr. Leonida Gherasim

ANNEX A

FORMAT OF THE MANUFACTURING AUTHORISATION

Summary:

- Form - Manufacturing Authorisation
- ANNEXES 1 and/or 2 – Scope of authorisation
- ANNEX 3 – Address(es) of contract manufacturing sites
- ANNEX 4 – Address(es) of contract laboratories
- ANNEX 5 – Qualified Person(s)
- ANNEX 6 – Person(s) responsible for manufacturing/quality control
- ANNEX 7 - Date of inspection on which authorisation was grant
- ANNEX 8 – Medicinal products authorised for manufacturing/import

Format for Manufacturing Authorisation[1,2]

1. Authorisation Number .....

2. Authorisation Holder .....

3. Address(es) of the manufacturing site(s):
.....……
(All authorised sites should be listed if not covered by separate authorisations.)

4. Legally registered address of the Authorisation Holder

5. Scope of authorisation and dosage forms[2] — Annex 1 and/or Annex 2
[Separate Annexes for different sites should be used if not covered by separate authorisations.]

6. Legal basis for authorisation:

7. Responsible person of the National Agency for Medicines and Medical Devices (the Romanian competent authority granting the manufacturing/import authorisation): …….....

8. Annexes……..

9. Date……

[1] The authorisation referred to under Art. 748 (1) of Law 95/2006 is also required for imports from third countries.
[2] A Guideline on the interpretation of this template is available in the EudraGMP database

10. Annexes attached	Annex 1 and/or Annex 2 Annex 3 (Address(es) of contract manufacturing sites) Annex 4 (Address(es) of contract laboratories) Annex 5 (Qualified Person(s)) Annex 6 (Person(s) responsible for manufacturing/quality control) Annex 7 (Date of inspection on which the authorisation was granted) Annex 8 (Medicinal products authorised for manufacturing/import)[3]

[3] The National Agency for Medicines and Medical Devices is responsible for establishing agreement between the authorisation and the manufacturer's application (Art. 750 (3) of Law 95/2006).

ANNEX 1

SCOPE OF AUTHORISATION (please delete the sections which do not apply)

Site name and address:

☐ Medicinal products for human use

AUTHORISED OPERATIONS
☐ Manufacturing operations (according to Part 1)
☐ Importation of medicinal products (according to Part 2)

Part 1 MANUFACTURING OPERATIONS	
1.1	Sterile products
	1.1.1 Aseptically prepared (processing operations for the following dosage forms) 1.1.1.1. Large volume liquids 1.1.1.2. Lyophilisates 1.1.1.3. Semi-solid preparations 1.1.1.4. Small volume liquids 1.1.1.5. Solids and implants 1.1.1.6. Other aseptically prepared products <free text>
	1.1.2 Terminally sterilised (processing operations for the following dosage forms) 1.1.2.1 Large volume liquids 1.1.2.2. Semi-solid preparations 1.1.2.3. Small volume liquids 1.1.2.4. Solids and implants 1.1.2.5. Other terminally sterilised <free text>
	1.1.3 Batch certification

1.2	**Non-sterile products**
	1.2.1 Non-sterile products(processing operations for the following dosage forms) 1.2.1.1. Capsules, hard shell 1.2.1.2. Capsules, soft shell 1.2.1.3. Chewable gums 1.2.1.4. Impregnated matrices 1.2.1.5. Liquids for external use 1.2.1.6. Liquids for internal use 1.2.1.7. Medicinal gases 1.2.1.8. Other solid dosage forms 1.2.1.9. Pressurised preparations 1.2.1.10. Radionuclide generators 1.2.1.11. Semi-solid preparations 1.2.1.12. Suppositories 1.2.1.13. Tablets 1.2.1.14. Transdermal therapeutic systems 1.2.1.15. Other non-sterile products <free text>
	1.2.2 Batch certification
1.3	**Biological medicinal products**
	1.3.1 Biological medicinal products (list of product types) 1.3.1.1 Blood products 1.3.1.2 Immunological products 1.3.1.3 Cell therapy products 1.3.1.4 Gene therapy products 1.3.1.5 Biotechnologicals 1.3.1.6 Human or animal tissue extracted products 1.3.1.7 Tissue engineered products 1.3.1.8 Other biological medicinal products <free text>
	1.3.2 Batch certification (list of product types) 1.3.2.1 Blood products 1.3.2.2 Immunological products 1.3.2.3 Cell therapy products 1.3.2.4 Gene therapy products 1.3.2.5 Biotechnology products 1.3.2.6 Human or animal tissue extracted products 1.3.2.7 Tissue engineered products 1.3.2.8 Other biological medicinal products <free text>
1.4	**Other products or manufacturing activity**
	1.4.1 Manufacture of: 1.4.1.1. Herbal products 1.4.1.2. Homeopathic products 1.4.1.3. Other <free text>
	1.4.2 Sterilisation of active substances/excipients/finished products: 1.4.2.1. Filtration 1.4.2.2. Dry heat 1.4.2.3. Moist heat 1.4.2.4. Chemical 1.4.2.5. Gamma radiation

	1.4.2.6. Electron beam
	1.4.3 Other <free text>
1.5	**Packaging**
	1.5.1 Primary packaging 1.5.1.1. Capsules, hard shell 1.5.1.2. Capsules, soft shell 1.5.1.3. Chewable gums 1.5.1.4. Impregnated matrices 1.5.1.5. Liquids for external use 1.5.1.6. Liquids for internal use 1.5.1.7. Medicinal gases 1.5.1.8. Other solid dosage forms 1.5.1.9. Pressurised preparations 1.5.1.10. Radionuclide generators 1.5.1.11. Semi-solid preparations 1.5.1.12. Suppositories 1.5.1.13. Tablets 1.5.1.14. Transdermal therapeutic systems 1.5.1.15. Other non-sterile products <free text>
	1.5.2 Secondary packaging
1.6	**Quality control tests**
	1.6.1 Microbiological: sterility
	1.6.2 Microbiological: no sterility testing
	1.6.3 Physico/Chemical products
	1.6.4 Biological

Any restrictions or clarifying remarks related to the scope of these manufacturing operations:

.....

.....

Part 2 IMPORTATION OF MEDICINAL PRODUCTS	
2.1	**Quality control testing of imported medicinal products**
	2.1.1 Microbiological: sterility
	2.1..2 Microbiological: no sterility testing
	2.1.3 Physico/Chemical products
	2.1.4 Biological
2.2	**Batch certification of imported medicinal products**
	2.2.1 Sterile products 2.2.1.1 Aseptically prepared 2.2.1.2 Terminally sterilised
	2.2.2 Non-sterile products
	2.2.3 Biological medicinal products 2.2.3.1 Blood products 2.2.3.2 Immunological products 2.2.3.3 Cell therapy products 2.2.3.4 Gene therapy products 2.2.3.5 Biotechnology products 2.2.3.6 Human or animal tissue extracted products 2.2.3.7 Tissue engineered products 2.2.3.8 Other biological medicinal product <free text>
2.3	**Other import activities** (any relevant import activity not mentioned above)
	2.3.1 Site of physical importationation
	2.3.2 Importation of intermediate products which undergo further processing
	2.3.3 Biological active substance
	2.3.4 Other <free text>

Any restrictions or clarifying remarks related to the scope of these importing operations:

.....

.....

SCOPE OF THE AUTHORISATION (delete the sections which do not apply or use yes/no)

Name and address of the site:

☐ Investigational medicinal products (optional)

AUTHORISED OPERATIONS
☐ Manufacturing Operations of Investigational Medicinal Products (according to Part 1)
☐ Importation of Investigational Medicinal Products (according to Part 2)

Part 1 MANUFACTURING OPERATIONS OF INVESTIGATIONAL MEDICINAL PRODUCTS	
1.1	**Sterile Investigational Medicinal Products**
	1.1.1 Aseptically prepared (processing operations for the following dosage forms) 1.1.1.1. Large volume liquids 1.1.1.2. Lyophilisates 1.1.1.3. Semi-solid preparations 1.1.1.4. Small volume liquids 1.1.1.5. Solids and implants 1.1.1.6. Other aseptically prepared products<free text>
	1.1.2 Terminally sterilised (processing operations for the following dosage forms) 1.1.2.1 Large volume liquids 1.1.2.2. Semi-solid preparations 1.1.2.3. Small volume liquids 1.1.2.4. Solids and implants 1.1.2.5. Other terminally sterilised products <free text>
	1.1.3 Batch certification
1.2	**Non-sterile investigational medicinal products**
	1.2.1 Non-sterile products (processing operations for the following dosage forms) 1.2.1.1. Capsules, hard shell 1.2.1.2. Capsules, soft shell 1.2.1.3. Chewable gums 1.2.1.4. Impregnated matrices 1.2.1.5. Liquids for external use 1.2.1.6. Liquids for internal use 1.2.1.7. Medicinal gases 1.2.1.8. Other solid dosage forms 1.2.1.9. Pressurised preparations 1.2.1.10. Radionuclide generators 1.2.1.11. Semi-solid preparations 1.2.1.12. Suppositories 1.2.1.13. Tablets

	1.2.1.14. Transdermal therapeutic systems 1.2.1.15. Other non-sterile product <free text>
	1.2.2 Batch certification
1.3	**Biological investigational medicinal products**
	1.3.1 Biological medicinal products (product list) 1.3.1.1 Blood products 1.3.1.2 Immunological products 1.3.1.3 Cell therapy products 1.3.1.4 Gene therapy products 1.3.1.5 Biotechnologicals 1.3.1.6 Human or animal tissue extracted products 1.3.1.7 Tissue engineered products 1.3.1.8 Other Biological medicinal products <free text>
	1.3.2 Batch certification (product list) 1.3.2.1 Blood products 1.3.2.2 Immunological products 1.3.2.3 Cell therapy products 1.3.2.4 Gene therapy products 1.3.2.5 Biotechnologicals 1.3.2.6 Human or animal tissue extracted products 1.3.2.7 Tissue engineered products 1.3.2.8 Other Biological medicinal products <free text>
1.4	**Other investigational medicinal products or manufacturing activity**
	1.4.1 Manufacture of: 1.4.1.1. Herbal products 1.4.1.2. Homeopathic products 1.4.1.3. Others <free text>
	1.4.2 Sterilisation of active substances/excipients/finished products: 1.4.2.1. Filtration 1.4.2.2. Dry heat 1.4.2.3. Moist heat 1.4.2.4. Chemical 1.4.2.5. Gamma radiation 1.4.2.6. Electron beam
	1.4.3 Others <free text>
1.5	**Packaging**
	1.5.1 Primary packaging 1.5.1.1. Capsules, hard shell 1.5.1.2. Capsules, soft shell 1.5.1.3. Chewable gums 1.5.1.4. Impregnated matrices 1.5.1.5. Liquids for external use 1.5.1.6. Liquids for internal use 1.5.1.7. Medicinal gases 1.5.1.8. Other solid dosage forms 1.5.1.9. Pressurised preparations

	1.5.1.10. Radionuclide generators 1.5.1.11. Semi-solid preparations 1.5.1.12. Suppositories 1.5.1.13. Tablets 1.5.1.14. Transdermal therapeutic systems 1.5.1.15. Other non-sterile products <free text>
	1.5.2 Secondary packaging
1.6	**Quality control testing**
	1.6.1 Microbiological: sterility
	1.6.2 Microbiological: no sterility testing
	1.6.3 Physico/Chemical products
	1.6.4 Biological

Any restrictions or clarifying remarks related to the scope of these manufacturing operations:

.....

.....

Part 2 IMPORTATION OF INVESTIGATIONAL MEDICINAL PRODUCTS	
2.1	**Quality control testing of imported investigational medicinal products**
	2.1.1 Microbiological: sterility
	2.1..2 Microbiological: no sterility testing
	2.1.3 Physico/Chemical
	2.1.4 Biological
2.2	**Batch certification of imported investigational medicinal products**
	2.2.1 Sterile products 2.2.1.1 Aseptically prepared 2.2.1.2 Terminally sterilised
	2.2.2 Non-sterile products
	2.2.3 Biological products 2.2.3.1 Blood products 2.2.3.2 Immunological products 2.2.3.3 Cell therapy products 2.2.3.4 Gene therapy products 2.2.3.5 Biotechnological products 2.2.3.6 Human or animal tissue extracted products 2.2.3.7 Tissue engineered products 2.2.3.8 Other biological medicinal products <free text>
	Other importation activities (any other relevant import authority not included above)
2.3	*2.3.1 Site of physical importation*
	2.3.2 Import of intermediate which undergoes further processing
	2.3.3 Biological active substances
	2.3.4 Other <free text>
	Quality control testing of imported medicinal products

Any restrictions or clarifying remarks related to the scope of these importing operations:

.....

.....

ANNEX 3

Address(es) of contract manufacturing sites:

.....

.....

.....

ANNEX 4

Address(es) of contract laboratories:

.....

.....

.....

ANNEX 5

Qualified Person(s)

.....

.....

.....

Person(s) responsible for quality control:

.....

.....

.....

Person(s) responsible for manufacturing:

.....

.....

.....

ANNEX 7

Date of inspection on which authorisation was granted dd / mm / yyyy

Scope of latest inspection

.....

.....

.....

ANNEX 8

Medicinal products authorised for manufacturing/importation (in accordance with Art. 749 and 750 of Title XVII – The medicinal product of Law no. 95 /2006 on healthcare reform)

.....

.....

.....

.

ANNEX B
to Scientific Council Decision no. 7/22.04.2013

FORM

GOOD MANUFACTURING PRACTICE CERTIFICATE

(HEADER OF THE NATIONAL AGENCY FOR MEDICINES AND MEDICAL DEVICES)

Certificat Nr.: ___/___/___
Certificate No:____/____/____

CERTIFICAT PRIVIND CONFORMITATEA CU BUNA PRACTICĂ DE FABRICAȚIE[4,5]
CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER[1,2]

Partea 1
Part 1

Emis în urma unei inspecții în acord cu art. 111(5) al Directivei 2001/83/EC sau art. 15 al Directivei 2001/20/EC*
*Issued following an inspection in accordance with Art. 111(5) of Directive 2001/83/EC or Art. 15 of Directive 2001/20/EC**

sau
or

Emis în baza prevederilor Acordului de Recunoaştere Mutuală între Uniunea Europeană şi [*Partenerul ARM*].*
*Issued under the provisions of the Mutual Recognition Agreement between the European Union and [MRA Partner].**

Autoritatea competentă AGENȚIA NAȚIONALĂ A MEDICAMENTULUI ŞI A DISPOZITIVELOR MEDICALE din ROMÂNIA confirmă următoarele:
The competent authority NATIONAL AGENCY FOR MEDICINES AND MEDICAL DEVICES in ROMANIA confirms the following:

Fabricantul
The manufacturer
.....

Adresa locului de fabricație
Site address
.....……..

A fost inspectat în cadrul programului național de inspecție referitor la autorizația de fabricație nr. ..... în acord cu art. 40 al Directivei 2001/83/CE consolidată/art. 13 al Directivei 2001/20/EC* transpuse în legislația națională prin art. 748 din Legea nr. 95/2006 privind reforma în domeniul sănătății, Titlul XVII, Medicamentul/art. 48 din Ordinul ministrului sănătății publice nr. 904/2006 pentru aprobarea Reglementărilor privind implementarea regulilor de bună practică în desfăşurarea studiilor clinice efectuate cu medicamente de uz uman*

Has been inspected under the national inspection programme in connection with manufacturing authorisation no. ..... in accordance with Art. 40 of Directive 2001/83/EC/Art. 13 of Directive 2001/20/EC transposed in the following national legislation: art. 748 of Law no. 95/2006 on healthcare reform, Title XVII, The medicinal*

[4] Acest certificat la care se face referire în art. 823(5) din Legea 95/2006 Titlul XVII, Medicamentul este aplicabil şi importatorilor.
The certificate referred to in paragraph 111 (5) of Directive 2001/83, is also applicable to importers.
[5] Îndrumări privind interpretarea acestui format pot fi găsite în meniul de Ajutor al bazei de date EudraGMP.
Guidance on the interpretation of this template can be found in the Help menu of EudraGMP database.

product/art. 48 of Order of the Minister of Public Health no. 904/2006 for approval of Regulations relating to implementation of Good clinical practice in the conduct of clinical trials on medicinal products of human use**

sau

or

A fost inspectat în legătură cu autorizația(autorizațiile) de punere pe piață care se referă la fabricanți situați în afara Spațiului Economic European în acord cu art. Art. 8(2)/33(2)/19(3)/44(3)* al Regulamentului (EC) 726/2004* sau cu art. 111(4) al Directivei 2001/83/CE transpusă în legislația națională prin art. 823 alin. 4 din Legea nr. 95/2006 privind reforma în domeniul sănătății, Titlul XVII, Medicamentul*

Has been inspected in connection with marketing authorisation(s) listing manufacturers located outside of the European Economic Area in accordance with Art. 8(2)/33(2)/19(3)/44(3) of Regulation (EC) 726/2004* or Art. 111(4) of Directive 2001/83/EC transposed in the following national legislation: art. 823 (4) of Law no. 95/2006 on healthcare reform, Title XVII, The medicinal product**

şi/sau)*

*and/or**

Este un fabricant de substanță activă care a fost inspectat în acord cu art. 111(1) al Directivei 2001/83/CE transpusă în legislația națională prin art. 823 alin. 1 din Legea nr. 95/2006 privind reforma în domeniul sănătății, Titlul XVII, Medicamentul*

*Is an active substance manufacturer that has been inspected in accordance with Art. 111(1) of Directive 2001/83/EC transposed in the following national legislation: art. 823 (1) of Law no. 95/2006 on healthcare reform, Title XVII, The medicinal product**

şi/sau*

*and/or**

Este un fabricant de excipient care a fost inspectat în acord cu art. 111(1) al Directivei 2001/83/CE transpusă în legislația națională prin art. 823 alin. 1 din Legea nr. 95/2006 privind reforma în domeniul sănătății, Titlul XVII, Medicamentul*

Is an excipient manufacturer that has been inspected in accordance with Art. 111(1) of Directive 2001/83/EC transposed in the following national legislation art. 823 (1) of Law no. 95/2006 on healthcare reform, Title XVII, The medicinal product**

*sau**

*or**

Altele (se va specifica):.....

Other (please specify): .....

Din informațiile acumulate în timpul inspecției la acest fabricant, ultima fiind efectuată în ...../...../..... [data], se apreciază că acesta respectă cerințele de Bună Practică de Fabricație[3] la care se face referire în Acordul de Recunoaştere Mutuală între Uniunea Europeană şi *[Partenerul ARM]/* Principiile şi ghidurile pentru Buna Practică de Fabricație stabilite în Directiva 2003/94/CE[3]/Principiile BPF pentru substanțe active[3] la care se face referire în art. 47 al Directivei 2001/83/EC*, la un nivel adecvat al BPF conform art. 46(f) al Directivei 2001/83/EC.

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ...../...../..... [date], it is considered that it complies with the Good Manufacturing Practice requirements[1] referred to in the Agreement of Mutual Recognition between the European Union and [MRA partner]/The principles and guidelines of Good Manufacturing Practice laid down in Directive 2003/94/EC[6]/The principles of GMP for active

[6] Aceste cerințe îndeplinesc recomandările de bună practică de fabricație ale Organizației Mondiale a Sănătății
These requirements fulfill the GMP recommendations of WHO

substances[3] referred to in Article 47 of Directive 2001/83/EC. an appropriate level of GMP as referred to in Article 46(f) of Directive 2001/83/EC.*

Acest certificat reflectă statutul locului de fabricație la data inspecției menționată mai sus şi nu mai poate fi luat în considerație dacă de la data acestei inspecții au trecut mai mult de trei ani. Această perioadă de valabilitate poate fi redusă folosind principii de management al riscului în activitatea de reglementare, printr-o remarcă menționată la rubrica „Restricții sau observații care să clarifice".

Acest certificat este valid numai dacă are toate paginile incluse precum şi ambele Părți (1şi 2).

Autenticitatea acestui certificat poate fi verificată în baza de date EudraGMP. Dacă nu este inclus în această bază de date, vă rugăm să contactați autoritatea emitentă.

This certificate reflects the status of the manufacturing site at the time of the inspection noted above and should not be relied upon to reflect the compliance status if more than three years have elapsed since the date of that inspection. However, this period of validity may be reduced or extended using regulatory risk management principles by an entry in the Restrictions or Clarifying remarks field.

This certificate is valid only when presented with all pages and both Parts 1 and 2.

The authenticity of this certificate may be verified in EudraGMP. If it does not appear, please contact the issuing authority.

Partea a 2-a
Part 2

☐ Medicamente de uz uman* *Human Medicinal Products*)* ☐ Medicamente de uz uman pentru investigație clinică* *Human Investigational Medicinal Products**	
1. OPERAȚII DE FABRICAȚIE - MEDICAMENTE* ***MANUFACTURING OPERATIONS – MEDICINAL PRODUCTS***	
11.1	**Produse sterile** ***Sterile Products***
	1.1.1. *Preparate aseptic (operații de procesare pentru următoarele forme dozate*) *Aseptically prepared (processing operations for the following dosage forms)* 1.1.1.1. Lichide volume mari *Large volume liquids* 1.1.1.2. Liofilizate *Lyophilisates* 1.1.1.3. Semisolide *Semi-solids* 1.1.1.4. Lichide volume mici *Small volume liquids* 1.1.1.5. Solide şi implanturi *Solids and implants* 1.1.1.6. Alte medicamente preparate aseptic <se va completa> *Other aseptically prepared products <free text>*
	1.1.2. *Sterilizate final (operații de procesare pentru următoarele forme dozate*) *Terminally sterilised (processing operations for the following dosage forms)* 1.1.2.1. Lichide volume mari *Large volume liquids* 1.1.2.2. Semisolide *Semi-solids* 1.1.2.3. Lichide volume mici *Small volume liquids* 1.1.2.4. Solide şi implanturi *Solids and implants* 1.1.2.5. Alte medicamente sterilizate final <se va completa> *Other terminally sterilised prepared products <free text>*
	1.1.3. Numai certificarea seriei *Batch certification only*
11.2	**Produse nesterile** ***Non-sterile products***
	1.2.1. Produse nesterile (operații de procesare pentru următoarele forme dozate) *Non-sterile products (processing operations for the following dosage forms)* 1.2.1.1. Capsule *Capsules, hard shell* 1.2.1.2. Capsule moi *Capsules, soft shell*

	1.2.1.3. Gume masticabile *Chewing gums* 1.2.1.4. Matrici impregnate *Impregnated matrices* 1.2.1.5. Lichide pentru uz extern *Liquids for external use* 1.2.1.6. Lichide pentru uz intern *Liquids for internal use* 1.2.1.7. Gaze medicinale *Medicinal gases* 1.2.1.8. Alte forme solide dozate *Other solid dosage forms* 1.2.1.9. Preparate presurizate *Pressurised preparations* 1.2.1.10. Generatoare de radionuclizi *Radionuclide generators* 1.2.1.11. Semisolide *Semi-solids* 1.2.1.12. Supozitoare *Suppositories* 1.2.1.13. Comprimate *Tablets* 1.2.1.14. Sisteme terapeutice transdermice *Transdermal patches* 1.2.1.15. Alte medicamente nesterile <se va completa> *1.2.1.15. Other non-sterile medicinal product <free text>*
	1.2.2. Certificarea seriei *Batch certification*
11.3	**Medicamente biologice** ***Biological medicinal products***
	1.3.1. Medicamente biologice *Biological medicinal products* 1.3.1.1. Produse din sânge *Blood products* 1.3.1.2. Produse imunologice *Immunological products* 1.3.1.3. Produse pentru terapia celulară *Cell therapy products* 1.3.1.4. Produse pentru terapia genică *Gene therapy products* 1.3.1.5. Produse obținute prin biotehnologie *Biotechnology products* 1.3.1.6. Produse extrase din țesuturi umane sau animale *Human or animal tissue extracted products* 1.3.1.7. Produse obținute prin inginerie tisulară *Tissue engineered products* 1.3.1.8. Alte medicamente biologice <se va completa> *Other biological medicinal products <free text>*
	1.3.2. Certificarea seriei (lista tipurilor de produse) *Batch certification (list of product types*) 1.3.2.1. Produse din sânge *Blood products* 1.3.2.2. Produse imunologice

	Immunological products 1.3.2.3. Produse pentru terapia celulară *Cell therapy products* 1.3.2.4. Produse pentru terapia genică *Gene therapy products* 1.3.2.5. Produse obținute prin biotehnologie *Biotechnology products* 1.3.2.6. Produse extrase din țesuturi umane sau animale *Human or animal tissue extracted products* 1.3.2.7. Produse obținute prin inginerie tisulară *Tissue engineered products* 1.3.2.8. Alte medicamente biologice <se va completa> *Other biological medicinal products <free text>*
11.4	**Alte medicamente sau activități de procesare** ***Other products or processing activity***
	1.4.1. Fabricație de: *Manufacture of*: 1.4.1.1. Produse din plante *Herbal products* 1.4.1.2. Produse homeopate *Homoeopathic products* 1.4.1.3. Altele <se va completa> *Other <free text>*
	1.4.2. Sterilizarea substanțelor active/excipienților/produselor finite *Sterilisation of active substances/excipients/finished product:* 1.4.2.1. prin filtrare *Filtration* 1.4.2.2. cu căldură uscată *Dry heat* 1.4.2.3. cu căldură umedă *Moist heat* 1.4.2.4. chimică *Chemical* 1.4.2.5. cu radiații Gamma *Gamma irradiation* 1.4.2.6. prin bombardare cu electroni *Electron beam*
	1.4.3. Altele <se va completa> *Other <free text>*
11.5	**Ambalare** ***Packaging***
	1.5.1. Ambalare primară *Primary packing* 1.5.1.1. Capsule *Capsules, hard shell* 1.5.1.2. Capsule moi *Capsules, soft shell* 1.5.1.3. Gume masticabile *Chewing gums* 1.5.1.4. Matrici impregnate *Impregnated matrices* 1.5.1.5. Lichide pentru uz extern *Liquids for external use*

	1.5.1.6. Lichide pentru uz intern *Liquids for internal use* 1.5.1.7. Gaze medicinale *Medicinal gases* 1.5.1.8. Alte forme solide dozate *Other solid dosage forms* 1.5.1.9. Preparate presurizate *Pressurised preparations* 1.5.1.10. Generatoare de radionuclizi *Radionuclide generators* 1.5.1.11. Semisolide *Semi-solids* 1.5.1.12. Supozitoare *Suppositories* 1.5.1.13. Comprimate *Tablets* 1.5.1.14. Sisteme terapeutice transdermice *Transdermal patches* 1.5.1.15. Other non-sterile products <se va completa> *Other non-sterile medicinal products <free text>*
	1.5.2. Ambalare secundară *Secondary packing*
11.6	**Teste pentru controlul calității** ***Quality control testing***
	1.6.1. Microbiologice: sterilitate *Microbiological: sterility*
	1.6.2. Microbiologice: fără testul de sterilitate *Microbiological: non-sterility*
	1.6.3. Fizico-chimice *Chemical/Physical*
	1.6.4. Biologice *Biological*

2. IMPORTUL MEDICAMENTELOR* ***IMPORTATION OF MEDICINAL PRODUCTS****	
2.1	**Teste pentru controlul calității medicamentelor importate** ***Quality control testing of imported medicinal products***
	2.1.1. Microbiologice: sterilitate *Microbiological: sterility*
	2.1.2. Microbiologice: fără testul de sterilitate *Microbiological: non-sterility*
	2.1.3. Fizico-chimice *Chemical/Physical*
	2.1.4. Biologice *Biological*
2.2	**Certificarea seriei medicamentelor importate** ***Batch certification of imported medicinal products***
	2.2.1. Produse sterile *Sterile Products* 2.2.1.1. preparate aseptic *Aseptically prepared* 2.2.1.2. sterilizate final *Terminally sterilised* *2.2.2. Produse nesterile* *Non-sterile products*
	2.2.3. Medicamente biologice *Biological medicinal products* 2.2.3.1. Produse din sânge *Blood products* 2.2.3.2. Produse imunologice *Immunological products* 2.2.3.3. Produse pentru terapia celulară *Cell therapy products* 2.2.3.4. Produse pentru terapia genică *Gene therapy products* 2.2.3.5. Produse obținute prin biotehnologie . *Biotechnology products* 2.2.3.6. Produse extrase din țesuturi umane sau animale *Human or animal extracted products* 2.2.3.7. Produse obținute prin inginerie tisulară *Tissue engineered products* 2.2.3.8. Alte medicamente biologice <se va completa> *Other biological medicinal products <free text >*
2.3	***Alte activități de import*** ***Other importation activities***
	2.3.1 Locul fizic al importului *Site of physical importation*
	2.3.2 Import de produse intermediare care vor fi supuse unor procesări ulterioare *Importation of intermediate which undergoes further processing*
	2.3.3 Altele <se va completa> *Other <free text>*

Orice restricții sau observații care să clarifice domeniul acoperit de acest certificat*:
Any restrictions or clarifying remarks related to the scope of this certificate:*

.....
….....

3. OPERAȚII DE FABRICAȚIE – SUBSTANȚE ACTIVE ***MANUFACTURING OPERATIONS – ACTIVE SUBSTANCES*** Substanța(substanțe) activă(active): *Active substance(s):*	
3.1	**Fabricația de substanțe active prin sinteză chimică** ***Manufacture of Active substance by chemical synthesis***
	3.1.1 Fabricație de intermediari de substanță activă *Manufacture of active substance intermediates* *3.1.2 Fabricație de substanțe active brute* *Manufacture of crude active substance* *3.1.3 Etape de formare de săruri/purificare : <se va completa> (de ex. cristalizare)* *Salt formation/purification steps: <free text> (e.g. crystallization)* *3.1.4 Altele <se va completa>* *Other <free text>*
3.2	**Extracția de substanțe active din surse naturale** ***Extraction of Active Substance from natural sources***
	3.2.1 Extracția de substanțe din surse vegetale *Extraction of substance from plant source* *3.2.2 Extracția de substanțe din surse animale* *Extraction of substance from animal source* *3.2.3 Extracția de substanțe din surse umane* *Extraction of substance from human source* *3.2.4 Extracția de substanțe din surse minerale* *Extraction of substance from mineral source* *3.2.5 Modificarea sustanțelor extrase <se va specifica sursa 1,2,3,4>* *Modification of extracted substance <specify source 1,2,3,4>* *3.2.6 Purificarea substanțelor extrase < se va specifica sursa 1,2,3,4>* *Purification of extracted substance <specify source 1,2,3,4 >* *3.2.7 Altele <se va completa>* *Other <free text>*
3.3	**Fabricație de substanțe active prin procese biologice** ***Manufacture of Active Substance using Biological Processes***
	3.3.1 Fermentare *Fermentation* *3.3.2 Culturi celulare <se va specifica tipul celulelor> (de ex. e.g. de mamifere / bacteriene)* *Cell Culture <specify cell type> (e.g. mammalian / bacterial)* *3.3.3 Izolare/Purificare* *Isolation / Purification* *3.3.4 Modificare* *Modification* *3.3.5 Altele <se va completa>* *Other <free text>*
3.4	**Fabricație de substanțe active sterile (secțiunile 3.1, 3.2, 3.3 vor fi completate după caz)** ***Manufacture of sterile active substance (sections 3.1, 3.2, 3.3 to be completed as applicable)***
	3.4.1 Preparate aseptic *Aseptically prepared*

	3.4.2 Sterilizate final *Terminally sterilised*
3.5	**Etape generale finale** ***General Finishing Steps***
	3.5.1 Etape de procesare fizică <se va specifica> (de ex. uscare, măcinare/micronizare, sitare) *Physical processing steps < specify > (e.g. drying, milling / micronisation, sieving)* *3.5.2 Ambalare primară (ambalarea/sigilarea substanței active într-un material de ambalare care este în contact direct cu substanța)* *Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)* *3.5.3 Ambalare secundară (punerea ambalajului primar sigilat într-un ambalaj secundar sau recipient. Aceasta include orice etichetare a materialului care poate fi utilizată pentru identificarea şi trasabilitatea (număr de serie) substanței active)* *Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)* *3.5.4 Altele <se va completa> (pentru operații care nu sunt descrise mai sus)* *Other <free text> (for operations not described above)*
3.6	**Teste pentru controlul calității** **Quality control testing**
	3.6.1 Testare fizico-chimică *Physical/Chemical testing* *3.6.2 Testare microbiologică (fără testul de sterilitate)* *Microbiological testing (excluding sterility testing)* *3.6.3 Testare microbiologică (inclusiv testul de sterilitate)* *Microbiological testing (including sterility testing)* *3.6.4 Testare biologică* *Biological Testing*

4. ALTE ACTIVITĂȚI – SUBSTANȚE ACTIVE
OTHER ACTIVITIES – ACTIVE SUBSTANCES
<se va completa>
<free text>

Orice restricții sau observații care să clarifice domeniul acoperit de acest certificat*:
Any restrictions or clarifying remarks related to the scope of this certificate:*
.....
….....

..../..../.... [*data*]
[*date*]

Numele, titlul şi semnătura persoanei autorizate din Agenția Națională a Medicamentului şi a Dispozitivelor Medicale din România[3]
Name and signature of the authorised person of the National Agency for Medicines and Medical Devices from Romania[3]

.....
[*autoritatea națională, numerele de telefon şi fax*]
[*name, title, national authority,phone & fax numbers*]

(*): se va şterge ceea ce nu este aplicabil.
(*): delete that which does not apply.

---

[3] Semnătura, data şi detaliile de contact trebuie să apară pe fiecare pagină a certificatului.
[3] *The signature, date and contact details should appear on each page of the certificate.*

ANNEX C
to Scientific Council Decision no. 7/22.04.2013

FORM

WHOLESALE DISTRIBUTION AUTHORISATION

(MEDICINAL PRODUCTS FOR HUMAN USE)

FORMAT OF THE AUTHORISATION FOR WHOLESALE DISTRIBUTION (FOR MEDICINAL PRODUCTS FOR HUMAN USE)

1. Number of the authorisation

2. Marketing Authorisation Holder

3. Legally registered address of the Marketing Authorisation Holder

4. Address(es) of the site(s)
(All sites should be listed, if not covered by separate authorisation)

5. Scope of authorisation (please fill in for each site mentioned under Section 4)

6. Legal basis for authorisation

7. Responsible person of the National Agency for Medicines and Medical Devices

8. Signature

9. Date

10. Annexes attached:

ANNEX 1 Scope of wholesale distribution authorisation

ANNEX 2 Address(es) of contract wholesale distribution site(s) and its/their authorisation numbers

ANNEX 3 Name(s) of responsible person(s)

ANNEX 4 Date of inspection on which authorisation was granted

ANNEX 1

SCOPE OF WHOLESALE DISTRIBUTION AUTHORISATION

Name and address of the site:

1. MEDICINAL PRODUCTS

1.1 ☐ with a marketing authorisation in European Economic Area (EEA) country/countries

1.2 ☐ without marketing authorisation in European Economic Area (EEA) country/countries and intended for the European Economic Area* market

1.3 ☐ without marketing authorisation in European Economic Area country/countries and intended for exportation

2. AUTHORISED WHOLESALE DISTRIBUTION OPERATIONS

2.1 ☐ Procurement

2.2 ☐ Holding

2.3 ☐ Supply

2.4 ☐ Export

2.5 ☐ Other activities <please specify>

3. Medicinal products with additional requirements

3.1 ☐ Medicinal products according to Art. 794 of Law 95/2006 – Title XVII[7]

- **3.1.1** ☐ Narcotic or psychotropic products
- **3.1.2** ☐ Medicinal Products derived from blood
- **3.1.3** ☐ Immunological medicinal products
- **3.1.4** ☐ Radiopharmaceuticals (radionuclide kits included)

3.2 ☐ Medicinal gases

3.3 ☐ Cold chain products (requiring low temperature handling)

3.4 ☐ Other products: <please specify >

Any restrictions or clarifying remarks related to the scope of these wholesaling distribution operations:

.....

*Art. 699 of Law 95/2006 – Title XVII or Art. 83 of Regulation EC/726/2004

[7] Without prejudice to further authorisations as may be required according to national legislation

ANNEX 2

Address(es) of contract wholesale distribution site(s) and its/their authorisation number(s) .....
.....
.....

ANNEX 3

Name of responsible person(s) .....

ANNEX 4

Date of inspection on which authorisation was granted dd/mm/yyyy
.....

ANNEX D
to Scientific Council Decision no. 7/22.04.2013

FORM

GOOD DISTRIBUTION PRACTICE CERTIFICATE

(HEADER OF THE NATIONAL AGENCY FOR MEDICINES AND MEDICAL DEVICES)

Certificat Nr: _ _ _/_ _ _/_ _ _ / Pagina Nr__
Certificate No: _ _ _/_ _ _/_ _ _ / Page No__

CERTIFICAT PRIVIND CONFORMITATEA CU BUNA PRACTICĂ DE DISTRIBUȚIE

CERTIFICATE OF GDP COMPLIANCE OF A WHOLESALE DISTRIBUTOR

Emis în urma unei inspecții în acord cu art. 823 din Legea 95/2006 – Titlul XVII
Issued following an inspection in accordance with Art. 111 of Directive 2001/83/EC

Autoritatea competentă AGENȚIA NAȚIONALĂ A MEDICAMENTULUI ŞI A DISPOZITIVELOR MEDICALE confirmă următoarele:
The competent authority NATIONAL AGENCY FOR MEDICINES AND MEDICAL DEVICES confirms the following:

Distribuitorul angro
The wholesale distributor
…….
Adresa locului
Site address ……

A fost inspectat în cadrul programului național de inspecție referitor la autorizația numărul…. în acord cu art. 77 (1) al Directivei 2001/83/EC transpusă în legislația națională prin art. 788 alin. (1) din Legea 95/2006 privind reforma în domeniul sănătății,Titlul XVII, Medicamentul.

Has been inspected under the national inspection programme in connection with authorisation number …… in accordance with Art. 77 (1) of Directive 2001/83/EC transposed in the following national legislation: art. 788 (1) of Law 95/2006 on healthcare reform, Title XVII, The medicinal product.

Din informațiile acumulate în timpul inspecției la acest distribuitor angro, ultima fiind efectuată în …./…./…. [data], se apreciază că acesta respectă cerințele de Bună Practică de Distribuție la care se face referire în art. 795 din Legea 95/2006 privind reforma în domeniul sănătății,Titlul XVII, Medicamentul.

From the knowledge gained during inspection of this wholesale distributor, the latest of which was conducted on ...../……/…… [date], it is considered that it complies with the Good Distribution Practice requirements laid down in Article 795 of Law 95/2006 on healthcare reform, Title XVII, The medicinal product.

Acest certificat reflectă statutul locului de distribuție la data inspecției menționată mai sus şi nu mai poate fi luat în considerație dacă de la data acestei inspecții au trecut mai mult de cinci ani. Această perioadă de valabilitate poate fi redusă folosind principii de management al riscului în activitatea de reglementare, printr-o remarcă menționată la rubrica „Restricții sau observații care să clarifice".

This certificate reflects the status of the premises at the time of the inspection noted above and should not be relied upon to reflect the compliance status if more than five years have elapsed since the date of that inspection. However this period of validity may be reduced using regulatory risk management principles, by an entry in the Restrictions or Clarifying Remarks field.

Acest certificat este valid numai dacă are toate paginile incluse.
This certificate is valid only when presented with all pages.

Autenticitatea acestui certificat poate fi verificată în baza de date a Uniunii Europene. Dacă nu este inclus în această bază de date, vă rugăm să contactați autoritatea emitentă.
The authenticity of this certificate may be verified in the Union database. If it does not appear please contact the issuing authority.

Orice restricții sau observații care să clarifice domeniul acoperit de acest certificat:
Any restrictions or clarifying remarks related to the scope of this certificate:

.....

……/……/…… *[*Data*]*

Numele, titlul şi semnătura persoanei autorizate din Agenția Națională a Medicamentului și a Dispozitivelor Medicale din România[1]
Name and signature of the authorised person of the National Agency for Medicines and Medical Devices of Romania[8]
.....

[autoritatea națională, numerele de telefon şi e-mail pentru solicitări]
[name, title, national authority, phone, email in case of enquiries]

Detalii ale autorizației pot fi găsite în baza de date a Uniunii Europene.

Details of the authorisation can be found in the Union Database.

[8] Semnătura, data şi detaliile de contact trebuie să apară pe fiecare pagină a certificatului
The signature, date and contact details should appear on each page of the certificate.

