ROMANIA

Newsletter

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National Agency for Medicines and Medical Devices

Emergency Ordinance no. 91 of 12.12.2012 amending certain healthcare regulations

Report of the activities performed by the National Agency for Medicines and Medical Devices in 2010

Medicinal product batches recalled during the 4th quarter of 2012

Applications for marketing authorisation/marketing authorisation renewal submitted to the NAMMD during the 3rd quarter of 2012

Medicinal products authorised for marketing by the NAMMD during the 3rd quarter of 2012

EMA centrally authorised medicinal products for which a marketing price was established in Romania during the 3rd quarter of 2012

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THE GOVERNMENT OF ROMANIA

EMERGENCY ORDINANCE
amending certain healthcare regulations

Having regard to Directive 2011/62/EU of the European Parliament and of the Council of 8 June 2011 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use as regards the prevention of the entry into the legal supply chain of falsified medicinal products,

Taking into account Romania's obligation to observe deadlines for transposition of Directive 2011/62/EU into national law, namely by 31 December 2012,

To reduce the risk of action for failure to fulfil Member State obligations, according to art. 258 of the Treaty on the Functioning of the European Union,

Taking into account that transposition of the directives in question provide the necessary and obligatory conditions for achievement of quality medical intervention for citizens of Romania,

Having in mind that failure to meet these provisions entails the risk of decisions by the European Court of Justice imposing payment by Romania of financial penalties, according to art. 260(3) of the Treaty on the Functioning of the European Union, with major negative impact on the state budget,

Taking into account the Communication 2011/C 12/01 of the European Commission on Implementation of Article 260 (3) of the Treaty on the Functioning of the European Union, in particular the obligation of Member States to transpose directives within the deadlines laid down by the legislator and hence to ensure that Union legislation is genuinely effective,

Taking into account that failure to adopt emergency measures contained in this regulatory act may affect the rights of individuals, who may refer to national courts under the principle of the direct effect of directives, where harm has been done in result of non-compliance with European Union legislation on the prevention of the entry into the legal supply chain of falsified medicinal products,

Taking into account that the activities included in national health programs involve a combination of interventions intended for the therapeutic structure for patients with chronic diseases, such as rare diseases, transplants of organs, tissues or cells, cancer, diabetes mellitus and others, which require high costs for a certain number of affected persons, also intended for the public health structure, and for medical services whose costs are not covered by the DRG system financed from the budget of the Single National Social Health Insurance Fund,

Taking into account the undertaking of the Romanian Government concerning implementation before 31 December 2012 of the measures meant for reorientation of national healthcare programs towards primary public health field in accordance with the “Health Action Plan“,

For consistent regulation and adoption of immediate measures to ensure compliance with commitments of the Romanian Government in negotiations for loan agreements with financial institutions,

Taking into account that failure to adopt such immediate measures and their implementing regulations, by emergency ordinance, would cause major disruptions adversely affecting the health of the population, as well as for efficient use of healthcare human and financial resources,

Considering that these factors of major impact on public health concern the general public interest and represent emergency and extraordinary situations whose regulation may not be delayed,

Pursuant to Article 115(4) of the Romanian Constitution, republished,

The Government of Romania hereby adopts this Emergency Ordinance.

Art. I. - Law 95/2006 on healthcare reform, published in the Official Gazette of Romania, Part I, no. 372 of 28 April 2006, as amended, is hereby amended as follows:

1. Under Article 6 h), two new points, 9 and 10, are added after (8), as follows:

"9. Healthcare services for children;

10. Transfusion security services."

2. Under Article 6, a new point, i), is added after h), reading as follows:

"i) Medical and specific treatment of diseases with a major impact on public health (TB, HIV / AIDS, diseases, cancer, diabetes) and transplantation of organs, tissues or cells."

3. Under Article 8, c) is amended as follows:

"c) Activities within national health programs;"

4. Article 9 (3) and (5) are amended as follows:

"(3) National healthcare programs cover the main areas of intervention of public health and respond to national priorities identified by national health strategy.

.....

(5) National healthcare programs are developed by the Ministry of Health, with the participation of the National Health Insurance House; their development is carried out by the Ministry of Health and / or the National Health Insurance House as appropriate. "

5. Under Article 16 (1), points a) and c) are amended as follows:

"a) Establish national public health priorities, develop national healthcare programs and achieve coordination, monitoring, evaluation and control of the Ministry of Healthcare programs funded from the state budget and own revenues;

.....

c) Periodically assess population health indicators;"

6. Under Article 17 (2), o) is amended as follows:

"o) Ensure the implementation of national healthcare programs run by their own structures, coordination, monitoring and implementation of national public healthcare programs carried out under contracts with public institutions, healthcare providers network of local authorities, ministries and private health network institutions as well as private healthcare providers, as provided in the rules for performance of national public healthcare programs;".

7. Under Article 17, (2^1) is repealed.

8. Article 45 is amended as follows:

"Art. 45. - (1) For the purposes of this title, the terms and expressions below have the following meaning:

a) National healthcare programs - overall annual action directed towards the main areas of public healthcare intervention;

b) Development of national healthcare programs - the implementation, coordination, monitoring, evaluation and control of national healthcare programs;

c) Implementation of national healthcare programs, organisation of human, material and financial resources at the level of special units in order to ensure the goods, services or changes of behaviours and of living and working environment for the beneficiaries of these programs in response to certain health needs identified in objective data;

d) Specialised unit - structure of the public health system assigned to the implementation of national healthcare programs;

e) National/regional unit for national healthcare programs technical assistance and management units – the non-legal organisational structure of public institutions subordinated to the Ministry of Health, established by Order of the Minister of Health, responsible for providing national healthcare programs technical assistance and management units;

f) Technical assistance - all activities related to the training and information of special units responsible for the implementation of national healthcare programs and other activities undertaken to improve implementation of national healthcare programs;

g) Eligible expenditure - expenditure of goods and services carried out by specialised units assigned to the implementation of national healthcare programs, according to technical norms to achieve national healthcare programs.

(2) National healthcare programs address public health intervention areas as follows:

a) National public healthcare programs, which aim to ensure:

(i) The prevention, surveillance and control of communicable and non-communicable diseases;

(ii) Monitoring of the population health;

(iii) Promotion of health and a healthy lifestyle;

(iv) Monitoring of determinant factors in the living and working environment;

(v) Provision of specific public health services;

(vi) Provision of specific treatment for TB and HIV / AIDS;

(vii) Implementation of organ, tissue or cell transplantation procedures;

b) National healthcare programs ensuring specific treatment of diseases with a major impact on public health, other than TBC and HIV / AIDS and organ, tissue and cell transplantation."

9. In Article 48, s (1) and (2)-(4) are amended as follows:

"Article 48. - (1) National healthcare programs are developed by the Ministry of Health, with the participation of the National Health Insurance House, working separately, as follows:

a) By the Ministry of Health for public healthcare programs;

b) By the National Health Insurance for national healthcare programs.

.....

(2) The structure of national healthcare programs, their objectives, and any other terms and conditions needed in view of implementation and development are approved through Government decision on the proposal of the Ministry of Health.

(3) The technical standards to achieve national healthcare programs are approved as follows:

a) By the Minister of Health, for public healthcare programs;

b) By Order of the President of the National Health Insurance House, with the approval of the Ministry of Health, for national healthcare programs.

(4) In epidemiological risk, national public healthcare program beneficiaries, except for organ, tissue or cell transplant procedures are all Romanian citizens residing in the country, foreigners and stateless persons who have requested and obtained an extension of the right of temporary or permanent residence in Romania, as well as all citizens transiting Romania."

10. Under Article 48, s (5) and (6) are repealed.

11. Article 49 is amended as follows:

"Article 49. - (1) National healthcare programs are implemented by specialised units selected based on criteria approved by technical standards for national healthcare programs conduct.

(2) For the purposes of this law, specialised units are as follows:

a) Public institutions;

b) Public healthcare providers;

c) Private healthcare providers for medical services that exceed the capacity of public providers of medical services;

d) Private providers of medicinal products and medical devices.

(3) Specialised units under (2) may be employed to implement national healthcare programs as multiannual actions throughout implementation, in accordance with relevant legal provisions.

4) In order to perform the duties and activities included in national healthcare programs, specialised units mentioned under (2) may sign contracts for

services with physicians, medical assistants and other staff, as appropriate, as well as with legal persons, in accordance with the provisions of Law No. 287/2009 on the Code of Civil Procedure, republished, as amended, and under conditions as established through the technical Norms for implementation of national healthcare programs.

(5) Contracts for provision of services/temporary work contracts signed under the conditions laid down under (4) by the specialised units mentioned under (2) make provisions for multiannual actions, are of civil nature and are valid throughout the entire period of national healthcare programs implementation .

(6) Amounts necessary for the contracts referred to in (3) and (4) are included in the funds allocated to national healthcare programs. "

12. Article 49[1] is amended as follows:

"Art. 49[1]. - (1) National healthcare programs are implemented with Ministry of Health budget appropriations from the state budget and their own revenues, as follows:

a) Through public and healthcare providers under the Ministry of Health;

b) Through healthcare providers in the network of local authorities and ministries and institutions provided with their own health network, public and private healthcare providers, in compliance with Art. 49 (2) c) under contract with public health departments or, where appropriate, with public institutions subordinated to the Ministry of Health.

(2) National remedial healthcare programs are implemented with the amounts allocated from the budget of the Sole National Social Health Insurance Fund through assessed suppliers of medical services, medicinal products and medical devices, according to the contracts signed with health insurance houses."

13. Article 50 is amended as follows:

"Art. 50. - The responsibilities of Ministry of Health national healthcare programs are as follows:

a) To approve the strategy of national healthcare programs, integrant part of the national health strategy;

b) To propose for national healthcare programs Government approval;

c) To approve methodological norms for national public healthcare programs implementation;

d) To approve methodological norms for implementation of national remedial programs developed by the National Health Insurance House;

e) To organise national procedures for public acquisitions in view of procurement of goods and services needed to implement national healthcare programs, in compliance with legal provisions on public acquisitions;

f) To organise, monitor, assess and control the implementation of national public healthcare programs;

g) To finance national healthcare programs. "

14. Article 51 is amended as follows:

"Art. 51. – The responsibilities of the Ministry of Health structure concerning the development and coordination of national healthcare programs are:

a) To participate in the strategy concerning development of national healthcare programs, as integrant part of the national health strategy;

b) To elaborate the structure of national healthcare programs in collaboration with specialised departments of the Ministry of Health and the National Health Insurance House;

c) To substantiate the required financial resources for the development of national healthcare programs according to proposals form regional/national units for national healthcare programs technical assistance and management units and/or specialised departments of the Ministry of Health, as appropriate;

d) To propose technical standards for Minister of Health approval concerning implementation of national public healthcare programs, issued in cooperation with the specialised departments of the Ministry of Health;

e) To provide coordination, monitoring, assessment and control of the implementation of national public healthcare programs directly or through regional/national units for national healthcare programs technical assistance and management units, in cooperation with the specialised departments of the Ministry of Health;

f) To propose measures to the Minister of Health for better implementation of national healthcare programs.“

15. Article 52 is amended as follows:

“Art. 52. – In what concerns national healthcare programs, responsibilities of the National Health Insurance House are as follows:

a) To participate in the drafting of the Government Decision for approval of national healthcare programs;

b) To develop and approve the technical standards required for development of national remedial healthcare programs, with Ministry of Health consent;

c) To organise, monitor, assess and control implementation of national remedial healthcare programs;

d) To provide funding of national remedial healthcare programs;

e) To provide indicators of the national remedial programs to the structure responsible with the development and coordination of national healthcare programs, on a quarterly, annual basis and whenever necessary, and analyse their implementation. “

16. Article 53 is amended as follows:

“Art. 53. - (1) Through Order of the Minister of Health, the Ministry of Health assigns public institutions under its subordination to provide national healthcare programs technical assistance and management units and establishes technical and national healthcare programs management units within the institutions assigned.

(2) Units of national healthcare programs technical assistance and management units may be set up at national or regional level, as appropriate.

(3) A single unit for national healthcare programs technical assistance and management may be set up within a public institution subordinated to the Ministry of Health, able ensure technical assistance and management for one or several

national healthcare programs, as appropriate.

(4) The organisational structure of technical and management units of national healthcare programs, their duties and any other necessary condition for their operation are approved through the technical standards for implementation of national healthcare programs.

(5) Expenses for organisation and operation of technical and national healthcare programs management units are included in the amounts allocated to the national healthcare programs under their management, as established depending on thei complexity of their activity, with Ministry of Health approval.

(6) For implementation of technical and management functions of national healthcare programs, public institutions under (1) may employ personnel without exceeding the maximum number of positions approved by the Ministry of Health and its subordinate institutions, and / or may contract provision of services / civil agreements according to Art. 49 (3) - (6), pursuant to legal provisions in force. "

17. Article 54 is amended as follows:

"Art. 54. - (1) National healthcare programs are funded as follows:

a) From the Ministry of Health budget, the state budget and its own revenues for national remedial healthcare programs;

b) From the Sole National Health Insurance Fund for remedial healthcare programs;

c) From other sources, including donations and sponsorships, in accordance with the law;

(2) The amounts allocated to multiannual national healthcare programs are approved through state budget law in accordance with the provisions of Law 500/2002 on public finances, as amended.

(3) In case of national public healthcare programs, categories of eligible expenditures and the financing thereof are approved through the technical standards for national healthcare programs implementation.

(4) In case of national remedial healthcare programs, the medicinal products, healthcare materials, medical devices and such that are released through open circuit pharmacies and provided to beneficiaries included in national remedial programs are funded from the budget of the Sole National Social Health Insurance Fund, at discount price.

(5) Medicinal products, medical supplies, medical devices and such that are used in medical facilities for in-patient treatment during hospitalisation or, where applicable, released by in-house pharmacies for outpatient treatment of patients enrolled in national healthcare programs are paid by purchase price, which may not exceed the settlement price for medicinal products.

(6) The purchase of medicines, medical equipment, medical devices and such specified in (5) is done by public acquisition procedures organised by the Ministry of Health or by healthcare in-patient facilities implementing national healthcare programs, as appropriate, in accordance with legal provisions on public acquisitions.

(7) The List of medicinal products provided within national healthcare programs is approved by Government Decision.“

18. Article 55 is amended as follows:

“Article 55. - (1) The amounts allocated for healthcare programs are included in the revenue and expenditure of the specialised units of their implementation.

(2) The amounts referred to in (1) are posted on the website of the Ministry of Health.

(3) On their website, “Specialised Units“ publish the healthcare programs income and expenditure budget and its execution“.

19. Article 56 is amended as follows:

“Art. 56. - Specialised units implementing national healthcare programs use the funds without exceeding the budget assigned and according to the purpose specified by legal provisions and by the obligation concerning efficient management of material and financial resources as well as arrangement of accounting records for each program, according to budget classification subdivisions, for both the approved budget and the execution of the income and expenses budget. “

20. Article 57 is amended as follows:

“Article 57. - (1) The Ministry of Health provides funds for financing national healthcare programs at the request of national healthcare programs technical assistance and management units.

(2) The National Health Insurance House provides the funds required for the financing of national remedial programs on request by health insurance houses.