ANNEX E
to Scientific Council Decision no. 7/22.04.2013

FORM

GOOD DISTRIBUTION PRACTICE CERTIFICATE FOR ACTIVE SUBSTANCES TO BE USED AS STARTING MATERIALS IN MEDICINAL PRODUCTS FOR HUMAN USE

(HEADER OF THE NATIONAL AGENCY FOR MEDICINES AND MEDICAL DEVICES)

Certificat Nr: _ _ _/_ _ _/_ _ _/ Pagina Nr.
Certificate No: _ _ _/_ _ _/_ _ _ / Page No

CERTIFICAT PRIVIND CONFORMITATEA CU BUNA PRACTICĂ DE DISTRIBUȚIE PENTRU SUBSTANȚE ACTIVE CARE VOR FI UTILIZATE CA MATERII PRIME PENTRU MEDICAMENTE DE UZ UMAN
CERTIFICATE OF GDP COMPLIANCE OF A DISTRIBUTOR OF ACTIVE SUBSTANCES FOR USE AS STARTING MATERIALS IN MEDICINAL PRODUCTS FOR HUMAN USE

Emis în urma unei inspecții în acord cu art. 823 din Legea 95/2006 – Titlul XVII
Issued following an inspection in accordance with Art. 111 of Directive 2001/83/EC

Autoritatea competentă AGENȚIA NAȚIONALĂ A MEDICAMENTULUI ŞI A DISPOZITIVELOR MEDICALE confirmă următoarele:
The competent authority NATIONAL AGENCY FOR MEDICINES AND MEDICAL DEVICES confirms the following:

Distribuitorul substanței active
The active substance distributor
……..……

Adresa locului
Site address
……

A fost inspectat în acord cu art. 111(1) al Directivei 2001/83/EC transpusă în legislația națională prin art. 823 alin. (1) din Legea 95/2006 privind reforma în domeniul sănătății, Titlul XVII, Medicamentul

și în legătură cu numărul de înregistrare*:
has been inspected in accordance with Art. 111(1) of Directive 2001/83/EC transposed in the following national legislation: art. 823(1) of Law 95/2006 on healthcare reform, Title XVII, The medicinal product.

and in connection with registration no:*

……

Din informațiile acumulate în timpul inspecției la acest distribuitor angro, ultima fiind efectuată în …./…./…. [data], se apreciază că acesta respectă cerințele de Bună Practică de Distribuție la care se face referire în art. 795 din Legea 95/2006 privind reforma în domeniul sănătății,Titlul XVII, Medicamentul.
From the knowledge gained during inspection of this active substance distributor, the latest of which was conducted on ...../……/…… [Date], it is considered that it complies with the principles of good distribution practice for active substances referred to in article 795 of Law 95/2006 on healthcare reform, Title XVII, The medicinal product.

Acest certificat reflectă statutul locului de distribuție la data inspecției menționată mai sus

şi nu mai poate fi luat în considerație dacă de la data acestei inspecții au trecut mai mult de cinci ani. Această perioadă de valabilitate poate fi redusă folosind principii de management al riscului în activitatea de reglementare, printr-o remarcă menționată la rubrica „Restricții sau observații care să clarifice”.
This certificate reflects the status of the site at the time of the inspection noted above and should not be relied upon to reflect the compliance status if more than five years have elapsed since the date of that inspection. However this period of validity may be reduced using regulatory risk management principles, by an entry in the Restrictions or Clarifying Remarks field.

Autenticitatea acestui certificat poate fi verificată în baza de date a Uniunii Europene. Dacă nu este inclus în această bază de date, vă rugăm să contactați autoritatea emitentă.
The authenticity of this certificate may be verified in the Union database. If it does not appear please contact the issuing authority.

Orice restricții sau observații care să clarifice domeniul acoperit de acest certificat:
Any restrictions or clarifying remarks related to the scope of this certificate:

.....

.....

……/……/…… *[*Data*]*

Numele, titlul şi semnătura persoanei autorizate din Agenția Națională a Medicamentului şi a Dispozitivelor Medicale din România[1]
Name and signature of the authorised person of the National Agency for Medicines and Medical Devices of Romania[9]
.....

[autoritatea națională, numerele de telefon şi e-mail pentru solicitări]
[name, title, national authority, phone, email in case of enquiries]

Se şterge unde nu este aplicabil/*Delete where not applicable

[9] Semnătura, data şi detaliile de contact trebuie să apară pe fiecare pagină a certificatului
The signature, date and contact details should appear on each page of the certificate.

DECISION

No. 8/22.04.2013
on Procedure for dealing with serious GMP non-compliance or voiding/suspension of CEPS thus requiring co-ordinated administrative action

The Scientific Council of the National Agency for Medicines and Medical Devices (NAMMD), established based on Order of the Minister of Health no. 158/18.02.2013, reunited on summons of the President of the National Agency for Medicines and Medical Devices in the ordinary meeting of 22.04.2013, in accordance with Article 12(5) of Government Decision no. 734/2010 on establishment, organisation and operation of the National Agency for Medicines and Medical Devices, as amended, adopts the following

DECISION

Art. 1. – The Procedure for dealing with serious GMP non-compliance or voiding/suspension of CEPS thus requiring co-ordinated administrative action is approved, in accordance with the Annex which is integral part of this Decision.

Art. 2. – On this Decision coming into force, Scientific Council Decision no. 3/2009 on procedure for dealing with serious GMP non-compliance or voiding/suspension of CEPS thus requiring co-ordinated administrative action is repealed.

PRESIDENT
of the Scientific Council
of the National Agency for Medicines and Medical Devices,

Acad. Prof. Dr. Leonida Gherasim

ANNEX
to SCD no. 8/22.04.2013

PROCEDURE

for dealing with serious Good Manufacturing Practice (GMP) non-compliance or voiding/suspension of CEPS thus requiring co-ordinated administrative action

CHAPTER I

Scope

Art. 1. – This procedure is a translation into Romanian and an adaptation of Procedure EMA/INS/GMP/321252/2012 Rev 15 of the European Medicines Agency (EMA) for dealing with serious Good Manufacturing Practice (GMP) non-compliance or voiding/suspension of CEPS thus requiring co-ordinated administrative action.

CHAPTER II
Summary

Art. 2. – A consolidated procedure for dealing with all circumstances of serious GMP non-compliance, whether found at a manufacturing authorisation holder, third country manufacturer or active substance manufacturer is necessary to ensure a coordinated approach to potential risks to public health.

Art. 3. – (1) This document replaces Annex 3 of the Guideline on exchange of Information on Manufacturers and Manufacturing or Wholesale Distribution Authorisations between Competent Authorities in the European Economic Area, approved through Decision of the Scientific Council of the National Medicines Agency (NMA) no. 15/15.06.2007.

(2) The respective Annex deals with serious GMP non-compliance found at a third country manufacturing site where co-ordinated administrative action is necessary.

Art. 4. – Suspension or voiding of a Certificate of the European Pharmacopoeia (CEP) may be a recommended action following an inspection of an active substance manufacturer but this procedure additionally addresses action to be taken in the event of notification by the European Directorate for the Quality of Medicines (EDQM) that a CEP has been voided or suspended for reasons other than serious GMP non-compliance, as the actions and consequences are similar.

Art. 5. – The reporting inspectorate should enter the information on serious GMP non-compliance in EudraGMP, as referred in Article 823(6) of Law no. 95/2006 on healthcare reform, Title XVII - The medicinal product, as amended.

Art. 6. – (1) The procedure requires the inspectorate discovering serious GMP non-compliance to recommend appropriate action, involving other authorities that share supervisory responsibility in developing those recommendations, and to communicate the recommendations to all other authorities in the Community.

(2) Communication with partner authorities in the Mutual Recognition Agreement (MRA) may also be necessary.

Art. 7. – Provision is made in the procedure for a teleconference to give authorities receiving notification of serious GMP non-compliance an opportunity to seek clarifications and to confirm the appropriateness of the recommended actions before they are implemented at Community level.

Art. 8. – The Romanian competent authority, the National Agency for Medicines and Medical Devices, must take into account the information on serious GMP non-compliance

received and should follow the actions recommended, where the procedure requires it to do so, unless it can justify alternative action based on specific national considerations and where those alternative actions have no impact on other Member States.

Art. 9. – (1) With regard to actions, directly or consequential, against marketing authorisations, the Reference Member State takes the initiative for medicinal products authorised through mutual recognition/decentralised procedure.

(2) The European Medicines Agency (EMA) co-ordinates action for centrally authorised medicinal products.

(3) The NAMMD takes responsibility for marketing authorisations that exist purely at national level.

CHAPTER III
Definitions

Art. 10. – For the purposes of this procedure, serious GMP non-compliance is non-compliance with GMP that in the opinion of the reporting inspectorate is of such nature that administrative action is necessary to remove a potential risk to public health.

Art. 11. – For the purposes of this procedure, administrative action is one of the actions described in Chapter VII.

CHAPTER IV
Principles

Art. 12. – (1) The GMP inspection report should provide a sound conclusion on overall compliance/non-compliance with GMP principles and Guidelines, as defined in the Order of the Minister of Public Health no. 905/2006 on approval of the Principles and guidelines for good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use and in NAMMD Scientific Council Decision no. 5/2012 on the Guideline on Good Manufacturing Practice.

(2) It is understood that a company can be considered to be in general GMP compliant even if there is a certain degree of non-compliance, fact which, according to the inspector, can be resolved without administrative action being taken.

Art. 13. – (1) Action following the discovery of any non-compliance should be commensurate with the level of risk posed by the non-compliance.

(2) Serious non-compliance by definition requires administrative action to be taken.

Art. 14. – (1) All inspections carried out by the inspection services of any Member States are performed on behalf of the entire Community [10].

(2) The discovery of serious GMP non-compliance may have implications not only for the Member State carrying out the inspection but also other, possibly all, Member States.

(3) Therefore a mechanism that ensures consistent, co-ordinated action throughout the Community is required.

Art. 15. – Although Member States may make a reasoned request to another Member State to receive an inspection report, the authority that carries out the inspection, with first-hand information is best placed to assess the potential impact of, and to manage the risk posed by, the level of GMP non-compliance discovered.

Art. 16. – Exceptionally, where, following proper assessment, specific national factors alter the risk such that the agreed Community action in connection with a marketing authorisation, or a rapid alert is not considered, on balance, to be in the interest of public health in Romania, this Member State may, in accordance with Community legislation, decide to take

[10] This includes inspections requested by the European Commission, EMA and EDQM but excludes those performed under contract to WHO. Until further notice serious non-compliance discovered during an inspection on behalf of WHO is not subject to this procedure.

alternative action to that proposed by the Member State revealing the serious GMP non-compliance.

Art. 17. – (1) With regard to actions, directly or consequential, against marketing authorisations, the Reference Member State takes the initiative for medicinal products authorised through mutual recognition/decentralised procedure.

(2) EMA co-ordinates action for centrally authorised medicinal products.

(3) The NAMMD takes responsibility for marketing authorisations that exist purely at national level.

Art. 18. – Unnecessary communication of non-compliance should be avoided in order to make efficient use of the Community alert mechanisms.

CHAPTER V
Scope

Art. 19. – (1) Most GMP inspections reveal a degree of non-compliance and even if failures to comply are cited as being "major", or occasionally, "critical", matters can usually reach a satisfactory conclusion, sometimes involving follow-up inspections, without administrative action being taken.

(2) This procedure applies only when the level of non-compliance is such that the inspector concerned recommends that administrative action is taken to remove a potential risk to public health and that recommendation is ratified in accordance with internal national procedures.

(3) Procedures should require the adherence to timelines that ensure that serious non-compliance is dealt with in a timely manner.

Art. 20. – (1) This procedure applies to all GMP inspections where serious GMP non-compliance is discovered whether on the territory of the Supervisory Authority or, in third countries, including inspections requested by the manufacturer, European Commission, EMA or EDQM.

(2) It applies to inspections of active substance manufacturers, manufacturers of medicinal products, manufacturers of investigational medicinal products as well as quality control laboratories.

(3) It applies to inspections in third countries covered under the distant assessment procedure.

Art. 21. – In order to avoid unnecessary use of Community alert mechanisms, communication of serious GMP non-compliance in accordance with this procedure should not be initiated when the information and action is of no interest to any other Member State; examples are given in Article 40.

Art. 22. – All serious GMP non-compliance relating to active substance manufacturers and all types of manufacturers located in third countries must be communicated even if it is known that no other Member State has an interest at the time as it may be important for all Member States to have the information available in the future.

Art. 23. – (1) The discovery of serious GMP non-compliance at an active substance manufacturer associated with a CEP and inspected at the request of EDQM may lead to action by EDQM in connection with the CEP, such as suspension or voiding.

(2) However, this procedure must still be invoked in order to ensure coordinated, harmonised action regarding the serious GMP non-compliance itself.

Art. 24. – The procedure also deals with cases where a CEP is declared void by EDQM for reasons unrelated to an inspection outcome as consequential action may be needed, which must be properly implemented and coordinated.

CHAPTER VI
Responsibilities

Art. 25. – (1) Following a GMP inspection, the inspection report must conclude whether the inspected company complies with the principles and guidelines of GMP or not.

(2) If the conclusion is that the inspected company is not GMP compliant, then the inspector concerned should recommend what risk-mitigating action is necessary such as administrative action, including whether a rapid alert is necessary for medicinal products/batches released onto the market and/or whether a prohibition of supply should be enforced.

Art. 26. – With regard to inspections relating to medicinal products and investigational medicinal products, if the authority performing the inspection is not the Supervisory Authority it should involve the Supervisory Authority before issuing any non-compliance report so that any proposed regulatory action can be initially agreed.

Art. 27. – (1) As a national competent authority, the NAMMD should have an internal national procedure to review inspection reports from its own inspectors which recommend administrative action in order to decide whether to support the inspectors recommended action or whether alternative action is more appropriate.

(2) According to this procedure, this decision should be reached, and if administrative action is supported, communicated to other competent authorities in accordance with this procedure, within a timeframe appropriate to the potential threat to public health.

Art. 28. – The Supervisory Authority is responsible for taking action against manufacturing authorisation holders under its supervision and/or disciplinary action against Qualified Persons (QPs) connected with manufacturing authorisations under its supervision.

Art. 29. – With regard to marketing authorisations, any recommendations made by the authority reporting the serious GMP non-compliance must take account of the interests of the Community as a whole, regardless as to any specific national considerations as referred to in Article 16 above.

Art. 30. – (1) With regard to actions, directly or consequential, against marketing authorisations, the Reference Member State takes the initiative for medicinal products authorised through mutual recognition/decentralised procedure.

(2) The EMA co-ordinates action for centrally authorised medicinal products.

(3) The NAMMD takes responsibility for marketing authorisations that exist purely at national level.

Art. 31. - Prohibition of supply as a result of GMP non-compliance is action in connection with the marketing authorisation and responsibility should be taken as described in Article 30.

Art. 32. – (1) MRA partners are obliged to notify recipients of GMP certificates exchanged in the context of the MRA when those certificates are withdrawn due to GMP non-compliance.

(2) Since manufacturers themselves may also request GMP certificates to provide to MRA partner authorities, Member States inspectorates should notify all MRA partners when serious GMP non-compliance has been discovered.

Art. 33. – (1) Where an inspection of an active substance manufacturer has been carried out at the request of the EDQM in connection with the CEP scheme and serious GMP non-compliance is revealed the inspectors involved should bear in mind that they have a dual responsibility.

(2) They should follow the procedures established by EDQM to determine the consequences for the CEP(s) in question, and they have an obligation to the Community to follow this procedure for notifying the serious GMP non-compliance.

(3) Every effort should be made to issue the non-compliance statement at the same time as the notification from EDQM concerning affected CEPs.

Art. 34. – (1) In cases where a CEP has been voided for non-GMP reasons EDQM notifies all national competent authorities using the agreed contact points.

(2) In its notification EDQM should indicate the reasons for voiding in order that authorities receiving the information can decide whether the quality, safety or efficacy of medicinal products already on the market is adversely affected and whether therefore a rapid alert is needed.

Art. 35. – If the authority reporting the serious GMP non-compliance considers it necessary to remove medicinal products or certain batches from the market, it is responsible for issuing the Rapid Alert.

Art. 36. – In the event that a rapid alert is necessary in response to CEP voiding or suspension in the circumstances mentioned in Article 33, 34 and VIII.2, responsibility for issuing the rapid alert is as follows:

- the Reference Member State - for affected medicinal products subject to the Decentralised or Mutual Recognition procedures,
- the EMA will co-ordinate in the same way as a quality defect, for centrally authorised medicinal products,
- For medicinal products subject to national marketing authorisations only, a national recall may suffice. No rapid alert is necessary unless under the specific circumstances it is concluded that a class 1 defect is being handled, or, it is likely that the batches in question are on the market in other Member States.

Art. 37. – Where the agreed action is suspension of a clinical trial each National Competent Authority authorising the trial in question should make appropriate entry into the EudraCT database.

CHAPTER VII
Types and consequences of administrative action

Art. 38 – (1) Some actions may lead to consequential actions. For instance, if a manufacturing authorisation is revoked or suspended or a CEP is voided or suspended it will have an impact on one or more marketing authorisations.

(2) Serious GMP non-compliance found at an active substance manufacturer means that manufacturing authorisation holders using the active substance in question as a starting material have failed to fulfil their legal obligations and therefore action may be taken against the manufacturing authorisation or QPs connected with it.

(3) One or more of the following actions is/are possible.

(4) It is stressed that these are options and Romania should take measures that are the most appropriate to the specific circumstances:

VII.1 Community notification of GMP non-compliance

Art. 39. – Apart from the situations described under Art. 40, the information related to non-compliance with GMP should be introduced in the EudraGMP database.

Art. 40 – (1) Community notification of serious GMP non-compliance is not necessary where the action to be taken is of no interest to any other Member State. Examples include:

- Action restricted to disciplining a QP;
- Action restricted to refusal to grant a manufacturing authorisation or application to vary a manufacturing authorisation;
- For manufacturers located in the Community, action limited to the issue of a restricted GMP certificate without corresponding action being deemed necessary, at the time, with regard to the relevant manufacturing authorisation.

(2) Note: Such action would allow continued manufacture but would put pressure on the manufacturing authorisation holder concerned to take corrective action before taking steps against

the manufacturing authorisation are taken, and the remainder of this procedure invoked. This approach is not suitable for manufacturers located in third countries since the close level of supervision implied is not feasible. Furthermore the GMP certificate for a third country manufacturer carries more weight within the Community regulatory system than it does for manufacturers subject to a Community manufacturing authorisation, where the manufacturing authorisation is the primary means of confirming GMP compliance.

VII.2 Withdrawal of GMP certificate or Issue of GMP certificate with restricted scope

Art. 41. – (1) Existing valid GMP certificates with conflicting information will be superseded and should therefore be withdrawn according to Decision no. 22/28.09.2007 on approval of the Guideline for the procedure for the issue and update of GMP certificates.

(2) In some cases, if the non-compliance is partial e.g. involving a limited category of dosage forms a new GMP certificate might also be issued, but restricted as appropriate.

Art. 42. – (1) A GMP certificate may be restricted for reasons other than serious GMP non-compliance, for example where a third country manufacturer is only partly inspected.

(2) However, if a certificate is restricted because of serious non-compliance then this procedure must be followed and a notification of non-compliance entered into EudraGMP, unless Article 40 applies.

VII.3 Actions taken against a manufacturing/importing authorisation

Art. 43. – Except under the specific circumstances described in section 6.1.2, consequential administrative action will be required for any directly affected manufacturing authorisation; otherwise there will be an unintentional inconsistency in the information available in the EudraGMP database.

Art. 44. – The actions against a manufacturing authorisation may involve the following:

a. Refusal to grant a manufacturing authorisation or an application to vary a manufacturing authorisation.

b. Total or partial suspension or revocation of the manufacturing authorisation.

VII.4 Voiding or suspension of CEP

Art. 45. – (1) The EDQM is responsible for actions directly involving CEPs.

(2) However, if a CEP is voided, marketing authorisations depending solely on the CEP are invalid and should be suspended until the dossier is supplemented through variation with new information on the active substance.

(3) If the grounds for voiding the CEP are related to GMP non-compliance then an alternative active substance manufacturer would need to be added through a variation unless an alternative active substance manufacturer is already authorised, in which case the non-compliant active substance manufacturer should be removed through a variation procedure.

Art. 46 – (1) CEPs may be voided for reasons unrelated to inspections, for example failure to fulfil critical commitments.

(2) Upon such notification by EDQM, the NMA should establish whether it has issued national marketing authorisations that depend on the CEP(s) in question, and, where relevant, whether Romania is a Reference Member State.

(3) The EMA will assess any impact on centrally authorised medicinal products.

Art. 47. – (1) Marketing authorisations depending on the CEP are invalid and should be suspended until the dossier is supplemented through variation with new information on the active substance and should therefore be suspended, unless an alternative source of active substance is

authorised which is unaffected by the voided CEP.

(2) The Reference Member State should take the initiative in taking action against marketing authorisations subject to the mutual recognition or decentralised procedures.

(3) The EMA will co-ordinate the actions relating to centrally authorised medicinal products.

(4) The NAMMD takes action against the marketing authorisation in the case of medicinal products authorised solely on a national basis.

VII.5 Actions related to marketing authorisations

Art. 48 – (1) Actions that can be taken include refusal to grant a marketing authorisation or application for variation, suspension or withdrawal.

(2) A marketing authorisation holder may also decide to withdraw a marketing authorisation voluntarily.

Art. 49. – (1) In the context of this procedure actions against marketing authorisations may be a consequence of action against the manufacturing authorisation or as a result of suspension or voiding of a CEP.

(2) It is possible however that the most appropriate course of action is the one taken against the marketing authorisation(s) alone; for example, a marketing authorisation listing a seriously non-compliant third country manufacturing site may need to be suspended or revoked unless an alternative manufacturing site is already authorised.

(3) A seriously non-compliant third country manufacturing site may need to be removed from a marketing authorisation through a variation.

Art. 50. – (1) Automatically suspending marketing authorisations associated with a non-compliant manufacturing site, where no alternative manufacturing site is authorised may not always be the most appropriate approach since if the manufacturing activity is suspended then this alone should serve to safeguard public health.

(2) If the suspension or withdrawal of the manufacturing authorisation is partial then not all marketing authorisations listing the site will be affected.

Art. 51. – In this case, the Reference Member State, for medicinal products subject to decentralised or mutual recognition procedures, the EMA in the case of medicinal products authorised through centralised procedure, or the NAMMD in the case of medicinal products authorised on a national basis only takes action against the marketing authorisation.

VII.6 Impact on clinical trials

Art. 52. – (1) If serious GMP non-compliance is discovered at the manufacturer of investigational medicinal products the impact on any completed or ongoing clinical trials will need to be taken into account in the recommendations of the reporting inspectorate.

(2) Trials may need to be suspended.

(3) Furthermore in some cases the results of completed trials may be doubted. Interruption, suspension or prohibition of trial must be entered into EudraCT.

Art. 53. – (1) The authority that carried out the inspection should involve the sponsor as well as the manufacturer in order to identify all affected trials.

(2) If trials are prematurely terminated appropriate entries in EudraCT must be made.

VII.7 Rapid Alert

Art. 54. – Based on the information in the inspection report the authority reporting the serious GMP non-compliance should decide, in addition to any other action, whether or not it is necessary to take action with respect to batches of affected medicinal product(s) already on the market or being used in clinical trials.

Art. 55. - For CEP voiding by EDQM that is unrelated to the outcome of an inspection, the Reference Member State (or EMA in the exceptional case that centrally authorised medicinal products authorised are affected) should recommend whether any batches should be recalled and invoke any Rapid Alert based on the information provided by EDQM on the reasons for voiding or suspension in its notice of voiding/suspension or, if necessary, following discussion with EDQM.

Art. 56. – In the context of this procedure responsibility for issuing a rapid alert is outlined in Article 36.

VII.8 Prohibition on supply

Art. 57. – Based on the information in the inspection report the authority reporting the serious GMP non-compliance should decide, in addition to any other action, whether or not to recommend a prohibition on supply to prevent medicinal products or batches from being released to the market or for use in clinical trials.

VII.9 Disciplinary measures against the Qualified Person(s)

Art. 58. – (1) This action can be taken by the Supervisory authority if deemed appropriate. In some cases it may be the only required action.

(2) If this is the only action taken there is no impact on other Member States (see Article 40).

CHAPTER VIII
Communication

VIII.1 Serious GMP non-compliance

Art. 59. – Notification of serious GMP non-compliance should take place after national procedures for dealing with adverse inspection reports have been followed and the action recommended by the inspector ratified or alternative action decided upon.

Art. 60 – (1) In principle, unilateral action by one Member State should be avoided, unless justified.

(2) In order to facilitate co-ordinated action at Community level, notification of serious GMP non-compliance should be made prior to the execution of any action.

(3) In so far as is possible, the authority that carried out the inspection revealing the non-compliance should establish the following as appropriate:

- the identity of Member States with medicinal products directly affected by inspection findings;
- where relevant, the Reference Member State(s);
- whether centrally authorised medicinal products are involved;
- the identity of other Supervisory Authorities in the case of medicinal or investigational medicinal products;
- for investigational medicinal products the EudraCT trial reference numbers should be identified;
- In the case of active substance manufacturer whether CEPs are affected in addition to marketing authorisations directly affected.

(4) The authority that discovers the non-compliance should involve the manufacturer concerned, the importer and trial sponsor as appropriate to gather this information.

(5) It may be necessary to issue the notice of non-compliance without complete information if the risk to patient health is considered particularly severe.

Art. 61. – Where there is more than one Supervisory Authority they should all be consulted by the reporting authority on proposed actions before transmission of the non-compliance information.

Art. 62. – (1) The agreed Community GMP non-compliance format should be used to report the non-compliance information to the EudraGMP database.

(2) The rapid alert distribution list should be used for this purpose.

Art. 63. – The GMP non-compliance notification should explain the nature of any proposed action, or where justified, action already taken.

Art. 64. – (1) Any further communication with the issuing authority requesting clarification the non-compliance or providing relevant data, should be made via EudraGMP.

(2) All these questions and answers will then be available to all National Competent Authorities.

Art. 65. – (1) Where relevant, a contact telephone number should be given in the notification form together with a proposed time and date for a teleconference in which all affected member states can join, and in which co-ordinated action can be ratified.

(2) The EDQM should be invited to join the teleconference if a CEP is affected.

Art. 66. – (1) The outcome of the teleconference, if held, should be communicated in a follow-up message to confirm that the recommended action in the initial notification was agreed or to communicate any other agreed Community action.

(2) EudraGMP will be used for this.

Art. 67. – If an inspection of an active substance manufacturer has been carried out other than at the request of EDQM and serious non-compliance is found, EDQM should be included in the communication of the serious non-compliance, unless it is clear that no CEPs are affected.

Art. 68. – (1) MRA partners are obliged to notify recipients of GMP certificates issued in the context of the MRA withdrawing those certificates if serious non-compliance is discovered.

(2) MRA partners given access to EudraGMP will be notified automatically of GMP non-compliance statements placed into the database.

Art. 69. – (1) The issuing authority may amend the non-compliance information entered in the EudraGMP database, if necessary.

(2) Any new modification of the non-compliance information should be distributed to the rapid alert distribution list.

VIII.2 Voiding of CEPs for reasons other than GMP non-compliance

Art. 70. – (1) In cases where a CEP has been voided for non-GMP reasons EDQM notifies all national competent authorities using the agreed contact points.

(2) In its notification, the EDQM should indicate the reasons for voiding in order that authorities receiving the information can decide whether the quality, safety or efficacy of medicinal products already on the market is adversely affected and whether therefore a rapid alert is needed.

(3) Responsibilities are defined in Art. 36.

CHAPTER IX
Post-communication procedure: Serious GMP non-compliance

Art. 71. – (1) On receipt of a form notifying serious GMP non-compliance, either by fax or through EudraGMP, the NAMMD should check whether nationally authorised medicinal products in Romania are affected, and whether Romania is a Reference Member State for any affected medicinal products, seeking assistance from the inspectorate carrying out the inspection, if different, and the manufacturer(s) concerned as needed.

(2) If either applies, they should join the teleconference if there is to be one.

(3) If no teleconference is proposed, receiving authorities should, where appropriate, take the actions on its own territory that correspond with the actions proposed or already executed by the authority reporting the non-compliance.

(4) In the case of action against marketing authorisations subject to the decentralised/mutual recognition procedures, the Reference Member State should take the initiative in following the recommendations of the Authority reporting the non-compliance.

(5) The EMA will coordinate action relating to centrally authorised medicinal products.

Art. 72. – Disagreement with the actions proposed, if not resolved at the teleconference, should be dealt with through procedures established in accordance with Article 839 of Law no. 95/2006 on healthcare reform, Title XVII - The medicinal product, as amended.

Art. 73. – In the case of actions proposed for marketing authorisations subject to the Decentralised or Mutual Recognition procedures, the Co-ordination Group for Mutual Recognition and Decentralised Procedures [CMD (h)] may decide to discuss the coordination of actions at a meeting of the relevant group prior to implementation.

Art. 74. – (1) Exceptionally, where, following proper assessment, specific national factors alter the risk such that the agreed Community action in connection with a marketing authorisation, or a rapid alert is not considered, on balance, to be in the interest of public health in Romania, this may decide to take alternative action to that proposed by the Member State initiating this procedure so long as this does not affect any other Member State.

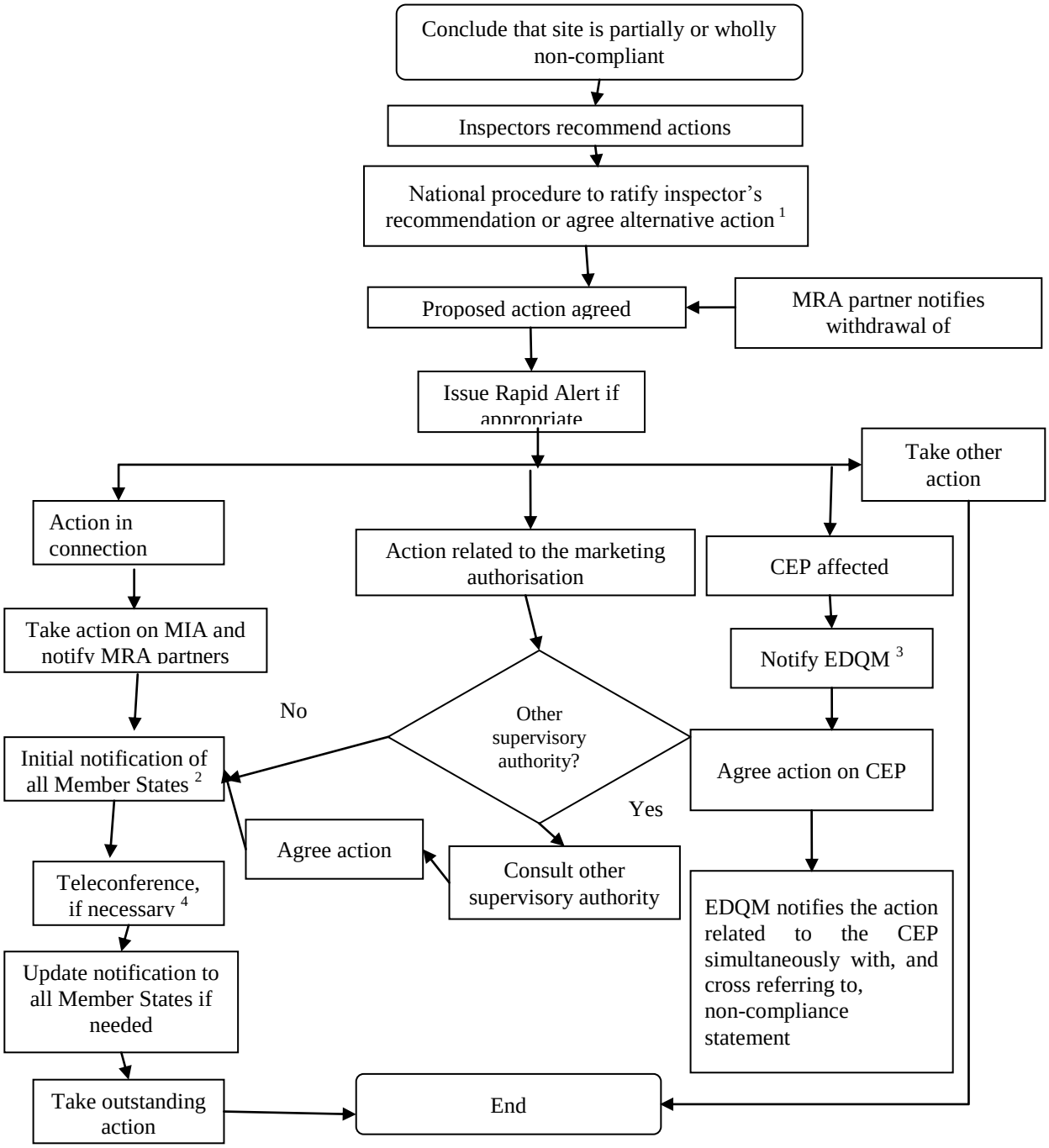
(2) In such cases, in line with Article 839 of Law no. 95/2006 on healthcare reform, Title XVII - The medicinal product, as amended, it is Romania's duty to notify the EMA and the European Commission.

(3) The Supervisory Authority or Reference Member State may find itself in this position but should nevertheless fulfil its responsibilities under chapter VI.

CHAPTER X
Legal References

- Law no. 95/2006 on healthcare reform, Title XVII - The medicinal product, as amended – Chapter XII Supervision and sanctions.
- Law no. 95/2006 on healthcare reform, Title XVII-The medicinal product, as amended – Chapter XIII General provisions.
- Regulation (EC) no. 726/2004 of the European Parliament and of the Council laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, Title II Chapter 2 Supervision and Penalties.
- The Compilation of Community Procedures for Inspections and the Exchange of Information, published by the European Commission [Article 4 of Order of the Ministry of Public Health no. 905/2006 on approval of Principles and guidelines for good manufacturing practice in respect of medicinal products for human use and investigational medicinal products (IMPs) for human use].

Annex 1 – Action taken by authority discovering GMP non-compliance



*MIA = Manufacturing/Importing authorisation

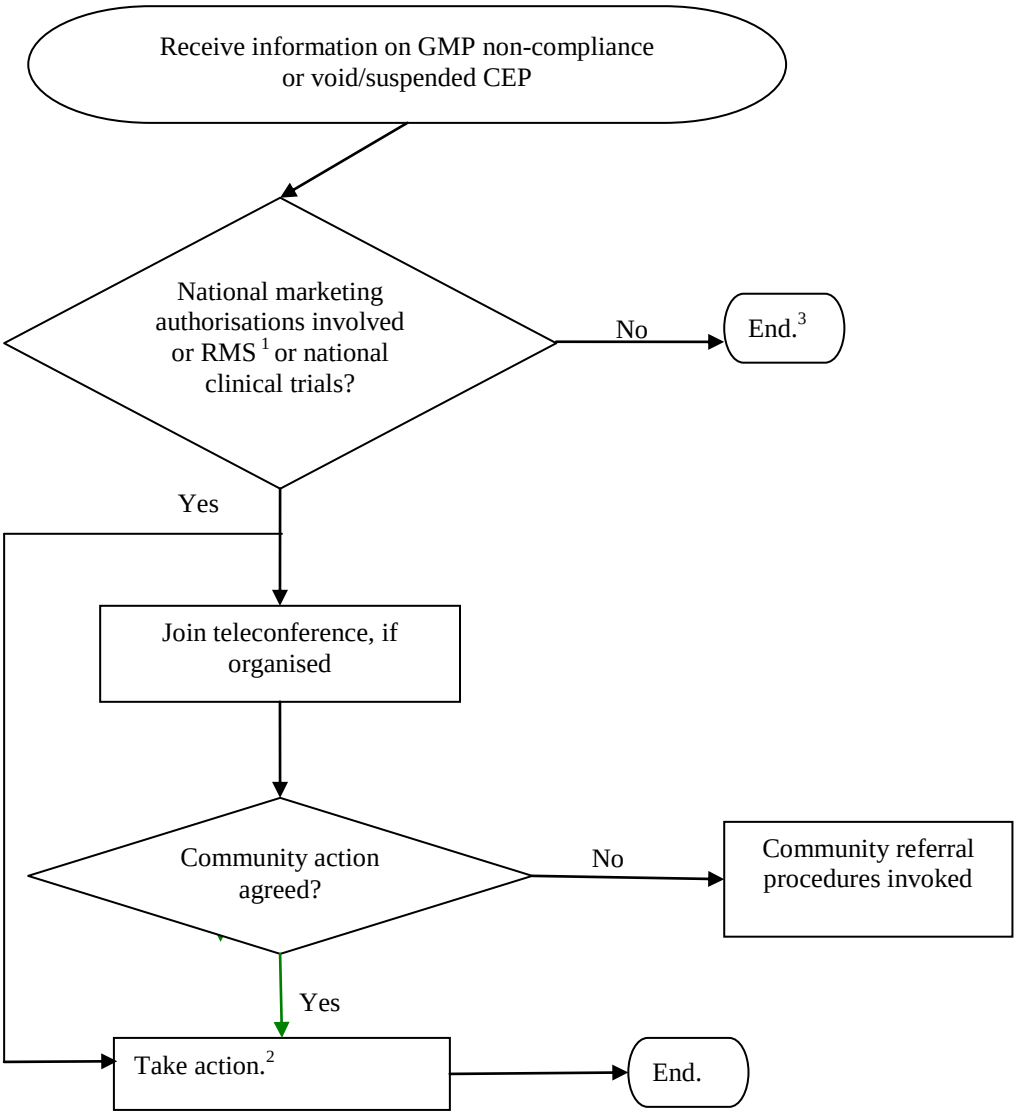
[1] If action against marketing authorisations is considered, the action ratified is that regarded as appropriate for the Community. If the reporting authority is not the Supervisory Authority the Supervisory Authority must be involved in the decision process.

[2] Via EudraGMP

[3] This is the starting point for CEPs voided for reasons unrelated to a GMP inspection.

[4] If a CEP is involved EDQM is invited to join. If desired, coordination of action in respect of marketing authorisations subject to the mutual recognition or decentralised procedures may be discussed at the next meeting of CMD(h).

Annex 2 – Action by Authorities following receipt of information of GMP non-compliance



[1]EMA co-ordinates action for centrally authorised medicinal products
[2]Reference Member States (RMSs) should take the agreed action at Community level
[3]Notwithstanding appropriate responses to consequential rapid alerts or other consequential actions agreed at Community level

(LETTERHEAD OF COMPETENT AUTHORITY)

Report No: _ _ _/_ _ _/_ __/_ _

STATEMENT OF NON-COMPLIANCE WITH GMP

Exchange of information between National Competent Authorities (NCAs) of the EEA following the discovery of serious GMP non-compliance at a manufacturer[11]

Part 1

Issued following an inspection in accordance with Art. 111(7) of Directive 2001/83/EC, Art. 80(7) of Directive 2001/82/EC or Art. 15 of Directive 2001/20/EC.*

The competent authority of.....*[Member State]* confirms the following:

The manufacturer .....

Site address .....

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on …../...…/..… *[date]*, it is considered that **it does not comply with the Good Manufacturing Practice** requirements referred to in the principles and guidelines of Good Manufacturing Practice laid down in Directive 2003/94/EC/Directive 91/412/EEC/ the principles of GMP for active substances referred to in Article 47 of Directive 2001/83/EC / Article 51 of Directive 2001/82/EC / an appropriate level of GMP as referred to in Article 46(f) of Directive 2001/83/EC*

[11] The statement of non-compliance referred to in paragraph 111(7) of Directive 2001/83/EC and 80(7) of Directive 2001/82/EC, as amended, is also applicable to importers.

Part 2

☐ Human Medicinal Products*

☐ Human Investigational Medicinal Products*

1 NON-COMPLIANT MANUFACTURING OPERATIONS- MEDICINAL PRODUCTS *	
1.1	*Sterile Products*
	1.1.1 Aseptically prepared (processing operations for the following dosage forms) 1.1.1.1 Large volume liquids 1.1.1.2 Lyophilisates 1.1.1.3 Semi-solids 1.1.1.4 Small volume liquids 1.1.1.5 Solids and implants 1.1.1.6 Other aseptically prepared products <free text>
	1.1.2 Terminally sterilised (processing operations for the following dosage forms) 1.1.2.1 Large volume liquids 1.1.2.2 Semi-solids 1.1.2.3 Small volume liquids 1.1.2.4 Solids and implants 1.1.2.5 Other terminally sterilised prepared products <free text>
	1.1.3 Batch certification
1.2	**Non-sterile products**
	1.2.1 Non-sterile products (processing operations for the following dosage forms) 1.2.1.1 Capsules, hard shell 1.2.1.2 Capsules, soft shell 1.2.1.3 Chewing gums 1.2.1.4 Impregnated matrices 1.2.1.5 Liquids for external use 1.2.1.6 Liquids for internal use 1.2.1.7 Medicinal gases 1.2.1.8 Other solid dosage forms 1.2.1.9 Pressurised preparations 1.2.1.10 Radionuclide generators 1.2.1.11 Semi-solids 1.2.1.12 Suppositories 1.2.1.13 Tablets 1.2.1.14 Transdermal patches 1.2.1.15 Other non-sterile medicinal product <free text >
	1.2.2 Batch certification
1.3	**Biological medicinal products**
	1.3.1 Biological medicinal products 1. Blood products 2. Immunological products 3. Cell therapy products 4. Gene therapy products 5. Biotechnology products 6. Human or animal tissue extracted products 7. Tissue engineered products 8. Other biological medicinal products <free text >

	1.3.2 Batch certification (list of product types) 1. Blood products 2. Immunological products 3. Cell therapy products 4. Gene therapy products 5. Biotechnology products 6. Human or animal tissue extracted products 7. Tissue engineered products 8. Other biological medicinal products <free text >
1.4	**Other products or manufacturing activity**
	1.4.1 Manufacture of: 1.4.1.1 Herbal products 1.4.1.2 Homoeopathic products 1.4.1.3 Other <free text >
	1.4.2 Sterilisation of active substances/excipients/finished product: 1.4.2.1 Filtration 1.4.2.2 Dry heat 1.4.2.3 Moist heat 1.4.2.4 Chemical 1.4.2.5 Gamma irradiation 1.4.2.6 Electron beam
	1.4.3 Others <free text>
1.5	Packaging
	1.5.1 Primary packing 1.5.1.1 Capsules, hard shell 1.5.1.2 Capsules, soft shell 1.5.1.3 Chewing gums 1.5.1.4 Impregnated matrices 1.5.1.5 Liquids for external use 1.5.1.6 Liquids for internal use 1.5.1.7 Medicinal gases 1.5.1.8 Other solid dosage forms 1.5.1.9 Pressurised preparations 1.5.1.10 Radionuclide generators 1.5.1.11 Semi-solids 1.5.1.12 Suppositories 1.5.1.13 Tablets 1.5.1.14 Transdermal patches 1.5.1.15 Other non-sterile medicinal products <free text >
	1.5.2 Secondary packing
1.6	Quality control testing
	1.6.1 Microbiological: sterility
	1.6.2 Microbiological: non-sterility
	1.6.3 Chemical/Physical
	1.6.4 Biological

2 NON-COMPLIANT IMPORTATION OPERATIONS*	
2.1	**Quality control testing of imported medicinal products**
	2.1.1 Microbiological: sterility
	2.1.2 Microbiological: non-sterility

	2.1.3 Chemical/Physical
	2.1.4 Biological
2.2	Batch certification of imported medicinal products
	2.2.1 *Sterile Products* 2.2.1.1 Aseptically prepared 2.2.1.2 Terminally sterilised
	2.2.2 Non-sterile products
	2.2.3 Biological medicinal products 2.2.3.1 Blood products 2.2.3.2 Immunological products 2.2.3.3 Cell therapy products 2.2.3.4 Gene therapy products 2.2.3.5 Biotechnology products 2.2.3.6 Human or animal extracted products 2.2.3.7 Tissue engineered products 2.2.3.8 Other biological medicinal products <free text >
2.3	**Other importation activities**
	2.3.1 Site of physical importation
	2.3.2 Importation of intermediate which undergoes further processing
	2.3.3 Other <free text>

Any restrictions or clarifying remarks related to the scope of this statement*:

.....

.....

3 MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES Active Substance(s):	
3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.1 Manufacture of active substance intermediates *3.1.2 Manufacture of crude active substance* *3.1.3 Salt formation / Purification steps : <free text> (e.g. crystallisation)* *3.1.4 Other <free text>*
3.2	**Extraction of Active Substance from Natural Sources**
	3.2.1 Extraction of substance from plant source *3.2.2 Extraction of substance from animal source* *3.2.3 Extraction of substance from human source* *3.2.4 Extraction of substance from mineral source* *3.2.5 Modification of extracted substance <specify source 1,2,3,4>* *3.2.6 Purification of extracted substance <specify source 1,2,3,4 >* *3.2.7 Other <free text>*
3.3	**Manufacture of Active Substance using Biological Processes**

	3.3.1 Fermentation *3.3.2 Cell Culture <specify cell type> (e.g. mammalian / bacterial)* *3.3.3 Isolation / Purification* *3.3.4 Modification* *3.3.5 Other <free text>*
3.4	**Manufacture of sterile active substance (sections 3.1, 3.2, 3.3 to be completed as applicable)**
	3.4.1 Aseptically prepared *3.4.2 Terminally sterilised*
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps < specify > (e.g. drying, milling / micronisation, sieving) *3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)* *3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)* *3.5.4 Other <free text> (for operations not described above)*
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing *3.6.2 Microbiological testing (excluding sterility testing)* *3.6.3 Microbiological testing (including sterility testing)* *3.6.4 Biological Testing*

4. OTHER ACTIVITIES- ACTIVE SUBSTANCES

<free text>

Any restrictions or clarifying remarks related to the scope of this statement*:

.....

.....

Part 3

1. Nature of non-compliance

<free text > .....

.....

2. Action taken/proposed by the NCA

☐ Suspension/Variation/Revocation* of the manufacturing authorisation no. …… in full/in part*

<free text > .....

.....

☐ Restriction of current valid GMP certificate no. .....

<free text > .....

.....

☐ Suspension/Revocation/Requested variation/ Refusal to grant * of Marketing Authorisation(s)

<free text> .....

.....

☐ Recall of batches already released (separate Rapid Alert to follow)

<free text > .....

.....

☐ Prohibition of supply

<free text >.....

.....

☐ Suspension or voiding of CEP (action to be taken by EDQM)

<free text > .....

.....

☐ Suspension of clinical trials

<free text > .....

.....

☐ Others <free text >

<free text > .....

.....

3. Additional comments

<free text > .....

.....

Teleconference Date		**Teleconference Time (CET)**		**Dial in no.**	
Products manufactured at site, if known	**Product**	**Dosage Form**	**Reference Member State, National or EMEA**		
Human medicinal product(s)					
Investigational medicinal product(s)	**EudraCT nos.**				

…../...…/.....… *[date]*

Name and signature of the authorised person of the Competent Authority of *[country]*[12]

[Name, title, national authority, phone & fax numbers in case of enquiries]

[12] The signature, date and contact details should appear on each page of the non-compliance document.

DECISION

No. 9/22.04.2013

on Procedure for dealing with serious good manufacturing practice (GMP) non-compliance information originating from third country authorities or international organisations

The Scientific Council of the National Agency for Medicines and Medical Devices (NAMMD), established based on Order of the Minister of Health no. 158/18.02.2013, reunited on summons of the President of the National Agency for Medicines and Medical Devices in the ordinary meeting of 22.04.2013, in accordance with Article 12(5) of Government Decision no. 734/2010 on establishment, organisation and operation of the National Agency for Medicines and Medical Devices, as amended, adopts the following

DECISION

Sole article. – The Procedure for dealing with serious Good Manufacturing Practice (GMP) non-compliance information originating from third country Authorities or international organisations is approved, in accordance with the Annex which is integral part of this Decision.

PRESIDENT
of the Scientific Council
of the National Agency for Medicines and Medical Devices,

Acad. Prof. Dr. Leonida Gherasim

ANNEX
to SCD no. 9/22.04.2013

Procedure for dealing with serious GMP non-compliance information originating from third country authorities or international organisations

CHAPTER I

Introduction

Art. 1. – This Procedure is a translation into Romanian and an adaptation of the procedure for dealing with serious GMP non-compliance information originating from third country authorities or international organisations included in the compilation of community procedures EMA/INS/GMP/321252/2012 Rev 15 issued by the European Medicines Agency (EMA).

CHAPTER II
Summary

Art. 2. – A consolidated procedure for dealing with all circumstances of serious GMP non-compliance information originating from third country authorities and international organisations is necessary to ensure a coordinated approach to potential risks to public health. Information may refer to API, finished product or IMP manufacturers and/or QC labs located either in the EU/EEA or in a third country.

Art. 3 – This document supplements the procedure in the Compilation of Community Procedures (CoCP) for dealing with serious Good Manufacturing Practice (GMP) non-compliance (transposed into national legislation by NAMMD Scientific Council Decision no. 3/2009), with regard to the receipt, dissemination and initial assessment of serious GMP non-compliance notifications which originate from third country (non-EU, non-MRA) authorities or international organisations (e.g. WHO).

Art. 4 – This procedure requires the Competent Authorities in the EEA involved in the receipt and coordination of serious GMP non-compliance notifications to disseminate relevant information to all other authorities in the Community in a timely manner, to enable the scope and impact of the notification to be confirmed, and subsequent recommendations for action to be made.

Art. 5 – Communication with authorities of those countries with which the Community has made appropriate arrangements on GMP (e.g. MRA) may also be necessary.

CHAPTER III
Definitions

Art. 6 – For the purposes of this procedure, serious GMP non-compliance is non-compliance with GMP that in the opinion of the reporting authority is of such nature that administrative action is necessary to remove a potential risk to public health. It should be noted that authorities in Third Countries issuing information may not share the same understanding.

CHAPTER IV
Principles

Art. 7 – (1) Notification of serious GMP non-compliance from a third country authority or an international organisation is to be assessed to determine the impact with respect to medicinal

products supplied to the Community. It is possible that the detailed GMP non-compliances identified in the notification may have limited or no impact on EU products, e.g.:

- in cases where the issues relate to facilities or products which are not involved in EU supply, or
- where the non-compliances do not relate to GMP principles and guidelines as defined in the relevant Directives and as interpreted in Guidelines on GMP published by the European Commission in Eudralex Volume 4, or
- Where the impact of the identified non-compliances, as interpreted in Guidelines on GMP published in Eudralex Volume 4, does not pose a significant risk to the quality or safety of products for EU supply.

(2) Therefore, it is important to determine the degree of Community impact as soon as possible following the initial notification.

Art. 8 – Action following the notification of any serious GMP non-compliance must be commensurate with the level of risk. Confirmation of serious non-compliance with the principles and guidelines of EU GMP by definition requires administrative action to be taken. Notification of GMP deficiencies which do not require administrative action is recorded in the relevant Supervisory Authority's model for risk based inspection planning, in accordance with CoCP.

Art. 9 – The notification of a serious GMP non-compliance may have implications not only for the Member State receiving the notification but also for other, possibly all, Member States. Therefore, a mechanism that ensures consistent, co-ordinated action throughout the Community is important, even though the final outcome may differ based on specific national factors.

CHAPTER V
Scope

Art. 10 – This procedure relates to the receipt, dissemination and initial assessment of the information relating to serious GMP non-compliance received from third country authorities. If, following assessment of the notification, the nature and severity of non-compliance is considered to pose a potential risk to public or animal health, coordinated administrative action applicable to the situation is to be considered in accordance with the detailed guidance provided in CoCP. Procedures require the adherence to timelines that ensure that serious non-compliance is dealt with in a timely manner.

Art. 11 – This procedure applies to all notifications of serious GMP non-compliance discovered by a third country authority or international organisations either in the territory of an EEA Supervisory Authority or in third countries. It applies to inspections of active substance manufacturers, manufacturers or importers of medicinal products, manufacturers or importers of investigational medicinal products as well as quality control laboratories.

Art. 12 – Notifications of serious non-compliance with Good Practice in the case of human blood, blood components or tissues, when used as a starting material in medicinal products, may also follow this procedure.

Art. 13 – All serious GMP non-compliance relating to active substance manufacturers and all types of manufacturers located in third countries must be communicated even if it is known that no other Member State has an interest at the time as it may be important for all Member States to have the information available in the future.

CHAPTER VI
Procedure and responsibilities

Art. 14 – Receipt of third country Authority notification

14.1 A Member State who receives notification from a third country authority relating to serious GMP non-compliance at a manufacturer must ensure that sufficient information is

obtained to permit an assessment of Community impact. Information is collected using the format given in Annex 1. The information to be recorded in this template includes:

- Contact details of single point of contact (SPoC) from the notifying authority;
- Manufacturer name and address;
- SPoC for manufacturer;
- Product-related information:
  - Human / Veterinary / IMP / API / export only;
  - Products / dosage forms / buildings / lines affected;
  - Centralised / DC / MRP / national marketing authorisations / products not subject to a MA;
- Non-compliance issues:
  - Serious EU GMP non-compliance;
  - Serious third country GMP non-compliance.

14.2 The Member State which receives the initial notification may need to request further information from either the notifying third country authority, or the manufacturing site to which the notification refers, in order to ensure that the original information can be validated, and that sufficient information is obtained to permit an impact assessment in all Member States.

14.3 If an EU National Competent Authority receives a third country notification which refers to a manufacturer on its own territory, the notified National Competent Authority will take the necessary action. If the notification refers to a site in a different EU Member State, the notified National Competent Authority will forward the information to the National Competent Authority of the Member State in which the manufacturing site is located[13].

14.4 If the third country authority notification refers to a site in a third country, the Member State who receives the initial non-compliance notification is responsible for dissemination to all EU Member States and EMA, using the rapid alert single point of contact (SPoC) list[1].

14.5 Member States may receive further updates to the initial notification as additional information becomes available. These updates are also to be circulated to ensure continuity of the information chain.

14.6 Each EU Competent Authority has an internal national procedure to review this type of non-compliance information and determine whether there is any potential impact to products on their territory. Information relating to these products is forwarded to the Member State who received the initial notification for collation, including information regarding product criticality (e.g. market share, and known availability of therapeutic alternatives).

14.7 The Member State who received the initial notification is responsible for arranging a teleconference with the concerned Member States to decide on the lead and on next steps. The selection of the coordinating Competent Authority is based on a hierarchy of factors such as:

Product type	**Coordinator**
Centralised product	Supervisory Authority will lead; EMA will co-ordinate actions.
DC/MRP	Supervisory Authority / Reference Member State
National Authorisation	Member State granting authorisation
IMP	Member State granting CTA

[13] Without prejudice to any confidentiality arrangements

API	Supervisory Authority of API site / Coordinator responsible for the product type containing the affected API(s)

14.8 In cases where there are no EU-coordinated marketing authorisations but there are various National Authorisations affecting more than one Member State, the coordinating Competent Authority is determined on the basis of product criticality or market volume. Consideration must also be given to inclusion of the Competent Authorities previously involved in GMP inspections of the site, as the Authority that has carried out previous inspections is best placed to assess the potential impact of the level of GMP non-compliance discovered.

14.9 Contact details for the coordinating Competent Authority SPoC are sent to the notifying third country authority and the manufacturing site to which the notification refers.

14.10 If additional information becomes available during the process which indicates that a change in coordinating Competent Authority is appropriate (e.g. due to additional information on affected products), this is agreed between the initial coordinator and the proposed new coordinator. Contact details of the new coordinator are to be sent to the concerned Member States, and the contacts listed in section 14.8 above. Care is taken to ensure that a change in coordinator is made only where absolutely necessary and are clearly communicated, in order to avoid confusion or delays in the assessment process.

14.11 The coordinating Competent Authority continues to gather further information and clarification on the detailed inspection findings, impact on EU GMP and public health. Coordination of issues with Marketing Authorisation Holders (MAHs) may be required at this point, in order to determine potential impact on maintaining supplies. In cases where product is certified to the market by the holder of a Manufacturing and Import Authorisation who is not the MAH, information is also obtained from the Qualified Person. Following collation of detailed GMP non-compliance and product related information, a risk assessment is performed to determine the actions to be taken. Further guidance on the administrative actions available for consideration is described in CoCP.

14.12 Consideration is given with regards to whether an EU GMP inspection is performed prior to taking any administrative action, or whether the significance of the issues notified require immediate action in the interest of public health.

14.13. If the initial dissemination of information by the Member State which received the initial notification indicated that more than one Member State is affected by the notification of serious GMP non-compliance, a contact telephone number is to be provided by the coordinating Competent Authority, together with a proposed time and date for a teleconference in which all affected Member States can join. This will assist in ratification of proposed administrative action. The European Directorate for the Quality of Medicines (EDQM) is invited to join the teleconference if a Certificate of the European Pharmacopoeia (CEP) is affected.

14.14 The coordinating Competent Authority is responsible for communicating the agreed administrative actions to the affected Member States using the template provided in Annex 1.

14.15 The post-communication procedure is to be followed as described in CoCP. An EU GMP inspection is performed in order to verify the third country notification of non-compliances before consideration of issuing a statement of serious GMP non-compliance. In cases where this is not possible due to a perceived enhanced physical threat to inspectors (for political reasons, health reasons or others), the use of a ‘distant assessment’, as described in CoCP may be an appropriate alternative means to inform the decision regarding the issuance of a statement of serious GMP non-compliance.

ANNEX 1

(LETTERHEAD OF COMPETENT AUTHORITY)

Report No: _ _ _/_ _ _/_ __/_ _

STATEMENT OF NON-COMPLIANCE WITH GMP

Exchange of information between National Competent Authorities (NCAs) of the EEA following notification of serious GMP non-compliance at a manufacturer.

Part 1

Issued by the competent authority of ……*[Member State]* following notification from a third country authority or international organisation in accordance with reference to CoCP here.

……..*[third country authority / International organisation name]* reports the following:

The manufacturer……..……..

Site address……
……...

DUNS Number (if known)…….....……

Site contact name, title, email, phone and fax number
……..

Third country authority / international organisation contact name, title, email, phone and fax number
……..

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on …../...…/...… *[date]*, it is considered that **it does not comply with the Good Manufacturing Practice** requirements referred to in the principles and guidelines of Good Manufacturing Practice laid down in……*[third country / international GMP standards or regulations used for assessment]* , relating to medicinal products/active substances/excipients*

Part 2

☐ Human Medicinal Products*
☐ Human Investigational Medicinal Products*

1 NON-COMPLIANT MANUFACTURING OPERATIONS- MEDICINAL PRODUCTS *	
1.1	**Sterile Products**
	1.1.1 Aseptically prepared (processing operations for the following dosage forms) 1.1.1.1 Large volume liquids 1.1.1.2 Lyophilisates 1.1.1.3 Semi-solids 1.1.1.4 Small volume liquids 1.1.1.5 Solids and implants 1.1.1.6 Other aseptically prepared products <free text>
	1.1.2 Terminally sterilised (processing operations for the following dosage forms) 1.1.2.1 Large volume liquids 1.1.2.2 Semi-solids 1.1.2.3 Small volume liquids 1.1.2.4 Solids and implants 1.1.2.5 Other terminally sterilised prepared products <free text>
	1.1.3 Batch certification
1.2	**Non-sterile products**
	1.2.1 Non-sterile products (processing operations for the following dosage forms) 1.2.1.1 Capsules, hard shell 1.2.1.2 Capsules, soft shell 1.2.1.3 Chewing gums 1.2.1.4 Impregnated matrices 1.2.1.5 Liquids for external use 1.2.1.6 Liquids for internal use 1.2.1.7 Medicinal gases 1.2.1.8.....Other solid dosage forms 1.2.1.9 Pressurised preparations 1.2.1.10 Radionuclide generators 1.2.1.11 Semi-solids 1.2.1.12 Suppositories 1.2.1.13 Tablets 1.2.1.14 Transdermal patches 1.2.1.15 Other non-sterile medicinal product <free text >
	1.2.2 Batch certification
1.3	**Biological medicinal products**
	1.3.1 Biological medicinal products 1.3.1.1 Blood products 1.3.1.2 Immunological products 1.3.1.3 Cell therapy products 1.3.1.4 Gene therapy products 1.3.1.5 Biotechnology products

	1.3.1.6 Human or animal extracted products 1.3.1.7 Tissue engineered products 1.3.1.8 Other biological medicinal products <free text >
	1.3.2 Batch certification (list of product types) 1.3.2.1 Blood products 1.3.2.2 Immunological products 1.3.2.3 Cell therapy products 1.3.2.4 Gene therapy products 1.3.2.5 Biotechnology products 1.3.2.6 Human or animal extracted products 1.3.2.7 Tissue engineered products 1.3.2.8 Other biological medicinal products <free text >
1.4	**Other products or manufacturing activity**
	1.4.1 Manufacture of: 1.4.1.1 Herbal products 1.4.1.2 Homoeopathic products 1.4.1.3 Other <free text >
	1.4.2 Sterilisation of active substances/excipients/finished product: 1.4.2.1 Filtration 1.4.2.2 Dry heat 1.4.2.3 Moist heat 1.4.2.4 Chemical 1.4.2.5 Gamma irradiation 1.4.2.6 Electron beam
	1.4.3 Others <free text>
1.5	**Packaging**
	1.5.1 Primary packing 1.5.1.1 Capsules, hard shell 1.5.1.2 Capsules, soft shell 1.5.1.3 Chewing gums 1.5.1.4 Impregnated matrices 1.5.1.5 Liquids for external use 1.5.1.6 Liquids for internal use 1.5.1.7 Medicinal gases 1.5.1.8 Other solid dosage forms 1.5.1.9 Pressurised preparations 1.5.1.10 Radionuclide generators 1.5.1.11 Semi-solids 1.5.1.12 Suppositories 1.5.1.13 Tablets 1.5.1.14 Transdermal patches 1.5.1.15 Other non-sterile medicinal products <free text >
	1.5.2 Secondary packing
1.6	**Quality control testing**
	1.6.1 Microbiological: sterility
	1.6.2 Microbiological: non-sterility
	1.6.3 Chemical/Physical
	1.6.4 Biological

2 NON-COMPLIANT IMPORTATION OPERATIONS*	
2.1	**Quality control testing of imported medicinal products**
	2.1.1 Microbiological: sterility
	2.1.2 Microbiological: non-sterility
	2.1.3 Chemical/Physical
	2.1.4 Biological
2.2	**Batch certification of imported medicinal products**
	2.2.1 Sterile Products 2.2.1.1 Aseptically prepared 2.2.1.2 Terminally sterilised
	2.2.2 Non-sterile products
	2.2.3 Biological medicinal products 2.2.3.1 Blood products 2.2.3.2 Immunological products 2.2.3.3 Cell therapy products 2.2.3.4 Gene therapy products 2.2.3.5 Biotechnology products 2.2.3.6 Human or animal extracted products 2.2.3.7 Tissue engineered products 2.2.3.8 Other biological medicinal products <free text >
2.3	**Other importation activities**
	2.3.1 Site of physical importation
	2.3.2 Importation of intermediate which undergoes further processing
	2.3.3 Other <free text>

Any restrictions or clarifying remarks related to the scope of this notification*:

3 MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES Active Substance(s):	
3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.1 Manufacture of active substance intermediates *3.1.2 Manufacture of crude active substance* *3.1.3 Salt formation / Purification steps : <free text> (e.g. crystallisation)* *3.1.4 Other <free text>*
3.2	**Extraction of Active Substance from Natural Sources**
	3.2.1 Extraction of substance from plant source *3.2.2 Extraction of substance from animal source* *3.2.3 Extraction of substance from human source* *3.2.4 Extraction of substance from mineral source* *3.2.5 Modification of extracted substance <specify source 1,2,3,4>* *3.2.6 Purification of extracted substance <specify source 1,2,3,4 >* *3.2.7 Other <free text>*

3.3	**Manufacture of Active Substance using Biological Processes**
	3.3.1 Fermentation *3.3.2 Cell Culture <specify cell type> (e.g. mammalian/bacterial)* *3.3.3 Isolation / Purification* *3.3.4 Modification* *3.3.5 Other <free text>*
3.4	**Manufacture of sterile active substance (sections 3.1, 3.2, 3.3 to be completed as applicable)**
	3.4.1 Aseptically prepared *3.4.2 Terminally sterilised*
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps < specify > (e.g. drying, milling / micronisation, sieving) *3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)* *3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)* *3.5.4 Other <free text> (for operations not described above)*
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing *3.6.2 Microbiological testing (excluding sterility testing)* *3.6.3 Microbiological testing (including sterility testing)* *3.6.4 Biological Testing*

Part 3

1. Nature of non-compliance (check all relevant boxes)	
☐ Analytical validation	☐ Housekeeping - cleanliness, tidiness
☐ Batch release procedures	☐ In-process controls - control and monitoring of production operations
☐ Calibration of measuring and test equipment	☐ Intermediate and bulk product testing
☐ Calibration of reference materials and reagents	☐ Investigation of anomalies
☐ Cleaning validation	☐ Line clearance, segregation and potential for mix-up
☐ Complaints and product recall	☐ Personnel issues: Duties of key personnel
☐ Computerised systems - documentation and control	☐ Personnel issues: Hygiene/Clothing
☐ Computerised systems - validation	☐ Personnel issues: Training
☐ Contamination, chemical/physical - potential for	☐ Process validation
☐ Contamination, microbiological - potential for	☐ Production planning and scheduling
☐ Design and maintenance of equipment	☐ Regulatory issues: Non-compliance with manufacturing authorisation
☐ Design and maintenance of premises	☐ Regulatory issues: Non-compliance with marketing authorisation
☐ Documentation - manufacturing	☐ Regulatory issues: Unauthorised activities
☐ Documentation - quality system elements/procedures	☐ Sampling - procedures and facilities
☐ Documentation - specification and testing	☐ Self-inspection
☐ Environmental control	☐ Starting material and packaging component testing
☐ Environmental monitoring	☐ Status labelling - work in progress, facilities and equipment
☐ Equipment qualification	☐ Sterility Assurance
☐ Finished product testing	☐ Supplier and contractor audit and technical agreements
☐ Handling and control of packaging components	☐ Warehousing and distribution activities

2. Action taken/proposed* by the third country authority or International organisation: ☐ Suspension, variation, revocation* of the manufacturing site approval in full or in part ☐ Withdrawal, of current valid GMP certificate / statement ☐ Suspension, Revocation or Requested Variation* of product registrations ☐ Recall of batches already released ☐ Prohibition of supply ☐ Suspension of clinical trials ☐ Others <free text >
3. Additional comments

Teleconference Date		**Teleconference Time (GMT)**		**Dial in no.**	
EU Products manufactured at site, if known	**Product**	**Dosage Form**	**Reference Member State, National or EMEA**		
Human medicinal product(s)					
Veterinary medicinal product(s)					
Investigational medicinal product(s)	**EudraCT nos.**				

Name of the authorised person of the Competent Authority of ……..…….*[Member State]*

…….
[Name, title, national authority, email, phone & fax numbers in case of enquiries]

…../..…/.....… *[date]*

(*): delete that which does not apply.

DECISION

No. 10/22.04.2013

on approval of the Guideline on training and qualification of inspectors performing inspections of wholesale distributors

The Scientific Council of the National Agency for Medicines and Medical Devices (NAMMD), established based on Order of the Minister of Health no. 158/18.02.2013, reunited on summons of the President of the National Agency for Medicines and Medical Devices in the ordinary meeting of 22.04.2013, in accordance with Article 12(5) of Government Decision no. 734/2010 on establishment, organisation and operation of the National Agency for Medicines and Medical Devices, as amended, adopts the following

DECISION

Sole article. – The Guideline on training and qualification of inspectors performing inspections of wholesale distributors is approved, in accordance with the Annex which is integral part of this Decision.

PRESIDENT
of the Scientific Council
of the National Agency for Medicines and Medical Devices,

Acad. Prof. Dr. Leonida Gherasim

ANNEX
to SCD no. 10/22.04.2013

GUIDELINE
on training and qualification of inspectors performing inspections of wholesale distributors

CHAPTER I

Introduction

Art. 1. – This Guideline is a translation into Romanian and a transposition of the Guideline on training and qualification of inspectors performing inspections of wholesale distributors which is part of the Compilation of Community Procedures on Inspections and Exchange of Information EMA/INS/GMP/321252/2012 Rev 15 published by the European Medicines Agency (EMA).

CHAPTER II
Summary

Art. 2. – (1) Taking into account the paramount importance of the management of inspection services, this guideline establishes some requirements concerning experience, training and qualifications of inspectors performing inspections of wholesale distributors.

(2) Objectivity, confidentiality, professional integrity, knowledge of technical matters, knowledge of legislation, and auditing skills are the main requirements of inspectors.

(3) Inspectors must be very well trained in all aspects of the distribution of medicinal products and in the way of conducting an inspection.

(4) This guideline provides information on minimal requirements; Member States may decide to add supplementary national requirements.

CHAPTER III
Scope

Art. 3. – This guideline applies to the training and qualifications required for an inspector of the National Agency for Medicines and Medical Devices (NAMMD) who shall conduct an inspection to verify compliance with the legal requirements for wholesale distribution[14]. Moreover, it identifies the requirements for ongoing training of inspectors as they advance from the "basic" to the "expert" level throughout a number of inspection fields, each field having its own technical, legislative and practical training requirements.

CHAPTER IV
Background

Art. 4. – General aspects

(1) The NAMMD appoints inspectors to inspect the sites of distributors, as specified in Law 95/2006.

(2) There must be sufficient resources at all levels to meet, effectively and efficiently, the EU requirements of verifying compliance with the legal requirements for the wholesale distribution of medicinal products.

[14] This includes compliance with the Good Distribution Practice for medicinal products for human use.

(3) The inspectors are officially appointed by the NAMMD in accordance with legal requirements.

(4) All inspectors must be competent to carry out their assigned duties and receive appropriate training.

(5) When needed, teams of inspectors may be nominated comprising inspectors with appropriate qualifications and experience to collectively fulfil the requirements necessary for conducting the inspection.

(6) The inspectors are to be made aware of and maintain confidentiality whenever they gain access to confidential information during inspections in accordance with the national legislation and European requirements.

Art. 5. – Personal qualities

(1) T he inter-personal skills of an inspector are important in helping to achieve the objectives of inspections.

(2) During an inspection, the inspector should help in creating an open atmosphere. Inspectors need to remain objective during the inspection and in this context should answer questions or provide clarification but avoid entering into the role of a consultant.

(3) The inspector should have a high level of personal integrity, maturity, be open-minded, understanding of complexity, possess sound judgement, assertiveness, analytical skills and tenacity and have the ability to perceive situations in a realistic way.

(4) The inspector should demonstrate competence in clearly and fluently expressing concepts and ideas orally and in writing in Romanian.

CHAPTER V
Qualification and training

Art. 6. – Qualification

Inspectors are qualified in accordance with national requirements.

Art. 7. – Training

(1) The inspectors have undergone training to the extent necessary to ensure their competence in the skills required for planning, carrying out and reporting inspections.

(2) The training and experience should be documented individually and evaluated within the requirements of the applicable quality system of the Inspectorate.

Art. 8. – Basic training

(1) Moreover, in order to be appointed as inspectors, the candidates must demonstrate their knowledge of the relevant matters in the pharmaceutical field, including:

- Good Distribution Practice (GDP);
- Basic knowledge of the Good Manufacturing Practice (GMP);
- Community and national pharmaceutical legislation;
- Compilation of Community procedures;
- Organisation and quality systems of national Competent Authorities;
- Principles of wholesale distribution and roles of the actors involved in the distribution system;
- Principles of quality management systems;
- Marketing, manufacturing and wholesale distribution authorisation systems and their relationship;
- Inspection techniques, including the skills required for inspection management i.e. planning, organisation, assessment of deficiencies and reporting, communication and information for the inspected entity. Such skills can be acquired by attending relevant courses and or/by accompanying and/or guided by qualified GMP inspectors during inspection;
- Interrelation of licensing, inspection, sampling and analysis, as required;
- Acknowledging the counterfeiting trend.

Art. 9. – Further training

(1) After recruitment and in addition to their basic training, new inspectors are trained by assigned senior inspectors. The theory of inspection should be explained and the practice should be shown in the field, so that concrete examples of the meaning and of the goals of inspections are given and can be discussed. New inspectors should participate, but only as observers, in on the spot inspections carried out during their training.

(2) Beside this and where needed, training courses in inspection techniques and audit, communication, reporting, languages, legal matters and management should be organised by national inspectorates.

(3) Prior to assuming responsibility for performing inspections at wholesale distributors, the new inspector should have gained experience by participation as team member in inspections led by senior inspectors. Preferably, the inspector starts with national GMP inspections as a member of a team and then deal progressively with more complex inspections to be able to act as a team leader. This is recorded within the requirements of the applicable quality system of the Inspectorate.

(4) Through suitable means, the inspector is to demonstrate his/her knowledge and capability of using the necessary management skills required in the conduct of an inspection, i.e. planning, announcing, conducting and reporting an inspection.

(5) The inspector demonstrates his/her capability to write reports in accordance with national and EU requirements.

Art. 10. – Continuous training

(1) Considering the rapid implementation of new manufacturing technologies, the ever more frequent utilisation of automatic and computerized systems both in production and quality control of medicinal products, inspectors also receive continuous training. This can be done by participating to courses, seminars, meetings and conferences organised by national inspectorates or by national/international scientific organisations.

(2) Where needed, joint inspections or training visits with other inspectors from Romania/other Member States could be a useful tip.

(3) The target of all inspectors performing inspections at wholesale distributor sites should be 5 days of training per year. This training should also include DP issues. This ongoing training may include training inspections, courses, symposia, conferences etc. These training days are planned and documented.

CHAPTER VI
Maintenance of competence

Art. 11. – (1) Inspectors have their performance and qualifications periodically reviewed within the requirements of the applicable quality system of the Inspectorate.

(2) Their competence must be maintained and updated by ongoing training, as described under Art. 10. This is documented and its effectiveness assessed.

CHAPTER VII
Harmonisation within the European Economic Area (EEA)

Art. 12. – (1) In order to promote international harmonisation in the interpretation of the principles and compliance, the Inspectorate's management facilitates training activities, including on the job training, at national and international levels.

(2) Consultations with the staff of other inspectorates and joint inspections or training visits are useful in this context and are to be encouraged.

(3) The management should also facilitate the exchange of information and practical experience gained by inspectors in the field of wholesale distribution.

CHAPTER VIII

Legal references

- Law 95/2006 Title XVII- The medicinal product
- Compilation of community procedures on inspections and exchange of information (Art. 3.3 of Directive 2003/94/EC transposed through Art. 4 of Order of the Minister of Public Health no. 905/2006 on the Principles and guidelines for good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use)

DECISION

No. 11/22.04.2013

on approval of the formats concerning statements of serious non-compliance with Wholesale Distribution Practice and Good Distribution Practice for active pharmaceutical substances

The Scientific Council of the National Agency for Medicines and Medical Devices (NAMMD), established based on Order of the Minister of Health no. 158/18.02.2013, reunited on summons of the President of the National Agency for Medicines and Medical Devices in the ordinary meeting of 22.04.2013, in accordance with Article 12(5) of Government Decision no. 734/2010 on establishment, organisation and operation of the National Agency for Medicines and Medical Devices, as amended, adopts the following

DECISION

Sole article. – The following forms are approved for statements of serious non-compliance with Wholesale Distribution Practice and Good Distribution Practice for active substances for use as starting materials in medicinal products for human use in accordance with the community legislation (the Compilation of Community Procedures on Inspections and Exchange of Information), in accordance with the Annexes which are integral part of this Decision:

- Annex A: Form - Statement of serious non-compliance with Good Distribution Practice (medicinal products for human use)
- Annex B: Form - Statement of serious non-compliance with Good Distribution Practice for active substances to be used as starting materials in medicinal products for human use.

PRESIDENT
of the Scientific Council
of the National Agency for Medicines and Medical Devices,

Acad. Prof. Dr. Leonida Gherasim

ANNEX A

FORM

STATEMENT OF SERIOUS NON-COMPLIANCE WITH GOOD DISTRIBUTION PRACTICE

(MEDICINAL PRODUCTS FOR HUMAN USE)

(LETTERHEAD OF COMPETENT AUTHORITY)

Report No: _ _ _/_ _ _/_ __/_ _

STATEMENT OF NON-COMPLIANCE WITH GDP

MEDICINAL PRODUCTS FOR HUMAN USE

Exchange of information between National Competent Authorities (NCAs) of the EEA following the discovery of serious GDP non-compliance at a wholesale distributor

Part 1

Issued following an inspection in accordance with Art. 111(7) of Directive 2001/83/EC as amended. The competent authority of .....*[Member State]* confirms the following: The wholesale distributor..... Authorisation number..... Site address.....

From the knowledge gained during inspection of this wholesaler distributor, the latest of which was conducted on …../..…/..… *[date]*, it is considered that **it does not comply with the Good Distribution Practice** requirements referred to in Article 84 of Directive 2001/83/EC.

Part 2

Wholesale distribution activity affected: <free text>

Part 3

1. Nature of non-compliance: <free text >
2. Action taken/proposed by the NCA: <free text >
3. Additional comments: <free text >

Teleconference Date:	Teleconference Time (CET):	Dial in no.:

…../..…/.....… *[date]* Name and signature of the authorised person of the Competent

Authority of *[country]*[15]

.....

.....

[name, title, name of authority, phone, email in case of enquiries]

[15] The signature, date and contact details should appear on each page of the statement.
Page 1 of <*insert number of pages*>

ANNEX B

FORM
STATEMENT OF SERIOUS NON-COMPLIANCE WITH GOOD DISTRIBUTION PRACTICE OF A DISTRIBUTOR OF ACTIVE SUBSTANCES FOR USE AS STARTING MATERIALS IN MEDICINAL PRODUCTS FOR HUMAN USE

(LETTERHEAD OF COMPETENT AUTHORITY)

Report No: _ _ _/_ _ _/_ __/_ _

STATEMENT OF NON-COMPLIANCE WITH GDP OF A DISTRIBUTOR OF ACTIVE SUBSTANCES FOR USE AS STARTING MATERIALS IN MEDICINAL PRODUCTS FOR HUMAN USE

Exchange of information between National Competent Authorities (NCAs) of the EEA following the discovery of serious GDP non-compliance at an active substance distributor

Part 1

Issued following an inspection in accordance with Art. 111(7) of Directive 2001/83/EC as amended. The competent authority of.....*[Member State]* confirms the following: The active substance distributor..... Site address .....

From the knowledge gained during inspection of this active substance distributor, the latest of which was conducted on …/…/… *[date]*, it is considered that **it does not comply with the Good Distribution Practice** for active substances referred to in Article 47 of Directive 2001/83/EC.

Part 2

□ All registered active substances distributed are affected □ Specify which Active Substances are affected : <free text >

Part 3

4. Nature of non-compliance: <free text >
5. Action taken/proposed by the NCA: <free text >
6. Additional comments: <free text >

Teleconference Date:	Teleconference Time (CET):	Dial in no.:

…/…/… *[date]*

Name and signature of the authorised person of the Competent Authority of *[country]*[16]

.....

.....

[Name, title, name of authority, phone, email in case of enquiries]

[16] The signature, date and contact details should appear on each page of this statement.

DECISION

No. 12/22.04.2013

on approval of new templates of package leaflet, summary of product characteristics and label information for medicinal products authorised for marketing through national procedure in Romania, in accordance with European models

The Scientific Council of the National Agency for Medicines and Medical Devices (NAMMD), established based on Order of the Minister of Health no. 158/18.02.2013, reunited on summons of the President of the National Agency for Medicines and Medical Devices in the ordinary meeting of 22.04.2013, in accordance with Article 12(5) of Government Decision no. 734/2010 on establishment, organisation and operation of the National Agency for Medicines and Medical Devices, as amended, adopts the following

DECISION

Art. 1. - The new templates of package leaflet, summary of product characteristics and label information for medicinal products authorised for marketing through national procedure in Romania, in accordance with European models are approved, in accordance with Annexes I–IV which are integral part of this Decision.

Art. 2. – (1) Provisions of this decision concern applications for marketing authorisation/marketing authorisation renewal and the applications for approval of variations to MA terms related to information concerning this medicinal product, submitted to the NAMMD following the entry into force of this Decision.

(2) For medicinal products not undergoing MA renewal procedure, provisions of this decision are applied throughout 3 years as of the entering into force of this procedure;

(3) Provisions of this decision do not concern the applications for approval of a variation to MA terms, other than a variation referring to the product information.

Art. 3. – This Decision shall enter into force on the date of its repeal, through:

- Order of the Minister of Health no. 1450/24.11.2010 on amendment of Annexes I-III to Order of the Minister of Health no. 399/2006 on approval of European templates of package leaflet, summary of product characteristics and label information for medicinal products authorised for marketing in Romania (which lead to the approval of NMA Scientific Council Decision no. 20/27.11.2009);

- Order of the Minister of Health no. 399/10.04.2006 on approval of European templates of package leaflet, summary of product characteristics and label information for medicinal products authorised for marketing in Romania (which lead to the approval of NMA Scientific Council Decision no. 2/27.01.2006).

PRESIDENT
of the Scientific Council
of the National Agency for Medicines and Medical Devices,

Acad. Prof. Dr. Leonida Gherasim

Package leaflet: Information for the <patient><user>

{ (Invented) name strength pharmaceutical form}
{Active substance(s)}

< ▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects. >

<**Read all of this leaflet carefully before you start <taking> <using> this medicine because it contains important information for you.>**
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your <doctor> <or> <pharmacist>.
- <This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.>
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your <doctor> <or> <pharmacist>.> See Section 4.>

<**Read all of this leaflet carefully before you start <taking> <using> this medicine because it contains important information for you.>**
Always <take> <use> this medicinal product in accordance with the indications listed in this leaflet or with the indications provided by your <doctor> <or> <pharmacist>.
- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your <doctor> <or> <pharmacist>.> See Section 4.
- You must contact a doctor if your symptoms worsen or do not improve <after {number of} days.>

In this leaflet:

1. What is X and what it is used for

- You must contact a doctor if your symptoms worsen or do not improve <after {number of} days.>

2. Before you <take> <use> X

Do not <take> <use> X <:>

- <if you are allergic (hypersensitive) to {active substance(s)} or any of the other ingredients of X (mentioned at point 6).>

Special warnings and precautions for use
Before you <take> <use> X, please contact your <doctor> <or> <pharmacist>.