(3) Requests for financing national healthcare programs under (1) and (2) above are made using specialised unit based applications requiring funding dependent on achievement of indicators and within the limits of the funds approved for this purpose.“

21. Under Article 80, d) is amended as follows:

“d) Contracts with local public health authorities or public institutions under the Ministry of Health for national public healthcare programs implementation.“

22. Under Article 81^1, (1) is amended as follows:

“Art. 81^1. - (1) The state budget, via the Ministry of Health budget, may provide funding for infrastructure investments in rural areas for construction, rehabilitation, minimum standard endowment of medical and non-medical areas where primary healthcare activities are conducted.“

23. A new article is introduced after Article 92, Article 92^1, which reads as follows:

“Art. 92^1. - (1) In the context of activities performed by ambulance services, namely pre-hospital emergency medical assistance and assisted medical transportation, activities carried out by the medical assistant, the emergency registry operator and the dispatcher/radio telephone operator, as well as of the ambulance driver are permanent.

(2) The activity performed by the medical assistant, the emergency registry operator and the dispatcher/radio telephone operator, as well as by the ambulance driver to ensure continuity in emergency medical care, outside the regular schedule hours, is assimilated with on-duty medical staff activity and as such has the same rights as mentioned in Chapter II Art. 3 of Annex III of Framework Law No. 284/2010 on unitary pay wage system for staff paid from public funding, as amended, when no adequate off-duty time can be granted to compensate for work performed beyond regular working hours."

24. Under Article 93, (1) is amended as follows:

"Art. 93. - (1) Funding of emergency public medical assistance is done via the Ministry of Health from the state budget and its own revenues, via the budget of the Ministry of Administration and Internal Affairs, of ministries and institutions provided with their individual healthcare network, from donations and sponsorships, as well as from other sources, as provided by law."

25. Under Article 93, (11) is amended as follows:

"(1^1) The financing of county ambulance services, namely of the Bucharest-Ilfov Ambulance Service is provided from the state budget through the Ministry of Health. Criteria for allocation of funds are approved through Order of the Minister of Health."

26. Under Article 93, a new paragraph, (2^1), is introduced after (1^1), which reads as follows:

"(1^2) Emergency domiciliary consultations and unattended medical transportation can also be achieved by private providers through direct contracting with the Health Insurance House, coordinated by public ambulance services."

27. Under Article 93, (3) is repealed.

28. Under Article 93, (4) is amended as follows:

"(4) Funds from emergency regional hospitals and level II emergency county hospitals, intended for management of with critical cases and whose expenditures cannot be covered from contracted funding with health insurance houses are granted from Ministry of Health budget, state budget and their own revenues."

29. Under Article 93, a new paragraph, (4^1), is introduced after (4), which reads as follows:

"(4^1) The list of hospitals and their departments, the description of expenditures, the manner of fund distribution as provided in (4), as well as any other terms and conditions are established through Order of the Minister of Health."

30. Under Article 93, paragraph (5) is amended as follows:

"(5) Emergency units and emergency admissions in emergency hospitals are financed from the state budget and from Ministry of Health revenues, from the state budget through the budgets of ministries and institutions with their own healthcare network covering staff expenditures, medicinal products, reagents and medical supplies, costs for laboratory investigations performed in these structures, without need for patient admission in the healthcare unit of which the respective emergency emergency unit / emergency admission pertains".

31. Under Article 107, paragraph (2) is amended as follows:

"(2) The department of emergency medical assistance works in a standby regime."

32. Under Article 110, paragraphs (1) and (2) are repealed.

33. Under Article 182, paragraph (1^1) is amended as follows:

"(1^1) The Manager negotiates and concludes contracts for supply of medical services with the health insurance house as well as with the public health department or, where appropriate, with public institutions subordinated to the Ministry of Health to implement national public healthcare programs and insurance costs referred to in Art. 190^1."

34. Under Article 184, paragraph (2) is amended as follows:

"(2) In public hospitals, jobs such as head of service, head of laboratory, chief medical assistant represent management positions and can only be assigned to physicians, biologists, chemists and biochemists or, where appropriate, by medical assistants, with at least 5 years' experience in the given field."

35. Under Article 184, a new paragraph, (2^1), is introduced after (2), which reads as follows:

"(2^1) In accordance with the law, the head pharmacist position in public hospitals can only be assigned to pharmacists with at least 2 years of work experience."

36. Under Article 189, paragraph (4) is amended as follows:

"(4) For the implementation of national remedial healthcare programs, public hospitals may sign contracts with health insurance houses as well as with county public healthcare departments and public healthcare departments in Bucharest or, where appropriate, with public institutions subordinated to the Ministry of Health, according to their respective organisational structure. "

37. Under Article 189^1, paragraph (1) is amended as follows:

"Art. 189^1. - (1) Income derived by public health units in line with healthcare contracts with health insurance funds cannot be used for:

a. Investments in infrastructure;

b. Provision of medical equipment worth more than 15,000 euro without VAT / medical equipment.

38. Under Article 190 paragraph (2), a), b) and f) are amended as follows:

"a) National healthcare programs implementation;

b) The purchase of medical equipment and other facilities independent of the nature of capital expenditure, in accordance with the law;

.....

f) Specific activities of ministries and institutions provided with their own individual healthcare network, approved by Government Decision;".

39. Under Article 190 paragraph (3), b) is amended as follows:

"b) Funds from the state budget and from personal revenues are granted for the implementation of national public health programs through Ministry of Health

budget, in line with the contracts signed with the Public Health Department of Bucharest or with other public institutions subordinated to the Ministry of Health, as required;".

40. Under Article 190[1], point a) is amended as follows:

"a) Implementation of national public health programs;".

41. Article 196[1] is amended as follows:

"Art. 196[1]. - (1) Medical assistants employed in the public system based on diploma/certificate awarded on graduation from specialised short-term upper /post-highschool medical education, graduates from related higher education, are employed in positions according to their higher education studies, while maintaining their "senior" status and pay scale on the date of their promotion.

(2) Medical assistants employed in the public system based on diploma/certificate awarded on graduation from specialised short-term upper /post-highschool medical education, graduates from related higher education, subsequently awarded "senior" status in their own field of higher education are granted the "senior medical assistant" status corresponding to the higher education graduated, while maintaining their pay scale on the date of their promotion."

42. Under Article 210 (1), points e), k) and l) are amended as follows:

"e) Minimum package of services - to be provided to persons not insured, including medical services delivered only in case of medical-surgical emergencies and of potentially endemoepidemic diseases, including monitoring of pregnancy progress and breastfeeding, family planning, as established through the frame contract;

.....

k) Reimbursement price - the price paid from the Sole National Social Health Insurance Fund for medicines, medical equipment, medical devices and such released through open circuit pharmacies for ensured employees included in national remedial healthcare programs. Their list and the reimbursement price are approved through Order of the Minister of Health;

l) Co-payment - the amount representing payment of the money to the ensured employees in line with the provisions of Art. 219 g) in order to receive medical services included in the basic package of services, in the context of the social health insurance system, according to the proportion and under conditions established through frame contract concerning provision of medical assistance in the context of the social health insurance system, pursuant to Art. 217 (3) k)".

43. Under Article 213[2], paragraph (5) is amended as follows:

"(5) Co-payment revenues represent incomes of healthcare providers and are used to improve service quality."

44. Under Article 217, paragraph (4) is amended as follows:

"(4) Where the law of the state budget is not approved until 31 December of the current year, the time limits in paragraphs (2) and (5) are extended until February 28 of the next year.'

45. Article 220 is amended as follows:

"Article 220. - People who cannot prove their insurant status only have access to healthcare services in case of surgical emergencies and endemic-epidemic diseases; they also have access to the monitoring of pregnancy, breastfeeding and family planning services in line with provisions of Art. 223, within a minimum package of healthcare services established by the frame contract."

46. Under Article 223 (2), point d) is repealed.

47. Under Article 233, paragraphs (6) and (7) are repealed.

48. Article 235 is amended as follows:

"Article 235. - Insurants are entitled to medical transportation required for delivery of healthcare services under the following circumstances:

a) Surgical emergencies;

b) Cases specified in the frame contract. "

49. Article 241 is amended as follows:

"Article 241. - In order to accomplish the objectives of the National health strategy, the Ministry of Health develops national healthcare programs in collaboration with the National Health Insurance House."

50. Article 242 is amended as follows:

"Art. 242. - Medicinal products delivered in outpatient care in the context of national remedial healthcare programs are ensured through pharmacies belonging to healthcare units in charge of their conduct or other pharmacies, as required."

51. Under Article 244, paragraph (2) is amended as follows:

"(2) The evaluation process comprises medical offices, ambulatory care units, hospitals, pharmacies, home care providers, medical device providers, private providers of emergency consultations at home and unattended medical transport as well as other natural or legal persons authorised in this respect by the Ministry of Health."

52. Article 252 (1), e) and g) are amended as follows:

"e) Settlement price for medicinal products, medical equipment, medical devices and such, released through open circuit pharmacies for insurants enrolled in remedial healthcare programs;

.....

g) The purchase price of medicinal products, medical equipment, medical devices and such used in in-patient medical facilities for treatment of patients during their hospitalisation or, where applicable, released through in house pharmacies for outpatient treatment of patients enrolled in national remedial healthcare programs;".

53. Article 255 is amended as follows:

"Article 255. – Emergency home consultations and unattended medical transportation provided by private providers is given by authorised and assessed specialised medical units."

54. Under Article 270 (1), point o) is amended as follows:

“o) To conclude and conduct supply contracts for dialysis medical services;“.

55. Under Article 281 (1), point h) is amended as follows:

“h) To submit quarterly and annual reports to the Ministry of Health, as well as in the context of functional analyses, all National Health Insurance House activities as related to medical services, medical devices provided to insurants as well as insurants included in national remedial healthcare programs, their contracting, reimbursement and financing within the social health insurance system, as well as budget execution.“

56. Article 322 is amended as follows:

“Article 322. – A European card is issued in case of insurant travels for temporary stay in a Member State of the European Union. Under exceptional circumstances, hindering use of the card by the insurant, the health insurance house issues a provisional certificate replacing the European card. The European card and its replacement entitle the holder to the same medical services. “

57. Article 362 is amended as follows:

“Art. 362. – Incomes referred to in Art. 361, managed by the Ministry of Health, are used for:

a) Investments in infrastructure and equipment of healthcare units included in the Ministry of Health network and of public hospitals included in the network of the local public administration authority, as provided in Art. 190^5 (1);

b) Funding of national healthcare programs;

c) The reserve of the Ministry of Health for special circumstances;

d) Amounts allocated through transfer to the budget of the Sole National Social Health Insurance Fund for medical services or medicinal products provided to insurants in out-patient care, with or without personal contribution, based on medical prescription, within the social health insurance system, as well as for settlement of payment obligations recorded at the end of 2012 within credit commitments approved for national healthcare programs;

e) Other destinations referred to in Art. 93 (11), Art. 93 (4), (5) and (5^1).“

58. Under Article 370, a new paragraph, (2), is introduced after (1), which reads as follows:

“(2) Notwithstanding provisions of Art. 371(1), (3) d) and Art. 372, physicians who are citizens of a third state may perform occasional professional activities for educational purposes in Romania, with the approval of the Ministry of Health and of the Romanian College of Physicians. In this case, such activities can be performed no more than 3 months and may be extended for a further 3 months period per year. The agreement methodology is approved through Order of the Minister of Health, on consent from the Romanian College of Physicians, and is published in the Official Gazette of Romania, Part I.“

59. Under Article 385, paragraphs (2) and (5) are amended and shall read as follows:

“(2) Upon request, physicians may retire under the terms of Law no. 263/2010 on the unitary system of public pensions, as amended.

.....

(5) In case of public healthcare units dealing with medical staff deficits, as well as public healthcare units located in disadvantaged areas, physicians may continue their activity after the age of retirement stipulated by law, on proposal by the public healthcare unit, with annual consent from the Romanian College of Physicians and of local county and Bucharest colleges and approval of the main credit accountant, until the jobs are filled by contest.“

60. Under Article 692, paragraphs (2) and (3) are amended as follows:

“(2) The National School for Public Health, Management and Ongoing Professional Healthcare Training can carry out activities related to analysis, evaluation and monitoring of healthcare services reimbursed from the Sole National Social Health Insurance Fund.

(3) The activities referred to in paragraph (2) are achieved through direct contract-based negotiations with the National Health Insurance House. “

61. Under Article 695, two new points, 2^1 and 2^2, are introduced after 2, which read as follows:

“2^1. Active substance - any substance or mixture of substances intended to be used in the manufacture of a medicinal product which, when used in its production, becomes an active ingredient of that product intended to exert a pharmacological, immunological or metabolic action with a view to restoring, correcting or modifying physiological functions or to make a medical diagnosis;

2^2. **Excipient -** any constituent of a medicinal product other than the active substance and the packaging material**;“.**

62. Under Article 695, a new point, 16^1, is introduced after 16, which reads as follows:

“16^1. Brokering of medicinal products - all activities in relation to the sale or purchase of medicinal products, except for wholesale distribution, that do not include physical handling and that consist of negotiating independently and on behalf of another legal or natural person;“

63. Under Article 695, a new point, 37, is introduced after 36, which reads as follows:

“37. Falsified medicinal product - **a**ny medicinal product with a false representation of:

a) Its identity, including its packaging and labelling, its name or its composition as regards any of the ingredients including excipients and the strength of those ingredients;

b) Its source, including its manufacturer, its country of manufacturing, its country of origin or its marketing authorisation holder;

c) Its history, including the records and documents relating to the distribution channels used.