Children <and teenagers>
<**Athletes**>

<Taking> <Using> other medicines

<Please tell your <doctor> <or> <pharmacist> if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.>

<Taking> <Using> X with <food> and <drink> and <alcohol>

<Pregnancy> and <breast–feeding>

<If you are pregnant or if you breastfeed, think you might be pregnant or intend to, ask your <doctor > <or> <pharmacist> for advice before taking this medicine.>

Driving and using machines

<X contains {name(s) of excipient(s)}>

3. How to <take> <use> X

<Always <take> <use> X exactly as your doctor <or pharmacist> has told you. You should check with your <doctor> <or> <pharmacist> if you are not sure.>

<The usual dose is …>

<Always <take> <use> X as described in this leaflet or exactly as your doctor <or pharmacist><or nurse> has told you. You should check with your <doctor> <or> <pharmacist> if you are not sure.>

<The usual dose is …>

<Use in children <and teenagers>>

<The scoreline is only to facilitate breaking for ease of swallowing and not to divide into equal doses.>
<The tablet can be divided into equal halves.>
<The scoreline is not meant for the division of the tablet.>

<If you <take> <use> more X than you should>

<If you forget to <take> <use> X>
<Do not take a double dose to make up for a forgotten <dose> <tablet>.>

<If you stop <taking> <using> X>
<If you have any further questions on the use of this product, ask your <doctor> <or> <pharmacist>.>

4. Possible side effects

Like all medicines, X can cause side effects, although not everybody gets them.

<Additional side effects in children <and teenagers>>

Reporting of side effects
If you encounter any side effects, please tell your <doctor> or <pharmacist>. These include any type of side effects not listed in this leaflet.
You could also report side effects via the national reporting system, whose details are published on the website of the National Agency for Medicines and Medical Devices, http://www.anm.ro/. By reporting the side effects, you could help with the supply of additional information related to the safety of this medicinal product.

5. How to store X

Keep out of the reach and sight of children.

Do not use X after the expiry date which is stated on the <label> <carton> <bottle> <...> <after {abbreviation used for expiry date}.> <The expiry date refers to the last day of that month.>

[For terms to be used in accordance with the storage conditions see Annex III to the Order of the Minister of Health no. 1446/2010]
<Do not use X if you notice {description of the visible signs of deterioration}.>

<Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.>

6. Further information

What X contains
- The active substance(s) is (are)…
- The other ingredient(s) excipient(s) is (are)...

What X looks like and contents of the pack

Marketing Authorisation Holder and Manufacturer

{Name and address}
<{tel}>
<{fax}>
<{e–mail}>

For any information about this medicinal product, please contact the local representatives of the Marketing Authorisation Holder:

Romania
{Name}
<{Address}
{City} {Postal code} – RO>
Tel: + {Telephone number}
<{e-mail}>

This leaflet was last approved in < {**MM/YYYY**}.>

<This medicinal product has been authorised under „special circumstances".
This means that, <due to the scarceness of the disease> <due to scientific reasons> <due to ethical reasons>, complete information about the product couldn't be gathered.
The National Agency for Medicines and Medical Devices shall yearly revise any new available information about this medicinal product and this leaflet is updated, as required.>

<Other sources of information>

You can find detailed information about this product on the website of the National Agency for Medicine and Medical Devices, http://www.anm.ro/

<----------

< The following information is intended for medical or healthcare professionals only:>>

SUMMARY OF PRODUCT CHARACTERISTICS

< ▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.>

1. NAME OF THE MEDICINAL PRODUCT

{(Invented) name strength pharmaceutical form}

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

<Excipient(s):>

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

<The scoreline is only to facilitate breaking for ease of swallowing and not to divide into equal doses.>
<The scoreline is not meant for the division of the tablet>
<The tablet can be divided into equal doses.>

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

<This medicinal product is for diagnostic use only.>

<{X} is indicated in <adults> <neonates> <infants> <children> <adolescents> <aged {x to y}> <years> <months>.>

4.2 Posology and method of administration

Posology

Children and teenagers

<The <safety> <and> <efficacy> of {X} in children aged {x to y} <months> <years> {or any other relevant subsets, e.g. weight, pubertal age, gender} <has> <have> not <yet> been established.>
<No data are available.>
<Currently available data are described in section <4.8> <5.1> <5.2> but no recommendation on a posology can be made.

<{X} should not be used in children aged {x to y} <years> <months> {or any other relevant subsets e.g. weight, pubertal age, gender} because of <safety> <efficacy> concern(s).>

<There is no relevant use of {X} <in the paediatric population> <in children aged {x to y} <years> <months> {or any other relevant subsets, e.g. weight, pubertal age, gender} <in the indication...>.

<{X} is contraindicated in children aged {x to y} <years> <months> {or any other relevant subsets, e.g. weight, pubertal age, gender} <in the indication...> (see Section 4.3).>

Method of administration

<Precautions to take prior to handling or administration of the medicinal product>
<For instructions on the <reconstitution> <dilution> of the medicinal product before administration, see Sections <6.6> <and> <12>.>

4.3 Contraindications

<Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1 <or {name of the residue(s)}>.>

4.4 Special warnings and precautions for use

<Children and teenagers>

<Athletes>

4.5 Interaction with other medicinal products and other forms of interaction

<No interaction studies have been performed.>

<Children and teenagers>

<Interaction studies have only been performed in adults.>

4.6 Pregnancy, lactation and fertility
[For Pregnancy and lactation statements see Annex I of the Order of the Minister of Health no. 1446/2010]

<Pregnancy>
<Lactation>
<Fertility>

4.7 Effects on ability to drive and use machines

<{Invented name} has <no <or negligible> influence> <minor or moderate influence> <major influence> on the ability to drive and use machines.>

<Not relevant.>

4.8 Side effects

<Children and teenagers>

Reporting suspected adverse reactions
It is important to report adverse reactions suspected after the product's authorisation. This allows a continual monitoring of the product's risk-benefit balance. Healthcare professionals are asked to report any adverse reaction suspected via the national reporting system, whose details are published on the website of the National Agency for Medicines and Medical Devices http://www.anm.ro.

4.9 Overdose

<Children and teenagers>

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: {group}, ATC code: {code} <blank>

<{Invented name} is a biosimilar medicinal product. You can find detailed information about this product on the website of the National Agency for Medicines and Medical Devices, http://www.anm.ro .>

<Mechanism of action>
<Pharmacodynamic effects>
<Clinical efficacy and safety>
<Children and teenagers>

<The European Medicines Agency has waived the obligation to submit the results of studies with {(Invented) Name} [or with generic medicinal products: <reference medicinal product containing {name of the active substance(s)}>] in all subsets of the paediatric population in {condition as per Paediatric Investigation Plan (PIP) decision, in the granted indication} (see section 4.2 for information on paediatric use).>

<The European Medicines Agency has deferred the obligation to submit the results of studies with {(Invented) Name} [or with generic medicinal products: <reference medicinal product containing {name of the active substance(s)}>] in one or more subsets of the paediatric population in {condition as per Paediatric Investigation Plan (PIP) decision, in the granted indication} (see section 4.2 for information on paediatric use).>

<This medicinal product has been authorised under 'exceptional circumstances'.
This means that <due to the rarity of the disease> <for scientific reasons> <for ethical reasons> it has not been possible to obtain complete information on this medicinal product.
The National Agency for Medicines and Medical Devices shall yearly review any new available information and this SPC is updated, if applicable.>

5.2 Pharmacokinetic properties

<Absorption>
<Distribution>
<Metabolisation>
<Disposal>
<Linearity/Nonlinearity >
<Pharmacokinetic/pharmacodynamic relationship(s)>

5.3 Preclinical safety data

<Non–clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.>
<Effects in non–clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.>
<Adverse reactions not observed in clinical studies, but seen in animals at exposure levels similar to clinical exposure levels and with possible relevance to clinical use were as follows:>

<Environmental Impact Assessment (EIA)>

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

<Not applicable.>

6.2 Incompatibilities

<Not applicable.>

<In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.>

<This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6 and section 12.>

6.3 Shelf life

<...> <6 months> <...> <1 year> <18 months> <2 years> <30 months> <3 years> <...>

6.4 Special precautions for storage

[For storage conditions statements see Annex III to the Order of the Minister of Health no. 1446/2010]
< For storage conditions of the <reconstituted> <diluted> medicinal product, see section 6.3.>

6.5 Nature and contents of container

<Not all pack sizes may be marketed.>

6.6 Special precautions for disposal <and other handling>

<Use in children and teenagers>

<No special requirements for disposal.>

<Any unused product or waste material should be disposed of in accordance with local requirements.>

7. MARKETING AUTHORISATION HOLDER

{Name and address}
<{tel}>
<{fax}>
<{e–mail}>

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<Date of first authorisation: <{month YYYY }>
<Date of most recent authorisation renewal: <{month YYYY }>

10. DATE OF REVISION OF THE TEXT

{MM/YYYY}

<11. DOSIMETRY>

<12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS >

< Any unused product or waste material should be disposed of in accordance with local requirements.>

You can find detailed information about this product on the website of the National Agency for Medicine and Medical Devices, http://www.anm.ro/

ANNEX 3
to SCD No.12/22.04.2013

Labelling

PARTICULARS TO APPEAR ON THE <OUTER PACKAGING> <AND> <THE IMMEDIATE PACKAGING>

{NATURE/TYPE}

{(Invented) name strength pharmaceutical form}
{Active substance(s)}

1. NAME OF THE MEDICINAL PRODUCT

{(Invented) name strength pharmaceutical form}
{Active substance(s)}

2. STATEMENT OF ACTIVE SUBSTANCE(S)

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

<Warnings for athletes – see Leaflet!>

<Pictogram (triangle shape **–** in accordance with the Order of the Minister of Health no. 759/2003**)**
(see leaflet for more information)


>]

8. EXPIRY DATE

[For terms on Expiry date see Annex IV to the Order of the Minister of Health no. 400/2006]

9. SPECIAL STORAGE CONDITIONS

[For terms on Storage condition see Annex III to the Order of the Minister of Health no. 1446/2010]

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

{Name and address}
<{Telephone number}>
<{Fax number}>
<{e-mail}>

12. MARKETING AUTHORISATION NUMBER(S)

{...../YYYY/01-...}

13. BATCH NUMBER

[For terms on Batch number see Annex IV to the Order of the Minister of Public Health no. 400/2006]

14. GENERAL CLASSIFICATION FOR SUPPLY

<Medicinal product subject to medical prescription -<PRF> <P6L> <PR> <PS>.>
< Medicinal product not subject to medical prescription.>

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

<Justification accepted for not including the information in Braille>

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS
{NATURE/TYPE}

{(Invented) name strength pharmaceutical form}
{Active substance(s)}

1. NAME OF THE MEDICINAL PRODUCT

{(Invented) name strength pharmaceutical form}
{Active substance(s)}

2. NAME OF THE MARKETING AUTHORISATION HOLDER

{Trade name}

3. EXPIRY DATE

[For terms on Expiry date see Annex IV to the Order of the Minister of Public Health no. 400/2006]

4. BATCH NUMBER

[For terms on Batch number, see Annex IV to the Order of the Minister of Public Health no. 400/2006]

5. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

{NATURE/TYPE}

{(Invented) name strength pharmaceutical form}
{Active substance(s)}

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

{(Invented) name strength pharmaceutical form}
{Active substance(s)}
{Route of administration}

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

[For terms on Expiry date, see Annex IV to the Order of the Minister of Public Health no. 400/2006 ("Terms on Batch number and Expiry date, both on the inner and outer packaging")]

4. BATCH NUMBER

[For terms on Batch number, see Annex IV to the Order of the Minister of Health no. 400/2006]

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

{Name/stamp of the Marketing Authorisation Holder}

SUMMARY OF PRODUCT CHARACTERISTICS

[NOTE: the following are those items of information required by Article 708 of Law no. 95/2006 on healthcare reform, Title XVII – The medicinal product, as amended, transposing the amended Directive 2001/83/EC.
For the full information to be included in each section and subsection of the SmPC, please refer to Scientific Council Decision no. 22/27.11.2009 on approval of the Guideline on Summary of Product Characteristics, published on the NAMMD website:
http://www.anm.ro/anmdm/med_legislatie_hcs.html, which is a translation into Romanian and a transposition of the Guideline EC/2009 on the Summary of Product Characteristics (SmPC). This Guideline should also be read in conjunction with other relevant Guidelines (a cross-reference is made in this document), published on the NAMMD website and/or on the European Medicines Agency (EMA) website, http://www.ema.europa.eu (e.g. "QRD Convention to be followed for the EMA-QRD templates",
http://www.ema.europa.eu/htms/human/qrd/docs/convention.pdf)

During the evaluation process, applicants may present SmPCs for different strengths in one document, clearly indicating with grey-shaded titles the strength or presentation to which alternative text elements refer.
However, the final printed material shall contain a separate SmPC per strength and per pharmaceutical form, containing all pack-sizes related to the strength and pharmaceutical form concerned.

Standard statements are given in the European template, which must be used whenever they are applicable. If the applicant needs to deviate from these statements to accommodate medicinal product-specific requirements, alternative or additional statements will be considered on a case-by-case basis.

Text colour convention:
Violet text: recommendations referring to the information to be included in each section and subsection.
Black text: standard mentions/text to be or not to be included, as required/information to be filled out.

Bracketing convention:
{text}: Information to be filled in
<text>: Text to be selected or deleted as appropriate.]

[ONLY for medicinal products subject to additional monitoring:
The black symbol and the specifications should precede Section 1. The black symbol should be an equilateral triangle oriented downwards: the symbol should be proportional to the size of the characters used in the text and each side of the triangle should be no longer than 5 mm. In view of submitting the information about the medicinal product, the black triangle shown here is used (see below).]

< ▼ This medicinal product is subject to an additional monitoring. This shall allow a rapid identification of new safety information. Healthcare professionals are asked to report any suspected adverse reaction. See Section 4.8 on the manner of reporting adverse reactions.>

1. NAME OF THE MEDICINAL PRODUCT

[The Guideline on the expression of strength in the trade name of medicinal products for human use, approved through Scientific Council Decision no. 11/07.06.2010, is available on the NAMMD website: http://www.anm.ro/anmdm/med_legislatie_hcs.html]

[The pharmaceutical form is stated in accordance with the Scientific Council Decisions concerning the approval of Romanian Standard Terms for pharmaceutical forms, starting materials, closure and administrative systems, in accordance with the European Standard Terms approved by the European Pharmacopoeia Commission, available on the NAMMD website: http://www.anm.ro/anmdm/med_legislatie_hcs.html]

{(Invented) name strength pharmaceutical form}

[No ® ™ symbols is attached here and throughout the text.]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

[The name(s) of the active substance(s) is written in Romanian.]

<Excipient(s) with known effect :>
<For the full list of excipients, see section 6.1.>

3. PHARMACEUTICAL FORM

<The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.>
<The score line is not intended for breaking the tablet.>
<The tablet can be divided into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

[Specify, if appropriate, <This medicinal product is for diagnostic use only.>]

<{X} is indicated in <adults> <neonates> <infants> <children> <adolescents> <aged {x to y}> <years> <months>.>

4.2 Posology and method of administration

Posology
[Additional subheadings such as "Elderly patients" or "Patients with renal impairment" can be stated if necessary.]

Paediatric population

<The <safety> <and> <efficacy> of {X} in children aged {x to y} <months> <years> {or any other relevant subsets, e.g. weight, pubertal age, gender} <has> <have> not <yet> been established.> [One of the following statements should be added:
<No data are available.>
or]<Currently available data are described in section <4.8> <5.1> <5.2> but no recommendation on a posology can be made.>

<{X} should not be used in children aged {x to y} <years> <months> {or any other relevant subsets e.g. weight, pubertal age, gender} because of <safety> <efficacy> concern(s).> [concern(s) to be stated with cross-reference to sections detailing data (e.g. 4.8 or 5.1).]

<There is no relevant use of {X} <in the paediatric population> <in children aged {x to y} <years> <months> {or any other relevant subsets, e.g. weight, pubertal age, gender} <in the indication...>.> [specify indication(s).]

<{X} is contraindicated in children aged {x to y} <years> <months> {or any other relevant subsets, e.g. weight, pubertal age, gender} <in the indication...> [specify indication(s).] (see section 4.3).>

Method of administration

<Precautions to be taken before handling or administering the medicinal product>

[Method of administration: directions for proper use by healthcare professionals or by the patient. Further practical details for the patient can be included in the package leaflet, e.g. in the case of inhalers, subcutaneous self-injection. Explanatory illustrations may be included, if necessary.]

<For instructions on <reconstitution> <dilution> of the medicinal product before administration, see section <6.6> <and> <12>.

4.3 Contraindications

[In case the active substance(s) is/are included on the List of the substances contraindicated to drivers, approved through Order of the Minister of Health no. 87/2003 supplemented through Order of the Minister of Health no. 759/2003, this subsection shall also state the fact that their use is contraindicated in drivers, with cross-reference to subsection 4.7.]

<Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1 <or {name of the residue(s)}>.

4.4 Special warnings and precautions for use

[Sub-headings (e.g. "Interference with serological testing" "Hepatic impairment", "QT prolongation") should be used where necessary to facilitate readability (i.e. identification of information in lengthy section).]

<Paediatric population>

<Athletes>
[State the active substance(s) included on the list of forbidden substances from the World Anti-doping Code in force established by the World Anti-doping Agency, http://www.wada-ama.org/en/ .]

<This medicinal product contains an <active substance(s)> which might determine whether anti-doping tests turned positive.>

[For excipients with a known effect, warnings is enforced in accordance with the Order of the Minister of Health no. 1202/02.10.2006, available on the NAMMD website: http://www.anm.ro/anmdm/med_legislatie_ordine.html]

4.5 Interaction with other medicinal products and other forms of interaction

<No interaction studies have been performed.>

<Paediatric population>

<Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation

[For standard statements referring to pregnancy and lactation, see Annex 1 to the Order of the Minister of Health no. 1446/2010, available on the NAMMD website, http://www.anm.ro/anmdm/med_legislatie_ordine.html]

<Pregnancy>
<Breastfeeding>
<Fertility>

[Additional sub-headings such as "Women of childbearing potential", "Contraception in males and females" can be stated, as appropriate.]

4.7 Effects on the ability to drive and use machines

< {Invented name} has <no or negligible influence> <minor influence> <moderate influence> <major influence> on the ability to drive and use machines.> <and its use is forbidden for drivers and those using machines (see Section 4.3.)
[Describe effects where applicable.]

<Not relevant.>

4.8 Undesirable effects

[For MedDRA frequency convention and system organ class database, see Annex II to the Order of the Minister of Health no. 1446/2010, available on the NAMMD website, http://www.anm.ro/anmdm/med_legislatie_ordine.html]

[Subheadings should be used to facilitate identification of information on each selected adverse reaction and on each relevant special population, e.g.: "Summary of the safety profile", "Tabulated list of adverse reactions", "Description of selected adverse reactions" (alternatively the subsection could be named with the name of the relevant adverse reaction), "Other special populations".]

<Paediatric population>

[For all medicinal products:
The following subtitle should also appear in the end of Section 4.8]

Reporting suspected adverse reactions
It is important to report adverse reactions suspected after the product's authorisation. This allows a continual monitoring of the product's risk-benefit balance. Healthcare professionals are asked to report any adverse reaction suspected via the national reporting system, whose details are published on the website of the National Agency for Medicines and Medical Devices http://www.anm.ro.

4.9 Overdose

[Additional sub-headings, such as "Symptoms" or "Management" can be stated, if necessary.]
<Paediatric population>

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: {group}, ATC code: {code} <not yet assigned>

[For medicinal product authorised as similar biological medicinal product, include the following statement:]
<{(Invented) Name} is a biosimilar medicinal product. Detailed information is available on the website of the National Agency for Medicines and Medical Devices, http://www.anm.ro/>.

[Tabular presentation of clinical efficacy and safety information may be used.]

<Mechanism of action>
<Pharmacodynamic effects>
<Clinical efficacy and safety>
<Paediatric population>

[If the European Medicines Agency has waived or deferred the obligation to submit the outcomes of the performed trials, the information should be given as follows:]

<The European Medicines Agency has waived the obligation to submit the results of studies with {(Invented) Name} [or with generic medicinal products: <reference medicinal product containing {name of the active substance(s)}>] in all subsets of the paediatric population in {condition as per Paediatric Investigation Plan (PIP) decision, in the granted indication} (see section 4.2 for information on paediatric use).>

<The European Medicines Agency has deferred the obligation to submit the results of studies with {(Invented) Name} [or with generic medicinal products: <reference medicinal product containing {name of the active substance(s)}>] in one or more subsets of the paediatric population in {condition as per Paediatric Investigation Plan (PIP) decision, in the granted indication} (see section 4.2 for information on paediatric use).>

<This medicinal product has been authorised under 'exceptional circumstances'.
This means that <due to the rarity of the disease> <for scientific reasons> <for ethical reasons> it has not been possible to obtain complete information on this medicinal product.
The National Agency for Medicines and Medical Devices will review any new information which may become available every year and this SmPC will be updated as necessary.>

5.2 Pharmacokinetic properties

<Absorption>
<Distribution>
<Biotransformation>
<Elimination>
<Linearity/non-linearity>
<Pharmacokinetic/pharmacodynamic relationship(s)>

[Additional sub-heading(s), such as "Renal impairment", "Hepatic impairment", "Elderly", "Paediatric population" or "Other special populations" (to be specified) should be used, where appropriate.]

5.3 Preclinical safety data

[Additional subheadings such as "Juvenile animal studies" can be included when necessary.]
<Nonclinical data have not shown any special risk in humans based on conventional pharmacological studies concerning safety assessment, toxicity after repeated doses, genotoxicity, carcinogenicity, toxicity on reproduction and development.>
<Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.>
<Adverse reactions not observed in clinical studies, but seen in animals at exposure levels similar to clinical exposure levels and with possible relevance to clinical use were as follows:>

<Environmental Risk Assessment (ERA)>

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

[Name of the excipient(s) in Romanian.]
<None>

6.2 Incompatibilities

<Not applicable.> [if appropriate, e.g. for solid oral pharmaceutical forms.]

<In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.> [e.g. for parenterals.]

<This medicinal product must not be mixed with other medicinal products except those mentioned in section <6.6> <and> <12>.>

6.3 Shelf life

[Information on the finished product shelf life and on the in-use stability after 1st opening and/or reconstitution/dilution should appear here. Only one overall shelf life for the finished product is to be given even if different components of the product may have a different shelf life (e.g. powder & solvent). For example, if the powder's shelf life is 2 years, and the solvent's, 3 years, the medicinal product's shelf life is 2 years.]
<...> <6 months> <...> <1 year> <18 months> <2 years> <30 months> <3 years> <...>

6.4 Special precautions for storage

[For standard statements referring to storage conditions, see Annex III to the Order of the Minister of Health no. 1446/2010, available on the NAMMD website, http://www.anm.ro/anmdm/med_legislatie_ordine.html]

[General storage conditions of the finished medicinal product should appear here, together with a cross-reference to section 6.3 where appropriate:
<For storage conditions after <reconstitution> <dilution> <first opening> of the medicinal product, see section 6.3.>

6.5 Nature and contents of container

<Not all pack sizes may be marketed.>

6.6 Special precautions for disposal <and other handling

[Include practical instructions for preparation and handling of the medicinal product, where applicable, including disposal of the medicinal product, and waste materials derived from the used medicinal product. Presentation of practical information using pictograms in addition to text may be considered, if necessary.]

<Use in the paediatric population>

<No special requirements <for disposal>.>

<Any unused medicinal product or waste material should be disposed of in accordance with local requirements.>

7. MARKETING AUTHORISATION HOLDER

[Country name in Romanian.]
{Name and address}
<{tel.}>
<{fax}>
<{e-mail}>

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[As per SmPC guideline, the date should be stated in the following format:]
<Date of first authorisation: {DD month YYYY}>
<Date of latest renewal: {DD month YYYY}
[The date should correspond to the initial authorisation of the medicinal product concerned.]

10. DATE OF REVISION OF THE TEXT

< {month YYYY}>

<11. DOSIMETRY>

<12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS>

<Any unused medicinal product or waste material should be disposed of in accordance with local requirements.>

Detailed information on this medicinal product is available on the website of the National Agency for Medicines and Medical Devices: http://www.anm.ro

LABELLING AND PACKAGE LEAFLET

[The lay-out of the labelling and package leaflet presented in this template is only intended for Annex I "Leaflet" and for Annex III "Labelling information" of the marketing authorisation. Recommendations about the optimal manner of conceiving and organising the information on the package and leaflet are available in the Scientific Council Decision no. 8/26.06.2009, available on the NAMMD website,
http://www.anm.ro/anmdm/med_legislatie_hcs.html]

[**B**oxed headings in Annex III are provided to help applicants when completing the European template; they are not to appear in the final printed packaging materials (mock-ups/specimens).
A separate text for outer and inner packaging labelling should be completed per strength and per pharmaceutical form. Different pack sizes of the same strength can be presented in one document.
A separate package leaflet should be provided per strength and per pharmaceutical form. During the evaluation process however, applicants may present package leaflets for different strengths in one document, clearly indicating the strength or presentation to which alternative text elements refer. Where applicants consider marketing a combined printed package leaflet, a detailed justification for such a combined package leaflet will have to be included at submission of the marketing authorisation/renewal application. The justification shall take into account the recommendations of the "Compilation of QRD decisions on stylistic matters", published on the website of the European Medicines Agency, http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/10/WC500004442.pdf.
Text which will not appear in the final printed material is to be presented as grey-shaded text].

[Patient alert card:
In case a patient alert card is to be included in the carton, then the text itself will have to be part of the product information (at the end of the inner packaging).]

LABELLING

[NOTE: these are all mandatory items listed in Title V, Labelling and leaflet of Law no. 95/2006 – Title XVII "The medicinal product", transposing Title V of Directive 2001/83/EC.
The data should be presented according to the template below, irrespectively of their sequence on the actual labelling and their position and possible repetition on the individual sides/flaps of the packaging.
Where the same text for outer and inner packaging is used, this should be clearly indicated in the first heading and in {nature/type}. Text which is identical for different presentations should be provided only once, e.g. text of inner vial label where such vial is part of different pack-sizes.

On the printed outer packaging material, an empty space should be provided for the prescribed dose.]

REGULARS TO APPEAR ON <THE OUTER PACKAGING> <AND> <THE IMMEDIATE PACKAGING>

{NATURE/TYPE}

1. NAME OF THE MEDICINAL PRODUCT

{(Invented) name strength pharmaceutical form} [as it appears in the SmPC under section 1.]
{Active substance(s)}

[The reference to the active substance should correspond to the strength expressed in the name,
e.g. (invented) name 60 mg capsules toremifene
(since 60 mg corresponds to toremifene, even if the active substance is actually present as toremifene citrate).]

[The Guideline on the expression of strength and trade name of medicinal products for human use, approved through Scientific Council Decision no. 11/07.06.2010, is available on the NAMMD website:
http://www.anm.ro/anmdm/med_legislatie_hcs.html]

[For mock-ups and specimens, this information may be presented on different lines of text or in different font sizes if necessary, provided that the appearance of the name is as an integrated item,
e.g. (invented) name Z mg/ml
solution for injection]

[The international non-proprietary name (INN) of the active substance(s) is included.
In addition, the different strengths of fixed-combination medicinal products should be presented separated by a "/". The names of the active substances should be presented separated by a "/" and in the same order relating to the strength,
e.g. (invented) name 150 mg/12.5 mg tablets
irbesartan/hydrochlorothiazide]

2. STATEMENT OF ACTIVE SUBSTANCE(S)

[Expressed qualitatively and quantitatively per dosage unit or according to the form of administration for a given volume or weight. Where the active substance is present as a salt, this should be clearly indicated, e.g. for the examples given above: "60 mg toremifene (as citrate)", "60 mg diltiazem hydrochloride". The statement should be based on the information on the active substance given in section 2 of the SmPC.]

3. LIST OF EXCIPIENTS

[Express qualitatively those excipients known to have a recognised action or effect and included in the Order of the Minister of Health no. 1202/02.10.2006, published on the NAMMD website,
http://www.anm.ro/anmdm/med_legislatie_ordine.html . However, if the medicinal product is a parenteral, a topical or an eye preparation or if used for inhalation, all excipients must be stated.]

4. PHARMACEUTICAL FORM AND CONTENTS

[The pharmaceutical form is expressed in accordance with the Scientific Council Decisions related to the approval of Romanian Standard Terms for pharmaceutical forms, primary packages, closure and administrative systems, in accordance with the European Standard Terms approved by the European Pharmacopoeia Commission, published on the NAMMD website, http://www.anm.ro/anmdm/med_legislatie_hcs.html. The full form of the Standard Terms is used. Pharmaceutical form patient-friendly terms will be considered on a case-by-case basis, in case of space constraints. If used, the pharmaceutical form patient-friendly term should be added in brackets in section 3 of the SmPC.
Contents by weight, by volume or by number of doses or number of units of administration of the medicinal product (i.e. pack size, including a reference to any ancillary items included in the pack such as needles, swabs, etc.). The information should be as simple and descriptive as possible using terms used in section 3 and 6.5 of the SmPC. Since the pharmaceutical form is already mentioned as part of the name of the medicinal product in section 1, it should be repeated here in grey shading, so that it will not appear several times on the final printed material.
In case of a combined labelling text covering different pack sizes of the same strength, each pack size should be listed on a separate line in grey shading,
e.g. 14 film-coated tablets
28 film-coated tablets
42 film-coated tablets]

[In case of a treatment initiation pack, please follow the below example:
"Treatment initiation pack
Each pack of 28 film-coated tablets for a 4 week treatment schedule contains:
7 film-coated tablets of X 5 mg
7 film-coated tablets of X 10 mg
7 film-coated tablets of X 15 mg
7 film-coated tablets of X 20 mg"]

5. METHOD AND ROUTE(S) OF ADMINISTRATION

[Method of administration: directions for proper use of the medicinal product, e.g. "Do not swallow", "Do not chew", "Shake well before use". In all cases, and especially if full details cannot be included on the outer packaging itself, a reference to the package leaflet must be made:]

Read the package leaflet before use.

[The Standard terms approved through the Scientific Council Decisions related to the approval of Romanian Standard Terms for pharmaceutical forms, primary packages, closure and administrative systems is used for the routes of administration, in accordance with the European Standard Terms approved by the European Pharmacopoeia Commission, published on the NAMMD website, http://www.anm.ro/anmdm/med_legislatie_hcs.html.]

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. SPECIAL WARNING(S), IF NECESSARY

[Special warnings on labelling should be reserved:

- To cases where they are considered very important in order to fulfil a risk minimisation objective (e.g. "Cytotoxic: Handle with caution", "May cause birth defects", etc.).]

- To cases where the active substance(s) of the medicinal product is/are included on the list of forbidden substances from the World Anti-doping Code in force established by the World Anti-doping Agency, http://www.wada-ama.org/en/, when the leaflet shall state:

<Warning for Athletes – see leaflet!>]

[If the active substance(s) is/are included on the List of substances contraindicated to drivers, approved through Order of the Minister of Health no. 87/2003 supplemented through Order of the Minister of Health no. 759/2003, this section shall contain the following statement and pictogram:

<Pictogram (a triangle, in accordance with the Order of the Minister of Health no. 759/2003**)**
(see leaflet for more information)

8. EXPIRY DATE

[For terms on Expiry date, see Annex IV to the Order of the Minister of Health no. 400/2006, published on the NAMMD website, http://www.anm.ro/anmdm/med_legislatie_ordine.html]

[The expiry date printed on medicinal products stating only month and year should be taken to mean the last day of that month. Expiry dates should be expressed with the month given as 2 digits or at least 3 characters and the year as 4 digits, e.g.: January 2012, Jan 2012, 02-2012.]

[Where applicable, shelf life after reconstitution, dilution or after first opening the container.
Please refer to CHMP "Note for Guidance on Maximum Shelf Life for Sterile Products for Human Use after First Opening or Following Reconstitution" (CPMP/QWP/159/96/corr). If however the maximum in-use shelf life for the reconstituted medicinal product varies, depending on how, or with what, it is reconstituted, then there should be a statement on the label, such as: "Read the leaflet for the shelf life of the reconstituted medicine".]

9. SPECIAL STORAGE CONDITIONS

[The statement(s) should reflect special precautions recommended in section 6.4 of the SmPC. For Storage condition statements, see Annex III to the Order of the Minister of Health no. 1446/2010, available on the NAMMD website.] http://www.anm.ro/anmdm/med_legislatie_ordine.html]

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

[The statement(s) should reflect special precautions recommended in section 6.6 or 12 of the SmPC, e.g. radiopharmaceuticals, cytostatics.]

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[Including town, postal code (if available) and country name of the MAH in Romanian. Telephone, fax numbers or e-mail addresses may be included (no MAH websites, no e-mails linking to MAH websites)].

{Name and address}
<{tel}>
<{fax}>
<{e-mail}>

12. MARKETING AUTHORISATION NUMBER(S)

[Item to be completed by the NAMMD once the Marketing Authorisation has been granted.]
[In case of a combined Annex III covering different pack sizes of the same strength, the respective pack sizes should be included in grey shading after the corresponding MA number and listed on a separate line,

e.g.

...../AAAA/01	14 film-coated tablets
...../AAAA/02	28 film-coated tablets
...../AAAA/03	42 film-coated tablets

13. MANUFACTURING BATCH

[For the terms to be used related to the number of the manufacturing batch, see Annex IV to the Order of the Minister of Health no. 400/2006, published on the NAMMD website, http://www.anm.ro/anmdm/med_legislatie_ordine.html]

14. GENERAL CLASSIFICATION FOR SUPPLY

[The classification for release is done in accordance with the Order of the Minister of Health no. 1602/31.12.2010 published on the NAMMD website, http://www.anm.ro/anmdm/med_legislatie_ordine.html]

< Medicinal product subject to medical prescription - <PRF> <P6L> <PR> <PS>.>
<Medicinal product not subject to medical prescription.>

15. INSTRUCTIONS ON USE

[Only for medicinal products **not subject** to medical prescription, include, in accordance with the available space and with provisions of Scientific Council Decision no. 8/26.06.2009:
- Therapeutic indication(s)
- Dose recommendations, contraindication(s) and warnings;
- General warnings and overdose warnings are not routinely required, but for certain medicinal products such warnings may be added during the procedure at the request of the NAMMD.]

16. INFORMATION IN BRAILLE

[Information that will appear in Braille on the printed outer packaging material should be mentioned here in normal text format; see also the Scientific Council Decision no. 12/15.07.2007, published on the NAMMD website, http://www.anm.ro/anmdm/med_legislatie_hcs.html]
[In cases where Braille is not included, according to the above mentioned guideline, the justification for such exclusion should be provided in module 1.3.6. Upon agreement by the NAMMD, the following statement should be included in this section in grey shading: <Justification for not including Braille accepted>.]

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

{NATURE/TYPE}

1. NAME OF THE MEDICINAL PRODUCT

{(Invented) name strength pharmaceutical form}
{Active substance(s)}

[The active substance is mentioned in accordance with the provisions in section 1 of the outer packaging.]

[Pharmaceutical form patient-friendly terms may be used in case of space limitation]

2. NAME OF THE MARKETING AUTHORISATION HOLDER

{Name} [Full/short name of the Marketing Authorisation Holder.]

3. EXPIRY DATE

[For terms on Expiry date, see Annex IV to the Order of the Minister of Health no. 400/2006, published on the NAMMD website, http://www.anm.ro/anmdm/med_legislatie_ordine.html]

4. MANUFACTURING BATCH

[For terms on Batch number, see Annex IV to the Order of the Minister of Health no. 400/2006, published on the NAMMD website, http://www.anm.ro/anmdm/med_legislatie_ordine.html]

5. OTHER

[Space permitting, any other information necessary for the correct use and administration of the medicinal product can be included here, e.g. Calendar days may be included if the product is taken as a single dose and that is packaged in blister strips that comprise multiples of seven.]

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

{NATURE/TYPE}

[Small immediate packaging units are defined as containers sized up to and including 10 ml. On a case-by-case basis the minimum particulars could also be considered for other containers where it is not feasible to include all the information. Such exceptional cases have to be justified, discussed and agreed with the NAMMD.
In case of radiopharmaceuticals, vials should be labelled in accordance with Art. 776 (3) of Law no. 95/2006, Title XVII – The medicinal product.]

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

{(Invented) name strength pharmaceutical form}
{Active substance(s)}
{Route of administration}

[In case of space-related limitations, patient-friendly terms may be used for the pharmaceutical forms; moreover, the abbreviations in the QRD table (containing standard abbreviations), published on the EMA website, http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/10/WC500004439.pdf, may be used as well.
Abbreviations should also be explained and stated in full in the relevant section of the package leaflet.]

[Where different labels apply to different constituents of the medicinal product, the pharmaceutical form in the name on the specific label should only refer to the constituent concerned (e.g. separate label for powder vial and solvent ampoule).]

[In case of a solvent container, section 1 should read:
"Solvent for X" (identify medicinal product name)
< {Route of administration}>]

2. METHOD OF ADMINISTRATION

[Method of administration: directions for proper use of the medicinal product, e.g. "Do not swallow", "Do not chew", "Shake well before use". If full details cannot be included on the immediate packaging itself, a reference to the package leaflet can be made, e.g. "Read the package leaflet before use".]

3. EXPIRY DATE

[For terms on Expiry date, see Annex IV to the Order of the Minister of Health no. 400/2006, published on the NAMMD website, http://www.anm.ro/anmdm/med_legislatie_ordine.html].

[Where applicable and if space permitting, shelf life after reconstitution, dilution or after first opening the container. For medicinal products which have a limited shelf life after opening or reconstitution, space and a statement inviting to record the date of opening or reconstitution is recommended, e.g. "reconstituted on: …", "EXPIRY DATE: …".

Please refer to "Note for Guidance on Maximum Shelf Life for Sterile Products for Human Use after First Opening or Following Reconstitution" (CPMP/QWP/159/96/corr).]

4. MANUFACTURING BATCH

[For terms on Batch number, see Annex IV to the Order of the Minister of Health no. 400/2006, published on the NAMMD website, http://www.anm.ro/anmdm/med_legislatie_ordine.html]

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

{Name/stamp of the Marketing Authorisation Holder}

[If space permitting, any other information related to the proper use and administration of the medicinal product, e.g. storage conditions, may be included.]

PACKAGE LEAFLET

[**NOTE**: the following items must appear in the package leaflet as required by Chapter V Labelling and Leaflet of Law no. 95/2006, Title XVII – The medicinal product, transposing Title V of Directive 2001/83/EC.
The package leaflet must be readable for the patient; see Scientific Council Decision no. 21/07.11.2008 and Scientific Council Decision no. 8/26.06.2009, published on the NAMMD website, http://www.anm.ro/anmdm/med_legislatie_hcs.html .
The package leaflet should be written in a language understandable by the patient and should reflect the terminology the patient is likely to be familiar with.
Throughout the text "X" stands for the (invented) name of the medicinal product.

The headings of the sections and subsections given in the European template must be used whenever they are applicable. If the applicant needs to deviate from these headings/statements to accommodate medicine-specific requirements (e.g. for medicines administered by healthcare professionals, "take"/"use" could be replaced by "are given" or "are administered"), alternative or additional headings/subheadings/statements different from those specified in the European template will be considered on a case-by-case basis (please also consider this for contraceptives).
When requested, applicants should justify the use of alternative headings/subheadings, different from European ones (e.g. by reference to user testing results).
For certain medicines not all items may be relevant, in this case the corresponding heading should not be included.

The purpose of the formats is to ensure that all the information required by Art. 769 of Law no. 95/2006, Title XVII – The medicinal product is included in the text versions of all packaging components in the order specified. Design and layout are key elements for the readability of the final printed material. Marketing authorisation holders will still need to format the resulting texts into the relevant full colour mock-ups for all packaging components.
European formats ensure the consistency of the presentation of information across medicinal products authorised through national procedure, and between these and the products authorised through European procedure.
Concerning the conception and organization of the information, as well as to the size, type and colour of characters from the printed leaflet, see Scientific Council Decision no. 8/26.06.2009.
The green recommendations refer to the sections/information in the SmPC corresponding to that section of the leaflet.
In accordance with Art. 14 (4) of Scientific Council Decision no. 12/15.07.2007, published on the NAMMD website, http://www.anm.ro/anmdm/med_legislatie_hcs.html, it is the responsibility of the Marketing Authorisation Holders to provide the leaflet at the request of patient organisations, in an adequate format and in its current version for blind people and for people suffering of visual impairment. As a consequence, MAHs are encouraged to include a statement at the end of each leaflet in view of informing the public about the availability of such formats.]

Package leaflet: Information for the <patient><user>
[Heading to be printed]

{(Invented) name strength pharmaceutical form}
{Active substance(s)}

[The (invented) name of the medicine (referred to as "this medicine" throughout the package leaflet, wherever practical) followed by the strength and pharmaceutical form (i.e. as it appears in section 1 of the SmPC) should be stated here in bold. This should be followed by the active substance(s) (as stated on the label section 1), which may be written on the line below. In the remainder of the document the invented name should appear in lower case without bold or underline and should not be used excessively throughout the text.]