This definition does not include unintentional quality defects and is without prejudice to infringements of intellectual property rights**.“**

64. Under Article 696, paragraph (3) is amended as follows:

“(3) Notwithstanding paragraph 1 of this Article and of **point d) in** Article

697, Chapter IV of this Title shall apply to the manufacture of medicinal products intended only for export and to intermediate products, active substances and excipients**.“**

65. Under Article 696, a new paragraph, (4), is introduced after paragraph (3), which reads as follows:

“(4) **Provisions of paragraph (1)** shall apply without prejudice **to Articles 761[2] and 796[1].“**

66. Under Article 699, paragraph (2) is amended as follows:

“(2) The National Agency for Medicines and Medical Devices may temporarily authorise the distribution of an unauthorised medicinal product in the event of a suspected epidemic or of a concerned epidemic with pathogens, toxins, as well as in the event of a (confirmed) suspected outbreak with chemical agents or nuclear radiations which could endanger public health or in other cases of need uncovered by authorised products, under the conditions established through Order of the Minister of Health.“

67. Under Article 702 (4), a new point, i[1]), is introduced after i), which reads as follows:

“i[1]) A written confirmation that the manufacturer of the medicinal product has verified compliance of the manufacturer of the active substance with principles and guidelines of Good Manufacturing Practice by conducting audits, in accordance with **Article 754 f).** The written confirmation shall contain a reference to the date of the audit and a declaration according to which the outcome of the audit confirms manufacturing compliance with GMP principles and guidelines.“

68. Under Article 748, (4) is amended as follows:

“(4) **The National Agency for Medicines and Medical Devices** shall enter the information relating to the authorisation referred to in **(1)** into the European Union database referred to in Article **823 (6).“**

69. Under Article 754, point f) is amended as follows:

“f) To comply with the principles and guidelines of Good Manufacturing Practice for medicinal products and to use only active substances, which have been manufactured in accordance with Good Manufacturing Practice for active substances and distributed in accordance with Good Distribution Practices for active substances. To this end, the holder of the manufacturing authorisation shall verify compliance by the manufacturer and distributors of active substances with Good Manufacturing Practice and Good Distribution Practices by conducting audits at the manufacturing and distribution sites of the manufacturer and distributors of active substances. The holder of the manufacturing authorisation shall verify such compliance either by himself or, without prejudice to his responsibility as provided for in this Law, through an entity acting on his behalf under a contract**.** The holder of the manufacturing authorisation shall ensure that the excipients are suitable for use in medicinal products by ascertaining what the appropriate Good Manufacturing Practice is. This shall be ascertained on the basis of a formalised risk assessment in accordance with the applicable guidelines referred to in point **d) of Article 756.** Such risk assessment shall take into account

requirements under other appropriate quality systems as well as the source and intended use of the excipients and previous instances of quality defects. The holder of the manufacturing authorisation shall ensure that the appropriate Good Manufacturing Practice so ascertained, is applied. The holder of the manufacturing authorisation shall document the measures taken under this **point;"**

70. Under Article 754, three new points are introduced after f), which read as follows:

"g) To immediately inform the **National Agency for Medicines and Medical Devices and** the marketing authorisation holder if they obtain information that medicinal products which come under the scope of his/her manufacturing authorisation are, or are suspected of being, falsified irrespective of whether those medicinal products were distributed within the legal supply chain or by illegal means, including illegal sale by means of information society services**;**

h) To verify that the manufacturers, importers or distributors from whom he obtains active substances are registered with the competent authority of the Member State in which they are established**;**

i) To verify the authenticity and quality of the active substances and the excipients**."**

71. A new Article, Article 755[1], is introduced after Article 755, which reads as follows:

"Art. 755[1]. - (1) **The National Agency for Medicines and Medical Devices** shall take appropriate measures to ensure that the manufacture, import and distribution on their territory of active substances, including active substances that are intended for export, comply with Good Manufacturing Practice and Good Distribution Practices for active substances.

(2) Active substances shall only be imported if the following conditions are met**:**

a) The active substances have been manufactured in accordance with standards of Good Manufacturing Practice at least equivalent to those laid down by the European Union pursuant to **point b) of Article 756;**

b) The active substances are accompanied by a written confirmation from the competent authority of the exporting third country of the following**:**

(i) The standards of Good Manufacturing Practice applicable to the plant manufacturing the exported active substance are at least equivalent to those laid down by the **European Union** pursuant to **point b) of Article 756;**

(ii) The manufacturing plant concerned is subject to regular, strict and transparent controls and to the effective enforcement of Good Manufacturing Practice, including repeated and unannounced inspections, so as to ensure public health protection at least equivalent to that in the **European Union;**

(iii) In the event of findings relating to non-compliance, information on such findings is supplied by the exporting third country to the **European Union** without any delay**.** This written confirmation shall be without prejudice to the obligations set out in **Article 702 and point f) of Article 754.**

(3) The requirement set out in point b) of **paragraph (2)** shall not apply if the exporting country is included in the list referred to in **Article 823[2].**

(4) Exceptionally and where necessary to ensure the availability of medicinal products, when a plant manufacturing an active substance for export has been inspected by a Member State and was found to comply with the principles and guidelines of Good Manufacturing Practice laid down pursuant to **point b) of Article 756, the Ministry of Health and the National Agency for Medicines and Medical Devices may waive** the requirement set out in point **b) of paragraph (2)** for a period not exceeding the validity of the GMP certificate**; the Ministry of Health and the National Agency for Medicines and Medical Devices shall inform the European Commission when** use is made of the possibility of such waiver**. "**

72. Article 756 is amended as follows:

"Art. 756. - **The National Agency for Medicines and Medical Devices pursues application of:**

a) The principles and guidelines of Good Manufacturing Practice for **medicinal products for human use, a**s provided for by Union law**;**

b) The principles and guidelines of Good Manufacturing Practice for **active substances referred to under Article 754 f) and Article 755[1], as** adopted by the **European** Commission**;**

c) The principles of Good Distribution Practice **for active substances referred to in Article 754 f),** adopted by the **Europe[a]n** Commission in the form of guidelines**;**

d) **The guidelines** on the formalised risk assessment for ascertaining the appropriate Good Manufacturing Practice for excipients referred to in **Article 754 f), as** adopted by the **European** Commission**."**

73. A new Article is introduced after Article 756, Article 756[1], which reads as follows:

"Art. 756[1]. - (1) **"Article 756[1]. - (1)** The safety features referred to in **Article 763 o)** shall not be removed or covered, either fully or partially, unless the following conditions are met**:**

a) The manufacturing authorisation holder verifies, prior to partly or fully removing or covering those safety features, that the medicinal product in question is authentic and that it has not been tampered with**;**

b) The manufacturing authorisation holder complies with **Article 763 o)** by replacing those safety features with safety features which are equivalent as regards the possibility to verify the authenticity, identification and to provide evidence of tampering of the medicinal product. Such replacement shall be conducted without opening the immediate packaging as defined in **Article 695 (23).** Safety features shall be considered equivalent if they comply with the requirements set out in the delegated acts adopted **by the European Commission** pursuant to **Article 763[1] (2), and** are equally effective in enabling the verification of authenticity and identification of medicinal products and in providing evidence of tampering with medicinal products**;**

c) The replacement of the safety features is conducted in accordance with applicable Good Manufacturing Practice for medicinal products**;**

d) The replacement of the safety features is subject to supervision by the **National Agency for Medicines and Medical Devices.**

(2) Manufacturing authorisation holders, including those performing the activities referred to in **paragraph (1),** shall be regarded as producers and therefore held liable for damages in the cases and under the conditions set forth in **Law no. 240/2004 concerning manufacturer liability for defective products, republished as amended.“**

74. Under Article 760, paragraph (1) is amended as follows:

“**Article 760. - (1) The National Agency for Medicines and Medical Devices shall take all steps required to ensure that, in the context of procedures provided for in Article 761 and without prejudice to the relationship with the manufacturing authorisation holder, the Qualified Person referred to in Article 757 shall be responsible for securing the following:**

a) **For medicinal products manufactured in Romania, that each medicinal product batch has been manufactured and verified compliant with laws in force in Romania as well as with marketing authorisation requirements;**

b) **For medicinal products from third countries, regardless of whether the medicinal product has been manufactured in the European Union, that each medicinal product batch has been subject to a full qualitative review in a Member State as well as to a quantitative review of at least all the active substances and to any other tests or checks required to ensure medicinal product quality according to the requirements provided in the marketing authorisation.**

For medicinal products intended for marketing in the European Union, the

Qualified Person referred to in Article 757 shall ensure that safety features referred to in Article 763 o) have been affixed on the packaging**. Medicinal product batches that have been subject to such controls in a Member State shall be exempt from such controls if marketed in Romania, accompanied by control reports signed by the Qualified Person.“**

75. Two new Articles, 761^1 and 761^2, are introduced after Article 761, which read as follows:

“Art. 761^1. - (1) Importers, manufacturers and distributors of active substances established in **Romania** shall register their activity with the **National Agency for Medicines and Medical Devices.**

(2) The registration form shall include at least the following information**:**

a) Name or corporate name and permanent address**;**

b) The active substances which are to be imported, manufactured or distributed**;**

c) Particulars regarding the premises and the technical equipment for their activity**.**

(3) The persons referred to in **paragraph (1)** shall submit the registration form to the **National Agency for Medicines and Medical Devices** at least 60 days prior to the intended commencement of their activity**.**

(4) Based on a risk assessment, **the National Agency for Medicines and Medical Devices** may **decide** to carry out an inspection. If **the National Agency for Medicines and Medical Devices** notifies the applicant within 60 days of the receipt of the registration form that an inspection will be carried out, the applicant's activity shall not begin before the **National Agency for Medicines and Medical Devices** has notified the applicant that he/she may commence the activity. If, within 60 days of the receipt of the registration form, the **National Agency for Medicines and Medical Devices** has not notified the applicant that an inspection will be carried out, the applicant may commence the activity**.**

(5) The persons referred to in **paragraph (1)** shall communicate annually to the **National Agency for Medicines and Medical Devices** an inventory of the changes which have taken place as regards the information provided in the registration form; any changes that may have an impact on the quality or safety of the active substances that are manufactured, imported or distributed must be notified immediately.

(6) **The National Agency for Medicines and Medical Devices** enters the information provided, pursuant to **paragraph (2),** into the European Union database referred to in **Article 823(6).**

(7) This Article shall be without prejudice to Article **823.**

Art. 761^2. - (1) Notwithstanding **Article 696(1) and** without prejudice to **Chapter VII, the National Agency for Medicines and Medical Devices and the other competent authorities** shall take the necessary measures in order to prevent medicinal products that are introduced into Romania, but are not intended to be placed on the Romanian market**,** from entering into circulation if there are sufficient grounds to suspect that those products are falsified**.**

(2) **In order to meet the requirements of paragraph (1), the National Agency for Medicines and Medical Devices and the other competent authorities, as applicable, shall apply measures established in delegated acts adopted by the European Commission,** supplementing **paragraph (1)** as regards the criteria to be considered and the verifications to be made when assessing the potential falsified character of medicinal products introduced into **Romania** but not intended to be placed on the Romanian market**.“**

76. Under Article 763, a new point, o), is introduced after n), which reads as follows:

"o) For medicinal products other than radiopharmaceuticals referred to in **Article 763^1 (1),** safety features enabling wholesale distributors and persons authorised or entitled to supply medicinal products to the public to verify the authenticity of the medicinal product**,** identify individual packs**,** as well as a device allowing verification of whether the outer packaging has been tampered with**.“**

77. A new Article is introduced after Article 763, Article 763[1], which reads as follows:

"Art. 763[1]. - (1) Medicinal products subject to prescription shall bear the safety features referred to **in Article 763 o),** unless they have been listed in accordance with the procedure pursuant to **point b) of paragraph (3).**

(2) Medicinal products not subject to prescription shall not bear the safety features referred to in **o) of Article 763,** unless, by way of exception, they have been listed in accordance with the procedure pursuant to **b) of (3),** after having been assessed to be at risk of falsification**.**

(3) **The National Agency for Medicines and Medical Devices shall adopt and apply** detailed rules for the safety features referred to in **o) of Article 763, in line with provisions of delegated acts adopted by the European Commission on** measures supplementing **Article 763 o). Such rules set out:**

a) The characteristics and technical specifications of the unique identifier of the safety features referred to in **Article 763 o)** that enable the authenticity of medicinal products to be verified and individual packs to be identified**;**

b) The lists containing the medicinal products or product categories which, in the case of medicinal products subject to prescription, shall not bear the safety features, and in the case of medicinal products not subject to prescription, shall bear the safety features referred to in **Article 763 o).** Those lists shall be established considering the risk of and the risk arising from falsification relating to medicinal products or categories of medicinal products. To this end, at least the following criteria shall be applied**:**

(i) The price and sales volume of the medicinal product**;**

(ii) The number and frequency of previous cases of falsified medicinal products being reported within the **European Union and** in third countries and the evolution of the number and frequency of such cases to date**;**

(iii) The specific characteristics of the medicinal product concerned**;**

(iv) The severity of the conditions intended to be treated**;**

(v) Other potential risks to public health**;**

c) The procedures for the notification to the European Commission provided for in paragraph 4 and an expedited system for evaluating and deciding on such notification for the purpose of applying **point b);**

d) The modalities for the verification of the safety features referred to in **Article 763 o)** by the manufacturers, wholesalers, pharmacists and persons authorised or entitled to supply medicinal products to the public and by competent authorities. Those modalities shall allow the verification of the authenticity of each supplied pack of the medicinal products bearing the safety features referred to in **Article 763 o) and the** assessment of the extent of such verification. When establishing those modalities, the particular characteristics of the supply chains in Member States, and the need to ensure that the impact of verification measures on particular actors in the supply chains is proportionate, shall be taken into account**;**

e) Provisions on the establishment, management and accessibility of the repositories system in which information on the safety features, enabling the

verification of the authenticity and identification of medicinal products, as provided for in **Article 763 o).** The costs of the repositories system shall be borne by the manufacturing authorisation holders of medicinal products bearing the safety features**.**

(4) **The National Agency for Medicines and Medical Devices** shall notify the **European** Commission of non-prescription medicinal products which they judge to be at risk of falsification and may inform the European Commission of medicinal products which they deem not to be at risk according to the criteria set out in **paragraph (2) b).**

(5) For the purposes of reimbursement or pharmacovigilance, the National Agency for Medicines and Medical Devices may extend the scope of application of the unique identifier referred to in **Article 763 o)** to any medicinal product subject to prescription or**, on request by the Ministry of Health, to** any medicinal product subject to reimbursement**.** For the purposes of reimbursement, pharmacovigilance or pharmacoepidemiology, **the National Agency for Medicines and Medical Devices and the Ministry of Health**, as applicable, may use the information contained in the repositories system referred to in point **e) of paragraph (2).**

For the purposes of patient safety, **the National Agency for Medicines and Medical Devices may** extend the scope of application of the anti-tampering device referred to in **Article 763 o)** to any medicinal product**.“**

78. Under Article 767, paragraph (1) is amended as follows:

“Art. 767. - (1) In compliance with Article 770, the National Agency for Medicines and Medical Devices shall require use of forms of medicinal product labelling allowing for indication of legal status of release to the patient, according to Chapter VI and identification and authenticity features pursuant to Article 763[1](5).“

79. The title of Chapter VII “Medicinal product distribution“ is amended as follows:

“Chapter VII - Wholesale distribution and brokering of medicinal products“

80. Under Article 787, paragraph (4) is amended as follows:

“(4) Any distributor, not being the marketing authorisation holder, who imports a medicinal product from another Member State, shall notify the marketing authorisation holder and the **National Agency for Medicines and Medical Devices** of their intention to import that product**.“**

81. Under Article 787, a new paragraph, (5), is introduced after (4), which reads as follows:

“(5) In the case of medicinal products which have been granted an authorisation **through the centralised procedure,** the distributor shall submit the notification in accordance with **paragraph (4)** to the marketing authorisation holder **and the European Medicines Agency.“**

82. Under Article 788, paragraphs (1), (5) and (6) are amended and shall read as follows:

“Art. 788. - (1) **The National Agency for Medicines and Medical Devices**

shall take all appropriate measures to ensure that the wholesale distribution of medicinal products is subject to owning an authorisation to engage in activity as a wholesaler of medicinal products, stating the premise(s) located in **Romania** for which it is valid**.**

.....