[ONLY for medicinal products subject to additional monitoring:
The black symbol and the specifications should precede Section 1. The black symbol should be an equilateral triangle oriented downwards: the symbol should be proportional to the size of the characters used in the text and each side of the triangle should be no longer than 5 mm. In view of submitting the information about the medicinal product, the black triangle shown here is used (see below).]

< ▼ This medicinal product is subject to an additional monitoring. This shall allow a rapid identification of new safety information. Healthcare professionals are asked to report any suspected adverse reaction. See last part of Section 4 on the manner of reporting adverse reactions.>

[For medicinal products available ONLY on prescription:]
<**Read all of this leaflet carefully before you start <taking> <using> this medicine because it contains important information for you.**
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your <doctor> <,> <or> <pharmacist> <or nurse>.
- <- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.> [Do not include this statement in case of hospital use.]
- If you get any side effects, talk to your <doctor> <,> <or> <pharmacist> <or nurse>. This includes any possible side effects not listed in this leaflet.> See Section 4.>

[For medicinal products available without prescription:]
<**Read all of this leaflet carefully before you start <taking> <using> this medicinal product because it contains important information for you.**
Always <take> <use> this medicine exactly as described in this leaflet or as your <doctor> <,> <or> <pharmacist> <or nurse> <has> <have> told you.
- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- If you get any side effects, talk to your <doctor> <,> <or> <pharmacist> <or nurse>. This includes any possible side effects not listed in this leaflet. See Section 4.
- You must talk to a doctor if you do not feel better or if you feel worse <after {number of} days>.>

What is in this leaflet:
[User testing to date has indicated that most patients value a content listing in the package leaflet. In order for this to be most useful it needs to be prominently displayed where it appears. The content listing would normally reflect the six main sections of the leaflet, where a flat leaflet is prepared. However, if a booklet format is used, or the flat leaflet contains many subsections, a more detailed content listing may be used (page numbers or column numbers may be added to enable readers to quickly find the information they are seeking).]

1. What X is and what it is used for

[Invented name, active substance(s) and pharmacotherapeutic group]

[You should first of all include the invented name of the medicinal product and the active substance(s) included in it, as per section 2 of the SmPC, e.g. "X contains the active substance Y". The pharmacotherapeutic group and/or type of activity, as per section 5.1 of the SmPC should also be stated (e.g. statins (used to lower cholesterol).]

[Therapeutic indications]
[The therapeutic indications in line with section 4.1 of the SmPC should be stated here. It should be stated in which age group the medicine is indicated, specifying the age limits, e.g. "X is used to treat {specify indication} in <adults> <new-born babies> <babies> <children> <adolescents> <aged {x to y}> <years> <months>".]

[Information on the benefits of using this medicinal product]
[On a case-by-case basis, information on the benefits of the treatment could be included in this section, as long as it is compatible with the SmPC, useful for the patient, and to the exclusion of any element of a promotional nature. This could be included under a separate subheading, e.g. entitled "How X works".
The information should be depicted in a clear and condensed way. For example, information could relate to:

- signs and symptoms of the target disease, in particular for non-prescription medicines, but also for medicines to be taken "on-demand" (e.g. treatment of migraine);
- the benefit(s) of taking the medicine could be summarised (e.g. "this medicine reduces pain associated with arthritis", "this medicine has been shown to reduce blood sugar, which helps to prevent complications from your diabetes"). This would be particularly important to encourage adherence to the treatment, e.g. for long-term and prevention treatment. Benefit may be described in terms of prevention of disease complications (e.g. anti-diabetic), if established. The timing of the effect may also be described if useful. In any case, information must be compatible with the SmPC, in particular section 5.1;
- information on the amount of time the medicine usually takes to work may be presented if relevant for the patient (pain-killer, antidepressant, etc).

<You must talk to a doctor if you do not feel better or if you feel worse <after {number of} days>.>.]

2. What you need to know before you <take> <use> X

[This section should include information which patients/users should be aware of before they start taking the medicine and while using it. This section of the package leaflet is the one which in user testing patients have most difficulty with due to its overall size. The inclusion of additional sub-headings (e.g. for information to particular category of users) with a clear hierarchy is therefore critical in helping patients to navigate this information.]

[Contraindications]
Do not <take> <use> X <:>
[All contraindications mentioned in section 4.3 of the SmPC should be included here in the same order as presented in the SmPC. Other precautions and special warnings should be presented in the next section.
Care must be taken to ensure that complex details are not omitted.
It is not acceptable to state only the common or major contraindications. Belief that a patient cannot understand a contraindication is not a reason for omitting it.]

- <if you are allergic to {active substance(s)} or any of the other ingredients of this medicine (listed in section 6).>

[Appropriate precautions for use; special warnings]
Warnings and precautions
Talk to your doctor <or> <pharmacist> <or nurse> before <taking> <using> X
[All warnings and precautions for use included in section 4.4 of the SmPC should be provided here (as in the SmPC, the order should be in principle determined by the importance of safety information provided) and it should also be made clear for each warning or precaution for use, what action the patient should take to minimise the potential risk. Detailed information on warnings and precautions relating to side effects that could occur while a patient is taking the medicine should be presented in section 4, with an appropriate cross-reference in section 2.]

[Warnings relating to interactions, fertility, pregnancy and breast-feeding, the ability to drive and use machines, or excipients should be presented in the relevant subsequent subsections, unless they are of major safety importance (contraindication) in which case they should also be highlighted in the subsection "Do not take/use X", above.]

[An additional sub-heading could be included for information on additional monitoring tests that the patient will be required to undergo during treatment.]

Children <and adolescents>
[When the medicine is indicated in children, the warnings and precautions which are specific to this population (and identified as such in section 4.4 of the SmPC) should be included under this sub-heading. Where relevant, parents/carers should also be alerted in this section of potential children/teenager specific warnings included under "driving and using machines".]

[If there is no indication in some or all subsets of the paediatric population, information should reflect those in subsection *Paediatric population* (section 4.2 of the SmPC), e.g. "Do not give this medicine to children between the ages of x and y <years> <months>, because of the <risk of [....]> <it does not work> <the potential benefits are not greater than the risks>, <it is unlikely to be safe>".]

<**Athletes**>
[State the active substance(s) included on the list of forbidden substances from the World Anti-doping Code in force established by the World Anti-doping Agency, http://www.wada-ama.org/en/ .]
<This medicinal product contains an <active substance(s)> which might determine whether anti-doping tests turned positive.>

[Interactions with other medicinal products]
Other medicines and X
<Tell your <doctor> <or> <pharmacist> if you are <taking> <using>, have recently <taken> <used> or might <take> <use> any other medicines.>

[Describe the effects of other medicines on the medicine in question and vice versa as per section 4.5 of the SmPC. Refer to other medicines by their pharmacotherapeutic group/type of activity and by their INN(s) (including the lay terms first and the INNs in brackets unless the interaction is only with one active in a class, e.g. „statin (medicine used to lower cholesterol)".]

[In some cases, where it may be helpful to the patient, you should describe in brief terms the consequence of the interaction. One possibility could be to distinguish the medicine which must not be used with the medicine, e.g.: "Do not take X with Y (a medicine used for Z) as this may result in the <loss of its effect> <side effect>", those for which the combination should be avoided and those for which the combination would require some precaution (e.g. dose adjustment; in such a case please cross-refer to section 3 of this leaflet). For example, if hormonal oral contraceptives are likely to become ineffective as a result of an interaction, patients should also be advised to use additional forms of contraceptives (e.g. barrier contraceptives).]

[Interactions with herbal or alternative therapies should be addressed if mentioned in section 4.5 of the SmPC.]

[Interactions with food and drink]
X with <food> <and> <,> <drink> <and> <alcohol>
[Interactions not related to medicines should be mentioned here if reference is made in section 4.5 of the SmPC. For example, patients should not consume milk in combination with tetracyclines and no alcohol should be consumed during treatment with benzodiazepines. This section should not be used to tell patients whether or not their medicine should be taken before, during or after meals as this should only be addressed in section 3 (below), but a cross-reference to section 3 can be included.]

[Use by pregnant or breastfeeding women, information on fertility]

Pregnancy <and> <,> breast-feeding <and fertility>
[Where the information is significantly different, pregnancy, breast-feeding and fertility information can be presented under separate sub-headings.]

[Include conclusion summary of the information given in section 4.6 of the SmPC, in addition to the following optional statement:]
<If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your <doctor> <or> <pharmacist> for advice before taking this medicine.>

[Please note that if the medicine is contraindicated in pregnancy and/or breast-feeding the same information should be presented in both subsections ("Do not take/use X" & "Pregnancy, breast-feeding and fertility") of the leaflet and should include information on teratogenicity where this is known.]

[Effects on the ability to drive or to use machines]
Driving and using machines
[Where there is cautionary advice in section 4.7 of the SmPC related to the affectation of the ability to drive or use equipment, this should be translated into meaning colloquial language for the patient, in this section.

MAHs should bear in mind that medicines taken by children may need specific advice. For example, regarding road safety, children who may not be old enough to drive may nevertheless cycle.
The advice should include an explanation as to why the patient is advised not to drive or undertake these tasks, and whether or not they should discuss this with their doctor if they wish to do so.]

[Excipient warnings]
<X contains {name the excipient(s)}>
[Warnings referring to known excipients is included, in accordance with the Order of the Minister of Health no. 1202/02.10.2006, available on the NAMMD website: http://www.anm.ro/anmdm/med_legislatie_ordine.html] This subsection should be omitted when the medicine does not contain any excipients of known effect. In case the information relates to another section of the package leaflet (e.g. alcohol), a cross reference to this section should be made. It will also be necessary to refer back to the excipients warning from those sections relating to the effects (e.g. pregnancy and breast-feeding, paediatric information, ability to drive and use equipment).]

3. How to <take> <use> X

[Dose (SmPC Section 4.2)]
[For medicines available on prescription only:]
<Always <take> <use> this medicine exactly as your doctor <or pharmacist> has told you.
Check with your <doctor> <or> <pharmacist> if you are not sure.>

<The recommended dose is …>

[For medicines available without prescription:]
<Always <take> <use> this medicine exactly as described in this leaflet or as your <doctor> <,> <or> <pharmacist> <or nurse> <has> <have> told you. Check with your <doctor> <or> <,> <pharmacist> <or nurse> if you are not sure.>

<The recommended dose is …>

[When available, information on maximum single, daily and/or total dose should also be included. Additional sub-headings may be included where the posology varies for different indications or for different populations (e.g. elderly, hepatic impairment, renal impairment). Include the recommended dose and specify, if necessary, the appropriate time(s) at which the medicine may or must be administered.]

<Use in children <and adolescents>>
[When the medicine is indicated in different age groups with a different dose, method of administration, frequency of administration or duration of treatment, specific instructions for use for each age group should be clearly identified.
If there are more appropriate strength(s) and/or pharmaceutical form(s) for administration in some or all subsets of the paediatric population (e.g. oral solution for infants), these should be mentioned, e.g. "Other form(s) of this medicine may be more suitable for children; ask your doctor or pharmacist.".]

[Route(s) of administration (SmPC section 4.2)]
[The route(s) of administration is/are given in accordance with the Scientific Council Decisions on approval of the Romanian Standard Terms for pharmaceutical forms, primary packages, closure and administration systems, in accordance with the European Standard Terms approved by the European Pharmacopoeia Commission, available on the NAMMD website: http://www.anm.ro/anmdm/med_legislatie_hcs.html. An additional patient-friendly explanation may be given if necessary.
Method of administration: directions for a proper use of the medicine, e.g. "Do not swallow", 'Do not chew", "Shake well before use" (user testing experience has shown it is useful to state the reasons for the inclusion of such a statement, e.g. "Do not break or crush the tablet(s). If you do, there is a danger you could overdose because this medicine will be absorbed into your body too quickly").
When applicable, there should be descriptions (if useful with illustrations) of opening techniques for child-resistant containers and other containers to be opened in an unusual way.
Where relevant, guidance should always be included to clarify if the medicine must be taken with food, during/before meals, or clearly state if food/meals have no influence, etc.]
<The score line is only there to help you break the tablet if you have difficulty swallowing it whole.>
<The tablet can be divided into equal doses.>
<The score line is not intended for breaking the tablet.>

[Duration of treatment (SmPC section 4.2)]
[If appropriate, especially for medicines available without prescription, precise statements should be included on:

- the usual duration of the therapy;
- the maximum duration of the therapy;
- the intervals with no treatment;
- the cases in which the duration of treatment should be limited.]

[For some medicines it may be necessary to include some additional information in this section although this need not be covered in all cases.]

<If you <take> <use> more X than you should>

[Describe how to recognise symptoms if someone has taken an overdose and what to do as per SmPC section 4.9.]

<If you forget to <take> <use> X>

[Make clear to patients what they should do after irregular use of a medicine, e.g.: if information is available, try to include information on the maximum interval the missed dose can be caught up as per SmPC section 4.2.]

<Do not take a double dose to make up for a forgotten <tablet> <dose> <…>.>

<If you stop <taking> <using> X>

[Indicate withdrawal effects and how to minimise them as per SmPC section(s) 4.2 and/or 4.4**.**

A statement on the potential consequences of stopping the treatment before finishing the course of treatment and the need for a prior discussion with the treating physician, for medicines released on prescription, and with the pharmacist or nurse, for medicines released without prescription should be included as appropriate.]

[Close this section with:]

<If you have any further questions on the use of this medicine, ask your <doctor> <,> <or> <pharmacist> <or nurse>.>

4. Possible side effects

[Description of side effects]

[Begin this section with:]

Like all medicines, this medicine can cause side effects, although not everybody gets them.

[The section should generally be divided into two sections bearing in mind that there should be sufficient patient-friendly description of the overt clinical signs and symptoms to enable the patient to recognise all side effects which may occur as set out in section 4.8 of the SmPC:

1) summary safety profile as per section 4.8 of the SmPC: the most serious side effects need to be listed prominently first with clear instructions to the patients on what action to take (e.g. to stop taking the medicine and/or seek urgent medical advice; the use of the words "straight away" or "immediately" may be helpful in this context), together with the most frequently occurring side effects.

2) then a list of all other side effects (without repeating the most serious and most frequent included above).

Within each section, side effects should be arranged by frequency. The following frequency convention is recommended:

Very common: may affect more than 1 in 10 people
Common: may affect up to 1 in 10 people
Uncommon: may affect up to 1 in 100 people
Rare: may affect up to 1 in 1,000 people
Very rare: may affect up to 1 in 10,000 people
Not known: frequency cannot be estimated from the available data

This frequency convention should not appear before the list of side effects as this takes up space and has shown in user testing to be misleading to patients.

In any case, when expressing the likelihood of side effects it is important to include verbal terms and numerical data, as far as possible. Bear in mind that user testing has shown that double sided expressions such as "affects more than 1 in 100 but less than 1 in 10" are not well understood and should not be used.
System organ class listings should not be used. However, patient-friendly terms for parts of the body may be used as headings where the frequency is not known (e.g. for older medicines) in order to break up an otherwise long list, e.g. skin, stomach and gut, etc.]

<Additional side effects in children <and teenagers>>

[If appropriate (and in line with information stated in section 4.8 of the SmPC), a subsection should highlight any clinically relevant differences in terms of side effects in any relevant subset of the paediatric population compared to another or to the adult population.]

[For all medicinal products:
The following subtitle should show up in the end of Section 4]

Reporting of side effects
If you encounter any side effects, please tell your <doctor> or <pharmacist>. These include any type of side effects not listed in this leaflet.
You could also report side effects via the national reporting system, whose details are published on the website of the National Agency for Medicines and Medical Devices, http://www.anm.ro/. By reporting the side effects, you could help with the supply of additional information related to the safety of this medicinal product.

5. How to store X

Keep this medicine out of the sight and reach of children.

[Expiry date]
[Where a specific abbreviation for Expiry date is used on the labelling, it should be mentioned here.] Do not use this medicine after the expiry date which is stated on the <label> <carton> <bottle> <...> <after {abbreviation used for expiry date}.> <The expiry date refers to the last day of that month.>

[Storage conditions]
[Information should be compliant with section 6.4 of the SmPC; for storage condition statements, see Annex III to the Order of the Minister of Health no. 1446/2010, available on the NAMMD website, http://www.anm.ro/anmdm/med_legislatie_ordine.html]

[Where applicable, shelf life after reconstitution, dilution or after first opening the container]
[Information should be in accordance with section 6.3 of the SmPC; please also refer to "Note for Guidance on Maximum Shelf Life for Sterile Products for Human Use after First Opening or Following Reconstitution" (CPMP/QWP/159/96/corr).]

[Where appropriate, warnings against certain visible signs of deterioration]
<Do not use this medicine if you notice {description of the visible signs of deterioration}.>

< Do not throw away any medicines via wastewater <or household waste>. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.>

6. Contents of the package and other information

[Full statement of the active substance(s) and excipient(s)]
What X contains
[The active substance(s) (expressed qualitatively and quantitatively) and the other ingredients (expressed qualitatively) should be identified using their names as given in sections 2 and 6.1 of the SmPC and in Romanian.]
- The active substance(s) is (are)… [e.g. "Each <tablet> <capsule> contains x <gram> <milligram>…{active substance}".]
- The other <ingredient(s)> <(excipient(s))> is (are)... [A cross-reference to section 2 "X contains {name the excipients}" should be included when applicable.]

[Pharmaceutical form, nature and contents of container in weight, volume or units of dose]
What X looks like and contents of the package
[The pharmaceutical form should be stated according to the Scientific Council Decisions referring to the approval of the Romanian Standard Terms for pharmaceutical forms, primary packages, closure and administrative systems, in accordance with the European Standard Terms approved by the European Pharmacopoeia Commission, available on the NAMMD website: http://www.anm.ro/anmdm/med_legislatie_hcs.html
It is recommended to include a physical description, e.g. shape, colour, imprint, etc. as per section 3 of the SmPC.]

[All pack sizes for this pharmaceutical form and strength should be detailed here as per section 6.5 of the SmPC, including the reference to any ancillary items included in the pack such as needles, swabs etc.
If appropriate, indicate that not all pack sizes may be marketed. A cross-reference to other pharmaceutical forms and strengths may be included.]
[Name and address of the marketing authorisation holder and of the manufacturer responsible for batch release, if different]

Marketing Authorisation Holder and Manufacturer

{Name and address}
<{tel}>
<{fax}>
<{e-mail}>
[State the name and address of the Marketing Authorisation Holder as per section 7 of the SmPC and identify as such, e.g. "Marketing Authorisation Holder: ABC Ltd, etc." State the full address of the MAH, including the city, postal code (if available) and Member State in Romanian. Telephone, fax numbers or e-mail addresses may be included. The inclusion of the holding companies' websites and links sent via e-mails to the websites of holding companies are forbidden.]

[State the name and address of the manufacturer responsible for batch release, e.g. „Manufacturer: ABC …. etc". Please specify the full address of the manufacturer responsible for batch release, including the city, postal code (if available) and name of the Member State in Romanian. Telephone or fax numbers, e-mail addresses or websites are not allowed.]

[If MAH and manufacturer are the same, the general heading "Marketing Authorisation Holder and Manufacturer" can be used.]
[In cases where more than 1 manufacturer responsible for batch release is designated, all should be listed here (with or without grey-shading, depending on the option chosen for the printed package leaflet).
The printed package leaflet of the medicinal product must clearly identify the manufacturer responsible for the release of the concerned batch or mention only the specific manufacturer responsible for the release of that batch.]

[The local representative may be stated, without this being a mandatory requirement, when appropriate. There are cases in which the local representative and the MAH are one and the same. In such cases, nothing is stated.]

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder:

Romania
{Name}
<{Address}
{City} {Postal code} – RO>
Tel: + {Telephone number}
<{e-mail}>

This leaflet has been revised in <{**month YYYY**}.>
[The date of the release of the marketing authorisation/approval of the most recent variation implying changes in the leaflet or in the transfer of a Marketing Authorisation Holder.]

<This medicinal product has been authorised under 'exceptional circumstances'.
This means that <for scientific reasons> <for ethical reasons> it has not been possible to obtain complete information on this medicinal product.
The National Agency for Medicines and Medical Devices shall yearly revise any new available information about this product and this leaflet is updated, as required.>

<Other information sources>
[This subsection should include references to other information sources which are useful for the patient. These information sources should be compatible with the Summary of Product Characteristics and should not be promotional:
- Details referring to the manner in which patients can access this information randomly, e.g. Braille, audio, CD-ROM, for blind people or in adequate written format (e.g. font size: Sans serif, 16-20 points; contrast: black letters on white background; word spacing, text alignment, row spacing, aspect, quality of the paper) for blind persons (see Scientific Decision no. 12/2007. These details should have a larger font, so that blind persons are aware of the availability of information.]
Detailed information related to this medicinal product is available on the website of the National Agency for Medicines and Medical Devices, http://www.anm.ro/

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[For parenteral medicinal products, other products particularly used in the hospital or in the exceptional case of extemporaneous preparation (when a product is not suitable for use in children and when an adequate formulation

for children has not been developed (based on justified scientific reasons)), practical information relevant for healthcare professionals, e.g. preparation and/or handling, non-compliances, doses, overdosage or monitoring measures and laboratory investigations can be added in this section, when applicable, and a cross-reference to section 3 should also be included. In this case, the section shall start with the following statement:

<The following information is only meant for healthcare professionals>

[If additional scientific information must be included in the leaflet at the request of healthcare professionals, this can be done:

- either by providing a full SmPC as a separate document in the package;
- or by adding the entire SmPC as a document which can be attached at the end of the printed leaflet, so that the information meant for patients (in other terms, the leaflet) and the information meant for healthcare professionals (namely the SmPC) can be easily differentiated.

The intention of including a complete SmPC and the manner in which this issue will be solved should be explained by the applicant and indicated in the end of Annex 1 "Leaflet", without overtly repeating the last SmPC approved.
Applicants must decide whether the inclusion of scientific information on the package is proper, given the type of the medicinal product.]

DECISION

No. 14/22.04.2013

on approval of the Guideline on Good Pharmacovigilance Practices – Annex I - Definitions

The Scientific Council of the National Agency for Medicines and Medical Devices (NAMMD), established based on Order of the Minister of Health no. 158/18.02.2013, reunited on summons of the President of the National Agency for Medicines and Medical Devices in the ordinary meeting of 22.04.2013, in accordance with Article 12(5) of Government Decision no. 734/2010 on establishment, organisation and operation of the National Agency for Medicines and Medical Devices, as amended, adopts the following

DECISION

Sole article. – The Guideline on Good Pharmacovigilance Practices – Annex I – Definitions is approved, in accordance with the Annex which is integral part of this Decision.

PRESIDENT
of the Scientific Council
of the National Agency for Medicines and Medical Devices,

Acad. Prof. Dr. Leonida Gherasim

ANNEX
to SCD no. 14/22.04.2013

GUIDELINE ON GOOD PHARMACOVIGILANCE PRACTICES (GFP) Rev.1

Date of entry into force: December 2012

ANNEX I - DEFINITIONS

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Abuse of a medicinal product
Persistent or sporadic, intentional excessive use of medicinal products which is accompanied by harmful physical or psychological effects [Art. 695 (15) of Law 95/2006, as amended].

Advanced therapy medicinal product (ATMP)
A medicinal product for human use that is either a gene therapy medicinal product, a somatic cell therapy product or a tissue engineered products as defined in provisions of Art. 2 (1) a) of (EC) Regulation 1394/2007.

Adverse event (AE); synonym: Adverse experience
Any untoward medical occurrence in a patient or clinical trial subject administered a medicinal product, and which does not necessarily have a causal relationship with this treatment [Art. 21(m) of Order of the Minister of Health no. 904/25.07.2006 on approval of rules relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use].
An adverse event can therefore be any unfavourable and unintended sign (e.g. an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

Adverse reaction; synonyms: Adverse drug reaction (ADR), Suspected adverse (drug) reaction, Adverse effect, Undesirable effect
A response to a medicinal product which is noxious and unintended [Art. 695 (10) of Law 95/2006, as amended][17].
Response in this context means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility (see Annex IV, ICH-E2A Guideline).
Adverse reactions may arise from use of the product within or outside the terms of the marketing authorisation or from occupational exposure [Art. 812 (1) of Law 95/2006, as amended]. Conditions of use outside the marketing authorisation include off-label use, overdose, misuse, abuse and medication errors.
See also ***Adverse event, Serious adverse reaction, Unexpected adverse reaction, Off-label use, Overdose, Misuse of a medicinal product, Abuse of a medicinal product, Occupational exposure to a medicinal product***

[17] In the context of clinical trials, an adverse reaction is defined as all untoward and unintended responses to an investigational medicinal product related to any dose administered [Art. 2(n) of Directive 2001/20/EC].

Audit
A systematic, disciplined, independent and documented process for obtaining audit evidence and evaluating it objectively to determine the extent to which the audit criteria are fulfilled (see ISO 19011 (3.1)[2]).

Audit finding(s)
Results of the evaluation of the collected audit evidence against audit criteria (see ISO 19011 (3.4)[18]).
Audit evidence is necessary to support the auditor's results of the evaluation, i.e. the auditor's opinion and report; it is cumulative in nature and is primarily obtained from audit procedures performed during the course of the audit.
See also ***Audit***

Audit plan
Description of activities and arrangement for an individual audit (see ISO19011 (3.12)[19]]
See also ***Audit***

Audit programme
Set of one or more audits planned for a specific timeframe and directed towards a specific purpose (see ISO 19011 (3.11)[20])
See also ***Audit***

Audit recommendation
Describes the course of action management might consider to rectify conditions that have gone awry, and to mitigate weaknesses in systems of management control (see Sawyer LB et al, 20036).
Audit recommendations should be positive and as specific as possible. They should also identify who is to act on them (Sawyer LB et al, 2003).
See also ***Audit***

Clinical trial
Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more investigational medicinal product(s), and/or to identify any adverse reactions to one or more investigational medicinal product(s) and/or to study absorption, distribution, metabolism and excretion of one or more investigational medicinal product(s) with the objective of ascertaining its (their) safety and/or efficacy. This includes clinical trials carried out in either one site or multiple sites, whether in one or more Member State [Art. 21 a) of Order of the Minister of Public Health no. 904/2006].
See also ***Ongoing clinical trial, Completed clinical trial, Investigational medicinal product***

Closed signal
In periodic benefit-risk evaluation reports, a signal for which an evaluation was completed during the reporting interval (see Annex IV, ICH- E2C(R2) Guideline).
This definition is also applicable to periodic safety update reports.
See also **Signal**

Company core data sheet (CCDS)
For medicinal products, a document prepared by the marketing authorisation holder (MAH) containing, in addition to safety information, material related to indications, dosing,

[18] International Organisation for Standardisation (ISO); www.iso.org
[19] The International Organisation for Standardisation (ISO); www.iso.org
[20] The International Organisation for Standardisation (ISO); www.iso.org

pharmacology and other information concerning the product (see Annex IV, ICH-E2C(R2) Guideline).
See also Company core safety information

Company core safety information (CCSI)
For medicinal products, all relevant safety information contained in the company core data sheet prepared by the marketing authorisation holder and which the marketing authorisation holder requires to be listed in all countries where the company markets the product, except when the local regulatory authority specifically requires a modification (see Annex IV, ICH-E2C(R2) Guideline).
It is the reference information by which listed and unlisted are determined for the purposes of periodic reporting for marketed products, but not by which expected and unexpected are determined for expedited reporting (see Annex IV, ICH-E2C(R2) Guideline).
See also ***Company core data sheet***

Compassionate use of a medicinal product
Making a medicinal product available for compassionate reasons to a group of patients with a chronically or seriously debilitating disease or whose disease is considered to be life-threatening, and who cannot be treated satisfactorily by an authorised medicinal product (the medicinal product concerned must either be subject of an application for a central marketing authorisation or must be undergoing clinical trials) [Art. 83 (2) of Regulation (EC) 726/2004].

Completed clinical trial
Study for which a final clinical study report is available (see ICH-E2F Guideline, Volume 10 of the Rules Governing Medicinal Products in the EU).
See also Clinical trial

Consumer
For the purpose of reporting cases of suspected adverse reactions, a person who is not a healthcare professional such as a patient, lawyer, friend or relative/parent/child of a patient (see Annex IV, ICH-E2D Guideline).

Data lock point
For a periodic safety update report (PSUR), the date designated as the cut-off date for data to be included in a PSUR.
For a periodic benefit-risk evaluation report (PBRER), the date designated as the cut-off date for data to be included in a PBRER, based on the international birth date (see Annex IV, ICH-E2C(R2) Guideline).
For a development safety update report (DSUR), the date designated as the cut-off date for data to be included in a DSUR, based on the development international birth date (see ICH-E2F Guideline, Volume 10 of the Rules Governing Medicinal Products in the EU).
Date includes day and month (see ICH-E2F Guideline, Volume 10 of the Rules Governing Medicinal Products in the EU).
See also ***Periodic safety update report, Development safety update report, International birth date, Development international birth date***

Development international birth date (DIBD)
Date of first approval (or authorisation) for conducting an interventional clinical trial in any country (see ICH-E2F Guideline, Volume 10 of the Rules Governing Medicinal Products in the EU).

Development safety update report (DSUR)
Format and content for periodic reporting on drugs under development (see ICH-E2F Guideline, Volume 10 of the Rules Governing Medicinal Products in the EU).

EU reference date; synonym: Union reference date
For medicinal products containing the same active substance or the same combination of active substances, the date of the first marketing authorisation in the EU of a medicinal product containing that active substance or that combination of active substances; or if this date cannot be ascertained, the earliest of the known dates of the marketing authorisations for a medicinal product containing that active substance or that combination of active substances [Art. 819^3 (5) of Law 95/2006, as amended].

Generic medicinal product
A medicinal product which has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product, and whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies (Art. 704 (2) b) of Law 95/2006, as amended).

Good pharmacovigilance practices (GVP) for the European Union
A set of guidelines for the conduct of pharmacovigilance in the EU, drawn up based on art. 820^1 of Law 95/2006, as amended, by the European Medicines Agency in cooperation with competent authorities in Member States and interested parties, and applying to Marketing Authorisation Holders in the EU, the Agency and competent authorities in Member States.

Healthcare professional
For the purposes of reporting suspected adverse reactions, healthcare professionals are defined as medically qualified persons, such as physicians, dentists, pharmacists, nurses and coroners (see Annex IV, ICH-E2D Guideline).

Herbal medicinal product
Any medicinal product, exclusively containing as active ingredients one or more herbal substances or one or more herbal preparations, or one or more such herbal substances in combination with one or more such herbal preparations [Art. 695 (31) of Law 95/2006, as amended].
Herbal substances are all mainly whole, fragmented or cut plants, plant parts, algae, fungi, lichen in an unprocessed, usually dried, form, but sometimes fresh. Certain exudates that have not been subjected to a specific treatment are also considered to be herbal substances. Herbal substances are precisely defined by the plant part used and the botanical name according to the binominal system [Art. 695 (32) of Law 95/2006, as amended].
Herbal preparations are preparations obtained by subjecting herbal substances to treatments such as extraction, distillation, expression, fractionation, purification, concentration or fermentation. These include comminuted or powered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates [Art. 695 (33) of Law 95/2006, as amended].

Homeopathic medicinal product
Any medicinal product prepared from substances called homeopathic stocks in accordance with a homeopathic manufacturing procedure described by the European Pharmacopoeia or, in the absence thereof, by the pharmacopoeias currently used officially in EU Member States. A homeopathic medicinal product may contain a number of active principles (Art. 695 (4) of Law 95/2006, as amended).

Identified risk
An untoward occurrence for which there is adequate evidence of an association with the medicinal product of interest (see ICH-E2F Guideline, Volume 10 of the Rules Governing Medicinal Products in the EU).
Examples include:

 an adverse reaction adequately demonstrated in non-clinical studies and confirmed by clinical data;

 an adverse reaction observed in well-designed clinical trials or epidemiological studies for which the magnitude of the difference, compared with the comparator group on a parameter of interest suggests a causal relationship;

 an adverse reaction suggested by a number of well-documented spontaneous reports where causality is strongly supported by temporal relationship and biological plausibility, such as anaphylactic reactions or application site reactions (see ICH-E2F Guideline, Volume 10 of the Rules Governing Medicinal Products in the EU).

In a clinical trial, the comparator may be placebo, an active substance or non-exposure.
Adverse reactions included in section 4.8 of the summary of product characteristics (SmPC) are also considered identified risks, unless they are class-related reactions which are mentioned in the SmPC but which are not specifically described as occurring with this product (these would normally be considered as a potential risk)).
See also ***Risks related to use of a medicinal product, Important identified risk and Important potential risk, Important missing information, Unexpected adverse reaction***

Illegal purposes
See ***Misuse for illegal purposes***.

Immunological medicinal product
Any medicinal product consisting of vaccines, toxins, serums or allergen products:

a) Vaccines, toxins and serums shall cover in particular agents used to produce active immunity (such as cholera vaccine, BCG, polio vaccine, smallpox vaccine);
b) Agents used to diagnose the state of immunity (including in particular tuberculin and tuberculin PPD, toxins for the Schick and Dick Tests, brucellin);
c) Agents used to produce passive immunity (such as diphtheria antitoxin, anti-smallpox globulin, antilymphocytic globulin).

Allergen products shall mean any medicinal product which is intended to identify or induce a specific acquired alteration in the immunological response to an allergizing agent [Art. 695 (3) of Law 95/2006, as amended].

Important identified risk and important potential risk
An identified risk or potential risk that could have an impact on the risk-benefit balance of the product or have implications for public health (see ICH-E2F Guideline, Volume 10 of the Rules Governing Medicinal Products in the EU).
What constitutes an important risk will depend upon several factors, including the impact on the individual, the seriousness of the risk and the impact on public health. Normally, any risk that is likely to be included in the contraindications or warnings and precautions section of the product information should be considered important (see Annex IV, ICH-E2C(R2) Guideline).
See also ***Risk-benefit balance, Identified risk, Potential risk, Safety concern***

Important missing information
Critical gaps in knowledge for specific safety issues or populations that use the marketed product (see Annex IV, ICH-E2C(R2) Guideline).
See also ***Missing information, Safety concern***

Important potential risk
See ***Important identified risk*** *and* ***Important potential risk***

Individual case safety report (ICSR); synonym: Adverse (drug) reaction report

Format and content for the reporting of one or several suspected adverse reactions to a medicinal product that occur in a single patient at a specific point of time[21].
*See also **Minimum criteria for reporting***

International birth date (IBD)
The date of the first marketing authorisation for any product containing the active substance granted to any company in any country in the world (see Annex IV, ICH-E2C(R2) Guideline).

Investigational drug
Experimental product under study or development. This term is more specific than investigational medicinal product, which includes comparators and placebos (see ICH-E2F Guideline, Volume 10 of the Rules Governing Medicinal Products in the EU).
*See also **Investigational medicinal product***

Investigational medicinal product
An investigational medicinal product is a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including products already with a marketing authorisation but used or assembled (formulated or packaged) in a way different from the authorised form, or when used for an unauthorised indication, or when used to gain further information about the authorised form [Art. 21 d) of Order of the Minister of Health no. 904/2006].
*See also **Clinical trial***

Labelling
Information on the immediate or outer packaging [Art. 695 (25) of Law 95/2006, as amended].

Medicinal product
Any substance or combination of substances:
 presented as having properties for treating or preventing disease in human beings; or

 which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis [art. 695 (1) of Law 95/2006, as amended].

Medicinal product derived from human blood or human plasma
Any medicinal product based on blood constituents which is prepared industrially by a public or private establishment, such as a medicinal product including, in particular, albumin, coagulating factor(s) and immunoglobulin(s) of human origin [art. 695 (9) of Law 95/2006, as amended].

Minimum criteria for reporting
For the purpose of reporting cases of suspected adverse reactions, the minimum data elements for a case are: an identifiable reporter, an identifiable patient, an adverse reaction and a suspect medicinal product (see Annex IV, ICH-E2D Guideline).
For the purpose of validation of individual case safety reports as qualifying for reporting in the EU, see Module VI.
*See also I**ndividual case safety report***

[21] In the context of clinical trials, an individual case is an information provided by a primary source to describe suspected unexpected serious adverse reactions related to the administration of one or more investigational medicinal products to an individual patient at a particular point of time.

Missing information
Information about the safety of a medicinal product which is not available at the time of submission of a particular risk management plan and which represents a limitation of the safety data with respect to predicting the safety of the product in the marketplace.
Examples of missing information include populations not studied (e.g. pregnant women or patients with severe renal impairment) or where there is a high likelihood of off-label use.
See also ***Off-label use***

Misuse of a medicinal product
Situations where the medicinal product is intentionally and inappropriately used not in accordance with the authorised product information.
See also ***Misuse of a medicinal product for illegal purposes***

Misuse of a medicinal product for illegal purposes
Misuse for illegal purposes is misuse with the additional connotation of an intention of misusing the medicinal product to cause an effect in another person. This includes, amongst others: the sale, to other people, of medicines for recreational purposes and use of a medicinal product to facilitate assault.
See also ***Misuse of a medicinal product***

Name of the medicinal product
The name which may be either an invented name not liable to confusion with the common name, or a common or scientific name accompanied by a trade mark or the name of the marketing authorisation holder [Art. 695 (20) of Law no. 95/2006, as amended].
The common name is the international non-proprietary name (INN) recommended by the World Health Organization (WHO), or, if one does not exist, the usual common name [Art. 695 (21) of Law no. 95/2006, as amended].
The complete name of the medicinal product is the name of the medicinal product followed by the strength and pharmaceutical form.

Newly identified signal
In periodic benefit-risk evaluation reports, a signal first identified during the reporting interval, prompting further actions or evaluation
(see Annex IV, ICH-E2C(R2) Guideline).
This definition could also apply to a previously closed signal for which new information becomes available in the reporting interval prompting further action or evaluation (see Annex IV, ICH-E2C(R2) Guideline).
This definition is also applicable to periodic safety update reports.
See also **Signal, Closed signal**

Non-interventional trial; synonym: Non-interventional study
A study where the medicinal product(s) is (are) prescribed in the usual manner in accordance with the terms of the marketing authorisation; the assignment of the patient to a particular therapeutic strategy is not decided in advance by a trial protocol but falls within current practice and the prescription of the medicine is clearly separated from the decision to include the patient in the study; no additional diagnostic or monitoring procedures is applied to the patients and epidemiological methods is used for the analysis of collected data [Art. 21 (c) of Order of the Minister of Public Health no. 904/2006].
Thus, a trial is non-interventional if the following requirements are cumulatively fulfilled:
- the medicinal product is prescribed in the usual manner in accordance with the terms of the marketing authorisation;

• the assignment of the patient to a particular therapeutic strategy is not decided in advance by a trial protocol but falls within current practice and the prescription of the medicine is clearly separated from the decision to include the patient in the study; and
• no additional diagnostic or monitoring procedures are applied to the patients and epidemiological methods are used for the analysis of collected data (see Volume 10 of the Rules Governing Medicinal Products in the EU, Questions & Answers, Version 10.0).
Non-interventional studies are defined by the methodological approach used and not by the scientific objectives.
Non-interventional studies include database research or review of records where all the events of interest have already happened (this may include case-control, cross-sectional, cohort and other study designs making secondary use of data). Non-interventional studies also include those involving primary data collection (e.g. prospective observational studies and registries in which the data collected derive from routine clinical care), provided that the conditions set out above are met. In these studies, interviews, questionnaires and blood samples may be performed as normal clinical practice. Non-interventional trials do not fall in the scope of Order of the Minister of Public Health no. 904/2006.

Occupational exposure to a medicinal product
For the purpose of reporting cases of suspected adverse reactions, an exposure to a medicinal product as a result of one's professional or non-professional occupation.

Off-label use
Situations where a medicinal product is intentionally used for a medical purpose not in accordance with the authorised product information.

Ongoing clinical trial
Trial where enrolment has begun, whether a hold is in place or analysis is complete, but for which a final clinical study report is not available (see ICH-E2F Guideline, Volume 10 of the Rules Governing Medicinal Products in the EU).
See also ***Clinical trial, Completed clinical trial***

Ongoing signal
In periodic benefit-risk evaluation reports, a signal that remains under evaluation at the data lock point (see Annex IV, ICH-E2C(R2) Guideline).
This definition is also applicable to periodic safety update reports.
See also **Signal, Data lock point**

Overdose
Administration of a quantity of a medicinal product given per administration or cumulatively which is above the maximum recommended dose according to the authorised product information. Clinical judgement should always be applied.

Package leaflet
A leaflet containing information for the user which accompanies the medicinal product [Art. 695 (26) of Law 95/2006, as amended].

Periodic safety update report (PSUR)
Format and content for providing an evaluation of the risk-benefit balance of a medicinal product for submission by the marketing authorisation holder at defined time points during the post-authorisation phase.
In the EU, periodic safety update reports should follow the format described in Module VII.

Pharmacovigilance
Science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem (see WHO[22]).
In line with this general definition, underlying objectives of pharmacovigilance in accordance with the applicable EU legislation for are:
 preventing harm from adverse reactions in humans arising from the use of authorised medicinal products within or outside the terms of marketing authorisation or from occupational exposure; and
 promoting the safe and effective use of medicinal products, in particular through providing timely information about the safety of medicinal products to patients, healthcare professionals and the public.