(5) T**he National Agency for Medicines and Medical Devices** shall enter the information relating to the authorisations referred to in **paragraph (1)** into the **European Union** database referred to in **Article 823(6);** at the request of the European Commission or any Member State**, the National Agency for Medicines and Medical Devices** shall provide all appropriate information concerning the individual authorisations which they have granted under **paragraph (1).**

(6) Checks on the persons authorised to engage in activity as a wholesaler in medicinal products, and the inspection of their premise(s), shall be carried out under the responsibility of the **National Agency for Medicines and Medical Devices** which has granted the authorisation for premise(s) located **in Romania.“**

83. Under Article 791, a new point, c[1]), is introduced after c), which reads as follows:

“c[1]) They must verify that the medicinal products received are not falsified, by checking the safety features on the outer packaging, in accordance with the requirements laid down in the delegated acts referred to in **Article 763[1](3);“**

84. Under Article 791, e) is amended as follows:

“e) They must keep records either in the form of purchase/sales invoices or on computer, or in any other form, for any transaction in medicinal products received, dispatched or brokered giving at least the following information**: date,** name of the medicinal product**, manufacturer’s name and country of origin, formulation, pharmaceutical form, active substances strength, package size, batch number and expiry date, quality certificate and test report, as applicable, quantity received, provided or brokered,** name and address of the supplier or consignee, as appropriate**, as well as** batch number of the medicinal products at least for products bearing the safety features referred to in **Article 763 o);”**

85. Under Article 791, two new points, points h) and i), are inserted after g), which shall read as follows:

“h) They must maintain a quality system setting out responsibilities, processes and risk management measures in relation to their activities**;**

i) They must immediately inform **the National Agency for Medicines and Medical Devices** and, where applicable, the marketing authorisation holder, of medicinal products received or granted which they identify as falsified or suspect to be falsified**.**

For the purposes of **point b),** where the medicinal product is obtained from another wholesale distributor, wholesale distribution authorisation holders must verify compliance with the principles and guidelines of Good Distribution Practices by the supplying wholesale distributor; this includes verifying whether the supplying wholesale distributor holds a wholesale distribution authorisation**.**

Where the medicinal product is obtained from the manufacturer or importer, wholesale distribution authorisation holders must verify that the manufacturer or importer holds a manufacturing authorisation.

Where the medicinal product is obtained through brokering, the wholesale distribution authorisation holders must verify that the broker involved meets the requirements set out in this regulatory document.“

86. Under Article 793, paragraph (1) is amended as follows:

“Art. 793. - (1) For all supplies of medicinal products to a person authorised to supply medicinal products to the public in Romania, the authorised wholesaler must enclose a document that makes it possible to ascertain: the date, name and pharmaceutical form of the medicinal product, the quantity supplied, the name and address of the supplier and consignee as well as the batch number of the medicinal products at least for products bearing the safety features referred to in (o) of Article **763.“**

87. Two new Articles, 796[1] and 796[2], are introduced after Article 796, which read as follows:

“Art. 796[1]. - **Article 787 and c) of Article 791** shall not apply in the case of wholesale distribution of medicinal products to third countries**. Points b) and c[1]) of Article 791** shall not apply where a product is directly received from a third country but not imported**.** The requirements set out in **Article 793** shall apply to supply of medicinal products to persons in third countries authorised or entitled to supply medicinal products to the public**.**

Art. 796[2]. - (1) Persons brokering medicinal products shall ensure that the brokered medicinal products are covered by a marketing authorisation granted pursuant to the centralised procedure or by **the National Agency for Medicines and Medical Devices** in accordance with this law**.** Persons brokering medicinal products shall have a permanent address and contact details in **Romania or a different Member State,** so as to ensure accurate identification, location, communication and supervision of their activities by **the National Agency for Medicines and Medical Devices or other competent authorities.** Requirements set out in points **d) to i) of Article 791** shall apply mutatis mutandis to the brokering of medicinal products**.**

(2) Persons may only broker medicinal products if they are registered with the **National Agency for Medicines and Medical Devices, when their permanent address referred to in paragraph (1) is in Romania.** Those persons shall submit, at least, their name, corporate name and permanent address in order to register**.** They shall notify the **National Agency for Medicines and Medical Devices** of any changes thereof within **30 days. The National Agency for Medicines and Medical Devices** shall enter the information referred to in the first subparagraph in a register that shall be publicly accessible**.**

(3) The guidelines referred to in **Article 795** shall include specific provisions for brokering.

(4) This Article shall be without prejudice to **Article 823. When the medicinal product broker is registered in Romania,** inspections referred to in

Article 823 shall be carried out under the responsibility of **the National Agency for Medicines and Medical Devices.** If a person brokering medicinal products does not comply with the requirements set out in this Article**, the National Agency for Medicines and Medical Devices** may decide to remove that person from the register referred to in **paragraph (2). The National Agency for Medicines and Medical Devices** shall notify that person thereof**."**

88. Under Article 823, paragraph (1) is amended as follows:

"Art. 823. - (1) The National Agency for Medicines and Medical Devices shall, in cooperation with the **European Medicines Agency,** ensure that the legal requirements governing medicinal products are met, by means of unannounced inspections, if need be**;** where appropriate**, the National Agency for Medicines and Medical Devices requires its own control laboratory or a NAMMD certified/approved control laboratory** to carry out tests on samples. This cooperation shall consist in sharing information with the **European Medicines Agency** on both inspections that are planned and that have been conducted**. The National Agency for Medicines and Medical Devices,** Member States and the **European Medicines Agency** shall cooperate in the coordination of inspections in third countries. The inspections shall include but not be limited to the ones mentioned in paragraphs **(1^1) to (1^6)."**

Implementation of the community legal status in matters of medicinal product sale at a distance to the public is to be the object of a separate ruling amending Law of Pharmacy no. 266/2008.

89. Under Article 823, 8 new paragraphs, (1^1)-(1^8), are introduced after paragraph (1), which read as follows:

"(1^1) Manufacturers located in the **European Union** or in third countries and wholesale distributors of medicinal products shall be subject to repeated inspections**.**

(1^2) **The National Agency for Medicines and Medical Devices** shall have a monitoring system including inspections at an appropriate frequency, depending on the risk level, at the premises of the manufacturers, importers, or distributors of active substances located in **Romania,** and effective follow-up thereof**.** Whenever it considers that there are grounds for suspecting non-compliance with the legal requirements laid down in this Directive, including the principles and guidelines of Good Manufacturing Practice and Good Distribution Practices referred to in **f) of Article 754 and in points b) and c) of Article 756, the National Agency for Medicines and Medical Devices** may carry out inspections at the premises of**:**

a) Manufacturers or distributors of active substances located in third countries**;**

b) Manufacturers or importers of excipients**.**

(1^3) Manufacturers or importers of excipients **(1^1) and (1^2)** may also be carried out in **the European Union** and in third countries at the request of **the National Agency for Medicines and Medical Devices,** of a Member State**, the European Commission or the European Medicines Agency.**

(1^4) Inspections may also take place at the premises of marketing

authorisation holders and of brokers of medicinal products**.**

(1[5]) In order to check whether the data submitted to obtain a certificate of compliance is in line with the monographs of the European Pharmacopoeia, the National Agency for Medicines and Medical Devices may answer the requests of the European Commission/the European Medicines Agency for performance of such inspections when the concerned starting material is subject to a monograph of the European Pharmacopoeia.

(1[6]) **The National Agency for Medicines and Medical Devices** may carry out inspections of starting material manufacturers at the specific request of the manufacturer**.**

(1[7]) Inspections shall be carried out by officials representing **the National Agency for Medicines and Medical Devices,** who shall be empowered to**:**

a) Inspect the manufacturing or commercial establishments of manufacturers of medicinal products, of active substances or of excipients, and any laboratories employed by the holder of the manufacturing authorisation to carry out checks pursuant to the provisions of **Article 725;**

b) Take samples including with a view to independent tests being carried out by **a laboratory of the National Agency for Medicines and Medical Devices or a National Agency for Medicines and Medical Devices certified/approved control laboratory; costs of samples taken in the frame of the surveillance activity are borne by the manufacturer or the distribution unit, as applicable; costs of tests performed by the National Agency for Medicines and Medical Devices or the National Agency for Medicines and Medical Devices certified/approved control laboratory are covered from the National Agency for Medicines and Medical Devices budget if the product is complaint or by the liable manufacturer or distributor, if the product is non-complaint;**

c) Examine any documents relating to the object of the inspection, subject to the **national** provisions in force placing restrictions on these powers with regard to the description of the manufacturing method**;**

d) Inspect the premises, records, documents and pharmacovigilance system master file of the marketing authorisation holder or any firms employed by the marketing authorisation holder to perform the activities described in C**hapter X.**

(1[8]) Inspections shall be carried out in accordance with the guidelines referred to in **Article 823[1].“**

90. Under Article 823, paragraphs (3)-(8) are amended and shall read as follows:

“(3) After every inspection as referred to in paragraph (1), **the National Agency for Medicines and Medical Devices** shall report on whether the inspected entity complies with the principles and guidelines of Good Manufacturing Practice and Good Distribution Practices referred to in Articles **756 and 795,** as applicable, or on whether the marketing authorisation holder complies with the requirements laid down in **Chapter X;** the content of those reports shall be communicated to the inspected entity**.** Before adopting the report**, the National Agency for Medicines and Medical Devices** shall allow the inspected entity concerned to submit

comments**.**

(4) Without prejudice to any arrangements concluded between **the European Union and** third countries**, the National Agency for Medicines and Medical Devices, the European Commission or the European Medicines Agency** may require a manufacturer established in a third country to submit to an inspection as referred to in this Article**.**

(5) Within 90 days of an inspection as referred to in **(1),** a certificate of Good Manufacturing Practice or Good Distribution Practices shall, when applicable, be issued to the inspected entity if the outcome of the inspection shows that it complies with the principles and guidelines of Good Manufacturing Practice / Good Distribution Practices as provided for by national legislation**;** if inspections are performed as part of the certification procedure for the monographs of the European Pharmacopoeia, a Good Manufacturing Practice certificate are drawn up**.**

(6) **The National Agency for Medicines and Medical Devices** shall enter the issued certificates of Good Manufacturing Practice and Good Distribution Practices into the **European Union database** managed by the **European Medicines Agency** on behalf of **the European Union.** Pursuant to **paragraph (7) of** Article **76$1^{1}$, the National Agency for Medicines and Medical Devices may also** enter information in that database regarding the registration of importers, manufacturers and distributors of active substances. The database shall be available to the public**.**

(7) **If the outcome of the inspection referred to in (1^{7}) or the outcome of an inspection conducted on a medicinal product / active substance distributor or an excipient manufacturer shows that the inspected unit is not compliant with legal requirements and/or Good Manufacturing Practice or Good Distribution Practice principles and guidelines provided in national legislation, information shall be entered into the European Union database referred to in paragraph (6).**

(8) Inspections **referred to under (1^{7}) d) may also be performed on request by an EU Member State, the European Commission or the European Medicines Agency.“**

91. Two new Articles, 82$3^{1}$ and 82$3^{2}$, are introduced after Article 823, , which read as follows:

“Art. 82$3^{1}$. - **The National Agency for Medicines and Medical Devices shall apply the** detailed guidelines laying down the principles applicable to inspections referred to in **Article 823, as adopted by the European Commission; the National Agency for Medicines and Medical Devices shall transpose the form and** content of the authorisation referred to in Articles **748 (1) and 788 (1),** of the reports referred to in **Article 823 (3),** of the certificates of Good Manufacturing Practice and of the certificates of Good Distribution Practices referred to in **Article 823(5), set up by the European Medicines Agency.**

Art. 82$3^{2}$. - (1) **Pursuant to Article 75$5^{1}$(3), Romania takes count of the list of active substance exporting third countries set up by the European Medicines Agency on request by an exporting third, based on** assessment of

whether that country's regulatory framework applicable to active substances exported to the European Union and the respective control and implementation activities ensure a level of protection of public health equivalent to that of the **European** Union.

(2) **The National Agency for Medicines and Medical Devices cooperate with the European Commission, the European Medicines Agency and competent authorities in the other member States in conducting the assessment referred to in (1).“**

92. Article 828 is amended as follows:

“Art. 828. - (1) The National Agency for Medicines and Medical Devices shall suspend, withdraw or change a marketing authorisation whenever it deems that the medicinal product is harmful or lacks in therapeutic efficacy, its risk/benefit ratio is unfavourable or its qualitative and quantitative composition is different from that declared; therapeutic efficacy is absent if the conclusion is reached that therapeutic outcomes cannot be achieved with the medicinal product concerned.

(2) **A marketing authorisation can also be suspended, withdrawn or changed if data presented in support of the application referred to in Articles 702, 704, 705, 706, 707 or 708 are inaccurate or have not been changed pursuant to Article 728, when conditions established in Articles726[1], 727 or 727[1] have not been met or when controls referred to in Article 824 have not been conducted.**

(3) **Paragraph (2) also applies to cases when medicinal product manufacturing is not compliant with information provided according to Article 702(4) e), or when controls** are not carried out in compliance with the control methods described pursuant to **Article 702(4) i).“**

93. After Article 829, a new article, 829[1], is added, reading as follows:

“Art. 829[1]. - (1) **Competent authorities shall adopt regulatory documents whose aim is to prevent** medicinal products that are suspected to present a danger to health from reaching the patient**.**

(2) **The regulatory documents referred to paragraph (1)** shall cover the receipt and handling of notifications of suspected falsified medicinal products as well as of suspected quality defects of medicinal products**. They shall also** cover recalls of medicinal products by marketing authorisation holders or withdrawals of medicinal products from the market ordered by the **National Agency for Medicines and Medical Devices** from all relevant actors in the supply chain both during and outside normal working hours**. Such regulatory documents** shall also make it possible to recall, where necessary with the assistance of healthcare professionals, medicinal products from patients who received such products**.**

(3) If the medicinal product in question is suspected of presenting a serious risk to public health**, the National Agency for Medicines and Medical Devices** identified shall, without any delay, transmit a rapid alert notification to all Member States and all actors in the supply chain in **Romania.** In the event of such medicinal products being deemed to have reached patients, urgent public

announcements shall be issued within 24 hours in order to recall those medicinal products from the patients. Those announcements shall contain sufficient information on the suspected quality defect or falsification and the risks involved**.**

(4) **By 22 July 2013, the National Agency for Medicines and Medical Devices shall** notify the Commission of the details of their respective national systems referred to in this Article**.“**

94. Three new Articles are introduced after Article 830, articles 830[1]-830[3], which read as follows:

“Art. 830[1]. - **By 2 January 2013, the National Agency for Medicines and Medical Devices shall notify the European Commission on internal rule provisions adopted for transposition of Directive 2011/62/EU** of the European Parliament and of the Council of 8 June 2011 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, as regards the prevention of the entry into the legal supply chain of falsified medicinal product and notify any changes thereof without delay.

Art. 830[2]. - T**he National Agency for Medicines and Medical Devices** shall organise meetings involving patient and consumer organisations/associations and, as necessary, enforcement officers in Romania, in order to communicate public information about the actions undertaken in the area of prevention and enforcement in view of combating the falsification of medicinal products.