Pharmacovigilance is therefore an activity contributing to the protection of patients' and public health.

Pharmacovigilance system
A system used by the marketing authorisation holder and by Member States to fulfil the tasks and responsibilities listed in Section X of Law 95/2006 and designed to monitor the safety of authorised medicinal products and detect any change to their risk-benefit balance [Art. 695 (28^1) c) of Law 95/2006, as amended].
In general, a pharmacovigilance system is a system used by an organisation to fulfil its legal tasks and responsibilities in relation to pharmacovigilance and designed to monitor the safety of authorised medicinal products and detect any change to their risk-benefit balance.

Pharmacovigilance system master file (PSMF)
A detailed description of the pharmacovigilance system used by the marketing authorisation holder with respect to one or more authorised medicinal products [Art. 695 point 28^1 d) of Law 95/2006, as amended].
See also ***Pharmacovigilance system***

Post-authorisation safety study (PASS)
Any study relating to an authorised medicinal product conducted with the aim of identifying, characterising or quantifying a safety hazard, confirming the safety profile of the medicinal product, or of measuring the effectiveness of risk management measures [Art. 695 (14) of Law 95/2006, as amended]. A post-authorisation safety study may be an interventional clinical trial or may follow an observational, non-interventional study design.
See also ***Clinical trial, Non-interventional trial***

Potential risk
An untoward occurrence for which there is some basis for suspicion of an association with the medicinal product of interest but where this association has not been confirmed (see ICH-E2F Guideline, Volume 10 of the Rules Governing Medicinal Products in the EU).
Examples include:
 non-clinical toxicological findings that have not been observed or resolved in clinical studies;
 adverse events observed in clinical trials or epidemiological studies for which the magnitude of the difference, compared with the comparator group (placebo or active substance, or unexposed group), on the parameter of interest raises a suspicion of, but is not large enough to suggest, a causal relationship;
 a signal arising from a spontaneous adverse reaction reporting system;
 an event known to be associated with other active substances within the same class or which

[22] World Health Organisation (WHO) "The importance of pharmacovigilance: safety monitoring of medicinal products", Geneva, WHO; 2002.

could be expected to occur based on the properties of the medicinal product (see ICH-E2F Guideline, Volume 10 of the Rules Governing Medicinal Products in the EU).

See also ***Adverse event, Signal***

Quality adherence
Carrying out tasks and responsibilities in accordance with quality requirements [IR Art. 8(3)]
See also ***Quality requirements***

Quality assurance
See ***Quality control and assurance***

Quality control and assurance
Monitoring and evaluating how effectively the structures and processes have been established and how effectively the processes are being carried out [IR Art 8(3) of Enforcment Regulation (ER) 520/2012].
This applies for the purpose of fulfilling quality requirements.
See also Quality requirements

Quality improvements
Correcting and improving the structures and processes where necessary [IR 520/2012 - Art 8(3)].
This applies for the purpose of fulfilling quality requirements.
See also ***Quality requirements***

Quality objectives
Performance of tasks and responsibilities in accordance with the quality requirements [IR Art. 8 (3)].
See ***Quality requirements***

Quality of a pharmacovigilance system
All characteristics of the pharmacovigilance system which are considered to produce, according to estimated likelihoods, outcomes relevant to the objectives of pharmacovigilance.
See also ***Pharmacovigilance system, Quality system of a pharmacovigilance system***

Quality planning
Establishing structures and planning integrated and consistent processes [Art. 8(3) of IR 520/2012].
This applies for the purpose of fulfilling quality requirements.
See also ***Quality requirements***

Quality requirements
Those characteristics of a system which are likely to produce the desired outcome, or quality objectives.
See also ***Pharmacovigilance system, Quality system of a pharmacovigilance system***

Quality system of a pharmacovigilance system
The organisational structure, responsibilities, procedures, processes and resources of the pharmacovigilance system as well as appropriate resource management, compliance management and record management [IR Art. 10 (2)].
The quality system is part of the pharmacovigilance system.
See also ***Pharmacovigilance system, Quality of a pharmacovigilance system***

Reference safety information
In periodic benefit-risk evaluation reports for medicinal products, all relevant safety information contained in the reference product information (e.g. the company core data sheet) prepared by the marketing authorisation holder and which the marketing authorisation holder requires to be listed in all countries where it markets the product, except when the local regulatory authority specifically requires a modification (see Annex IV, ICH-E2C(R2) Guideline).
It is a subset of information contained within the marketing authorisation holder's reference product information for the periodic benefit-risk evaluation report. Where the reference product information is the company core data sheet, the reference safety information is the company core safety information (see Annex IV, ICH-E2C(R2) Guideline).
See also ***Company core data sheet, Company core safety information***

Registry
An organised system that uses observational methods to collect uniform data on specified outcomes in a population defined by a particular disease, condition or exposure.

Risk management plan (RMP)
A detailed description of the risk management system [see Art. 695 (28)[1] b) of Law 95/2006, as amended].
To this end, it must identify or characterise the safety profile of the medicinal product(s) concerned, indicate how to characterise further the safety profile of the medicinal product(s) concerned, document measures to prevent or minimise the risks associated with the medicinal product, including an assessment of the effectiveness of those interventions and document post-authorisation obligations that have been imposed as a condition of the marketing authorisation [Art. 30 of IR 520/2012].
See also ***Risk management system, Risk minimisation activity***

Risk management system
A set of pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to a medicinal product, including the assessment of the effectiveness of those interventions [Art. 695 (28[1]) a) of Law 95/2006, as amended].

Risk minimisation activity; synonym: Risk minimisation measure
A public health intervention intended to prevent or reduce the probability of the occurrence of an adverse reaction associated with the exposure to a medicine, or to reduce its severity should it occur. (see Annex IV, Guideline ICH-E2C(R2)).
These activities may consist of routine risk minimisation (e.g. product information) or additional risk minimisation activities (e.g. healthcare professional or patient communications/educational materials) (see Annex IV, Guideline ICH-E2C(R2)).

Risk-benefit balance
An evaluation of the positive therapeutic effects of the medicinal product in relation to the risks (Art. 695 (29) of Law 95/2006, as amended), i.e. any risk relating to the quality, safety or efficacy of the medicinal product as regards patients' health or public health [Art. 695 (28), first point of Law 95/2006, as amended]).
See also ***Risks related to use of a medicinal product***

Risks related to the use of a medicinal product
Any risk relating to the quality, safety or efficacy of the medicinal product as regards patients' health or public health and any risk of undesirable effects on the environment [Art. 695(28) of Law 95/2006, as amended].

Safety concern
An important identified risk, important potential risk or important missing information (see Annex IV, ICH-E2C(R2) Guideline).
See also ***Important identified risk and Important potential risk, Important missing information***

Serious adverse reaction
An adverse reaction which results in death, is life-threatening, requires in-patient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a congenital anomaly/birth defect [Art. 695 (11) of Law 95/2006, as amended].
"Life-threatening" in this context refers to a reaction in which the patient was at risk of death at the time of the reaction; it does not refer to a reaction that hypothetically might have caused death if more severe (see Annex IV, ICH-E2D Guideline).
Medical and scientific judgement should be exercised in deciding whether other situations should be considered serious reactions, such as important medical events that might not be immediately life threatening or result in death or hospitalisation but might jeopardise the patient or might require intervention to prevent one of the other outcomes listed above. Examples of such events are intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalisation or development of dependency or abuse (see Annex IV, ICH-E2D Guideline).
Any suspected transmission via a medicinal product of an infectious agent is also considered a serious adverse reaction.
See also ***Adverse reaction***

Signal
Information arising from one or multiple sources, including remarks and experiments, which suggests a new potentially causal association, or a new aspect of a known association between an intervention and an event or set of related events, either adverse or beneficial, that is judged to be of sufficient likelihood to justify verificatory action [IR Art 19(1)].
For the purpose of monitoring data in the EudraVigilance database, only signals related to an adverse reaction is considered [IR Art 19(1)].
For the purpose of Section 16.2 of the periodic benefit-risk evaluation report, signals relate to adverse effects (see Annex IV, ICH-E2C(R2) Guideline).
See also ***Validated signal, Newly identified signal, Closed signal, Ongoing signal, Signal management process, Adverse reaction***
Signal management process
Includes the following activities: signal detection, signal validation, signal confirmation, signal analysis and prioritisation, signal assessment and recommendation for action [IR Art 21(1)].
It therefore is a set of activities performed to determine whether, based on an examination of individual case safety reports (ICSRs), aggregated data from active surveillance systems or studies, literature information or other data sources, there are new risks causally associated with an active substance or a medicinal product or whether known risks have changed.
See also Signal validation

Signal validation
Process of evaluating the data supporting a detected signal in order to verify that the available documentation contains sufficient evidence demonstrating the existence of a new potentially causal association, or a new aspect of a known association, therefore justifying further analysis of the signal [see Annex IV, Guideline ICH-E2D].
See also ***Validated signal***

Solicited sources of individual case safety reports
Organised data collection systems, which include clinical trials, registries, post-authorisation

named - patients use programmes, other patient support and disease management programmes, surveys of patients or healthcare providers or information gathering on efficacy or patient compliance. For the purpose of safety reporting, solicited reports should not be considered spontaneous but classified as individual case safety reports from studies and therefore should have an appropriate causality assessment by a healthcare professional or the marketing authorisation holder (see Annex IV, ICH-E2D).
See also ***Clinical trial, Post-authorisation safety study, Non-interventional trial***

Spontaneous report, synonym: Spontaneous notification
An unsolicited communication by a healthcare professional or consumer to a company, regulatory authority or other organisation (e.g. the World Health Organization, a regional centre, a poison control centre) that describes one or more adverse reactions in a patient who was given one or more medicinal products and that does not derive from a study or any organised data collection scheme (see Annex IV, ICH-E2D).
In this context, an adverse reaction refers to a suspected adverse reaction.
Stimulated reporting can occur in certain situations, such as after a direct healthcare professional communication (DHPC), a publication in the press or questioning of healthcare professionals by company representatives, and adverse reaction reports arising from these situations are considered spontaneous reports (see Annex IV, ICH-E2D), provided the report meets the definition above. Reporting can also be stimulated by invitation from patients' or consumers' organisations to their members. Reporting made in the context of early post-marketing phase vigilance (EPPV), e.g. in Japan, is also considered stimulated reporting.
See also ***Adverse reaction***

Stimulated reporting
See Spontaneous report

Substance
Any matter irrespective of origin which may be human (e.g. human blood and human blood products), animal (e.g. micro-organisms, whole animals, parts of organs, animal secretions, toxins, extracts, blood products), vegetable (e.g. micro-organisms, plants, part of plants, vegetable secretions, extracts), chemical (e.g. elements, naturally occurring chemical materials and chemical products obtained by chemical change or synthesis) [Art. 695 (2) of Law 95/2006, as amended].

Summary of product characteristics (SmPC)
Part of the marketing authorisation of a medicinal product setting out the agreed position of the product as distilled during the course of the assessment process which includes the information described in Art. 708 of Law 95/2006. It is the basis of information for healthcare professionals on how to use the product safely and effectively. The package leaflet is drawn in accordance with the summary of product characteristics (based on A Guideline on Summary of Product Characteristics, Volume 2C of the Rules Governing Medicinal Products in the EU).

Target population (treatment); synonym: Treatment target population
The patients who might be treated with the medicinal product in accordance with the indication(s) and contraindication(s) in the authorised product information.

Traditional herbal medicinal product
A herbal medicinal product that fulfils the conditions laid down in Art. 714 (1) of Law 95/2006, as amended, i.e.
(a) it has (an) indication(s) exclusively appropriate to traditional herbal medicinal products which, by virtue of their composition and purpose, are intended and designed for use without the supervision of a medical practitioner for diagnostic purposes or for prescription

or monitoring of treatment;
(b) it is exclusively for administration in accordance with a specified strength and posology;
(c) it is an oral, external and/or inhalation preparation;
(d) the period of traditional use as laid down in Article 716 (1)(c) has elapsed;
(e) the data on the traditional use of the medicinal product are sufficient; in particular the product proves not to be harmful in the specified conditions of use and the pharmacological effects or efficacy of the medicinal product are plausible on the basis of long-standing use and experience [Art. 695 (30) and Art. 714 (1) of Law 95/2006, as amended]. Regarding (d), the product must have been in medicinal use throughout a period of at least 30 years, including at least 15 years within the EU (see Art. 716 (1) c) and European Commission Questions & Answers Document on Registration of Traditional Herbal Medicinal Products, 2011).
See also ***Herbal medicinal product***

Unexpected adverse reaction
An adverse reaction, the nature, severity or outcome of which is not consistent with the summary of product characteristics [Art. 695 (12) of Law 95/2006, as amended][23].

This includes class-related reactions which are mentioned in the summary of product characteristics (SmPC) but which are not specifically described as occurring with this product. For products authorised nationally, the relevant SmPC is that authorised by the competent authority in the Member State to whom the reaction is being reported. For centrally authorised products, the relevant SmPC is the SmPC authorised by the European Commission. During the time period between a CHMP opinion in favour of granting a marketing authorisation and the Commission decision granting the marketing authorisation, the relevant SmPC is the SmPC annexed to the CHMP opinion.
See also ***Summary of product characteristics***

Upper management
Group of persons in charge of the highest executive management of an organisation.
Membership of this group is determined by the governance structure of the organisation.
While it is envisaged that the upper management usually is a group, the head of the organisation is the one person at the top of the organisation with ultimate responsibility for ensuring that the organisation complies with relevant legislation.

Valid individual case safety report
See ***Individual case safety report***

Validated signal
A signal where the signal validation process of evaluating the data supporting the detected signal has verified that the available documentation contains sufficient evidence demonstrating the existence of a new potentially causal association, or a new aspect of a known association, and therefore justifies further analysis of the signal [based on IR Art 21 (1)].
See also **Signal**

[23] For investigational medicinal products, an unexpected adverse reaction is an adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g. the investigator's brochure for an unauthorised investigational product or the summary of product characteristics for an authorised product) [Order of the Minister of Health No. 904/2006, Art 2(p)]

DECISION

No. 15/22.04.2013

on approval of the Guideline on Good Pharmacovigilance Practices – Module I – Pharmacovigilance systems and their quality systems

The Scientific Council of the National Agency for Medicines and Medical Devices (NAMMD), established based on Order of the Minister of Health no. 158/18.02.2013, reunited on summons of the President of the National Agency for Medicines and Medical Devices in the ordinary meeting of 22.04.2013, in accordance with Article 12(5) of Government Decision no. 734/2010 on establishment, organisation and operation of the National Agency for Medicines and Medical Devices, as amended, adopts the following

DECISION

Sole article. – The Guideline on Good Pharmacovigilance Practices – Module I – Pharmacovigilance systems and their quality systems is approved, in accordance with the Annex which is integral part of this Decision.

PRESIDENT
of the Scientific Council
of the National Agency for Medicines and Medical Devices,

Acad. Prof. Dr. Leonida Gherasim

Guideline on Good Pharmacovigilance Practices (GPP)

Date for coming into effect: 2 July 2012

Module I – PHARMACOVIGILANCE SYSTEMS AND THEIR QUALITY SYSTEMS

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I.A. Introduction

This Module contains guidance for the establishment and maintenance of quality assured pharmacovigilance systems for marketing authorisation holders, competent authorities of Member States and the European Medicines Agency. How the systems of these organisations interact while undertaking specific pharmacovigilance processes is described in each respective Module of GVP.
The definition of a pharmacovigilance system is provided in Article 1 of Directive 2001/83/EC as a system used by the marketing authorisation holder and by Member States to fulfil the tasks and responsibilities listed in Section X of Law 95/2006, as amended, and designed to monitor the safety of authorised medicinal products and detect any change to their risk-benefit balance. The Agency likewise maintains a pharmacovigilance system to fulfil its pharmacovigilance activities.
For performing their pharmacovigilance activities, marketing authorisation holders, competent authorities of Member States and the Agency shall establish and use quality systems that are adequate and effective for this performance.
The legal requirement for quality systems was introduced by Emergency Government Ordinance no. 35/2012 implemented within Law 95/2006, as amended, and by Regulation (EU) 1235/2010 on amendment of Regulation (EC) 726/2004 (the latter is referenced as REG) to strengthen pharmacovigilance in the EU. The minimum requirements of these quality systems are set out in the Commission Implementing Regulation (EU) no. 520/2012 on the Performance of Pharmacovigilance Activities Provided for in Regulation (EC) no. 726/2004 and Directive 20 01/83/EC (the Implementing Regulation is referenced as IR).
While there has to be compliance with these legal requirements, the implementation of a quality system should be adapted to the respective organisation.
By following the overall quality objectives in I.B.4. and the guiding principle in I.B.5. to meet the needs of patients, healthcare professionals and the public in relation to the safety of medicines, the application of the quality system should be adapted to how crucial each pharmacovigilance task is for fulfilling the quality objectives for each medicinal product covered by a quality system. The guidance on quality systems in this Module is consistent with the general principles of the ISO 9000 Standards on good quality management practices, specifically the ISO 9001-2008 Standards on quality management systems, issued by the International Organization for Standardization (ISO). The general application of quality management to pharmacovigilance systems is described under I.B. and requirements specific to the operation of the EU network in I.C..
In this Module, all applicable legal requirements are referenced in the way explained in the GVP Introductory Cover Note and are usually identifiable by the modal verb “shall”. Guidance for the implementation of legal requirements is provided using the modal verb “should”.

I.B. Structures and processes

I.B.1. Pharmacovigilance system

A pharmacovigilance system is defined as a system used by an organisation to fulfil its legal tasks and responsibilities in relation to pharmacovigilance and designed to monitor the safety of authorised medicinal products and detect any change to their risk-benefit balance [Art. 695 (28^1) c) of Law 95/2006, as amended].

A pharmacovigilance system, like any system, is characterised by its structures, processes and outcomes. For each specific pharmacovigilance process, including its necessary structures, a dedicated Module is included in GVP.

I.B.2. Quality, quality objectives, quality requirements and quality system

For the purpose of GVP, which provides guidance on structures and processes of a pharmacovigilance system, the quality of a pharmacovigilance system can be defined as all the characteristics of the system which are considered to produce, according to estimated likelihoods, outcomes relevant to the objectives of pharmacovigilance.
In general terms, quality is a matter of degree and can be measured. Measuring if the required degree of quality has been achieved necessitates pre-defined quality requirements. Quality requirements are those characteristics of a system that are likely to produce the desired outcome, or quality objectives. The overall quality objectives for pharmacovigilance systems are provided under I.B.4.
Specific quality objectives and quality requirements for the specific structures and processes of the pharmacovigilance systems are provided in each Module of GVP as appropriate.
The quality system is part of the pharmacovigilance system and consists of its own structures and processes. It shall cover organisational structure, responsibilities, procedures, processes and resources of the pharmacovigilance system as well as appropriate resource management, compliance management and record management [IR Art. 8 (2)].

I.B.3. Quality cycle

The quality system is based on all of the following activities:

• quality planning: establishing structures and planning integrated and consistent processes;
• quality adherence: carrying out tasks and responsibilities in accordance with quality requirements;
• quality control and assurance: monitoring and evaluating how effectively the structures and processes have been established and how effectively the processes are being carried out; and
• quality improvements: correcting and improving the structures and processes where necessary [IR Art. 8 (3)].

I.B.4. Overall quality objectives for pharmacovigilance

The overall quality objectives of a pharmacovigilance system are:
• complying with the legal requirements for pharmacovigilance tasks and responsibilities;
• preventing harm from adverse reactions in humans arising from the use of authorised medicinal products within or outside the terms of marketing authorisation or from occupational exposure;
• promoting the safe and effective use of medicinal products, in particular through providing timely information about the safety of medicinal products to patients, healthcare professionals and the public; and
• contributing to the protection of patients' and public health.

I.B.5. Principles for good pharmacovigilance practices

With the aim of fulfilling the overall quality objectives in I.B.4., the following principles should guide the design of all structures and processes as well as the conduct of all tasks and responsibilities:
• The needs of patients, healthcare professionals and the public in relation to the safety of medicines should be met.
• Upper management should provide leadership in the implementation of the quality system and motivation for all staff members in relation to the quality objectives.
• All persons within the organisation should be involved in and support the pharmacovigilance system on the basis of task ownership and responsibility in a degree according to their tasks and assigned responsibilities.
• All persons involved with the entire organisation should engage in continuous quality

improvement following the quality cycle in I.B.3..
• Resources and tasks should be organised as structures and processes in a manner that will support
the proactive, risk-proportionate, continuous and integrated conduct of pharmacovigilance.
• All available evidence on the risk-benefit balance of medicinal products should be sought and all relevant aspects, which could impact on the risk-benefit balance and the use of a product, should be considered for decision-making.
• Good cooperation should be fostered between marketing authorisation holders, competent authorities, public health organisations, patients, healthcare professionals, learned societies and other relevant bodies in accordance with the applicable legal provisions.

I.B.6. Responsibilities for the quality system within an organisation

A sufficient number of competent and appropriately qualified and trained personnel is available for the performance of pharmacovigilance activities [IR 520/2012, Art. 13 (1), Art. 18 (1)]. Their responsibility should include adherence to the principles defined in I.B.5.
For the purpose of a systematic approach towards quality in accordance with the quality cycle (see I.B.3.), managerial staff (i.e. staff with management responsibilities) in any organisation should be responsible for:
• ensuring that the organisation documents the quality system as described in I.B.11.;
• ensuring that the documents describing the quality system are subject to document control in relation to their creation, revision, approval and implementation;
• ensuring that adequate resources are available and that training is provided (see I.B.7.);
• ensuring that suitable and sufficient premises, facilities and equipment are available (see I.B.8.);
• ensuring adequate compliance management (see I.B.9.);
• ensuring adequate record management (see I.B.10.);
• reviewing the pharmacovigilance system including its quality system at regular intervals in risk-based manner to verify its effectiveness (see I.B.12.) and introducing corrective and preventive measures where necessary;
• ensuring that mechanisms exist for timely and effective communication, including escalation processes of safety concerns relating to medicinal products within an organisation;
• identifying and investigating concerns arising within an organisation regarding suspected non-adherence to the requirements of the quality and pharmacovigilance systems and taking corrective, preventive and escalation action as necessary;
• ensuring that audits are performed (see I.B.12.).
In relation to the management responsibilities described above, upper management within an organisation should provide leadership through:
• motivating all staff members, based on shared values, trust and freedom to speak and act with responsibility and through recognition of staff members' contributions within the organisation; and
• assigning roles, responsibilities and authorities to staff members according to their competencies and communicating and implementing these throughout the organisation.
For competent authorities, all persons involved in the procedures and processes of the quality system established for the performance of pharmacovigilance activities is responsible for the good functioning of that quality system and shall ensure a systematic approach towards quality and towards the implementation and maintenance of the quality system [IR Art 8(5)].

I.B.7. Training of personnel for pharmacovigilance

Achieving the required quality for the conduct of pharmacovigilance processes and their outcomes by an organization is intrinsically linked with the availability of a sufficient number of competent and appropriately qualified and trained personnel (see I.B.6.).

All personnel involved in the performance of pharmacovigilance activities shall receive initial and continued training [IR Art 10(3), Art 14(2)]. For marketing authorisation holders, this training shall relate to the roles and responsibilities of the personnel [IR Art 10(3)]
The organization shall keep training plans and records for documenting, maintaining and developing the competences of personnel [IR Art 10(3), Art. 14 (2)].
Training plans should be based on training needs assessment and should be subject to monitoring. The training should support continuous improvement of relevant skills, the application of scientific progress and professional development and ensure that staff members have the appropriate qualifications, understanding of relevant pharmacovigilance requirements as well as experience for the assigned tasks and responsibilities. All staff members of the organisation should receive and be able to seek information about what to do if they become aware of a safety concern.
There should be a process in place within the organisation to check that training results in the appropriate levels of understanding and conduct of pharmacovigilance activities for the assigned tasks and responsibilities, or to identify unmet training needs, in line with professional development plans agreed for the organisations as well as the individual staff members.
Adequate training should also be considered by the organisation for those staff members to whom no specific pharmacovigilance tasks and responsibilities have been assigned but whose activities may have an impact on the pharmacovigilance system or the conduct of pharmacovigilance. Such activities include but are not limited to those related to clinical trials, technical product complaints, medical information, terminologies, sales and marketing, regulatory affairs, legal affairs and audits.

I.B.8. Facilities and equipment for pharmacovigilance

Achieving the required quality for the conduct of pharmacovigilance processes and their outcomes is also intrinsically linked with appropriate facilities and equipment used to support the processes. Facilities and equipment should include office space, information technology (IT) systems and (electronic) storage space. They should be located, designed, constructed, adapted and maintained to suit their intended purpose in line with the quality objectives for pharmacovigilance (see I.B.4.) and also be available for business continuity (see I.B.11.3.).
Facilities and equipment which are critical for the conduct of pharmacovigilance (see I.B.11.3.) should be subject to appropriate checks, qualification and/or validation activities to prove their suitability for the intended purpose. There should be processes in place to keep awareness of the valid terminologies (see Module VI) in their valid versions and to keep the IT systems up-to-date accordingly.

I.B.9. Specific quality system procedures and processes

I.B.9.1. Compliance management by marketing authorisation holders

For the purpose of compliance management, marketing authorisation holders shall have specific quality system procedures and processes in place in order to ensure the following:
• the continuous monitoring of pharmacovigilance data, the examination of options for risk minimisation and prevention and that appropriate measures are taken by the marketing authorisation holder[IR Art. 11(1)(a)] (see Modules IX and XII);
• the scientific evaluation of all information on the risks of medicinal products as regards patients or public health, in particular as regards adverse reactions in human beings arising from use of the product within or outside the terms of its marketing authorisation or associated with occupational exposure [IR Art 11(1)(b)] (see Modules VI, VII, VIII, IX);

- the submission of accurate and verifiable data on serious and non-serious adverse reactions to the competent authorities within the legally required time-limits [IR Art. 11(1)(c)] (see Modules VI and IX);
- the quality, integrity and completeness of the information submitted on the risks of medicinal products, including processes to avoid duplicate submissions and to validate signals [IR Art. 11 (1)(d)] (see Modules V, VI, VII, VIII and IX);

- effective communication by the marketing authorization holder with competent authorities, including communication on new or changed risks (see Module XII and XV), the pharmacovigilance system master file (see Module II), risk management systems (see Module V), risk minimisations measures (see Modules V and XVI), periodic safety update reports (see Module VII), corrective and preventive actions (see Modules II, III and IV) and post-authorisation safety studies (see Module VIII)[IR Art. 11 (1)(e)];

• the update of product information by the marketing authorisation holder in the light of scientific knowledge [IR Art. 11 (1)(f)] (see Module XII);

• appropriate communication of relevant safety information to healthcare professionals and patients (see Module XII and XV) [IR Art. 11 (1) (g)].

I.B.9.2. Compliance management by competent authorities

I.B.9.2. Compliance management by competent authorities

For the purpose of compliance management, competent authorities shall establish specific quality system procedures and processes in order to achieve all of the following objectives:

• ensuring the evaluation of the quality, including completeness, of pharmacovigilance data submitted [IR Art. 15 (1)(a)];

• ensuring the assessment of pharmacovigilance data and its processing in accordance with the legal timelines [IR Art. 15 (1)(b)];

• ensuring independence in the performance of pharmacovigilance activities [IR Art. 15 (1)(c)];

• ensuring effective communication with patients, healthcare professionals, marketing authorisation holders and the general public [IR Art. 15 (1)(d)];

• conducting inspections, including pre-authorisation inspections [IR Art. 15 (1) (f)].

Independence in the performance of pharmacovigilance activities is interpreted in the sense that all regulatory decisions on medicinal products should be taken in the sole interest of patients' and public health.

I.B.10. Record management

The organisation shall record all pharmacovigilance information and ensure that it is handled and stored so as to allow accurate reporting, interpretation and verification of that information [IR Art. 12(1), Art 16(1)].

A record management system is put in place for all documents used for pharmacovigilance activities, ensuring their retrievability as well as traceability of the measures taken to investigate safety concerns, of the timelines for those investigations and of decisions on safety concerns, including their date and the decision-making process [IR Art. 12 (1), Art. 16 (1)].

The record management system should support:

• the management of the quality of pharmacovigilance data, including their completeness, accuracy and integrity;

• timely access to all records;

• effective internal and external communication; and

• the retention of documents relating to the pharmacovigilance systems and the conduct of pharmacovigilance for individual medicinal products, in accordance with the applicable retention periods.

In addition, marketing authorisation holders shall establish mechanisms enabling the traceability and follow-up of adverse reaction reports [IR Art 12 (1)].

In this context, it should be ensured that the fundamental right to personal data protection is fully and effectively granted in all pharmacovigilance activities in conformity with legal provisions.

The purpose of safeguarding public health constitutes a substantial public interest and consequently the processing of personal data should be justified if identifiable personal data are processed only where necessary and only where the parties involved assess this necessity at every stage of the pharmacovigilance process (IR Recital 17). As part of a record management system, specific measures should therefore be taken at each stage in the storage and processing of pharmacovigilance data to ensure data security and confidentiality. This should involve strict

limitation of access to documents and to databases to authorised personnel respecting the medical and administrative confidentiality of the data.
There should be appropriate structures and processes in place to ensure that pharmacovigilance data and records are protected from destruction during the applicable record retention period.
The record management system should be described in a record management policy.

I.B.11. Documentation of the quality system

All elements, requirements and provisions adopted for the quality system is documented in a systematic and orderly manner in the form of written policies and procedures, such as quality plans, quality manuals and quality records [IR Art. 8 (4)].
A quality plan documents the setting of quality objectives and sets out the processes to be implemented to achieve them. A procedure is a specified way to carry out a process and may take the format of a standard operating procedure and other work instruction or quality manual.
A quality manual documents the scope of the quality system, the processes of the quality system and the interaction between the two.
A quality record is a document stating results achieved or providing evidence of activities performed.
In order to have a systematic approach, the organisation should define in advance:
• quality objectives specific to their organisations in accordance with the overall quality objectives provided under I.B.4. and the structure- and process- specific quality objectives in accordance with each Module of GVP; and
• methods for monitoring the effectiveness of the pharmacovigilance system (see I.B.12.).
The quality system is documented by:
• documents on organisational structures and assignments of tasks to personnel (see I.B.11.1. and I.B.11.2.);
• training plans and records (see I.B.7.) [IR Art. 10 (3), Art. 14 (2)];
• instructions for the compliance management processes (see I.B.9.) [IR Art 11 (1), Art 15 (1)];
• appropriate instructions on the processes to be used in case of urgency, including business continuity (see I.B.11.3.) [IR Art 10 (4), Art 14 (3)];
• performance indicators where they are used to continuously monitor the good performance of pharmacovigilance activities [IR Art 9 (1)];
• reports of quality audits and follow-up audits, including their dates and results [IR Art. 13 (2), Art 17 (2)].
Training plans and records is kept and made available for audit and inspection [IR Art 10 (3), Art 14 (2)].
It is recommended that the documentation of the quality system also includes:
• the methods of monitoring the efficient operation of the quality system and, in particular, its ability to fulfil the quality objectives;
• a record management policy;
• records created as a result of pharmacovigilance processes which demonstrate that key steps for the defined procedures have been taken;
• records and reports relating to the facilities and equipment including functionality checks, qualification and validation activities which demonstrate that all steps required by the applicable requirements, protocols and procedures have been taken;
• records to demonstrate that deficiencies and deviations from the established quality system are monitored, that corrective and preventive actions have been taken, that solutions have been applied to deviations or deficiencies and that the effectiveness of the actions taken has been verified.

I.B.11.1. Additional quality system documentation by marketing authorisation holders

In addition to the quality system documentation in accordance with I.B.11., marketing authorisation holders shall document:

• their human resource management in the pharmacovigilance system master file (PSMF) (see Module II) [IR Art 2 (5) (b)];
• job descriptions defining the duties of the managerial and supervisory staff [IR Art 10 (2)];
• an organisational chart defining the hierarchical relationships of managerial and supervisory staff [IR Art 10 (2)];
• instructions on critical processes (see I.B.11.3.) in the pharmacovigilance system master file (PSMF) (see Module II); and
• their record management system in the pharmacovigilance system master file (PSMF) (see Module II) [IR Art 2 (5) (c)].
It is recommended that the documentation of the quality system additionally includes the organisational structures and assignments of tasks, responsibilities and authorities to all personnel directly involved in pharmacovigilance tasks.
For the requirements of documenting the quality system in the pharmacovigilance system master file (PSMF) or its annexes, see Module II.

I.B.11.2. Additional quality system documentation by competent authorities

In addition to the quality system documentation in accordance with I.B.11., the organisational structures and the distribution of tasks and responsibilities is clear and, to the extent necessary, accessible [IR Art 14(1)].
It is recommended that the documentation of the quality system additionally includes the organisational structures and assignments of tasks, responsibilities and authorities to all personnel directly involved in pharmacovigilance tasks.
Contact points is established [IR Art 14(1)], in particular to facilitate interaction between competent authorities, marketing authorisation holders and persons reporting information on the risks of medicinal products as regards patients' or public health.

I.B.11.3. Critical pharmacovigilance processes and business continuity

The following pharmacovigilance processes should be considered as critical include:
• continuous safety profile monitoring and benefit-risk evaluation of authorised medicinal products;
• establishing, assessing and implementing risk management systems and evaluating the effectiveness of risk minimisation;
• collection, processing, management, quality control, follow-up for missing information, coding, classification, duplicate detection, evaluation and timely electronic transmission of individual case safety reports (ICSRs) from any source;
• signal management;
• scheduling, preparation (including data evaluation and quality control), submission and assessment of periodic safety update reports;
• meeting commitments and responding to requests from competent authorities, including provision of correct and complete information;
• interaction between the pharmacovigilance and product quality defect systems;
• communication about safety concerns between marketing authorisation holders and competent authorities, in particular notifying changes to the risk-benefit balance of medicinal products;
• communicating information to patients and healthcare professionals about changes to the risk-benefit balance of products for the aim of safe and effective use of medicinal products;
• keeping product information up-to-date with the current scientific knowledge, including the conclusions of the assessment and recommendations from the applicable competent authority;
• implementation of variations to marketing authorisations for safety reasons according to the urgency required.
Business continuity plans should be established in a risk-based manner and should include:
• provisions for events that could severely impact on the organisation's staff and infrastructure in general or on the structures and processes for pharmacovigilance in particular; and

• back-up systems for urgent exchange of information within an organisation, amongst organisations sharing pharmacovigilance tasks as well as between marketing authorisation holders and competent authorities.

I.B.12. Monitoring of the performance and effectiveness of the pharmacovigilance system and its quality system

Processes to monitor the performance and effectiveness of a pharmacovigilance system and its quality system should include:
• reviews of the systems by those responsible for management;
• audits;
• compliance monitoring;
• inspections;
• evaluating the effectiveness of actions taken with medicinal products for the purpose of minimising risks and supporting their safe and effective use in patients.

The organisation may use performance indicators to continuously monitor the good performance of pharmacovigilance activities [IR Art 9(1)] in relation to the quality requirements. The quality requirements for each pharmacovigilance process are provided in each Module of GVP as appropriate.

The requirements for the quality system itself are laid out in this Module and its effectiveness should be monitored by managerial staff, who should review the documentation of the quality system (see I.B.11.) at regular intervals, with the frequency and the extent of the reviews to be determined in a risk-based manner. Pre-defined programmes for the review of the system should therefore be in place. Reviews of the quality system should include the review of standard operating procedures and work instructions, deviations from the established quality system, audit and inspections reports as well as the use of the indicators referred to above.

Risk-based audits of the quality system is performed at regular intervals to ensure that it complies with the requirements for the quality system, the human resource management, the compliance management, the record management and the data retention and to ensure its effectiveness [IR Art 13 (1), Art 17 (1)].

Audits of the quality system should include audit of the pharmacovigilance system which is the subject of the quality system.

The methods and processes for the audits are described in Module IV. In relation to the pharmacovigilance system of a marketing authorisation holder, a report is drawn up on the results for each quality audit and any follow-up audits be sent to the management responsible for the matters audited [IR Art 13 (2)].

The report should include the results of audits of organisations or persons the marketing authorisation holder has delegated tasks to, as these are part of the marketing authorisation holder‘s pharmacovigilance system. For competent authorities, the audit report is sent to the management responsible for the matters audited [IR Art 17(2)].

As a consequence of the monitoring of the performance and effectiveness of a pharmacovigilance system and its quality system (including the use of audits), corrective and preventive measures should be implemented when deemed necessary. In particular as a consequence of audits, corrective action(s), including a follow-up audit of deficiencies, is taken where necessary [IR Art 13(2), Art 17(2)].

Additionally, the competent authorities should have in place arrangements for monitoring the compliance of marketing authorisations holders with legally required pharmacovigilance tasks and responsibilities. They shall further ensure compliance with the legal requirements by means of conducting inspections of marketing authorisation holders [Art. 823 (1) of Law 95/2006, as amended] (see Module III). Guidance on compliance monitoring for each pharmacovigilance process is provided in each Module of GVP as appropriate.

Requirements and methods for evaluating the effectiveness of actions taken upon medicinal products for the purpose of minimising risks and supporting the safe and effective use of medicines in patients are described in Module XVI.

I.B.13. Preparedness planning for pharmacovigilance in public health emergencies

Any pharmacovigilance system should be adaptable to public health emergencies and preparedness plans should be developed as appropriate. For preparedness planning in the EU, see I.C.4..

I.C. Operation of the EU network

I.C.1. Overall pharmacovigilance responsibilities of the applicant and marketing authorisation holder in the EU

The marketing authorisation holder in the EU is responsible for the respective pharmacovigilance tasks and responsibilities laid down in Law 95/2006, as amended, Regulation (EC) no. 726/2004 and the Commission Implementing Regulation (EU) no. 520/2012 on the Performance of Pharmacovigilance Activities Provided for in Regulation (EC) no. 726/2004 and Directive 2001/83/EC in order to assure responsibility and liability for its authorised medicinal products and to ensure that appropriate action can be taken, when necessary.
For this purpose, the marketing authorisation holder shall operate a pharmacovigilance system [Art. 815 (1) of Law 95/2006, as amended] and shall establish and use a quality system that is adequate and effective for performing its pharmacovigilance activities [IR Art 8(1)].
There may be circumstances where a marketing authorisation holder may establish more than one pharmacovigilance system, e.g. specific systems for particular types of products (e.g. vaccines, products available without medical prescription (OTCs) etc.).
A description of the pharmacovigilance system is developed by the applicant for a marketing authorisation in the format of a pharmacovigilance system master file (PSMF) and be maintained by the marketing authorisation holder for all authorised medicinal products (see Module II). The applicant or the marketing authorisation holder is also responsible for developing and maintaining product-specific risk management systems (see Module V).
Guidance on the structures and processes on how the marketing authorisation holder should conduct the pharmacovigilance tasks and responsibilities is provided in the respective GVP Modules.

I.C.1.1. Responsibilities of the marketing authorisation holder in reaction to the qualified person responsible for pharmacovigilance in the EU

As part of the pharmacovigilance system, the marketing authorisation holder shall have permanently and continuously at its disposal an appropriately qualified person responsible for pharmacovigilance in the EU (QPPV) [Art. 815 (3) of Law 95/2006, as amended].
The marketing authorisation holder shall submit the name and contact details of the QPPV to the competent authorities in Member States and the Agency [Art. 815 (3), last paragraph of Law 95/2006, as amended].
Changes to this information should be submitted in accordance with Regulation (EC) no. 1234/2008 on variations to the terms of marketing authorisation and the Communication from the Commission - Guideline on the Details of the Various Categories of Variations to the Terms of Marketing Authorisations for Medicinal Products for Human Use and Veterinary Medicinal Products[24].
The duties of the QPPV is defined in a job description [IR Art 10 (2)]. The hierarchical relationship of the QPPV is defined in an organisational chart together with those of other managerial and supervisory staff [IR Art 10 (2)]. Information relating to the QPPV is included in the pharmacovigilance systems master file (PSMF) [IR Art. 2 (1)] (see Module II).
Each pharmacovigilance system can have only one QPPV. A QPPV may be employed by more than one marketing authorisation holder, for a shared or for separate pharmacovigilance systems or may fulfil the role of QPPV for more than one pharmacovigilance system of the same marketing authorisation holder, provided that the QPPV is able to fulfil all obligations.