Art. 830[3]. - In applying this law, **the Ministry of Health and the National Agency for Medicines and Medical Devices** shall take the necessary measures to ensure cooperation between competent authorities for medicinal products and customs authorities**.“**

95. Under Article 836 paragraph (1), points a), c), d), f), g) and h) are amended and shall read as follows:

“a) A 10,000 lei to 30,000 lei fine to the manufacturer and closure of the unit, when the manufacturing unit operates in the absence of a manufacturing authorisation granted by the National Agency for Medicines and Medical Devices; the wholesale distributor shall be punished with the same penalty, as well as with the closure of the wholesale distribution unit for medicinal products that operates without an authorisation issued by the National Agency for Medicines and Medical Devices;

.....

c) A 5,000 to 10,000 lei fine applied to the manufacturer/importer or wholesale distributor, as appropriate, for performance of activities other than authorised in the manufacturing/wholesale distribution unit, for supply by the manufacturer/wholesale distributors of medicinal products to other units unauthorised by the National Agency for Medicines and Medical Devices (wholesale distributors) or by the Ministry of Health (pharmacies, drugstores, other units authorised to perform healthcare activities) in accordance with the law, the distribution (by suppliers) to drugstores of medicinal products other than released without medical prescription, participation of unqualified persons in technical

operations requiring specialised training in the fields of manufacturing and distribution processes, as well as non-compliance with provisions related to the printing of medicinal product leaflets, advertising, reporting of changes in manufacturing/distribution activity, non-compliance of Marketing Authorisation Holder with good pharmacovigilance practice rules in, participation of unqualified persons to technical operations requiring specialised qualification in the manufacturing and wholesale distribution processes, as well as non-compliance with provisions concerning the printing and package leaflet of medicinal products, advertising, reporting of changes in manufacturing/import/distribution, Marketing Authorisation Holder non-compliance with good pharmacovigilance practice rules, non-compliance with storage conditions of medicinal products and export legislation, donation and supply of medicinal product samples;

d) A 10,000 to 30,000 lei fine to the manufacturer/importer or wholesale distributor in case of non-compliance with conditions for authorisation of the unit handling manufacture/import/product distribution processes or in case of non-compliance with the Guideline on the Good Manufacturing Practice and with the Guideline on the Good Wholesale Distribution Practice;

.....

f) A 5,000 to 10,000 lei fine for unavailability of the head pharmacist or their alternates during working hours of the distribution unit; unavailability of the person responsible for the quality or their alternates during the working hours of the unit, as far as distribution units authorised for purchase/marketing activities are concerned, shall be fined the same amount;

g) A fine ranging from 10,000 to 30,000 lei and suspension of the authorisation of the manufacturer/wholesale distribution unit for a one-year period, if any of the infringements detected during a 3-month period reoccurs, as stipulated under c) and e);

h) A 5,000 to 20,000 lei fine and suspension of the wholesale distribution authorisation, in case of non-compliance with the Guideline on Good Wholesale Distribution Practice, until remedied; brokers who fail to comply with the specific provisions of the Guideline on Good Wholesale Distribution Practice shall be fined the same amount;".

96. Under Article 836 (1), î) is repealed.

97. Thirteen new points, l)-v), are introduced under Article 836 (1) k), which read as follows:

"l) A 10,000 to 30,000 lei fine and prohibition of activity for lack of National Medicines Agency notification by brokers about performance of brokerage of medicinal products/active pharmaceutical substances on Romanian territory;

m) A 10,000 to 30,000 lei fine and temporary suspension of the marketing authorisation for a 6-month period, for importer's failure to fulfil their commitment to submit to the National Agency for Medicines and Medical Devices the import status as well as for manufacturers' / importers' / wholesalers' failure to comply with their commitment concerning submission to the National Medicines Agency

of the report regarding distributed products, in accordance with the law;

n) A 10,000 to 30,000 lei fine, in the event of non-compliance with the obligation referred to in Art. 729 (2);

o) A 10,000 to 20,000 lei fine, in the event of incorrect release of the medicinal product batch manufactured/imported in Romania performed by the manufacturer's/importer's qualified person;

p) A 10,000 lei to 30,000 lei fine and suspension of the certificate attesting "qualified person" status for one year, in case of reoccurrence of the respective infringement during a 6-month period, as shown in n); the suspension shall be abolished only on account of proof attesting that the qualified person has undertaken relevant training during suspension;

q) A 10,000 lei to 30,000 lei fine applied to the investigator and suspension of the trial in case of performance in Romania of clinical trials not authorised by the National Agency for Medicines and Medical Devices (NAMMD) or for which the National Ethics Committee/Institutional Ethics Committee has issued an unfavourable opinion;

r) A 10,000 lei to 30,000 lei fine applied to the investigator and suspension of the study in case of performance in Romania of clinical trials in units which are unauthorised for performance of clinical trials in the field of medicinal products for human use by the Ministry of Health;

s) A 10,000 to 20,000 lei fine applied to the sponsor in the event of supply of an investigator/institution with the investigational medicinal product before it was granted full necessary documentation (e.g. approval of the National Ethics Committee/Institutional Ethics Committee and of the National Agency for Medicines and Medical Devices;

ş) A 2,000 to 5,000 fine lei applied to the sponsor for failure to fulfil their obligations concerning the evaluation of the safety of the investigational medicinal product during the trial;

t) A 2,000 to 5,000 lei fine applied to the investigator for failure to fulfil their obligations on reporting serious adverse events arising after administration of the investigational medicinal product during the study;

ţ) A 10,000 to 30,000 lei fine for not allowing the inspection staff of the National Agency for Medicines and Medical Devices access to the documents and facilities of the inspected unit;

u) A 10,000 to 30,000 lei fine to the manufacturer/importer/supplier of active substances for non-compliance with provisions of this Law related to the manufacturing, importation, distribution and export of active substances;

v) A 10,000 to 30,000 lei fine to the manufacturer of medicinal products in for non-compliance with Art. 754 f) provisions."

98. Under Article 836, paragraph (2) is amended as follows:

"(2) The offences and penalties provided in paragraph (1) are determined by inspectors of the National Agency for Medicines and Medical Devices and the Ministry of Health, as appropriate."

Article II. - (1) Competent authorities shall adopt provisions to ensure

implementation of art. I, section 73, 74, 76 and 77 of this law within three years from the date of publication of the delegated acts referred to in art. I (77) of this Law.

(2) Persons referred to in Art. 76^{1} (1) and Art. 79^{2} (2) of Law no. 95/2006 on healthcare reform, as amended, employed before the entry into force of this law shall submit the registration form to the National Agency for Medicines and Medical Devices before March 2, 2013.

Art. III. - Paragraph (2) of Article 16 of Law no. 584/2002 on measures to prevent the spread of AIDS in Romania and protection of HIV infected or AIDS affected people, published in the Official Gazette of Romania, Part I, no. 814 of November 8, 2002, as amended, is amended as follows:

"(2) Therapeutic activities and medical treatment are funded from the budget of the Ministry of Health or, where appropriate, from the budget of the National Health Insurance House, in accordance with the law."

Art. IV. – Article 5 of Law 263/2004 regarding insurance of permanent primary medical assistance through primary care clinics, published in the Official Gazette of Romania, Part I, no. 568 of 28 June 2004, as amended, is amended as follows:

"Art. 5. – The assignments of public health directors on the functioning of primary care clinics are the following:

a) Territorial assignation of cities to permanent centres;

b) Control of the planning and performance of the activity;

c) Insurance of approval of monthly schedule of physicians to ensure permanent primary medical assistance in primary care clinics, established by the centre coordinating physician, before day 25 of the current month concerning the following month."

Art. V. – The national plan for implementation of the International Health Regulation (2005) referred to in Art. 5 b) of Government Decision no. 758/2009 for implementation of the International Health Regulation (2005) shall ensure the handling of all provisions of the International Health Regulation (2005), from the scope of responsibility of each competent authority, and shall be submitted for approval through common order of competent authorities for implementation of International Health Regulation (2005) provisions.

Article VI. - Article I, sections 1-22, 24-26, 31-33, 36-40, 42, 45-55 and 60 and Art. III and IV shall come into force on 1 March 2013.

Art. VII. - In 2013, the financing of national healthcare programs is also performed through transfers from state budget and personal revenues, through the Ministry of Health, to the Single National Social Health Insurance Fund for:

a) The discharge of registered payment liabilities limited to commitment appropriations approved for national healthcare programs whose financing is ensured until 1 March 2013 through transfer from the budget of the Ministry of Health to the budget of the National Social Health Insurance Fund;

b) The discharge of registered payment liabilities limited to commitment

appropriations approved for the National program of transmissible diseases whose financing is ensured until 1 March 2013 from the budget of the Single National Social Health Insurance Fund.

This Emergency Ordinances transposes Directive 2011/62/EU of the European Parliament and of the Council of 8 June 2011 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, as regards the prevention of the entry into the legal supply chain of falsified medicinal products, published in the Official Journal of the European Union, L, 174/74 of 1 July 2011, except for Art. 1 (20).

PRIME MINISTER
VICTOR-VIOREL PONTA

Countersigned:
Minister of Health,
Raed Arafat
Minister of Administration and Internal Affairs,
Mircea Duşa
Minister-delegate for Administration,
Radu Stroe
Minister of National Defence,
Sebastian Huluban,
Secretary of State,
Minister of Labour, Family and Social Protection
Mariana Campeanu
Minister for Infrastructure and Transport,
Ovidiu Ioan Silaghi
Vice prime minister,
Minister of Public Finances,
Florin Georgescu

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REPORT

on National Agency for Medicines and Medical Devices activities in 2010,
published in accordance with provisions of Art. 5 (3) of Law no. 544/2001for free access to public information

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INTRODUCTORY WORD

In 2010, as national competent authority in the field of medicinal products for human use, the National Agency for Medicines and Medical Devices fulfilled its attributions and duties, even in the context of the international financial crisis. The efforts made by the Agency's employees were deemed even more substantial since during the previous two years, the institution has undergone ongoing major transformations. Ever since 2009, several changes in the inner structure of the Agency have been performed, in view of improving its activity, starting with the manner of structuring and operation of the European Medicines Agency (EMA). If by the end of 2009, the National Medicines Agency (NMA) has been reorganised as a public institution entirely financed from the state budget, in accordance with Law no. 329/2009 related to the restructuring of some public authorities and institutions, in 2010, the National Agency for Medicines and Medical Devices (NAMMD) has been founded in accordance with Government Emergency Ordinance no. 72 of June 2010, after the NMA and the Technical Office for Medical Devices merged. The organisation and operation of the NAMMD have been subsequently established through Government Decision no. 734 of July 2010.

As shown in the contents of Government Emergency Ordinance no. 72/30 June 2010 on reorganisation of healthcare facilities, the reasons for establishing the NAMMD were increased efficiency of healthcare institutions work, in accordance with Government priorities for public administration reform, initiation of economic and financial measures at the level of state budget financed institutions under the Ministry of Health, in consequence of the severe economic crisis. This resulted in supplementation of the Agency's mission with other tasks, related to the medical device field, such as:

- maintaining an elevated level of performance and security of medical devices in use throughout Romanian healthcare networks, regardless of their type of ownership;

- strictest assessment of technical-medical units providing services in the medical device field, so that prosthetic services of any type and medical device repair- maintenance services be carried out at optimal quality and competence levels;

- development of specific medical devices technical procedures.

At the same time, permanent contribution to the shaping of medical devices secondary legislation has been added to strategic objectives specific to a European authority in the medicinal product field.

NMA/NAMMD activity developed at the same pace as required by time-specific dynamics: assessment and marketing authorisation of medicinal products, conduct of Good Manufacturing Practice (GMP) inspections, Good Distribution Practice (GDP) inspections, Good Clinical Practice (GCP) inspections, **Good Analytical Laboratory Practice** (GALP) inspections, pharmacovigilance activities, communication with stakeholders on most recent and most accurate medicinal product information, provided to healthcare professionals, the media, patients and, last but not least, the general public..

The Agency displayed enhanced openness for improved communication with all partners in the field - meetings were organised in that respect with Marketing Authorisation Holders (MAHs), Romanian and international associations of medicinal product manufacturers, patients, associations of clinical trial coordinating companies, associations of medicinal product distributors etc.. This is considerable proof of the true partnership established between the Agency and the other stakeholders, meant to practically ensure a pharmaceutical market that is both balanced and accessible to the general public. This is also proof of transparency in Agency activity conducted by the, based on cooperation with all its partners, in the context of the decision-making process.

Under such circumstances of reorganisation imposed by the severe financial recession as well, the Agency had to carry on its work and fulfil its mission. Through consistent effort of its specialists and auxiliary personnel, the NAMMD has remained a European regulatory authority in the field of medicinal products for human use, fully in line with community requirements.

Apart from current, priority NMA/NAMMD work, representing in fact the very mission of the Agency, a certain activity started in 2009 was carried on, namely the Agency's preparations for the *"peer-review"* type of the quality management system audit within the *Benchmarking European Medicines Agencies (BEMA)* self-assessment exercise, initiated by the Heads of European Medicines Agencies; the audit is to be conducted in May 2011.

This is an ongoing, accurate and realistic process related to self-assessment of the Agency's performance, depending on pre-established performance indicators as well as to use of assessment results in view of constantly meeting the proposed strategic goals. The BEMA ultimate target is to improve the European pharmaceutical regulatory system in the field, based on a medicines agencies network that operates at full capacity, as well as to contribute to the development of the international regulatory system in the pharmaceutical field.

In 2010, the NMA/NAMMD was faced with a significant shortage of specialised staff. Despite this fact, the Agency managed to fulfil its target objectives and continued, in its 4th year of EU accession, its active involvement in

activities of European bodies in the medicinal product field. The activity of NAMMD departments in 2010 has been particularly complex; its main purpose has been to fulfil the main mission of the Agency, namely assessment at the highest scientific level of the authorisation dossier, so as to ensure marketing of quality, safe and effective medicinal products for human use and supervision of the safety of human medicinal products in therapeutic circuit by means of inspection and pharmacovigilance activities.

Moreover, in 2010, the structures of the Authorisation Department (AD) and the Post-Authorisation Department (PAD) have been changed and the two have been reorganised in two new departments:

- The National Procedures Department (NPD) – assessing documents for marketing authorisation / marketing authorisation renewal of medicinal products for which authorisation through national procedure has been sought;

- The European Procedures Department (EPD) – assessing documents for marketing authorisation / marketing authorisation renewal of medicinal products for which the authorisation through European procedure has been sought.

Whereas the number of Marketing Authorisations (MAs) granted through European Procedure (EP) [(decentralised procedure (DCP), Mutual Recognition Procedure (MRP) and Repeat-use mutual recognition procedure] has increased, namely:

MAs granted through European procedure: 2010 - 623 as compared to 2009 - 568,

The number of Marketing Authorisations granted through National Procedure (NP) has decreased in 2010, as compared to 2009, as follows:

MAs granted through national procedure: 2010 - 190 as compared to 2009 – 359.

This is, however, to ne expected, considering that the NMA/NAMMD represents an EU member state with a pharmaceutical market undergoing the harmonisation process with European requirements.

However, the overall number of MAs granted by the Agency in 2010 has been smaller than in 2009. Thus:

MAs granted through national and European procedure: 2010 - 813 compared to 2009 - 927.

Reason for this decrease was lack of staff that the Agency has recently been confronted with and not a smaller number of applications!

The number of decisions related to MA discontinuation on Marketing Authorisation Holders (MAHs) request for commercial reasons has increased in 2010, as compared to 2009, namely**:**

Discontinued MAHs: 2010 - 202 as compared to 2009 - 134.

Moreover, in 2010, 3 years after Romania's accession to the EU, the "*sunset clause"* has been enforced for 177 MAs for products which had not actually been marketed between 2007 - 2010.

At the end of 2010, the Index of Medicinal Products included 8168 trade names, corresponding to 1252 International Non-proprietary Names (INNs).

The activity of the National Pharmacovigilance Centre operating within the NMA/NAMMD was particularly complex in 2010, ensuring handling of safety data issued from spontaneous reporting and periodic safety update reports concerning medicinal products, as well as a wide range of pharmacovigilance activities within the system of EU national authorities, coordinated by the EMA and within the rapid alert/non-urgent information, in addition to assessment of requirements concerning description of the pharmacovigilance system of the Marketing Authorisation applicant through national and European procedures.