[24] See Volume 2C of the *Rules Governing Medicinal Products in the EU*; http://ec.europa.eu/health/documents/eudralex/vol-2/index_en.htm

In addition to the QPPV, competent authorities in Member States are legally provided with the option to request the nomination of a pharmacovigilance contact person at national level reporting to the QPPV. Reporting in this context relates to pharmacovigilance tasks and responsibilities and not necessarily to line management. A contact person at national level may also be nominated as the QPPV.
The marketing authorisation holder shall ensure that the QPPV has sufficient authority to influence the performance of the quality system and the pharmacovigilance activities of the marketing authorisation holder [IR Art 10 (2)].
The marketing authorisation holder should therefore ensure that the QPPV has access to the pharmacovigilance system master file (PSMF) as well as authority over it and is notified of any changes to it in accordance with Module II (see I.C.1.3). The authority over the pharmacovigilance system and the PSMF should allow the QPPV to implement changes to the system and to provide input into risk management plans (see Module V) as well as into the preparation of regulatory action in response to emerging safety concerns (see Module XII).
Overall, the marketing authorisation holder should ensure that structures and processes are in place, so that the QPPV can fulfil the responsibilities listed in I.C.1.3.. In order to do this, the marketing authorisation holder should ensure that mechanisms are in place so that the QPPV receives all relevant information and that the QPPV can access all information the QPPV considers relevant, in particular on:
• emerging safety concerns and any other information relating to the benefit-risk evaluation of the medicinal products covered by the pharmacovigilance system;
• ongoing or completed clinical trials and other studies the marketing authorisation holder is aware of and which may be relevant to the safety of the medicinal products;
• information from sources other than from the specific marketing authorisation holder, e.g. from those with whom the marketing authorisation holder has contractual arrangements;
and
• the procedures relevant to pharmacovigilance which the marketing authorisation holder has in place at every level in order to ensure consistency and compliance across the organisation.
The outcome of the regular reviews of the quality system referred to in I.B.6. and I.B.12. and the measures introduced should be communicated by the managerial staff to the QPPV.
Compliance information should be provided to the QPPV on a periodic basis. Such information may also be used to provide assurance to the QPPV that commitments in the framework of risk management plans and post-authorisation safety systems are being adhered to.
The managerial staff should also inform the QPPV of scheduled pharmacovigilance audits. The PPV should be able to trigger an audit where appropriate. The managerial staff should provide the QPPV with a copy of the corrective and preventive action plan following each audit relevant to the pharmacovigilance system the QPPV is responsible for, so that the QPPV can assure that appropriate corrective actions are implemented.
In particular with regard to its adverse reaction database (or other systems to collate adverse reaction reports), the marketing authorisation holder should implement a procedure to ensure that the QPPV is able to obtain information from the database, for example, to respond to urgent requests for information from the competent authorities or the Agency, at any time. If this procedure requires the involvement of other personnel, for example database specialists, then this should be taken into account in the arrangements made by the marketing authorization holder for supporting the QPPV outside of normal working hours.
When a marketing authorisation holder intends to expand its product portfolio, for example, by acquisition of another company or by purchasing individual products from another marketing authorisation holder, the QPPV should be notified as early as possible in the due diligence process in order that the potential impact on the pharmacovigilance system can be assessed and the system be adapted accordingly. The QPPV may also have a role in determining what pharmacovigilance data should be requested from the other company, either pre- or post-acquisition. In this situation, the QPPV should be made aware of the sections of the contractual

arrangements that relate to responsibilities for pharmacovigilance activities and safety data exchange and have the authority to request amendments.
When a marketing authorisation holder intends to establish a partnership with another marketing authorisation holder, organisation or person that has a direct or indirect impact on the pharmacovigilance system, the QPPV should be informed early enough and be involved in the preparation of the corresponding contractual arrangements (see I.C.1.5.) so that all necessary provisions relevant to the pharmacovigilance system are included.

I.C.1.2. Qualifications of the qualified person responsible for pharmacovigilance in the EU

The marketing authorisation holder shall ensure that the QPPV has acquired adequate theoretical and practical knowledge for the performance of pharmacovigilance activities [IR Art 10 (1)].
The QPPV should have skills for the management of pharmacovigilance systems as well as expertise or access to expertise in relevant areas such as medicine, pharmaceutical sciences as well as epidemiology and biostatistics.
Where the QPPV has not completed basic medical training in accordance with Law 200/2004 on the recognition of diplomas and professional qualifications for regulated professions in Romania, as amended, transposing Directive 2005/36/EC on the recognition of professional qualifications, the marketing authorisation holder shall ensure that the QPPV is assisted by a medically trained person (i.e. in accordance with Article 24 of Directive 2005/36/EC) and this assistance is duly documented [IR Art 10(1)].
The expectation is that the applicant or marketing authorisation holder will assess the qualification of the QPPV prior to appointment by, for example, reviewing university qualifications, knowledge of EU pharmacovigilance requirements and experience in pharmacovigilance.
The applicant or marketing authorisation holder should provide the QPPV with training in relation to its pharmacovigilance system, which is appropriate for the role prior to the QPPV taking up the position and which is appropriately documented. Consideration should be given to additional training, as needed, of the QPPV in the medicinal products covered by the pharmacovigilance system.

I.C.1.3. Role of the qualified person responsible for pharmacovigilance in the EU

The qualified person responsible for pharmacovigilance in the EU (QPPV) is a natural person[25].
The QPPV appointed by the marketing authorisation holder is appropriately qualified (see I.C.1.2.) and is at the marketing authorisation holder's disposal permanently and continuously (see I.C.1.1.) [Art. 815 (3)(a) of Law 95/2006, as amended].
The QPPV shall reside and operate in the EU [Art. 815 (3), the last paragraph of Law 95/2006, as amended]. Following European Economic Area (EEA) agreements, the QPPV may also reside and operate in Norway, Iceland or Liechtenstein. Back-up procedures in the case of absence of the QPPV is in place [IR Art 2(1)(d)] and should be accessible through the QPPV's contact details.
The QPPV should ensure that the back-up person has all necessary information to fulfil the role.
The QPPV is responsible for the establishment and maintenance of the marketing authorisation holder's pharmacovigilance system [Art. 815 (3), the last paragraph of Law 95/2006, as amended] and therefore shall have sufficient authority to influence the performance of the quality system and the pharmacovigilance activities [IR Art 10 (2)] and to promote, maintain and improve compliance with the legal requirements [IR Art 2 (1)(a)]. Hence, the QPPV should have access to the pharmacovigilance system master file (PSMF) (see Module II) and be in a position of authority to ensure and to verify that the information contained in the PSMF is an accurate and up-to-date reflection of the pharmacovigilance system under QPPV's responsibility.

[25] A natural person is a real human being, as distinguished from a corporation which is often treated at law as a fictitious person.

In relation to the medicinal products covered by the pharmacovigilance system, specific additional responsibilities of the QPPV should include:
• with an overview of medicinal product safety profiles and any emerging safety concerns;
• with awareness of any conditions or obligations adopted as part of the marketing authorizations and other commitments relating to safety or the safe use of the products;
• with awareness of risk minimisation measures;
• being aware of and having sufficient authority over the content of risk management plans;
• being involved in the review and sign-off of protocols of post-authorisation safety studies conducted in the EU or pursuant to a risk management plan agreed in the EU;
• with awareness of post-authorisation safety studies requested by a competent authority including the results of such studies;
• ensuring conduct of pharmacovigilance and submission of all pharmacovigilance-related documents in accordance with the legal requirements and GVP;
• ensuring the necessary quality, including the correctness and completeness, of pharmacovigilance data submitted to the competent authorities in Members States and the Agency;
• ensuring a full and prompt response to any request from the competent authorities in Member States and from the Agency for the provision of additional information necessary for the benefit-risk evaluation of a medicinal product;
• providing any other information relevant to the benefit-risk evaluation to the competent authorities in Members States and the Agency;
• providing input into the preparation of regulatory action in response to emerging safety concerns (e.g. variations, urgent safety restrictions, and communication to patients and healthcare professionals);
• acting as a single pharmacovigilance contact point for the competent authorities in Member States and the Agency on a 24-hour basis and also as a contact point for pharmacovigilance inspections.
This responsibility for the pharmacovigilance system means that the QPPV has oversight over the functioning of the system in all relevant aspects, including its quality system (e.g. standard operating procedures, contractual arrangements, database operations, compliance data regarding quality, completeness and timeliness of expedited reporting and submission of periodic update reports, audit reports and training of personnel in relation to pharmacovigilance). Specifically for the adverse reaction database, if applicable, the QPPV should be aware of the validation status of the database, including any failures that occurred during validation and the corrective actions that have been taken to address the failures. The QPPV should also be informed of significant changes that are made to the database (e.g. changes that could have an impact on pharmacovigilance activities).
The QPPV may delegate specific tasks, under supervision, to appropriately qualified and trained individuals, for example, acting as safety experts for certain products, provided that the QPPV maintains system oversight and overview of the safety profiles of all products. Such delegation should be documented.

I.C.1.4. Specific quality system processes of the marketing authorisation holder in the EU

In applying the requirements set out in I.B.9.1. in the EU, the marketing authorisation holder shall put in place the following additional specific quality system processes for ensuring:
• the submission of adverse reaction data to EudraVigilance within the legal timelines [IR Art 11 (c)];
• the monitoring of the use of terminology referred to in IR Art 25(1) either systematically or by regular random evaluation [IR Art 25(3)];
• the retention of minimum elements of the pharmacovigilance system master file (PSMF) (see IR Art 2 and Module II) as long as the system described in the PSMF exists and for at least further 5 years after it has been formally terminated by the marketing authorisation holder [IR Art 12 (2)];

• the retention of pharmacovigilance data and documents relating to individual authorized medicinal products as long as the marketing authorization exists and for at least further 10 years after the marketing authorisation has ceased to exist [IR Art 12 (2)];
• that the product information is kept up-to-date by the marketing authorisation holder in the light of scientific knowledge, including the assessments and recommendations made public via the European medicines web-portal and on the basis of a continuous monitoring by the marketing authorisation holder of information published on the European medicines web-portal [IR Art 11 (1)(g)].
The retention periods above apply unless the documents is retained for a longer period where EU or national law so requires [IR Art 12 (2)].
During the retention period, retrievability of the documents should be ensured.
Documents can be retained in electronic format, provided that the electronic system has been appropriately validated and appropriate arrangements exist for system security, access and back-up of data. If documents in paper format are transferred into an electronic format, the transfer process should ensure that all of the information present in the original format is retained in a legible manner and that the media used for storage will remain readable over time.
Documents transferred in situations where the business of the marketing authorisation holder is taken over by another organisation should be complete.

I.C.1.5. Quality system requirements for pharmacovigilance tasks subcontracted by the marketing authorisation holder

The marketing authorisation holder may subcontract certain activities of the pharmacovigilance system to third parties [IR Art 6(1)], i.e. to another organisation or person (where the same requirements apply to a person as for an organisation). This may include the role of the QPPV.
The marketing authorisation holder shall nevertheless retain full responsibility for the completeness and accuracy of the pharmacovigilance system master file (PSMF) (see Module II) [IR Art 6(1)]. The ultimate responsibility for the fulfilment of all pharmacovigilance tasks and responsibilities and the quality and integrity of the pharmacovigilance system always remains with the marketing authorisation holder.
Where a marketing authorisation holder has subcontracted some tasks of its pharmacovigilance tasks, it shall retain responsibility for ensuring that an effective quality system is applied in relation to those tasks [IR Art 11 (2)]. All guidance provided in GVP is also applicable to the other organisation to which the tasks have been subcontracted.
When subcontracting tasks to another organisation, the marketing authorisation holder shall draw up subcontracts [IR Art 6(2)] and these should be detailed, up-to-date and clearly document the contractual arrangements between the marketing authorisation holder and the other organisation, describing arrangements for delegation and the responsibilities of each party. A description of the subcontracted activities and/or services is included in the pharmacovigilance system master file (PSMF) [IR Art 2 (6)] and a list of the subcontracts is included in an annex to the PSMF, specifying the product(s) and territory(ies) concerned [IR Art 6 (2)] (see Module II).
The other organisations may be subject to inspection at the discretion of the competent or supervisory authority in the relevant Member State.
Contractual arrangements should be prepared with the aim of enabling compliance with the legal requirements by each party involved. When preparing contractual arrangements, the marketing authorisation holder should include sufficiently detailed descriptions of the delegated tasks, the related interactions and data exchange, together with, for example, agreed definitions, tools, assignments and timelines. The contractual arrangements should also contain clear information on the practical management of pharmacovigilance as well as related processes, including those for the maintenance of pharmacovigilance databases. Further, they should indicate which processes are in place for checking whether the agreed arrangements are being adhered to on an ongoing basis. In this respect, regular risk-based audits of the other organisation by the marketing authorisation holder or introduction of other methods of control and assessment are recommended.

With respect to centrally authorised products, contractual arrangements between different marketing authorisation holders should also be in place in relation to separately authorised medicinal products with the application of Article 82(1) of Regulation (EC) No 726/2004 in order to ensure conduct of pharmacovigilance on the basis of complete worldwide data sets. For responsibilities of the marketing authorisation holder towards the QPPV in this context, see I.C.1.1..

I.C.2. Overall pharmacovigilance responsibilities within the EU regulatory network

The NAMMD, the competent authorities in Member States and the Agency are responsible for the respective pharmacovigilance tasks and responsibilities imposed on them by Law 95/2006, as amended, Regulation (EC) No 726/2004 and the Commission Implementing Regulation (EU) No 520/2012 on the Performance of Pharmacovigilance Activities Provided for in Regulation (EC) No 726/2004 and Directive 2001/83/EC in order to ensure that appropriate action can be taken, when necessary.
For this purpose, the NAMMD, each competent authority in a Member State as well as the Agency shall operate a pharmacovigilance system [812 (1) of Law 95/2006, as amended] and shall establish and follow an adequate and effective quality system for performing their pharmacovigilance activities [IR Art. 8 (1)].
The Agency and the Member States shall cooperate to continuously develop pharmacovigilance systems capable of achieving high standards of public health protection for all medicinal products, regardless of the routes of marketing authorisation, including the use of collaborative approaches, to maximise use of resources available within the EU [REG Art. 28e]. The requirement in I.B.11.2. according to which competent authorities shall keep accessible clear descriptions of the organisational structures, assignment of tasks and responsibilities as well as contact points [IR Art. 14(1)], should relate to the interaction between competent authorities in Member States, the Agency, the European Commission, marketing authorisation holders and persons reporting information on the risks of medicinal products.
Guidance on the structures and processes to enable the competent authorities in Member States and the Agency to conduct the pharmacovigilance tasks and responsibilities is provided in the respective Modules of GVP.

I.C.2.1. Role of the competent authorities in Member States

Each Member State shall designate a competent authority for the performance of pharmacovigilance [Art. 812 (3) of Law 95/2006, as amended].
This authority is usually the same as the competent authority responsible for granting national marketing authorisations. The NAMMD is the Romanian competent authority.
Just like the other competent authorities in Member States, the NAMMD must operate a pharmacovigilance system for the fulfilment of their pharmacovigilance tasks and their participation in EU pharmacovigilance activities [Art. 812 (1) of Law 95/2006, as amended].
In this context, the NAMMD (the Romanian competent authority) is responsible for the safety monitoring of each medicinal product, independent of its route of authorisation, on its territory at Member State. In particular, the NAMMD is responsible for monitoring data originating in their territory [IR Art 18 (4)].
For nationally authorised products, including those authorised through the mutual recognition or the decentralised procedure, the NAMMD is responsible for granting, varying, suspending and revoking a marketing authorisation. The pharmacovigilance tasks and responsibilities of competent authorities in Member States for each process in relation to such products are detailed in the respective Modules of GVP.
For products authorised through the mutual recognition or the decentralised procedure, one Member State acts as the Reference Member State. For practical reasons, the competent authority of the Reference Member State should coordinate communication with the marketing authorisation holder on pharmacovigilance matters and monitor the compliance of the marketing authorisation holder with legal pharmacovigilance requirements. These arrangements do not

replace the legal responsibilities of the marketing authorisation holder with respect to individual competent authorities and the Agency.
Nationally authorised products, including those authorised through the mutual recognition or the decentralised procedure may become subject to regulatory procedures at EU level on pharmacovigilance grounds. If a Commission Decision for a nationally authorised product exists as an outcome of such a procedure, the NAMMD and the other competent authorities in Member States are responsible for the implementation of the Commission Decision and also for its follow-up, unless exceptionally further action by the Agency and the European Commission has been foreseen in the Commission Decision reflecting the outcome of the regulatory procedure (see Chapter 3 of the Notice to Applicants and the Agency's and HMA Procedural Advice on Referral Procedures for Safety Reasons).
The pharmacovigilance tasks and responsibilities of the NAMMD in relation to centrally authorised products are also detailed in the respective Modules of GVP. They include the collaboration in signal detection (see Module IX) and implementation of Commission Decisions regarding risk management of centrally authorised products addressed to Member States (see Module V). Where urgent action is essential to protect human health or the environment, the NAMMD, on its own initiative or at the European Commission's request, may suspend the use of a centrally authorised product in its territory (see Module XII).
The NAMMD is responsible for pharmacovigilance inspections of organisations in their territory in relation to medicinal products. This is independent of the route of marketing authorisation as well as which competent authority granted the marketing authorisation for the respective medicinal product (see Module III).
In relation to the various aspects of the role described above, the NAMMD should ensure that all pharmacovigilance data are shared between competent authorities in other Member States, the European Commission and the Agency for each process in accordance with the legislation and the guidance in the respective GVP Modules.

I.C.2.2. Role of the European Commission

The European Commission is the competent authority for medicinal products authorised through the centralised procedure and is responsible for granting, varying, suspending and revoking their marketing authorisations by adoption of Commission Decisions on the basis of Opinions adopted by the Committee for Medicinal Products for Human Use (CHMP) (see I.C.2.3.3.).
Further, the European Commission adopts Commission Decisions in relation to nationally authorised medicinal products subject to regulatory procedures at EU level, including on pharmacovigilance grounds. The European Commission may also initiate such procedures (see Chapter 3 of the Notice to Applicants and the Agency's and HMA Procedural Advice on Referral Procedures for Safety Reasons).

I.C.2.3. Role of the European Medicines Agency

I.C.2.3.1. General role of the Agency and the role of the Agency's secretariat

The role of the Agency is to coordinate the monitoring of medicinal products for human use authorised in the EU and to provide advice on the measures necessary to ensure their safe and effective use, in particular, by coordinating the evaluation and implementation of legal pharmacovigilance requirements and the monitoring of such implementation. The tools established and maintained by the Agency for the coordination are presented in the GVP Modules for each process.
The Agency provides coordination and technical, scientific and administrative support to the Pharmacovigilance Risk Assessment Committee (PRAC) (see I.C.2.3.2.) and the Committee for Medicinal Products for Human Use (CHMP) (see I.C.2.3.3.) and coordination and technical and administrative support to the Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh) (see I.C.2.3.4.), as well as coordination between the committees and the CMDh.

Pharmacovigilance for centrally authorised products is conducted by the Agency with the involvement of the Rapporteurs, the PRAC and the CHMP. The Agency should take the lead for communicating with the marketing authorisation holders of centrally authorised products. The respective responsibilities for each pharmacovigilance process are detailed in the GVP Modules.
For nationally authorised products, the Agency coordinates regulatory procedures at EU level on pharmacovigilance grounds through providing support to the CMDh and CHMP (see Chapter 3 of the Notice to Applicants and the Agency's and HMA Procedural Advice on Referral Procedures for Safety Reasons).
The Agency also cooperates with other EU bodies as necessary.
Specific pharmacovigilance tasks of the Agency include:
• running the EudraVigilance database [REG Art 57 (d)];
• monitoring selected medical literature for reports of suspected adverse reactions to medicinal products containing certain active substances [REG Art 27] (see Module VI);
• running processes for the EU coordination of the assessment of periodic safety update reports (see Module VII) and oversight of post-authorisation safety studies (see Module VIII);
• tasks relating to signal detection [REG Art 28 (1)(c), IR Art 18 - 24] (see Module IX);
• tracking of follow-up of safety concerns and other pharmacovigilance matters at EU level (see Module XII);
• assisting Member States with the rapid communication of information on safety concerns to healthcare professionals and coordinating the safety announcements of the national competent authorities [REG Art 57(e)] (see Module XV);
• distributing appropriate information on safety concerns to the general public, in particular by setting up and maintaining the European medicines web-portal [REG Art 57(f)] (see Module XV);
• coordination of safety announcements between national competent authorities for active substances contained in medicinal products authorised in more than one Member State, including the provision of timetables for the publication of information [818[1] (3) of Law 95/2006, as amended] (see Module XV);
and specifically in relation to centrally authorised products:
• assessing updates to risk management systems [REG Art 28 a(1)(b)] (see Module V);
• monitoring the outcome of risk minimisation measures [REG Art 28 a (1)(a)] (see Module XVI).

I.C.2.3.2. Role of the Pharmacovigilance Risk Assessment Committee (PRAC)

The Pharmacovigilance Risk Assessment Committee (PRAC) is responsible for providing recommendations to the Committee for Medicinal Products for Human Use (CHMP) and the Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh) on any question relating to pharmacovigilance activities in respect of medicinal products for human use and on risk management systems, including the monitoring of the effectiveness of those risk management systems [REG Art 56(1)(aa)]. The Details on the responsibilities for each process are presented in the respective GVP Modules. The Mandate and Rules of Procedure of the PRAC are published on the Agency's website[26].

I.C.2.3.3. Role of the Committee for Medicinal Products for Human Use (CHMP)

The Committee for Medicinal Products for Human Use (CHMP) is responsible for evaluating applications and formulating Opinions serving as a basis for granting, varying, suspending or withdrawing marketing authorisations for centrally authorised products. The CHMP also prepares Opinions on safety concerns emerging after a marketing authorisation has been granted for centrally authorised products or, for nationally authorised products, including those through the mutual recognition or the decentralised procedure, in the framework of regulatory procedures

[26] http://www.ema.europa.eu

at EU level in which at least one centrally authorised product is involved (see Chapter 3 of the Notice to Applicants and the Agency's and HMA Procedural Advice on Referral Procedures for Safety Reasons), procedures for the assessment of periodic safety update reports (PSURs) (see Module VII) and procedures for post-authorisation safety studies (see Module VIII). For questions
related to pharmacovigilance activities and risk management systems, the CHMP relies on the recommendations from the Pharmacovigilance Risk Assessment Committee (PRAC). The specific responsibilities of each party for each pharmacovigilance process are described in the GVP Modules. The Rules of Procedure of the CHMP are published on the Agency's website[27].

I.C.2.3.4. Role of the Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh)

The Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh) is responsible for examining any question relating to marketing authorisations for medicinal products authorised through the mutual recognition or the decentralised procedure and questions on the variation of marketing authorisations granted by the Member States as well as questions arising for nationally authorised products from assessments of periodic safety update reports (see Module VII), post-authorisation safety studies (see Module VIII) and during regulatory procedures at EU level. The CMDh shall reach a position, based on a PRAC recommendation, on regulatory procedures at EU level when only nationally authorised products, including those authorised through the mutual recognition or the decentralised procedure, are involved [Art. 819[11] of Law 95/2006, as amended] (see Chapter 3 of the Notice to Applicants and the Agency's and HMA Procedural Advice on Referral Procedures for Safety Reasons). The responsibilities of the CMDh for each pharmacovigilance process are described in the respective GVP Modules. The Rules of Procedure of the CMDh and the Functions and Tasks for CMDh are published on the HMA website[28].

I.C.2.4. Specific quality system processes of the quality systems of competent authorities in Member States and the Agency

In applying the requirements set out in I.B.9.2. in the EU, the competent authorities in Member States and the Agency shall put in place the following additional specific quality system processes for:

• monitoring and validating the use of terminology referred to in IR Art 25(1), either systematically or by regular random evaluation [IR Art 25(3)];
• assessing and processing pharmacovigilance data in accordance with the timelines provided by legislation [IR Art 15 (1)(b)];
• ensuring effective communication within the EU regulatory network in accordance with the provisions on safety announcements in Article 106a of Directive 2001/83/EC [IR Art 15 (1) (d)] (see Module XV);
• granting that the NAMMD, competent authorities in Member States and the Agency inform each other and the European Commission of their intention to make announcements relating to the safety of a medicinal product or an active substance contained in a medicinal product authorised in several Member State (see Modules XII and XV) [IR Art 15 (1)(e)];
• arranging for the essential documents describing their pharmacovigilance systems to be kept as long as the system exists and for at least further 5 years after they have been formally terminated [IR Art 16 (2)];
• ensuring that pharmacovigilance data and documents relating to individual authorised medicinal products are retained as long as the marketing authorisation exists or for at least further 10 years after the marketing authorisation has expired [IR Art 16 (2)].

[27] http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000095.jsp&murl=menus/about_us/about_us.jsp&mid=WC0b01ac0580028c7a
[28] http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000095.jsp&murl=menus/about_us/about_us.jsp&mid=WC0b01ac0580028c7a

In this context, documents relating to a medicinal product include documents of a reference medicinal product where this is applicable.
The retention periods above apply unless the documents is retained for a longer period where EU or national law so requires [IR Art 16 (2)]. During the retention periods referred to above, retrievability of the documents should be ensured.
Documents can be retained in electronic format, provided that the electronic system has been appropriately validated and appropriate arrangements exist for system security, access and back-up of data. If pharmacovigilance documents in paper format are transferred into an electronic format, the transfer process should ensure that all of the information present in the original format is retained in a legible manner and that the media used for storage will remain readable over time. The legal requirements for record management (see I.B.10.) imply accessibility to the records from within the EU, preferably at a single point.
In addition to the above, competent authorities in Member States shall establish procedures for collecting and recording all suspected adverse reactions that occur in their territory (see Module VI) [IR Art 15 (2)].
In addition to the above, the Agency shall establish procedures for literature monitoring in accordance with Article 27 of Regulation (EC) No 726/2004 (see Module VI) [IR Art 15 (3)].
In addition to the quality system documentation in accordance with I.B.11. and I.B.11.2., competent authorities in Member States and the Agency shall clearly determine, and to the extent necessary, keep accessible the organisational structures and the distribution of tasks and responsibilities [IR Art 14(1)] as well as establish contact points [IR Art 14(1)], in particular to facilitate interaction between competent authorities in Member States, the Agency, marketing authorisation holders and persons reporting information on the risks of medicinal products as regards patients' or public health.
Quality audits of the NAMMD, Member States' and Agency's pharmacovigilance systems (see I.B.12.) is performed according to a common methodology [IR Art 17(1)].
The results of audits is reported by the NAMMD and competent authorities in Member States in accordance with Art. 812 (2) of Law 95/2006 as amended and by the Agency in accordance with Article 28f of Regulation (EC) No 726/2004 (see Module IV).

I.C.2.5. Quality system requirements for pharmacovigilance tasks delegated or transferred by competent authorities in Member States

Competent authorities in a Member State, the NAMMD included, may delegate any pharmacovigilance task to another Member State subject to a written agreement of the latter Member State [Art. 814 of Law 95/2006, as amended]. The written agreement should be reflected by exchange of letters, defining the scope of the delegation.
The NAMMD may transfer any or all of the pharmacovigilance tasks to another organization, but the ultimate responsibility for the fulfilment of all pharmacovigilance tasks and responsibilities and the quality and integrity of the pharmacovigilance system always remains with the NAMMD.
Where tasks are transferred to another organisation, the NAMMD should ensure that the tasks are subject to a quality system compliant with the legal requirements applicable to their own organisation.

I.C.2.6. Transparency of the quality system of the EU regulatory network

The European Commission (EC) shall publish every three years a report on the performance of pharmacovigilance based on the reports submitted by the NAMMD and the other competent authorities in Member States (first EC report due on 21 July 2015) and by the Agency (first EC report due on 2 January 2014) on the results of their regular pharmacovigilance system audits (see Module IV) [DIR Art. 101(2), Art. 108b, REG Art 28f, Art 29].

I.C.3. Data protection in the EU

All legal requirements of the IR, including those relating to the record management described in I.B.10., shall apply without prejudice to the obligations of the NAMMD and marketing

authorisation holders relating to their processing of personal data under Directive 95/46/EC or the obligations of the Agency relating to its processing of personal data under Regulation (EC) no. 45/2001 [IR Art 39].

I.C.4. Preparedness planning in the EU for pharmacovigilance in public health emergencies

The pharmacovigilance systems of marketing authorisation holders, the NAMMD and the Agency should be adaptable to public health emergencies. Preparedness plans should be developed as appropriate (see I.B.13.).

A public health emergency is a public health threat duly recognised either by the World Health Organization (WHO) or the Community in the framework of Decision no. 2119/98/EC of the European Parliament and of the Council. Pharmacovigilance requirements for public health emergencies should be considered by the NAMMD, the competent authorities in Member States, the European Commission and the Agency on a case-by-case basis and appropriately notified to marketing authorisation holders and the public. The Agency publishes its notifications on the Agency's website.

DECISION

No. 16/22.04.2013

on approval of new Romanian standard terms for pharmaceutical forms, primary packaging, closure systems and administration devices, routes and manners of administration, in line with terms adopted by the European Pharmacopoeia Commission

The Scientific Council of the National Agency for Medicines and Medical Devices (NAMMD), established based on Order of the Minister of Health no. 158/18.02.2013, reunited on summons of the President of the National Agency for Medicines and Medical Devices in the ordinary meeting of 22.04.2013, in accordance with Article 12(5) of Government Decision no. 734/2010 on establishment, organisation and operation of the National Agency for Medicines and Medical Devices, as amended, adopts the following

DECISION

Sole article. - The new Romanian standard terms for pharmaceutical forms, primary packaging, closure systems and administration devices, routes and manners of administration, in line with terms adopted by the European Pharmacopoeia Commission are approved, in accordance with the Annex which is integral part of this Decision.

PRESIDENT
of the Scientific Council
of the National Agency for Medicines and Medical Devices,

Acad. Prof. Dr. Leonida Gherasim

ANNEX

to SCD no. 16/22.04.2013

New Romanian standard terms

Part 1: Pharmaceutical forms

Preparate bucofaringiene *Oromucosal preparations*			
Normal terms		No.[1)] monogr. of Ph.Eur.	**Remarks**
Romanian	**English**		
Film sublingual	*Sublingual film*	No. 1807	Fasciae/films made of one or several layers of appropriate material(s); to be administered in the oral cavity for systemic effect.
Spray sublingual, soluție	*Sublingual spray, solution*	No. 1807	
Spray sublingual, suspensie	*Sublingual spray, suspension*	No. 1807	
Spray sublingual, emulsie	*Sublingual spray, emulsion*	No. 1807	
Spray sublingual	*Sublingual spray*	No. 1807	**- use of the term "sublingual spray" is no longer recommended**; - as required, use of terms such as sublingual spray, sublingual spray/solution, sublingual spray/suspension, sublingual spray, emulsion is recommended ,.
Spray bucofaringian	*Oromucosal spray*	No. 1807	**- use of the term "oromucosal spray" is no longer recommended;** - as required, use of terms to use terms such as oromucosal spray, oromucosal spray/solution, oromucosal spray/suspension, oromucosal spray, emulsion is recommended.

Preparate dentare *Preparations for dental use*			
Normal terms		No.[1] monogr. of Ph.Eur.	**Remarks**
Romanian	**English**		
Pastă dentară	*Dental paste*	-	Single dose or multidose semi-solid preparation containing particles finely dispersed into an appropriate basis, administered on the tooth or inside it. Toothpaste is excluded

Preparate orale – forme lichide şi semisolide *Oral preparations – liquid and semi-solid forms*			
Normal terms		No.[1] monogr. of Ph.Eur.	**Remarks**
Romanian	**English**		
Concentrat pentru soluție orală	*Concentrate for oral solution*	nr. 672	Liquid preparation diluted into a prescribed liquid, for oral solution
Concentrat pentru suspensie orală	*Concentrate for oral suspension*	nr. 672	Liquid preparation diluted into a prescribed liquid, for oral suspension

Preparate cutanate şi transdermice *Cutaneous and transdermal preparations*			
Normal terms		No.[1] monogr. of Ph.Eur.	**Remarks**
Romanian	**English**		
Soluție transdermică	*Transdermal solution*	nr. 927, 523	Single- or multidose preparation containing one or several active substances dissolved in an appropriate solvent, meant for transdermal administration.

Preparate parenterale *Parenteral preparations*			
Normal terms		No.[1)] monogr. of Ph.Eur.	**Remarks**
Romanian	**English**		
Suspensie injectabilă cu eliberare prelungită	*Prolonged-release suspension for injection*	No. 520	Single- or multidose preparation containing a suspension meant for administration by injection; the active substance is released over a longer period of time.

Part 2: Routes of administration

Căi şi moduri de administrare *Routes and method of administration*		
Romanian	**English**	**Remarks**
Submucoasă	*Submucosal use*	Injection of a medicinal product directly under the mucous membrane
Intracamerală	*Intracameral use*	Administration of a medicinal product directly in the anterior chamber of the eyeball.

Part 3: Containers, closures and administration devices

Ambalaje primare, sisteme de închidere şi dispozitive de administrare *Containers, closures and administration devices*		
Romanian	**English**	**Remarks**
Recipient multidoză cu pompă dozatoare	*Multidose container with metering pump*	Multidose container with integrated dosing pump.

DECISION

No. 17/22.04.2013

on approval of amendment of SCD no. 8/5.04.2011 on supplementation of the Regulation on organisation and operation of the Scientific Council of the National Agency for Medicines and Medical Devices

The Scientific Council of the National Agency for Medicines and Medical Devices (NAMMD), established based on Order of the Minister of Health no. 158/18.02.2013, reunited on summons of the President of the National Agency for Medicines and Medical Devices in the ordinary meeting of 22.04.2013, in accordance with Article 12(5) of Government Decision no. 734/2010 on establishment, organisation and operation of the National Agency for Medicines and Medical Devices, as amended, adopts the following

DECISION

Art. 1. – Amendment of SCD no. 8/5.04.2011 on supplementation of the Regulation on organisation and operation of the Scientific Council of the National Agency for Medicines and Medical Devices is approved, as follows:

Chapter 2. – Article 9 (3) is amended under Organisation and operation, reading as follows:

"(3) A juridical approval is to be mentioned on all draft and final decisions of the Scientific Council".

Art. 2. – On this Decision coming into force, SCD no. 8/5.04.2011 on approval of the supplementation of the Regulation on organisation and operation of the Scientific Council of the National Agency for Medicines and Medical Devices is amended.

PRESIDENT
of the Scientific Council
of the National Agency for Medicines and Medical Devices,

Acad. Prof. Dr. Leonida Gherasim

Medicinal product batches recalled during the 2nd quarter of 2013

No. crt.	Product recalled	Pharmaceutical form	Strength	INN	Manufacturer/ MAH	Batch	Grounds for recall	Action proposed	Date of recall
1	IBANDRONIC ACID, SANDOZ	film-coated tablets	50 mg	Ibandronic acid	Pharmathen GREECE,/Sandoz Pharmaceuticals GmbH, Germany	CB1633	Out-of-specification results under parameter "dissolution testing''	Recall and destruction	10.04.2013
2	SOLPADEINE 500 mg/8 mg/ 30 mg	effervescent tablets	500 mg/ 8 mg/30 mg	Combinations	GSK Durgarvan, Ireland	Batches with previous MAs (3300/2003/03)	In accordance with Order of the Minister of Health no. 279/2005, following expiry of the 2-year period as of issuance of a new marketing authorisation	Voluntary recall and destruction	16.05.2013
3	MEPROBAMAT	tablets	400 mg	Meprobamat	Sanofi-Aventis Romania SRL	All batches	Expiry of the NAMMD approved marketing due date (15 months), following the date of discontinuation of MA renewal procedure	Voluntary recall and destruction	10.06.2013
4	RELAXAM	film-coated tablets	50 mg	Tetrazepam	AC Helcor Pharma S.R.L.	All batches	European Commission Decision C(2013)3344/ 29.05.2013	Voluntary recall and destruction	20.06.2013
5	CILEST	tablets		Combinations	Janssen Pharmaceutica, Belgium/Johnson & Johnson D.O.O., Slovenia	BKS3600, CCS5U00, CDS1P00, CFS2J00, CIS0900, CJS4M00, DAS1300, DAS3E00, AHS3300, BAS0Z00	Out-of-specification results under parameter "dissolution testing''	Voluntary recall and destruction	27.05.2013
6	SERETIDE DISKUS	pressurised inhalation suspension	50µg/500µg, 50µg/250µg	Combinations	Glaxo Wellcome Production, FRANCE/Glaxo Wellcome, Great Britain	4668, 4632, 4740A	Improper packing of 60-dose batches	Recall and destruction	29.05.2013

No. crt.	Product recalled	Pharmaceutical form	Strength	INN	Manufacturer/ MAH	Batch	Grounds for recall	Action proposed	Date of recall
7	MAGNEGITA	solution for injection	500 micromole/ml	Gadopentetic acid	Farmak, Ukraine/ Afa Healthcare Imaging Agens, Germany	20710/3RO, 140910/3RO, 150910/3RO, 150910/3RO, 160809/3RO, 10710/3RO, 11409/3RO, 161211/3RO, 40710/4RO, 181010/4RO, 30211/4RO, 40211/4RO, 50211/4RO, 50710B/4RO, 141211/4RO, 161112/4RO, 70311/6RO, 181211/6RO	Particles inside the solution for injection	Recall and destruction	06.06.2013
8	Fervex „pentru adulti”	granules for oral solution		Combinations	Bristol-Myers Squibb – FRANCE/ Bristol Myers Squibb Kft - Hungary	All batches	Precautionary recall for products manufactured with a potentially contaminated excipient	Recall and destruction	24.05.2013
9	Fervex „pentru copii”	granules for oral solution		Combinations	Bristol-Myers Squibb – FRANCE/ Bristol Myers Squibb Kft - Hungary	All batches	Precautionary recall for products manufactured with a potentially contaminated excipient	Recall and destruction	24.05.2013

Applications for marketing authorisation/marketing authorisation renewal submitted to the NAMMD during the 1st quarter of 2013

During the 1st quarter of 2013, 273 marketing authorisation/renewal applications for medicinal products corresponding to the following therapeutic groups have been submitted:

A02 - Drugs for acid related disorders
A03 – Drugs for functional gastrointestinal disorders
A10 – Drugs used in diabetes
A11 – Vitamins
B01 – Antithrombotic agents
B06 – Other haematological agents
C01 – Cardiac therapy
C07 – Beta blocking agents
C08 – Calcium channel blockers
C09 – Agents acting on the renin-angiotensin system
C10 – Lipid modifying agents
D01 – Antifungals for dermatological use
D07 – Corticosteroids, dermatological preparations
D08 – Dermatologicals
G03 – Sex hormones and modulators of the genital system
G04 – Urologicals
J01 – Antibacterials for systemic use
J02 – Antimycotics for systemic use
J04 – Antimycobacterials
J05 – Antivirals for systemic use
J07 – Vaccines
L01 – Antineoplastic agents
L02 – Endocrine therapy
L04 – Immunosuppressants
M01 – Anti-inflammatory and antirheumatic products
M02 – Topical products for joint and muscular pain
M05 – Drugs for treatment of bone diseases
N01 – Anesthetics
N02 – Analgesics
N03 – Antiepileptics
N04 – Anti-parkinson drugs
N05 – Psycholeptics
N06 – Psychoanaleptics
N07 – Other nervous system drugs
P02 – Anthelmintics
R01 – Nasal preparations

201R03 – Drugs for obstructive airway diseases
R05 – Cough and cold preparations
R06 – Antihistamines for systemic use
S01 – Ophthalmologicals
V03 – All other therapeutic products
V08 – Contrast media

Medicinal products authorised for marketing by the NAMMD during the 1st quarter of 2013