During 28–29 September 2010, the NAMMD European Procedures Department – The Pharmacovigilance and risk management service received the visit of a delegation from the World Health Organisation **Centre** for **Adverse** Drug **Reaction** Reporting, the Uppsala Monitoring Centre - UMC. The discussions focused on the theoretical and practical aspects concerning spontaneous reports in the Agency's pharmacovigilance activity in line with European legislation, as well as cooperation with the UMC for reporting to the „*VIGIMED"* through the „*Vigiflow"* and possibilities for signal detection by means of „*VIGISEARCH".*

The NMA/NAMMD similarly performed concentrated work in the pharmaceutical inspection field. Intense NMA pharmaceutical inspection activity represented a consequence of amendments to Law no. 95/2006 on healthcare reform, regarding supplementation of NMA assignments with authorisation for operation as well as inspection of medicinal product wholesale distribution units.

Started as early as 2009, through amendment of Law no. 95/2006 on healthcare reformTitle XVII – The medicinal product, activities related to Good Distribution Practice inspection (GDP) performed in 2010 were the following:

- 112 inspections for authorisation purposes;
- 70 wholesale distribution authorisations have been granted.

7 units were not granted wholesale distribution authorisations, in result of critical deficiencies found during authorisation inspections;

In 2010, following 40 unannounced inspections at the sites of wholesale distribution units, 17 authorisations were suspended and 3 withdrawn. This activity was carried on in 2010; apart from GDP inspections, other types of inspections were carried out, e.g. inspections to assess compliance with Good Manufacturing Practice (GMP) rules, Good Laboratory Practice (GLP) rules and Good Analytical Laboratory Practice (GALP) rules, Good Clinical Practice (GCP) rules, pharmacovigilance inspections.

Activities concerning surveillance of the quality of medicinal products authorised for marketing in Romania have involved both inspectors in the central headquarters and those in the 12 territorial inspection units (TIUs). This is a complex activity, yearly aiming to:

- meet the sampling plan concerning the supervision of the quality of medicinal products (sampling, analysis, results);
- supervise the quality of medicinal products in the distribution chain (warehouses, pharmacies), inspections conducted by TIU inspectors;
- assess the quality of the oxygen used in hospital units;

- cooperate with other bodies for resolution of certain issues related to legislation in the field of the medicinal product for human use and/or the quality of certain medicinal products marketed in Romania;
- handle complaints concerning potential quality non-compliances in medicinal products for human use;
- recall from the market of non-compliant products;
- handle rapid alerts issued in the context of the EMA, PIC/S rapid alert system;
- handle rapid alerts for counterfeit medicinal products received from the Working Group of Enforcement Officers (WGEO) of the Heads of Medicines Agencies (HMA);
- cooperate with European bodies: the European Medicines Agency (EMA), the European Directorate for the Quality of Medicines and Healthcare (EDQM), European competent authorities in surveillance of the quality of starting material/finished product manufacturing in third countries;
- introduce into the EudraGMP database information related to NAMMD manufacturing/import authorisation activity and GMP certification activity.

Activities regarding quality control of medicinal products were aligned to the Agency's general policy and conducted within the following two departments: the Department for medicinal product quality control (DMQC) and the Department for biological products control (BPCD).

As in previous years, in 2010 as well the NAMMD continued its cooperation with well-known European institutions in the quality control field, by taking part in studies initiated and coordinated by the European Directorate for the Quality of Medicines & HealthCare (EDQM), namely:

- the Proficiency Testing Scheme (PTS), performed yearly, whose purpose is to test each laboratory included in the Official Medicines control laboratories (OMCL) network to assess their ability to deal with highly difficult issues related to medicinal product quality control;

- studies concerning surveillance of the quality of medicinal products authorised through European procedures;

- Market Surveillance Studies (MSSs) for surveillance of the European market. In 2010, the professional activity of the BPCD distinguished itself through involvement in a Proficiency Testing Scheme (PTS) study, conducted at the initiative and under the coordination of the EDQM, for which the laboratory was rated "Satisfactory". Once again, the result confirmed the competitiveness of the BPCD laboratory testing.

The NAMMD regulatory activity continued at a fast pace in 2010, considering that medicinal product legislation undergoes ongoing development/update/amendment, in accordance with technical and scientific progress of research/development in the medicinal product fields, both in the EU and worldwide.

As always, the NMA/NAMMD Scientific Council supported the Agency in its regulatory mission in the field of medicinal products for human use; by

assessing and adopting/updating norms, scientific guidelines and procedures**,** it contributed to harmonious performance of Agency work and that of its external partners.

As a competent authority in the field of medicinal products for human use, the NAMMD has fully undertaken its important role in fight against the counterfeiting of medicinal products and illegal marketing of medicinal products, thus carrying on information and warning of the general public, as well as developing cooperation relationships with other institutions and bodies involved in this activity. In that respect, the NAMMD continued cooperation with national institutions involved in fight against counterfeit medicinal products sold online, as well as with similar institutions in EU member states and other countries outside the EU, to restrict such illegal phenomena, with sometimes serious consequences on public health.

Proceeding have thus continued towards preparing the framework for implementation of provisions of the upcoming European directive on prevention of the entry into the legal supply chain of falsified medicinal products, as regards their identity, history or source, now in draft stage submitted to debate by the European Parliament and the EU Council, where the NAMMD assigned representative also takes part, explaining and supporting Romania's view on the matter.

For ongoing information of the public in that respect, the "Counterfeiting" section on the Agency website has been further updated in 2010, comprising data related to counterfeiting as forwarded through the rapid alert system.

Year 2010 also meant active participation in scientific committees and working groups of the EMA, the Heads of Medicines Agencies (HMA), the European Union Council, the European Commission, the European Council, the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S), the European Pharmacopoeia Commission, the Official Medicines Control Laboratories (OMCL).

NAMMD specialists assigned to participate in meetings of the EU Council Working Group for medicinal products and medical devices have presented and supported Romania's viewpoints concerning directive drafts amending Directive 2001/83/EC, as regards both prevention of the entry into the legal supply chain of falsified medicinal products and pharmacovigilance. The draft directive on pharmacovigilance was approved in final form on 15 December 2010, as Directive 2010/84/EU of the European Parliament and of the Council amending, as regards pharmacovigilance, Directive 2001/83/EC on the community code relating to medicinal products for human use.

Just as in the previous year, participation in monthly meetings of the Paediatric Committee (PDCO) was as intent as ever, carried out through:

- assessment as Rapporteur/CoRapporteur of 20 Paediatric Investigation Plans (PIPs) and applications for amendment thereof,
- participation in teleconferences for applicant counselling,

- set up of reports and stage presentations of procedures during Committee meetings.

NAMMD involvement in activities of the EU competent authorities network also manifested in participation in Good Clinical Practice (GCP) and Good Manufacturing Practice (GMP) inspections concerning EMA centrally authorised medicinal products.

Moreover, numerous papers were presented in scientific events such as congresses, conferences and seminars held in Romania and abroad.

As for the previous year, the NMA/NAMMD carried out various activities not only for development of relationships with European partners, but with international partners as well, such as China and India, countries undergoing rapid development in the fields of research and manufacture. For promotion of true safeguarding of public health, the NAMMD continued to develop cooperation with countries it views as potential major medicinal product suppliers for the Romanian pharmaceutical market.

Particular attention was given to ensure communication with stakeholders and work transparency.

This year as well, the Agency manifested openness towards communication with partners in this field; several meetings were organised with Marketing Authorisation Holders, with associations of medicinal product manufacturers (foreign and Romanian), patient associations, associations of clinical trial coordinating companies, associations of medicinal product suppliers etc. The goal was to ensure transparency in the Agency's activity. Topics of these meetings were the main fields for cooperation between parts involved in the pharmaceutical market, as well as means to improve communication in these fields.

Moreover, communication with the media was enhanced and issues of general interest have been approached, such as safe use of medicinal products.

A large amount of useful data has been posted on the NMA/NAMMD website, meant for both healthcare professionals and the general public.

The Agency carried on implementation of provisions of Law no. 95/2006, Title XVII – The medicinal product on transparent activity of competent medicinal product authorities in the EU, by such proceedings as periodic update of Regulations on organisation and operation of Agency specialist commissions (the Marketing Authorisation Commission, the Commission for GMP, GDP, GLP, GALP, GCP and pharmacovigilance inspections) and their publication on the website after approval by the Agency Administration Council, set up, on request, of public versions of agendas and press releases of the Marketing Authorisation Commission and of the Commission for GMP, GDP, GLP, GALP, GCP and pharmacovigilance inspections, as well as of public versions of reports concerning assessment of product authorisation dossiers.

In 2010 as well, the NAMMD top management paid proper attention to the Quality Management System (QMS) and showed interest in implementation of a process-based approach.

The NMA owns a well established Quality Management System, based on

international standards in force.

In its effort towards attainment of its objectives in 2010, the NMA/NAMMD was supported by the Administrative Council (AC), in 6 ordinary meetings (4 of the NMA and 2 of the NAMMD); 42 Administrative Council Decisions (ACDs) have been approved, of which 27 as NMA ACDs and 15 as NAMMD ACDs. Three of these have been approved through Order of the Minister of Health. Although 2 regulatory decisions have been initiated (approval of tariffs for new activities, identified after set up of the Order of the Minister of Health no. 716/2009), they could not be completed.

Thematically speaking, ACDs have covered various aspects of current activities, but the main weight was derived from current circumstances, and consisted of decision documents regulating organisational issues – consecutive structure-related changes within the institution, change of the collective labour contract at unit level, approval of the job list and organisational structure, and other issues related to the current activity.

As regards fulfilment of the objective of the Human Resources Department (reorganised in 2010 as the Human Resources and Payroll Department), to secure qualified staff, it is worth mentioning that, as of April 2009 and throughout 2010, this was obviously rendered difficult by the legal framework enforced by Emergency Government Ordinance no. 34/2009. Moreover, the negative impact upon human resource management has been increased by the unfavourable economic circumstances created by Law no. 118/2010 on measures needed for budget balance restoration. Implementation of these economic and legislative measures resulted in leave of a significant number of employees trained by the NMA. As a consequence of legal provisions implemented in 2010, the human resources deficit encountered since 2009 increased by termination of a large number of individual work contracts.

In 2010, the relocation to the NMA headquarters of the Biological Product Evaluation and Control Department, formerly located in Demostene street, was completed; this move result in creation of an optimal environment for laboratory work, and resolution of the problem of biological samples transportation from the former location to NMA headquarters.

As in previous years, in 2010 as well, the General Administration Department (i.e. the GAD, set up through reorganisation during the year of the former Department of General Administration and Heritage - DGAH) managed to fulfil its objectives and answer promptly and efficiently to requests of other NMA/NAMMD structures.

Therefore, the GAD most substantial achievements consisted of performance and completion of various acquisitions for endowment and renovation of the NAMMD building. Several important acquisitions have been:

- **the access control system in the building of NAMMD headquarters;**
- **video surveillance systems (for both the headquarters and 20, Demostene Street), purchased to ensure safe and effective measures to protect the location, by eliminating the possibility of unauthorised persons entering**

areas containing secret or confidential documents.

The NAMMD carried on such activities as maximisation of headquarter areas, performance of sanitation activities, division of certain areas for transformation into offices and a wide range of activities related to workplace arrangement.

Moreover, the Agency carried on its policy for automation and extension of its internal computer network.

The goal established for 2010 could only be accomplished through adequate financial policy, based on strict financial discipline, through compliance with legal provisions on budget execution for judicious spending of allocated resources in accordance with the approved income and expenses budget.

In 2010, the NAMMD Economic Department set up and managed a balanced budget of revenues and expenditures from the state budget. In spite of all difficulties encountered, the new NAMMD department – The Technical Laboratory Department managed to adequately perform its activity in line with Law no. 176/2000 on medical devices, as amended, and maintain an acceptable level of medical devices performance and safety.

In 2010, within the "CERF" project on improved expertise in pharmaceutical regulation, the NMA/NAMMD and the "Carol Davila" University of Medicine and Pharmacy initiated and held several classes and workshops:

1. The "Advertising of medicinal products" workshop – 17 May 2010;
2. "New regulations on the set up of the Summary of Product Characteristics of medicinal products for human use" – 25 May 2010;
3. "Manners of consultation with target patient groups for the leaflet" – 7 June 2010;
4. "Regulations concerning the pharmacovigilance activity in accordance with the legislation in force" – 24 June 2010;
5. "Basic criteria and requirements on the documentation of the active substance dossier" – 16 September 2010;
6. "Module 3 – Quality of product authorisation dossier" – 17 September 2010;
7. "Overview of assessment of the quality of biological medicinal products for human use" – 18 September 2010;
8. "Regulations concerning conduct of clinical trials in Romania in accordance with legislation in force" – 24 September 2010;
9. "Performance of clinical trials at the investigator's site in accordance with Good Clinical Practice rules" – 13 October 2010;
10. The "Advertising of medicinal products" workshop – 2 November 2010;
11. "Conduct of clinical trials at the investigator's site in accordance with Good Clinical Practice rules" – 9 November 2010;
12. "Norms on the administrative procedure of the National Agency for Medicines and Medical Devices on the handling of variations" – 18 November 2010;
13. Bioequivalence course – 10 December 2010;

14. Pharmacovigilance course – 17 December 2010.

In 2010, the NMA/NAMMD and the Competition Council carried on their cooperation based on a cooperation protocol ended in the last quarter of 2009, to ensure and promote competition in the field of the medicinal products for human use, in accordance with provisions of Law no. 21/1996 on competition, forbidding withdrawal, hindrance or distortion of competition on the Romanian market. Extrapolating to the Romanian pharmaceutical market, the management of the two institutions found it useful to coordinate their activities for consistent implementation of general legislation and specific legislation without prejudice to any of the participants, be they manufacturers of innovative medicines or importers/distributors.

In December 2010, the first meeting took place between the NAMMD management and stakeholders involved in the set up of a Romanian regulatory framework concerning medicinal product traceability; the purpose of this meeting was detection of all elements able to act as starting points in finding feasible solutions for the set up of this framework.

As a decision factor in the field of the medicinal product for human use, the Agency must and intends to become involved in all issues involving regulatory aspects to attain balance on the medicinal product market, in line with the European Commission recommendation, for the good of the final consumer: the patient.

NMA/NAMMD ACTIVITIES IN 2010

1. Activity of the Scientific Council (SC) of the National Medicines Agency/National Agency for Medicines and Medical Devices

During the first half of 2010, the NMA Scientific Council activities developed in line with provisions of Section 3 "Scientific Council organisation and operation" of Government Ordinance no. 125/1998 on the set up, organisation and operation of the National Medicines Agency, approved by Law no. 594/2002, as amended.

After issuance of Emergency Government Ordinance no. 72 of June 2010, leading to the establishment of the National Agency for Medicines and Medical Devices (NAMMD), the organisation and operation of the NAMMD and its Scientific Council have been regulated through Government Decision no. 734 of 21 July 2010.

It is to be noted that, from institutional viewpoint, as opposed to administrative procedures set up by Government Ordinance no. 125/1998, Scientific Council decisions no longer require approval by the Minister of Health within 15 days from their adoption; the competent minister is strictly informed about the matter in question. As far as regulatory Scientific Council Decisions are concerned, these are subject to general jurisdiction provisions – approval through

Order of the Minister of Health and publication in the Official Gazette of Romania, Part I.

The new NAMMD Scientific Council has been set up based on Order of the Minister of Health no. 1123/18.08.2010; its activity is performed in line with provisions of Art. 12 of Government Ordinance no. 734/21.07.2010 related to the set up, organisation and operation of the National Agency for Medicines and Medical Devices and the NAMMD Organisation and Operation Rules, approved SCD no. 18 in the meeting of 03.09.2010, subsequently repealed by SCD no. 33/13.12.2010.

The Scientific Council establishes the NAMMD scientific policy, in accordance with the Agency's tasks.

The regulations concerning NAMMD professional activity are discussed and approved as Scientific Council Decisions (SCDs) during Scientific Council meetings.

Regulatory decisions of the Scientific Council are sent for approval to the Minister of Health and published as Minister Orders in the Official Gazette of Romania, Part I; the other decisions are first forwarded to the Ministry of Health, then posted on the NAMDM website and published in the NAMMD Newsletter

In 2010, the Scientific Council was summoned in 5 working sessions; 33 SCDs have been adopted.

Out of the 33 decisions, 3 have been approved through Order of the Minister of Health and published in the Official Gazette of Romania, Part I; 2 are undergoing approval through Order of the Minister of Health. Of the above, 31 are posted on the NAMMD website and published in the bilingual NAMMD Newsletter .

As in previous years, the activity of the Scientific Council mainly consisted of adopting regulations, guidelines and procedures ensuring quality performance of NAMMD activities as well as of its partners with direct interests in the medicinal product for human use. The Scientific Council regulatory activity is described in detail in what follows, under section 3.

It is worth mentioning that the Agency 2010 – 2014 organisational strategy (SCD no. 1/23.03.2010) and communication strategy (SCD no. 9/07.06.2010) have been approved during Scientific Council meetings. These strategies, of maximum importance for attainment of NAMMD goals, are subject to yearly update.

Moreover, in line with the new legislative framework of Government Decision no. 734/2010, the following actions were deemed mandatory:

- election of a NAMMD Scientific Council President (SCD no. 17/03.09.2010);
- adoption of a new regulation on NAMMD Scientific Council organisation and operation (initially through SCD no. 18/03.09.2010, then repealed through SCD no. 33/13.12.2010);
- approval according to which all NMA SCDs issued prior to Government Decision no. 734/2010, shall remain in force until new regulations are issued (SCD no. 19/03.09.2010).

2. **Activity of the NMA/NAMMD Administrative Council (AC)**

During the first 6 months of 2010, the activity of the NMA Administrative Council was performed in line with provisions shown under section 2 "The Organisation and operation of the Administrative Council" of Government Ordinance no. 125/1998 on the set up, organisation and functioning of the National Medicines Agency, approved as amended through Law no. 594/2002, as amended.

After issuance of Emergency Government Ordinance no. 72 of June 2010, leading to the set up of the National Agency for Medicines and Medical Devices (NAMMD), the organisation and operation of the unit, as well as the organisation and operation of the Administrative Council, have been regulated through Government Decision no. 734 of 21 July 2010.

The new NAMMD Administration Council has been set up based on Order of the Minister of Health no. 1275/2010; it works in line with provisions of Art. 10 and 11 of Government Decision no. 734/21.07.2010 on the organisation and operation of the National Agency for Medicines and Medical Devices and with the Agency's Regulation for Organisation and operation, adopted during the first meeting of the Administrative Council of 31 August 2010.

From an institutional viewpoint, it should be noted that, as compared to administrative procedures provided for in Government Ordinance no. 125/1998, the Administrative Council Decisions no longer require approval of the Minister of Health within 15 days as of their adoption; the Minister is only informed about such decisions; as regards regulatory documents, these are subject to general jurisdiction provisions – approval of the Minister of Health and publication in the Official Gazette of Romania, Part I.

In 2010, the Administrative Council carried out 6 ordinary meetings (4 of the NMA, 2 of the NAMMD), adopting 42 Administrative Council Decisions (ACDs), 27 of which belong to the NMA and 15 to the NAMMD, 3 of which have been approved through Orders of the Minister of Health. Although 2 regulatory decisions have been initiated (approval of tariffs for new activities, detected after the Order of the Minister of Health no. 716/2009), these could not be completed.

Thematically speaking, ACDs have covered various aspects of current activities, but the main weight was derived from current circumstances, and consisted of decision documents regulating organisational issues – consecutive structure-related changes within the institution, change of the collective labour contract at unit level, approval of the job list and organisational structure, and other issues related to the current activity.

Here are a few important issues of the current activity:

- approval of the 2009 Activity Report of the NAMMD;
- approval for grant of additional remuneration for particular working conditions;
- update of Regulations on the organisation and operation of NMA Commissions;
- approval for decomission of certain fixed assets such as inventory objects,

as well as the depreciation and decomission of certain material goods.

3. **Regulatory activity**

The activity of the NAMMD in the field of legislative regulation continued at a fast pace in 2010, taking into consideration that medicinal product legislation undergoes a continual process of development/update/change, to keep up with technical and scientific progress in research/development of medicinal products.

Some regulatory decisions approved by the Scientific Council in 2010 have been/are to be approved through Order of the Minister of Health; these SCDs refer to:

- Approval of Norms on NMA administrative procedure for the handling of variations (SCD no. 4/23.03.2010 approved through Order of the Minister of Health no. 1483/9.12.2010);
- Approval of amendment to SCD no. 10/2006 on approval of the Analytical, pharmacotoxicological and clinical norms and protocols in respect of the testing of medicinal products, as regards advanced therapy medicinal products (SCD no. 8/26.04.2010, approved through Order of the Minister of Health no. 615/2010);
- Approval of Norms on the classification for supply of medicinal products for human use (SCD no. 12/07.06.2010, approved through Order of the Minister of Health no. 1602/2010);
- Supplementation of the Guideline on Good Wholesale Distribution Practice, approved through Order of the Minister of Health no. 1963/2008 (SCD no. 2/23.03.2010, SCD no. 34/13.12.2010, undergoing approval through Order of the Minister of Health).

Other SCDs of 2010 refer to approval/supplementation/amendment of certain guidelines, namely:

- Approval of the Guideline on consultations with target patient groups for the package leaflet (SCD no. 6/23.03.2010). The Guideline provides recommendations on consultations with target patient groups by listing chapters to be included in the study report and outline thereof. The purpose of such consultations with target patient groups is to ensure and assess the legibility, accuracy and ease of leaflet use;
- Change of the deadline for implementation/supplementation of the Guideline on consultations with target patient groups for the package leaflet, approved through SCD no. 6/23.03.2010 (SCD no. 16/07.06.2010 and SCD no. 35/13.12.2010). Considering the numerous applications for marketing authorisation/ marketing authorisation renewal/ marketing authorisation variation, Art. 4 of the Guideline approved through SCD no. 6/23.03.2010 has been amended through supplementation with several provisions related to the implementation term. SCD no. 35/13.12. 2010 approved the documentation concerning criteria for NAMMD accreditation and inspection of operators of consultations with target patient groups for the package leaflet;
- Approval of the Guideline on expression of strength in the trade name of

medicinal products for human use (SCD no. 11/07.06.2010). This Guideline is a translation into Romanian and a transposition of the „Recommendations on the expression of strength in the name of centrally authorised medicinal products for human use“, issued by the Working Group on Quality Review of Documents (QRD) of the European Medicines Agency (EMA). The Guideline provides recommendation on the accurate expression of strength in the marketing authorisation, under section “Authorisation name“, as well as in its Annexes;

- Approval of the Guideline on Romanian specific “Blue box“ on the secondary packaging of medicinal products for human use authorised through centralised procedure (SCD no. 13/07.06.2010). The Guideline takes over basic principles included in the “Guideline on the packaging information of centrally authorised medicinal products for human use” published in the Notice to Applicants (NtA) in February 2008, describing the manner of implementation of provisions of Directive 2001/83/EC as updated;

- Approval of the Guideline on investigation of bioequivalence (SCD no. 15/07.06.2010). The Guideline specifies the requirements concerning design, conduct and assessment of results of bioequivalence studies on immediate-release pharmaceutical forms with systemic action.

- Approval of the Guideline on evaluation on advertising in medicinal products for human use (SCD no. 20/03.09.2010). This Guideline aims to facilitate implementation of legal norms in force through detailed clarification of certain issues. Thus, advertisement of any medicinal product, regardless of its presentation and target persons (general public/healthcare professionals), may be assessed by NAMMD specialists and endorsed by Romanian MAHs in compliance with legal norms in the field;

- Approval of Norms on implementation of rules on supply of free samples of medicines for human use authorised for marketing in Romania, approved through SCD No 17/27.11.2009 (SCD no. 3/23.03.2010). This SCD makes valuable specifications concerning regulation of one of the issues concerning human medicinal product advertising;

- Approval of certain rules for advertising of medicinal products for human use (SCD no. 31/01.11.2010). The SCD of November 2010 approved new rules in the field, which supplement the Guideline. Thus, through its Pharmaceutical Inspection Department, the NAMMD will be able to take all measures for compliance with the legal framework for recommended performance of such advertising;

- Approval of the Guideline on the wording of the marketing authorisation and its annexes (SCD no. 21/03.09.2010). The Guideline provides recommendations on the wording of the marketing authorisation and its annexes for medicinal products authorised by the NAMMD through national/ decentralised/ mutual recognition procedure, replacing former Norms;

- Approval of the amended detailed Guideline on the request for authorisation of a clinical trial on medicinal products for human use, notification of substantial amendments and declaration of the end of the clinical trial (SCD no. 22/03.09.2010

and SCD no. 32/18.11.2010). This Guideline is a translation into Romanian and an adaptation of the European Commission (EC) Communication (2010/C 82/01) on the request to the competent authorities for authorisation of a clinical trial on a medicinal product for human use, the notification of substantial amendments and the declaration of the end of the trial (CT-1).

Through SCD no. 32 of November 2010, two administrative amendments have been approved, related to the notion of "day zero" as the "day of receipt of the application" and to the "confirmation of payment in accordance with the tariff for assessment of documentation for authorising conduct of clinical trials with medicinal products for human use, in accordance with provisions of the Order of the Minister of Public Health no. 716/11.06.2009 and of the payment order";

- Approval of the Guideline on the Good Manufacturing Practice for medicinal products for human use (SCD no. 23/3.09.2010). While Order of the Minister of Health no. 905/2006 approves the Principles and guidelines for Good Manufacturing Practice (GMP) in respect of medicinal products for human use and investigational medicinal products for human use, transposing EC Directive 2003/94 into Romanian legislation, this Guideline details and explains these GMP principles and Guidelines. The Guideline consists of two parts: one containing the main requiremenst for medicinal product manufacturing and the other containing the main requirements for the active substances used as starting materials;

- Approval of the Guideline on elaboration of the assessment report on nonclinical documentation (SCD no. 27/01.11.2010). The Guideline is a translation into Romanian and a transposition of the *CHMP Day 80 Critical Assessment Report Non - clinical* EMA Guideline. The Guideline may be used in assessment of the documentation as shown in the CTD (Common Technical Document) and eCTD formats and contains recommendations concerning the set up of the assessment report of nonclinical documentation.

Moreover, SCDs related to the rules/norms for implementation of certain rules set up for various NAMMD activities have been approved, such as:

- Approval of regulations concerning NAMMD authorisation of clinical trials/notification to the NAMMD of non-interventional studies on medicinal products for human use in Romania (SCD no. 29/13.12.2010).

- Approval of the manner of resolution of applications for marketing authorisation/marketing authorisation renewal for medicinal products for human use submitted to the NMA prior to 2007 (SCD no. 24/03.09.2010).

4. **Activity of NMA/NAMMD commissions**

4.1. **Marketing authorisation commissions**

Between 01.01.2010 and 23.02.2010, a single Marketing Authorisation Commission (MAC) operated within the NMA, working in accordance with Decision no. 654/2009 of the NMA President and its own regulation for organisation and operation, approved through NMA Administrative Council

Decision. The setup of 3 commissions for marketing authorisation/marketing authorisation renewal was approved through ACD no. 2/23.02.2010, namely: CAPP – National Procedure, CAPP – European Procedures, CAPP - Renewals, whose structure has been established through Decision no. 165/25.03.2010 of the NMA President.

Assessment reports are discussed by the Commission, in order to provide an opinion concerning the marketing authorisation, as well as other aspects related to the marketing authorisation of medicinal products for human use.

In 2010, the Marketing Authorisation Commission conducted 47 working sessions to discuss 1172 evaluation reports for medicinal products for human use and formulate an opinion regarding their marketing authorisation.

Therefore, out of the 1172 medicinal products reviewed by the commission:

- 1118 medicinal products have been accepted for grant of marketing authorisation, and
- decision on 54 applications for marketing authorisation has been postponed.

On seeing the necessity to ensure continuity of Agency specific professional activity after issuance of Emergency Government Ordinance no. 72/2010 and Government Decision no. 734/2010 on the organisation and operation of the NAMMD, it has been convened through Decision no. 33/03.08.2010 of the NAMMD Interim President that the Marketing Authorisation/Marketing Authorisation Renewal Commissions set up through ACD no. 2/2010 should carry on their activity, in the same structure and with the same operating procedures.

4.2. **Commission for the Inspection of Good Manufacturing Practices (GMP), Good Distribution Practice (GDP), Good Laboratory Practices (GLP), Good Analytic Laboratory Practices (GALP), Good Clinical Practices (GCL) and Pharmacovigilance**

After establishment of the NAMMD, through Interim President Decision no. 33/03.08.2010, the commission was allowed to carry on its work in the structure previously updated through Decision no. 652/2009 of the NMA President and in accordance with NMA Regulation for organisation and operation approved through NMA Administrative Council Decision. The Commission receives inspection reports issued by Agency inspectors, concerning the manner of compliance by inspected units with Good Manufacturing Practice, Good Distribution Practice, Good Laboratory Practice, Good Analytical Laboratory Practice, Good Clinical Practice rules and/or with other issues concerning work of the Pharmaceutical Inspection Department.

The Commission acts as mediator in cases of inspecting decision disputed by the inspected unit and the decision lies with the majority of Commission votes.

In 2010, the Commission for GMP, GDP, GLP, GALP, GCL and Pharmacovigilance inspection conducted 14 working sessions for examination of 306 inspection reports (285 compliant and 21 non-compliant), of which:

- 70 inspection reports on compliance with Good Manufacturing Practice rules, of which 6 have found non-compliance with GMP rules;

- 207 inspection reports on compliance with Good Distribution Practice rules, of which 15 have found non-compliance with GDP rules;

- 18 inspection reports on compliance with Good Clinical Practice rules;

- 2 inspection reports on compliance with Good Laboratory Practice rules;

- 2 inspection reports on compliance with Good Analytical Laboratory Practice rules;

- 7 pharmacovigilance inspection reports.

4.3. **Commission for verification of compliance of NMA/NAMMD inspection staff with the professional ethic and deontology code**

The commission works based on Decision no. 651/2009 of the NMA President and according to its own organisational and operation rules, as approved by Administration Council decision.