INN	Invented name	Pharm. form	Strength	Manufacturer	Country	MA number		
ACIDUM ALENDRONICUM+CALCIU+ COLECALCIFEROLUM	ACID ALENDRONIC 70mg and CALCIU/VITAMINA D3 1000mg/880 UI SANDOZ	film-coated tablets + effervescent tablets	70mg/1000mg/ 880IU	SANDOZ S.R.L.	ROMANIA	5505	2013	06
ACIDUM ZOLEDRONICUM	ACID ZOLEDRONIC DR. REDDY'S 4mg/5 ml	concentrate for solution for infusion	4mg/5ml	DR. REDDY'S LABORATORIES ROMANIA S.R.L.	ROMANIA	5330	2013	08
ACIDUM ZOLEDRONICUM	ACID ZOLEDRONIC DR. REDDY'S 5mg/100 ml	solution for infusion	5mg/100ml	DR. REDDY'S LABORATORIES ROMANIA S.R.L.	ROMANIA	5331	2013	04
ACIDUM ZOLEDRONICUM	ACID ZOLEDRONIC GENTHON 4 mg/5 ml	concentrate for solution for infusion	4mg/5ml	GENTHON BV	HOLLAND	5332	2013	04
ACIDUM ZOLEDRONICUM	ACID ZOLEDRONIC GENTHON 5mg	solution for infusion	5mg	GENTHON BV	HOLLAND	5333	2013	01
AMLODIPINUM	ALNETA 5 mg	tablets	5mg	UAB "VVB"	LITHUANIA	5435	2013	08
AMLODIPINUM	ALNETA 10 mg	tablets	10mg	UAB "VVB"	LITHUANIA	5436	2013	08
AMOXICILLINUM	AMOXICILINA SANDOZ 500 mg	film-coated tablets	500mg	SANDOZ S.R.L.	ROMANIA	5474	2013	10
AMOXICILLINUM	AMOXICILINA SANDOZ 1000 mg	film-coated tablets	1000mg	SANDOZ S.R.L.	ROMANIA	5475	2013	10
AMOXICILLINUM	AMOXICILINA TRIHIDRAT SANDOZ 125 mg/5 ml	powder for oral suspension	125mg/5ml	SANDOZ S.R.L.	ROMANIA	5476	2013	02
AMOXICILLINUM	AMOXICILINA TRIHIDRAT SANDOZ 250 mg/5 ml	powder for oral suspension	250mg/5ml	SANDOZ S.R.L.	ROMANIA	5477	2013	02
AMOXICILLINUM + ACIDUM CLAVULANICUM	ENHANCIN 875 mg/125 mg	film-coated tablets	875mg/125mg	TERAPIA S.A.	ROMANIA	5309	2013	12
ANASTROZOLUM	EGISTROZOL 1 mg	film-coated tablets	1mg	EGIS PHARMACEUTICALS PLC	HUNGARY	5345	2013	19
ANASTROZOLUM	ENZAMIDEX 1 mg	film-coated tablets	1mg	LANNACHER HEILMITTEL GES.M.B.H.	AUSTRIA	5478	2013	19
BEMIPARINUM	ZIBOR 2500 IU/0.2 ml	solution for injection	2500IU/0.2 ml	FROSST IBERICA S.A.	SPAIN	5407	2013	04
BEMIPARINUM	ZIBOR 3500 IU/0.2 ml	solution for injection	3500IU/0.2ml	FROSST IBERICA S.A.	SPAIN	5348	2013	04
BENAZEPRILUM	CIBACEN 5 mg	film-coated tablets	5mg	NOVARTIS PHARMA GMBH	GERMANY	5384	2013	01
BENAZEPRILUM	CIBACEN 10 mg	film-coated tablets	10mg	NOVARTIS PHARMA GMBH	GERMANY	5385	2013	01
BENAZEPRILUM	CIBACEN 20 mg	film-coated tablets	20mg	NOVARTIS PHARMA GMBH	GERMANY	5386	2013	01
BRIMONIDINUM	BRIGLAU 2 mg/ml	eye drops,	2mg/ml	MEDANA PHARMA SA	POLAND	5397	2013	01

		solution						
CANDESARTANUM CILEXETIL	CANDESARTAN CILEXETIL TEVA 8 mg	tablets	8mg	TEVA PHARMACEUTICALS S.R.L.	ROMANIA	5294	2013	16
CANDESARTANUM CILEXETIL	CANDESARTAN CILEXETIL TEVA 16 mg	tablets	16mg	TEVA PHARMACEUTICALS S.R.L.	ROMANIA	5295	2013	16
CANDESARTANUM CILEXETIL	CANDESARTAN CILEXETIL TEVA 32 mg	tablets	32mg	TEVA PHARMACEUTICALS S.R.L.	ROMANIA	5296	2013	16
CAPECITABINUM	CAPECITABINA CIPLA 150 mg	film-coated tablets	150mg	CIPLA UK LTD.	GREAT BRITAIN	5413	2013	01
CAPECITABINUM	CAPECITABINA CIPLA 500 mg	film-coated tablets	500mg	CIPLA UK LTD.	GREAT BRITAIN	5414	2013	01
CAPECITABINUM	ARXEDA 150 mg	film-coated tablets	150mg	ROMASTRU TRADING SRL	ROMANIA	5442	2013	02
CAPECITABINUM	ARXEDA 500 mg	film-coated tablets	500mg	ROMASTRU TRADING SRL	ROMANIA	5443	2013	02
CAPECITABINUM	VOPECIDEX 150 mg	film-coated tablets	150mg	PHARMASWISS CESKA REPUBLIKA S.R.O.	THE CZECH REPUBLIC	5455	2013	06
CAPECITABINUM	VOPECIDEX 500 mg	film-coated tablets	500mg	PHARMASWISS CESKA REPUBLIKA S.R.O.	THE CZECH REPUBLIC	5456	2013	06
CHLORQUINALDOLUM	CLORCHINALDOL ARENA 100 mg (see P01AA04)	lozenges	100mg	ARENA GROUP S.A.	ROMANIA	5347	2013	03
CHLORQUINALDOLUM	CLORCHINALDOL ARENA 100 mg (see A07AXN1)	lozenges	100mg	ARENA GROUP S.A.	ROMANIA	5347	2013	03
CLOPIDOGRELUM	CLOPIDOGREL AUROBINDO 75 mg	film-coated tablets	75mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	5480	2013	10
COMBINATIONS	MULTILAC cu 2 mmol/l	hemofiltration solution	2mmol/l	FRESENIUS MEDICAL CARE DEUTSCHLAND GMBH	GERMANY	5403	2013	02
COMBINATIONS	MULTILAC FĂRĂ POTASIU	hemofiltration solution		FRESENIUS MEDICAL CARE DEUTSCHLAND GMBH	GERMANY	5402	2013	02
COMBINATIONS	ELEVIT	film-coated tablets		BAYER SRL ROMANIA	ROMANIA	5487	2013	02
COMBINATIONS (CALCII ACETAS+MAGNESII SUBCARBONAS)	OSVAREN 435 mg/235 mg	film-coated tablets	425mg/235mg	FRESENIUS MEDICAL CARE NEPHROLOGICA DEUTSCHLAND GM	GERMANY	5421	2013	01
COMBINATIONS (DESOGESTRELUM+ ETINILESTRADIOLUM)	JULIANE 150 micrograms/ 30 micrograms	tablets	150micrograms/ 30micrograms	ZENTIVA, K.S.	THE CZECH REPUBLIC	5360	2013	03
COMBINATIONS (DESOGESTRELUM+ ETINILESTRADIOLUM)	JULIANE 150 micrograms/ 20 micrograms	tablets	150micrograms/ 20micrograms	ZENTIVA, K.S.	THE CZECH REPUBLIC	5359	2013	03
COMBINATIONS (ESTRADIOLUM + NORETISTERONUM)	GYNAIKA 1 mg/0.5 mg	film-coated tablets	1mg/0.5 mg	ZENTIVA, K.S.	THE CZECH REPUBLIC	5379	2013	02
COMBINATIONS (FLUTICASONUM+ FORMOTEROLUM)	FLUTIFORM 50 micrograms/ 5 micrograms	pressurised inhalation suspension	50micrograms/ 5micrograms	MUNDIPHARMA GES.M.B.H	AUSTRIA	5437	2013	01
COMBINATIONS (FLUTICASONUM+ FORMOTEROLUM)	FLUTIFORM 125 micrograms/5 micrograms	pressurised inhalation suspension	125micrograms/ 5micrograms	MUNDIPHARMA GES.M.B.H	AUSTRIA	5438	2013	01
COMBINATIONS	FLUTIFORM	pressurised	250micrograms/	MUNDIPHARMA GES.M.B.H	AUSTRIA	5439	2013	01

(FLUTICASONUM+ FORMOTEROLUM)	250 micrograms/10 micrograms	inhalation suspension	10micrograms					
COMBINATIONS (FLUTICASONUM+ FORMOTEROLUM)	IFFEZA 50 micrograms/5 micrograms	pressurised inhalation suspension	50micrograms/ 5micrograms	MUNDIPHARMA GES.M.B.H	AUSTRIA	5449	2013	01
COMBINATIONS (FLUTICASONUM+ FORMOTEROLUM)	IFFEZA 125 micrograms/5 micrograms	pressurised inhalation suspension	125micrograms/ 5micrograms	MUNDIPHARMA GES.M.B.H	AUSTRIA	5450	2013	01
COMBINATIONS (FLUTICASONUM+ FORMOTEROLUM)	IFFEZA 250micrograms/10micrograms	pressurised inhalation suspension	250micrograms/ 10micrograms	MUNDIPHARMA GES.M.B.H	AUSTRIA	5451	2013	01
COMBINATIONS (LIDOCAINA+ LEVOMENTOL+FENOL)	DENTOCALMIN	dental solution		BIOFARM SA	ROMÂNIA	5459	2013	01
COMBINATIONS (NEBIVOLOLUM+ HYDROCHLOROTHIAZIDUM)	CO-NEBILET 5 mg/12.5 mg	film-coated tablets	5mg/12.5 mg	MENARINI INTERNATIONAL OPERATIONS	LUXEMBURG	5382	2013	03
COMBINATIONS (NEBIVOLOLUM+ HYDROCHLOROTHIAZIDUM)	CO-NEBILET 5 mg/25mg	film-coated tablets	5mg/25mg	MENARINI INTERNATIONAL OPERATIONS	LUXEMBURG	5383	2013	03
COMBINATIONS (PERINDOPRILUM+ INDAPAMIDUM)	HYPOPRILID 2.5 mg/0.625 mg	film-coated tablets	2.5 mg/0.625mg	TEVA PHARMACEUTICALS S.R.L.	ROMANIA	5334	2013	05
COMBINATIONS (PERINDOPRILUM+ INDAPAMIDUM)	HYPOPRILID 5 mg/1.25 mg	film-coated tablets	5mg/1.25mg	TEVA PHARMACEUTICALS S.R.L.	ROMANIA	5335	2013	05
COMBINATIONS (SODIUM SULFATE+ MAGNESIUM SULFATE+POTASSIUM SULFATE)	EZICLEN	concentrate for oral solution		IPSEN PHARMA	FRANCE	5417	2013	01
DOCETAXELUM	DOCETAXEL EGIS 20 mg/ml	concentrate for solution for infusion	20mg/ml	EGIS PHARMACEUTICALS PLC	HUNGARY	5398	2013	03
DOCETAXELUM	DOCETAXEL POLPHARMA 20 mg/ml	concentrate for solution for infusion	20mg/ml	PHARMACEUTICAL WORKS POLPHARMA SA	POLAND	5471	2013	03
DONEPEZILUM	DONESYN 10 mg	film-coated tablets	10mg	SYNTHON B.V.	HOLLAND	5416	2013	11
DONEPEZILUM	DONESYN 5 mg	film-coated tablets	5mg	SYNTHON B.V.	HOLLAND	5415	2013	11
DROTAVERINUM	DROTAVERINA LABORMED 40mg	tablets	40mg	LABORMED PHARMA S.A.	ROMANIA	5431	2013	05
DROTAVERINUM	DROTAVERINA LABORMED 80mg	tablets	80mg	LABORMED PHARMA S.A.	ROMANIA	5432	2013	05
EPLERENONUM	EPLERENONA LICONSA 25 mg	film-coated tablets	25mg	LABORATORIOS LICONSA S.A.	SPAIN	5469	2013	02
EPLERENONUM	EPLERENONA LICONSA 50 mg	film-coated tablets	50mg	LABORATORIOS LICONSA S.A.	SPAIN	5470	2013	02
ESOMEPRAZOLUM	ESOMEPRAZOL SANDOZ 20 mg	gastroresistant	20mg	SANDOZ S.R.L.	ROMANIA	5457	2013	33

		tablets						
ESOMEPRAZOLUM	ESOMEPRAZOL SANDOZ 40 mg	gastroresistant tablets	40mg	SANDOZ S.R.L.	ROMANIA	5458	2013	33
ESOMEPRAZOLUM	PRAGASTROL 20 mg	gastroresistant tablets	20mg	ALVOGEN IPCO S.A.R.L.	LUXEMBOURG	5311	2013	03
ESOMEPRAZOLUM	PRAGASTROL 40 mg	gastroresistant tablets	40mg	ALVOGEN IPCO S.A.R.L.	LUXEMBOURG	5312	2013	03
ETHAMBUTOLUM	ETAMBUTOL ARENA 400 mg	capsules	400mg	ARENA GROUP S.A.	ROMANIA	5393	2013	03
EXEMESTANUM	AROSTANIL 25 mg	film-coated tablets	25mg	SANDOZ S.R.L.	ROMANIA	5461	2013	08
HUMAN COAGULATION FACTOR VIII / VON WILLEBRAND FACTOR	IMMUNATE 250 IU	powder and solvent for solution for injection	250IU	BAXTER AG	AUSTRIA	5418	2013	01
HUMAN COAGULATION FACTOR VIII / VON WILLEBRAND FACTOR	IMMUNATE 500 IU	powder and solvent for solution for injection	500IU	BAXTER AG	AUSTRIA	5419	2013	01
HUMAN COAGULATION FACTOR VIII / VON WILLEBRAND FACTOR	IMMUNATE 1000 IU	powder and solvent for solution for injection	1000IU	BAXTER AG	AUSTRIA	5420	2013	01
FLUCONAZOLUM	FLUCOVIM 50	capsules	50mg	VIM SPECTRUM S.R.L.	ROMANIA	5315	2013	01
FLUCONAZOLUM	FLUCOVIM 100	capsules	100mg	VIM SPECTRUM S.R.L.	ROMANIA	5316	2013	01
FLUCONAZOLUM	FLUCOVIM 150	capsules	150mg	VIM SPECTRUM S.R.L.	ROMANIA	5317	2013	01
GALANTAMINUM	GALANTAMINA TEVA 8 mg	prolonged-release capsules	8mg	TEVA PHARMACEUTICALS S.R.L.	ROMANIA	5299	2013	10
GALANTAMINUM	GALANTAMINA TEVA 16 mg	prolonged-release capsules	16mg	TEVA PHARMACEUTICALS S.R.L.	ROMANIA	5300	2013	10
GALANTAMINUM	GALANTAMINA TEVA 24 mg	prolonged-release capsules	24mg	TEVA PHARMACEUTICALS S.R.L.	ROMANIA	5301	2013	10
GEMCITABINUM	GEMCITABINA KABI 40 mg/ml	concentrate for solution for infusion	40mg/ml	FRESENIUS KABI ONCOLOGY PLC.	GREAT BRITAIN	5344	2013	03
GLICLAZIDUM	GLYCLADA 60 mg	modified-release tablets	60mg	KRKA, D.D., NOVO MESTO	SLOVENIA	5467	2013	20
GLICLAZIDUM	GLICLAZIDA KRKA 60 mg	modified-release tablets	60mg	KRKA, D.D., NOVO MESTO	SLOVENIA	5468	2013	20
GRANISETRONUM	GRANISETRON KABI 1 mg/ml	solution for injection	1mg/ml	FRESENIUS KABI ROMANIA S.R.L.	ROMANIA	5462	2013	04
HEPARINUM	VIATROMB 2400 IU/g	cutaneous spray, emulsion	2400 IU/g	CYATHUS EXQUIRERE PHARMAFORSCHUNGS GMBH	AUSTRIA	5424	2013	02
IBUPROFENUM	IBUPROFEN SANDOZ 20 mg/ml	oral suspension	20mg/ml	SANDOZ S.R.L.	ROMANIA	5429	2013	03
IBUPROFENUM	IBUPROFEN SANDOZ 40 mg/ml	oral	40mg/ml	SANDOZ S.R.L.	ROMANIA	5430	2013	04

		suspension						
IBUPROFENUM	IBUPROFEN ROCKSPRING 200 mg	effervescent granules	200mg	ROCKSPRING HEALTHCARE LIMIT	GREAT BRITAIN	5503	2013	03
IMATINIBUM	IMAKREBIN 100 mg	film-coated tablets	100mg	ALVOGEN IPCO S.AR.L.	LUXEMBURG	5297	2013	07
IMATINIBUM	IMAKREBIN 400 mg	film-coated tablets	400mg	ALVOGEN IPCO S.AR.L.	LUXEMBURG	5298	2013	07
IMATINIBUM	IMATINIB ZENTIVA 100 mg	film-coated tablets	100mg	ZENTIVA, K.S.	THE CZECH REPUBLIC	5313	2013	04
IMATINIBUM	IMATINIB ZENTIVA 400 mg	film-coated tablets	400mg	ZENTIVA, K.S.	THE CZECH REPUBLIC	5314	2013	04
IMATINIBUM	IMATINIB ROMASTRU 100 mg	film-coated tablets	100mg	ROMASTRU TRADING SRL	ROMANIA	5336	2013	07
IMATINIBUM	IMATINIB ROMASTRU 400 mg	film-coated tablets	400mg	ROMASTRU TRADING SRL	ROMANIA	5337	2013	07
IMATINIBUM	IMATINIB GLENMARK 100 mg	film-coated tablets	100mg	GLENMARK PHARMACEUTICALS S.R.O.	THE CZECH REPUBLIC	5366	2013	08
IMATINIBUM	IMATINIB GLENMARK 400 mg	film-coated tablets	400mg	GLENMARK PHARMACEUTICALS S.R.O.	THE CZECH REPUBLIC	5367	2013	04
IMATINIBUM	VENZAN 400 mg	film-coated tablets	400mg	BIOFARM SP. ZO.O.	POLAND	5423	2013	03
IMATINIBUM	VENZAN 100 mg	film-coated tablets	100mg	BIOFARM SP. ZO.O.	POLAND	5422	2013	04
IMATINIBUM	NIBIX 100 mg	capsules	100mg	TERAPIA S.A.	ROMANIA	5472	2013	05
IMATINIBUM	NIBIX 400 mg	capsules	400mg	TERAPIA S.A.	ROMANIA	5473	2013	04
ANTI-D IMMUNOGLOBULIN	RHESONATIV 625 IU/ml	solution for injection	625IU/ml	OCTAPHARMA (IP) LIMITED	GREAT BRITAIN	5338	2013	03
HUMAN NORMAL IMMUNOGLOBULIN	INTRATECT 100 g/l	solution for infusion	100g/l	BIOTEST PHARMA GMBH	GERMANY	5454	2013	04
KALII CHLORIDUM	CLORURA DE POTASIU KABI 150mg/ml	concentrate for solution for infusion	150mg/ml	FRESENIUS KABI ROMANIA S.R.L.	ROMANIA	5479	2013	05
LATANOPROSTUM	MONOPOST 50 micrograms/ml	eye drops in single dose recipient, solution	50micrograms/ml	LABORATOIRES THEA	FRANCE	5346	2013	04
LATANOPROSTUM	AKISTAN 50 micrograms/ml	eye drops, solution	50micrograms/ml	PHARMASELECT INTERNATIONAL BETEILIGUNGS GMBH	AUSTRIA	5453	2013	01
LETROZOLUM	LORTANDA 2.5 mg	film-coated tablets	2.5 mg	KRKA, D.D., NOVO MESTO	SLOVENIA	5372	2013	10
LEVOCETIRIZINUM	LEVOCETIRIZINA STADA 5 mg	film-coated tablets	5mg	STADA ARZNEIMITTEL AG	GERMANY	5444	2013	20
LEVOCETIRIZINUM	CEZERA 5 mg	film-coated tablets	5mg	KRKA D.D. NOVO MESTO	SLOVENIA	5452	2013	22
LEVOTHYROXINUM	L-THYROXIN BERLIN-CHEMIE	tablets	100 micrograms	BERLIN-CHEMIE AG (MENARINI GROUP)	GERMANY	5464	2013	03
MACROGOLUM	OLOPEG	concentrate for oral solution		CNP PHARMA GMBH	GERMANY	5404	2013	04

MEMANTINUM	MEMANTINA TORRENT 10 mg	film-coated tablets	10mg	TORRENT PHARMA S.R.L.	ROMANIA	5481	2013	07
MEMANTINUM	MEMANTINA TORRENT 20 mg	film-coated tablets	20mg	TORRENT PHARMA S.R.L.	ROMANIA	5482	2013	07
MEMANTINUM	MEMANTINA TORRENT 5 mg+10 mg+15 mg+20 mg (Batch for treatment onset)	film-coated tablets	5mg+10mg+ 15mg+20mg	TORRENT PHARMA S.R.L.	ROMANIA	5483	2013	01
MEMANTINUM	MEMANTINA TEVA 5 mg/released dose	oral solution	5mg/dose	TEVA PHARMACEUTICALS S.R.L.	ROMANIA	5488	2013	03
METFORMINUM	METFORMIN AUROBINDO 500 mg	film-coated tablets	500mg	AUROBINDO PHARMA LIMITED	GREAT BRITAIN	5425	2013	19
METFORMINUM	METFORMIN AUROBINDO 850 mg	film-coated tablets	850mg	AUROBINDO PHARMA LIMITED	GREAT BRITAIN	5426	2013	19
METFORMINUM	METFORMIN AUROBINDO 1000 mg	film-coated tablets	1000mg	AUROBINDO PHARMA LIMITED	GREAT BRITAIN	5427	2013	11
METHYLFENIDATUM	CONCERTA 18 mg	prolonged-release tablets	18mg	JANSSEN PHARMACEUTICA N.V.	BELGIA	5339	2013	02
METHYLFENIDATUM	CONCERTA 36 mg	prolonged-release tablets	36mg	JANSSEN PHARMACEUTICA N.V.	BELGIA	5340	2013	02
METHYLFENIDATUM	CONCERTA 54 mg	prolonged-release tablets	54mg	JANSSEN PHARMACEUTICA N.V.	BELGIA	5341	2013	02
METOPROLOLUM	METOPROLOL TARTRAT AUROBINDO 50 mg	film-coated tablets	50mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	5391	2013	09
METOPROLOLUM	METOPROLOL TARTRAT AUROBINDO 100 mg	film-coated tablets	100mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	5392	2013	09
MICONAZOLUM	LORAMYC 50 mg	oral mucoadhesive tablets	50mg	BIOALLIANCE PHARMA	FRANCE	5302	2013	01
MISOPROSTOLUM	MISONE 400 micrograms	tablets	400micrograms	EXELGYN	FRANCE	5466	2013	08
MOMETASONUM	MOMETAZONA ATB 1 mg/g	ointment	1mg/g	ANTIBIOTICE SA	ROMANIA	5434	2013	01
MOMETASONUM	MOMETAZONA ATB 1 mg/g	cream	1mg/g	ANTIBIOTICE SA	ROMANIA	5433	2013	01
MONTELUKASTUM	MONTELUKAST ABBOTT 5 mg	chewable tablets	5mg	ABBOTT LABORATORIES LIMITED	GREAT BRITAIN	5396	2013	08
MONTELUKASTUM	MONTELUKAST ABBOTT 4 mg	chewable tablets	4mg	ABBOTT LABORATORIES LIMITED	GREAT BRITAIN	5395	2013	08
MONTELUKASTUM	MONTELUKAST ABBOTT 10 mg	film-coated tablets	10mg	ABBOTT LABORATORIES LIMITED	GREAT BRITAIN	5394	2013	08
NEBIVOLOLUM	NEBICARD 5 mg	tablets	5mg	BIOFARM SP. ZO.O	POLAND	5465	2013	06
NEVIRAPINUM	NEVIRAPINA SANDOZ 200 mg	tablets	200mg	SANDOZ S.R.L.	ROMANIA	5460	2013	03
OCTREOTIDUM	OCTREOTID KABI 0,1 mg/ml	solution for injection	0.1mg/ml	FRESENIUS KABI ROMANIA S.R.L.	ROMANIA	5463	2013	03
OLANZAPINUM	OLANZAPINA DR. REDDY'S 2.5 mg	film-coated tablets	2.5 mg	DR. REDDY'S LABORATORIES ROMÂNIA S.R.L.	ROMANIA	5373	2013	04
OLANZAPINUM	OLANZAPINA DR. REDDY'S 5mg	film-coated tablets	5mg	DR. REDDY'S LABORATORIES ROMÂNIA S.R.L.	ROMANIA	5374	2013	04
OLANZAPINUM	OLANZAPINA DR. REDDY'S 10mg	film-coated tablets	10mg	DR. REDDY'S LABORATORIES ROMÂNIA S.R.L.	ROMANIA	5376	2013	04
OLANZAPINUM	OLANZAPINA DR. REDDY'S 7.5	film-coated	7.5 mg	DR. REDDY'S LABORATORIES	ROMANIA	5375	2013	04

	mg	tablets		ROMÂNIA S.R.L.				
OLANZAPINUM	OLANZAPINA DR. REDDY'S 15 mg	film-coated tablets	15mg	DR. REDDY'S LABORATORIES ROMÂNIA S.R.L.	ROMANIA	5377	2013	04
OLANZAPINUM	OLANZAPINA DR. REDDY'S 20 mg	film-coated tablets	20mg	DR. REDDY'S LABORATORIES ROMANIA S.R.L.	ROMANIA	5378	2013	04
OLANZAPINUM	OLANZAPINA DR. REDDY'S 5 mg	orodispersible tablets	5mg	DR. REDDY'S LABORATORIES ROMANIA S.R.L.	ROMANIA	5352	2013	04
OLANZAPINUM	OLANZAPINA DR. REDDY'S 10 mg	orodispersible tablets	10mg	DR. REDDY'S LABORATORIES ROMANIA S.R.L.	ROMANIA	5353	2013	04
OLANZAPINUM	OLANZAPINA DR. REDDY'S 15 mg	orodispersible tablets	15mg	DR. REDDY'S LABORATORIES ROMANIA S.R.L.	ROMANIA	5354	2013	04
OLANZAPINUM	OLANZAPINA DR. REDDY'S 20 mg	orodispersible tablets	20mg	DR. REDDY'S LABORATORIES ROMANIA S.R.L.	ROMANIA	5355	2013	04
OLANZAPINUM	ATYZYO 2.5 mg	film-coated tablets	2.5 mg	ABBOTT LABORATORIES LTD.	GREAT BRITAIN	5387	2013	03
OLANZAPINUM	ATYZYO 5 mg	film-coated tablets	5mg	ABBOTT LABORATORIES LTD.	GREAT BRITAIN	5388	2013	03
OLANZAPINUM	ATYZYO 7.5 mg	film-coated tablets	7.5 mg	ABBOTT LABORATORIES LTD.	GREAT BRITAIN	5389	2013	03
OLANZAPINUM	ATYZYO 10 mg	film-coated tablets	10mg	ABBOTT LABORATORIES LTD.	GREAT BRITAIN	5390	2013	03
OXALIPLATINUM	OXALIPLATIN PHARMA RESOURCES 5mg/ml	concentrate for solution for infusion	5mg/ml	PHARMA RESOURCES GMBH	GERMANY	5303	2013	03
OXYMETAZOLINUM	AFRIN 0.5 mg/ml	nasal spray, solution	0.5 mg/ml	MERCK SHARP & DOHME ROMANIA S.R.L.	ROMANIA	5368	2013	01
OXYMETAZOLINUM	AFRIN MENTOL 0.5 mg/ml	nasal spray, solution	0.5 mg/ml	MERCK SHARP & DOHME ROMANIA S.R.L.	ROMANIA	5369	2013	01
OXYMETAZOLINUM	AFRIN LEMON 0.5 mg/ml	nasal spray, solution	0.5 mg/ml	MERCK SHARP & DOHME ROMANIA S.R.L.	ROMANIA	5370	2013	01
OXYMETAZOLINUM	AFRIN MUSETEL 0.5 mg/ml	nasal spray, solution	0.5 mg/ml	MERCK SHARP & DOHME ROMANIA S.R.L.	ROMANIA	5371	2013	01
PARACETAMOLUM	PARACETAMOL ACTAVIS 250 mg	orodispersible tablets	250mg	ACTAVIS GROUP PTC EHF.	ICELAND	5349	2013	10
PARACETAMOLUM	SUPOFEN 40 mg/ml	oral suspension	40mg/ml	LABORATORIOS BASI-INDUSTRIA FARMACEUTICA, S.A.	PORTUGAL	5428	2013	01
PARACETAMOLUM	PARACETAMOL ROCKSPRING 1000 mg	tablets	1000mg	ROCKSPRING HEALTHCARE LIMITED	GREAT BRITAIN	5504	2013	04
PERINDOPRILUM	PERINDOPRIL TOSILAT TEVA 2.5 mg	film-coated tablets	2.5 mg	TEVA PHARMACEUTICALS S.R.L.	ROMANIA	5289	2013	05
PERINDOPRILUM	PERINDOPRIL TOSILAT TEVA 5mg	film-coated tablets	5mg	TEVA PHARMACEUTICALS S.R.L.	ROMANIA	5290	2013	05
PERINDOPRILUM	PERINDOPRIL TOSILAT TEVA 10mg	film-coated tablets	10mg	TEVA PHARMACEUTICALS S.R.L.	ROMANIA	5291	2013	05
PRAMIPEXOLUM	PRAMIPEXOL AUROBINDO 0.18 mg	tablets	0.18 mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	5411	2013	11
PRAMIPEXOLUM	PRAMIPEXOL AUROBINDO 0.7 mg	tablets	0.7 mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	5412	2013	11

QUETIAPINUM	QUETIAPINA TEVA 150 mg	prolonged-release tablets	150mg	TEVA PHARMACEUTICALS S.R.L.	ROMANIA	5351	2013	11
QUETIAPINUM	KATHIRA 25 mg	film-coated tablets	25mg	ROMASTRU TRADING S.R.L.	ROMANIA	5361	2013	01
QUETIAPINUM	KATHIRA 100 mg	film-coated tablets	100mg	ROMASTRU TRADING S.R.L.	ROMANIA	5362	2013	01
QUETIAPINUM	KATHIRA 150 mg	film-coated tablets	150mg	ROMASTRU TRADING S.R.L.	ROMANIA	5363	2013	01
QUETIAPINUM	KATHIRA 200 mg	film-coated tablets	200mg	ROMASTRU TRADING S.R.L.	ROMANIA	5364	2013	01
QUETIAPINUM	KATHIRA 300 mg	film-coated tablets	300mg	ROMASTRU TRADING S.R.L.	ROMANIA	5365	2013	01
RANITIDINUM	RANITIDINA ACCORD 150 mg	film-coated tablets	150mg	ACCORD HEALTHCARE LIMITED	GREAT BRITAIN	5304	2013	03
RANITIDINUM	RANITIDINA ACCORD 300 mg	film-coated tablets	300mg	ACCORD HEALTHCARE LIMITED	GREAT BRITAIN	5305	2013	03
RIFAXIMINUM	TIXTELLER 550 mg	film-coated tablets	550mg	ALFA WASSERMANN S.P.A.	ITALY	5350	2013	05
RIVASTIGMINUM	RIVASTIGMINA TORRENT 4.6 mg/24 hours	transdermal patch	4.6 mg/24 hours	TORRENT PHARMA SRL	ROMANIA	5440	2013	07
RIVASTIGMINUM	RIVASTIGMINA TORRENT 9.5 mg/24 hours	transdermal patch	9.5 mg/24 hours	TORRENT PHARMA SRL	ROMANIA	5441	2013	07
RIVASTIGMINUM	RIVASTIGMINA TEVA 4.6 mg/24 hours	transdermal patch	4.6 mg/24 hours	TEVA PHARMACEUTICALS S.R.L.	ROMANIA	5485	2013	07
RIVASTIGMINUM	RIVASTIGMINA TEVA 9.5 mg/24 hours	transdermal patch	9.5 mg/24 hours	TEVA PHARMACEUTICALS S.R.L.	ROMANIA	5486	2013	07
ROPINIROLUM	ROPINIROL AUROBINDO 2 mg	prolonged-release tablets	2 mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	5408	2013	02
ROPINIROLUM	ROPINIROL AUROBINDO 4 mg	prolonged-release tablets	4 mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	5409	2013	02
ROPINIROLUM	ROPINIROL AUROBINDO 8 mg	prolonged-release tablets	8 mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	5410	2013	02
ROSUVASTATINUM	ROSUVASTATINA AUROBINDO 5mg	film-coated tablets	5mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	5445	2013	10
ROSUVASTATINUM	ROSUVASTATINA AUROBINDO 10 mg	film-coated tablets	10mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	5446	2013	10
ROSUVASTATINUM	ROSUVASTATINA AUROBINDO 20 mg	film-coated tablets	20mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	5447	2013	10
ROSUVASTATINUM	ROSUVASTATINA AUROBINDO 40 mg	film-coated tablets	40mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	5448	2013	10
SIMETHICONUM	VETRATE 41.2 mg/ml	oral drops, solution	41.2mg/ml	FARMACEUTICA REMEDIA S.A.	ROMANIA	5489	2013	02
SIMETHICONUM	VETRATE 42 mg	chewable tablets	42mg	FARMACEUTICA REMEDIA S.A.	ROMANIA	5490	2013	03
TACROLIMUSUM	TACROLIMUS PERGAMUS 0.5 mg	capsules	0.5 mg	PERGAMUS PHARMA LIMITED UK	GREAT BRITAIN	5399	2013	06
TACROLIMUSUM	TACROLIMUS PERGAMUS 1 mg	capsules	1mg	PERGAMUS PHARMA LIMITED UK	GREAT BRITAIN	5400	2013	06

TACROLIMUSUM	TACROLIMUS PERGAMUS 5 mg	capsules	5mg	PERGAMUS PHARMA LIMITED UK	GREAT BRITAIN	5401	2013	06
TAPENTADOLUM	PALEXIA 4 mg/ml	oral solution	4mg/ml	GRUNENTHAL GMBH	GERMANY	5293	2013	02
TELMISARTANUM	TELMISARTAN TORRENT 20 mg	tablets	20mg	TORRENT PHARMA S.R.L.	ROMANIA	5306	2013	03
TELMISARTANUM	TELMISARTAN TORRENT 40 mg	tablets	40mg	TORRENT PHARMA S.R.L.	ROMANIA	5307	2013	03
TELMISARTANUM	TELMISARTAN TORRENT 80 mg	tablets	80mg	TORRENT PHARMA S.R.L.	ROMANIA	5308	2013	03
TELMISARTANUM	STARAM 40 mg	tablets	40mg	SPECIFAR S.A.	GREECE	5342	2013	14
TELMISARTANUM	STARAM 80 mg	tablets	80mg	SPECIFAR S.A.	GREECE	5343	2013	14
TELMISARTANUM	MILSERTAN 40 mg	tablets	40mg	SPECIFAR S.A.	GREECE	5380	2013	14
TELMISARTANUM	MILSERTAN 80 mg	tablets	80mg	SPECIFAR S.A.	GREECE	5381	2013	14
TEMOZOLOMIDUM	NOGRON 5 mg	capsules	5mg	EGIS PHARMACEUTICALS PLC	HUNGARY	5318	2013	03
TEMOZOLOMIDUM	NOGRON 20 mg	capsules	20mg	EGIS PHARMACEUTICALS PLC	HUNGARY	5319	2013	03
TEMOZOLOMIDUM	NOGRON 100 mg	capsules	100mg	EGIS PHARMACEUTICALS PLC	HUNGARY	5320	2013	03
TEMOZOLOMIDUM	NOGRON 140 mg	capsules	140mg	EGIS PHARMACEUTICALS PLC	HUNGARY	5321	2013	03
TEMOZOLOMIDUM	NOGRON 180 mg	capsules	180mg	EGIS PHARMACEUTICALS PLC	HUNGARY	5322	2013	03
TEMOZOLOMIDUM	NOGRON 250 mg	capsules	250mg	EGIS PHARMACEUTICALS PLC	HUNGARY	5323	2013	03
TEMOZOLOMIDUM	TEMOZOLOMIDA POLPHARMA 5mg	capsules	5mg	PHARMACEUTICAL WORKS POLPHARMA SA	POLAND	5324	2013	03
TEMOZOLOMIDUM	TEMOZOLOMIDA POLPHARMA 20 mg	capsules	20mg	PHARMACEUTICAL WORKS POLPHARMA SA	POLAND	5325	2013	03
TEMOZOLOMIDUM	TEMOZOLOMIDA POLPHARMA 100 mg	capsules	100mg	PHARMACEUTICAL WORKS POLPHARMA SA	POLAND	5326	2013	03
TEMOZOLOMIDUM	TEMOZOLOMIDA POLPHARMA 140 mg	capsules	140mg	PHARMACEUTICAL WORKS POLPHARMA SA	POLAND	5327	2013	03
TEMOZOLOMIDUM	TEMOZOLOMIDA POLPHARMA 180 mg	capsules	180mg	PHARMACEUTICAL WORKS POLPHARMA SA	POLAND	5328	2013	03
TEMOZOLOMIDUM	TEMOZOLOMIDA POLPHARMA 250 mg	capsules	250mg	PHARMACEUTICAL WORKS POLPHARMA SA	POLAND	5329	2013	03
TEMOZOLOMIDUM	TEMOZOLOMIDA GLENMARK 5 mg	capsules	5mg	GLENMARK PHARMACEUTICALS S.R.O	THE CZECH REPUBLIC	5491	2013	03
TEMOZOLOMIDUM	TEMOZOLOMIDA GLENMARK 20 mg	capsules	20mg	GLENMARK PHARMACEUTICALS S.R.O	THE CZECH REPUBLIC	5492	2013	03
TEMOZOLOMIDUM	TEMOZOLOMIDA GLENMARK 100 mg	capsules	100mg	GLENMARK PHARMACEUTICALS S.R.O	THE CZECH REPUBLIC	5493	2013	03
TEMOZOLOMIDUM	TEMOZOLOMIDA GLENMARK 140 mg	capsules	140mg	GLENMARK PHARMACEUTICALS S.R.O	THE CZECH REPUBLIC	5494	2013	03
TEMOZOLOMIDUM	TEMOZOLOMIDA GLENMARK 180 mg	capsules	180mg	GLENMARK PHARMACEUTICALS S.R.O	THE CZECH REPUBLIC	5495	2013	03
TEMOZOLOMIDUM	TEMOZOLOMIDA GLENMARK 250 mg	capsules	250mg	GLENMARK PHARMACEUTICALS S.R.O	THE CZECH REPUBLIC	5496	2013	03
TEMOZOLOMIDUM	BRASTORYN 5 mg	capsules	5mg	ROMASTRU TRADING SRL	ROMANIA	5497	2013	03
TEMOZOLOMIDUM	BRASTORYN 20 mg	capsules	20mg	ROMASTRU TRADING SRL	ROMANIA	5498	2013	03
TEMOZOLOMIDUM	BRASTORYN 100 mg	capsules	100mg	ROMASTRU TRADING SRL	ROMANIA	5499	2013	03
TEMOZOLOMIDUM	BRASTORYN 140 mg	capsules	140mg	ROMASTRU TRADING SRL	ROMANIA	5500	2013	03
TEMOZOLOMIDUM	BRASTORYN 180 mg	capsules	180mg	ROMASTRU TRADING SRL	ROMANIA	5501	2013	03
TEMOZOLOMIDUM	BRASTORYN 240 mg	capsules	240mg	ROMASTRU TRADING SRL	ROMANIA	5502	2013	03

INACTIVATED TICK-BORNE ENCEPHALITIS VIRUS	ENCEPUR ADULȚI 1.5 µg/0.5 ml	suspension for injection in pre-filled syringe	1.5µg/0.5 ml	NOVARTIS VACCINES AND DIAGNOSTICS GMBH	GERMANY	5406	2013	04
INACTIVATED TICK-BORNE ENCEPHALITIS VIRUS	ENCEPUR COPII 0.75 µg/0.25 ml	suspension for injection in pre-filled syringe	0.75µg/0.25ml	NOVARTIS VACCINES AND DIAGNOSTICS GMBH	GERMANY	5405	2013	04
VACCIN RABIC INACTIVAT	VERORAB	powder and solvent for suspension for injection		SANOFI PASTEUR S.A.	FRANCE	5310	2013	03
VENLAFAXINUM	FOBILESS 37.5 mg	prolonged-release capsules	37.5 mg	LANNACHER HEILMITTEL GES.M.B.H	AUSTRIA	5356	2013	10
VENLAFAXINUM	FOBILESS 75 mg	prolonged-release capsules	75mg	LANNACHER HEILMITTEL GES.M.B.H	AUSTRIA	5357	2013	10
VENLAFAXINUM	FOBILESS 150 mg	prolonged-release capsules	150mg	LANNACHER HEILMITTEL GES.M.B.H	AUSTRIA	5358	2013	10
XYLOMETAZOLINUM	BIXTONIM XYLO AROMA 1mg/ml	nasal spray, solution	1mg/ml	BIOFARM S.A.	ROMANIA	5484	2013	01

EMA centrally authorised medicinal products for which a marketing price was established in Romania during the 1st quarter of 2013

INN	Invented name	Pharm. form	Strength	Manufacturer	Country	MA number		
ACIDUM ZOLEDRONICUM	ACID ZOLEDRONIC ACTAVIS 4mg/5ml	concentrate for solution for infusion	4mg/5ml	ACTAVIS GROUP PTC EHF	ICELAND	759	2013	01
COMBINATIONS (TELMISARTANUM+ HYDROCHLOROTHIAZIDUM)	ACTELSAR HCT 40 mg/12.5 mg	tablets	40mg/12.5 mg	ACTAVIS GROUP PTC EHF	ICELAND	817	2013	13
COMBINATIONS (TELMISARTANUM+ HYDROCHLOROTHIAZIDUM)	ACTELSAR HCT 80 mg/25mg	tablets	80mg/25mg	ACTAVIS GROUP PTC EHF.	ICELAND	817	2013	41
COMBINATIONS (TELMISARTANUM+ HYDROCHLOROTHIAZIDUM)	ACTELSAR HCT 80 mg/12.5 mg	tablets	80mg/12.5mg	ACTAVIS GROUP PTC EHF.	ICELAND	817	2013	28
IMATINIBUM	IMATINIB TEVA 100 mg	film-coated tablets	100mg	TEVA PHARMA B.V.	HOLLAND	808	2013	05
IMATINIBUM	IMATINIB TEVA 400 mg	film-coated tablets	400mg	TEVA PHARMA B.V.	HOLLAND	808	2013	14
NALMEFENUM	SELINCRO 18mg	film-coated tablets	18mg	H. LUNDBECK A/S	DENMARK	815	2013	05