The goal of the Commission is verification of compliance with the Ethic and deontology code by Agency inspecting staff, as approved through Order of the Minister of Health no. 160/2004.

In 2010, no violations of the Ethic and deontology code by NMA/NAMMD inspecting staff were notified.

4.4 **Commission for management of crisis situations caused by concerns for medicinal product quality, safety and/or efficacy**

The Commission for management of crisis situations works based on NAMMD President Decision and on its own rules for organisation and operation, as approved through decision of the NAMMD Administration Council.

In 2010, the membership of the commission was updated through NAMMD President Decision no. 55/2010.

In 2010, the Commission convened in 9 working sessions to discuss issues related to:

- assessment of the development stage of the clinical trial performed for administration in children of the Cantgrip pandemic vaccine;

- assessment of the situation arising in result of the numerous critical and major findings during Agency inspections on the Cantacuzino Institute site for grant of manufacturing authorisation concerning the Cantgrip and BCG vaccines;

- assessment of the Corrective Measures Plan proposed by the Cantacuzino Institute according to Agency inspection report on 08.02.2010, meant to propose rapid solutions to restart manufacturing of the Cantgrip vaccine, according to Agency approved conditions;

- assessment of the manner to implement corrective measures for critical findings detected by Agency inspection in the BCG vaccine manufacturing flow for grant of a new manufacturing authorisation, following expiry of the former

manufacturing authorisation.

Set up and operation of this commission proved their efficiency in the rapid, consistent and harmonised resolution of crisis situations through involvement of Agency specialised structures, with immediate and positive effect for the safety of medicinal products in therapeutic circulation in Romania.

5. **Marketing authorisation and related activities**

In 2010, activities related to the documentation submitted to the NAMMD in view of evaluation, marketing authorisation, renewal of marketing authorisation, post marketing authorisation surveillance were particularly complex and were conducted in line with National and European procedures (mutual recognition/decentralised/repeat-use mutual recognition procedure).

Throughout 2010, the National Procedure and European Procedures Departments were set up after the reorganisation of two departments, namely the Authorisation and Post-authorisation Departments; this reorganisation has been approved through Order of the Minister of Health no. 1275/30.09.2010.

The organisational structure of the National Procedure Department is as follows:

- The National procedure administration service
  - The administrative verification and product index bureau
  - The parallel import bureau
- The national procedure variation service
- The national procedure evaluation service
  - The medicinal products and active substances quality bureau
  - The efficacy bureau
  - The non-clinical safety bureau
  - The medicinal product information bureau
- The clinical trials service.
- The organisational structure of the European Procedures Department is as follows:
  - The European procedure administration service
  - The validation bureau
  - The centralised procedure administration bureau
  - The European procedure evaluation service
  - The medicinal products and active substances quality bureau
  - The non-clinical safety bureau
  - The efficacy bureau
  - The medicinal product information bureau
  - The European procedure variations service
  - The pharmacovigilance and risk management service.

5.1. **Marketing authorisation through national and European procedures**

Whereas the number of MAs granted through European Procedures (EPs) [(decentralised procedure (DCP)], mutual recognition procedure (MRP) and repeat use procedure] has increased:

MAs through EPs: 2009 - 568 as compared to 2010 - 623,

the number of MAs granted through national procedure (NP) was smaller in 2010 as compared to 2009, namely:

MAs through NP: 2009 - 359 as compared to 2010 - 190

This is only to be expected, given that Romania is a EU Member State with a pharmaceutical market undergoing harmonisation with European requirements.

However, on the whole, the number of MAs granted by the Agency in 2010 was smaller than in 2009. Thus: MAs through NP and EP: 2009 - 927 as compared to 2010 – 813.

The reason for this is not related to a smaller number of applications, but to the Agency's recent lack of staff.

The number of Decisions for MA discontinuation, on MAH request for commercial reasons has increased in 2010, namely:

Discontinued MAs: 2009 - 134 as compared to 2010 – 202.

Moreover, in 2010, 3 years after Romania's EU accession, the "*sunset clause"* was enforced for 177 MAs for medicinal products not actually marketed during 2007 - 2010.

5.2. Assessment of variations to Marketing Authorisation (MA) terms

5.2.1. In 2010, a number of 5211 applications for variation to MA terms were submitted for medicinal products authorised through national procedure or undergoing MA renewal procedure, of which 3296 applications for type I variations, 638 applications for type II variations, 151 applications for MA transfer, 261 applications for modification of design and package labelling and 865 applications for clinical variations.

The NMA assessed and approved 2922 applications for variations for medicinal products (received in 2007, 2008, 2009 and 2010) authorised through national procedure or undergoing MA renewal procedures, of which:

- 1666 type I variations;
- 357 type II variations;
- 94 applications for MA transfer;
- 116 applications for modification of the design and package labelling;
- 689 clinical variations.

5.2.2. As far as post-authorisation assessment of variations to terms of marketing authorisation (MA) granted through European procedures (except for clinical variations) is concerned, the Agency received the following in 2010:

- 1743 applications for type IA variations and 1936 applications for type IB variations;
- 575 applications for type II variations;
- 142 applications for MA transfer;

- 39 notifications in accordance with Art. 61 (3) of Directive 2001/83/EC.

In 2010, 2258 variations for medicinal products authorised through decentralised/mutual recognition/repeat-use mutual recognition procedure have been approved, namely:

- 965 type IA variations and 890 type IB variations;
- 403 type II variations;
- 102 applications for MA transfer;
- 9 notifications in accordance with Art. 61 (3) of Directive 2001/83/EC.

5.3. **Assessment of applications and documentation for approval of clinical trials on medicinal products for human use**

In 2010, the NMA/NAMMD received 266 applications for clinical trial approval, as follows:

- 10 applications for phase I clinical trial approval;
- 61 applications for phase II clinical trial approval;
- 173 applications for phase III clinical trial approval;
- 22 applications for phase IV clinical trial approval;
- 44 applications for observational clinical trials;
- 61 applications for bioequivalence studies.

Until the end of 2010, 215 clinical trials were assessed and 201 authorisations were issued for:

- 7 phase I clinical trials;
- 60 phase II clinical trials;
- 118 phase III clinical trials;
- 16 phase IV clinical trials.

The following have been assessed and approved:

- 44 observational clinical trials.

The following have been approved:

- 1267 amendments to submitted trials, of which
- 158 amendments for new clinical investigation sites.

The following have been assessed:

- 61 bioequivalence studies, of which 43 were authorised and 2 discontinued; protocol amendments were sent for 16 such studies.

5.4. **Monitoring and control of advertising material for medicinal products for human use**

In 2010, the National Medicines Agency assessed for approval 474 advertising materials to the general public concerning OTC medicinal products.

Of these, 7 notifications were issued on rejection of advertising approval, while 48 advertising materials for use in educational programmes were assessed and approved.

The content of 207 advertising materials addressing persons qualified for

medicinal product prescription or supply was assessed and approved.

Monitoring and control of advertising for medicinal products for human use found further concrete form in:

- grant of 37 responses to advertising related complaints.

In 2010, special emphasis has been placed upon regulatory, surveillance and control work concerning advertising of medicinal products for human use. Thus, a special heading, "Advertising", has been created on the Agency's website, containing important announcements for stakeholders on this topic as well as MAH penalties applied for non-compliance with advertising rules (e.g. broadcasting of unapproved advertising materials, use of unapproved advertising channels, broadcasting of different advertising materials than approved by the Agency etc.).

5.5. **Pharmacovigilance**

The NAMMD manages the safety of medicinal products currently authorised in Romania via the Pharmacovigilance and risk management service, which is part of the Agency's European Procedures Department, whose activity is entirely compliant with Law no. 95/2006 and specific European Guidelines. Pharmacovigilance represents an extremely dynamic and interactive field of activity, developed in time as a must for patient safety. Perhaps the most complex definition of pharmacovigilance is as seen in a Q&A public document of the European Commission (December 2010), stating that pharmacovigilance is the science which detects, assesses and prevents the occurrence of adverse reactions in medicinal products and all related activities.

Pharmacovigilance work already has a substantial history in Romania.

In 1973, the National Pharmacovigilance Network was founded in Romania, consisting of reference centres organised at the level of University hospitals and of pharmacovigilance centres organised in other Romanian hospitals. The coordination of the National Pharmacovigilance Network was assigned to the Institute for the State Control of Medicinal Products and Pharmaceutical Research (ICSMCF), subsequently transformed into the National Medicines Agency (NMA).

In 1976, Romania became a member of the WHO (World Health Organisation) Medicinal Product Monitoring Centre in Genoa, transformed in 1978 into the WHO Collaborative Centre for International Drug Monitoring of Uppsala, Sweden. The National Pharmacovigilance Centre was set up within the ICSMCF; its duty was to ensure a permanent relationship between Romania and the WHO centre for the Adverse Drug Reaction Monitoring Centre in Uppsala in view of valdating spontaneous reports of adverse reactions collected through the Pharmacovigilance Centre and preliminarily assessed by reference centres in university hospitals. In the '70s, the National Pharmacovigilance Centre published the "Pharmacovigilance" magazine, providing details on various issues of pharmacovigilance work and distributed free of charge to healthcare professionals, physicians and pharmacists. Unfortunately, after 1990, pharmacovigilance activity started to decline in Romania, thus leading to discontinuation of activities of the

National Pharmacovigilance Network as well as of publication of the "Pharmacovigilance" magazine and the drastic reduction of the number of spontaneous reports registered at the National Pharmacovigilance Centre.

After 1999, following transformation of the ICSMCF into the NMA, pharmacovigilance work was seriously reconsidered according to principles applied throughout the European Union. The starting moment was participation of NMA representatives in various forms of training available, as well as transposition of certain European pharmacovigilance regulations and Guidelines into NMA Scientific Council Decisions (SCDs).

After Romania's EU accession on 1 January 2007, Romania's pharmacovigilance activity was firmly relaunched, according to European laws, transposed and implemented as NMA Scientific Council Decision. Pharmacovigilance activity has been considerably enhanced, from assessment and transmission of adverse reactions through the EudraVigilance system (the European network for pharmacovigilance data-processing and management), to assessment of Periodic Safety Update Reports (PSURs), from the Pharmacovigilance systems of Holding companies, to assessment of Risk Management Plans, to harmonisation of Summary of Product Characteristics (SmPCs) by implementation of decisions of the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) in the sections referring to product safety. Moreover, pharmacovigilance work ensured (and still does) direct healthcare professional communications on special warnings on product safety, as well as translation and posting of press releases and Q&A documents (actually notifications from monthly CHMP meetings) on the NAMMD website. The Romanian pharmacovigilance field also answers to non-urgent information and to information from the European and International rapid alert system.

In order to encourage adverse reaction reporting, all types of available data related to medicinal product safety have been posted on the NMA/NAMMD website (from posting of rules for pharmacovigilance work and the reporting sheet, to other types of important information for stakeholders).

By means of symposia, national conferences and congresses, physicians receive a call for reporting of spontaneous suspected adverse reactions (ARs).

A useful incentive devised by the Agency for AR reporting, in cooperation with the Romanian College of Physicians was and still is grant of Ongoing Medical Education (CME) Credits to reporters (10 OME credits for each adverse reaction reported). Every adverse reaction validated by the NAMMD is confirmed through a thank-you note to the reporter, accompanied by an Adverse Reaction Reporting Form; the Romanian College of Physicians is quarterly informed about the number of adverse reactions reported by physicians in the country, so as to grant the OME credits.

Such incentives led to increased number of reports during the previous years in Romania. Whereas, for example, 280 spontaneous reports were recorded in 2004, 525 were reported in 2009 and 938 (serious and non-serious adverse

reactions) in 2010. The numbers are optimistic, since they reveal the increasing importance of safety in the administration of medicinal products shown by healthcare professionals.

In 2010, pharmacovigilance activities materialised in the following:

a) Management of safety data from spontaneous reporting;

- 938 adverse reactions (AR) reporting sheets from Romania;
- 1071 validations/confirmations of adverse reaction reports required by the monitoring of the single European electronic database of adverse reactions, EUDRAVIGILANCE, for medicinal products used in Romania and 805 transmissions/retransmissions of adverse reactions;
- 63 electronic transmissions of adverse reactions to the WHO database (the Uppsala Monitoring Centre) via the VigiFlow electronic channel;
- 4 notifications of the College of Physicians concerning spontaneous adverse reactions reported in Romania and validated by the NAMMD – the National Pharmacovigilance Centre.
- 333 letters confirming receipt of Spontaneous adverse reactions reporting sheets from physicians in the network;
- 225 information letters for physicians on grant of Ongoing Medical Education (OME) credits on adverse reactions reporting;
- 266 answers to MAH applications concerning adverse reactions transmitted to the NAMMD related to medicinal products authorised in Romania; 138 adverse reaction reports were handled;
- 141 letters of response to MAH requests concerning pharmacovigilance-related aspects.

b) Collection, validation and archiving of 2201 Periodic Safety Updated Reports (PSUR) related to safety of medicinal products;

- 1419 Periodic Safety Updated Reports (PSUR) related to the safety of imported medicinal products;
- 782 Periodic Safety Updated Reports (PSUR) related to the safety of Romanian medicinal products.

For medicinal products undergoing a MA renewal process through national procedure, 78 PSUR assessment reports have been issued.

c) Pharmacovigilance activities in the European national authority system coordinated by the EMA:

- handling of 42 EMA press releases, 16 EMA questions and answers documents, 24 Lines to take proposed by the EMA for request of information, 35 Direct Healthcare Professional Communications related to safety concerns raised by medicinal products, handling of 70 MAH information letters on medicinal products safety issues, 24 translations for SmPC harmonisation to be posted on the NAMMD website.

d) Pharmacovigilance activities within the rapid alert/non-urgent information system (RA/NUI):

- 9 NUI responses to solicitations by certain EU authorities;
- 2 actions in collaboration with the Pharmaceutical Inspection Department

with regard to rapid alerts;

- 1 response to complaints from patients concerning safety issues of medicinal products.

e) Assessment of compliance with requirements concerning accurate description of the pharmacovigilance system by the MA applicant:

- 815 assessment reports concerning summaries of the pharmacovigilance system of applicants for marketing authorisation through decentralised/mutual recognition/repeat-use mutual recognition procedure (with Romania as Concerned Member State);

- 211 assessment reports concerning summaries of the pharmacovigilance system of applicants for marketing authorisation through national procedure.

The new Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010 on amendment, as regards pharmacovigilance, of Directive 2001/83/EC on a community code relating to medicinal products for human use (to be transposed into Romanian legislation, amending the Pharmacovigilance chapter of Law no. 95/2006) will also envisage responsibilities for patients concerning reporting of adverse reactions to medicinal products. Thus, by physician-patient joint effort, detection is expected of as many adverse reactions as possible, enriching product information. Certainly, the final outcome will be attainment of the highest possible level of safety in the product administration within the EU.

5.6. **Other activities**

- Handling of the database represented by the index of medicinal products for human use consisted of introduction of new medicinal products authorised through national/European/centralised procedure, implementation of MA changes for already authorised medicinal products, introduction of approved variations to approved MA terms, keeping track of medicinal products undergoing MA renewal and of MA withdrawal/discontinuation decisions.

At Ministry of Health request, the statutes of innovative, original, generic, biosimilar and homeopathic products were established for medicinal products included in the successive Canamed versions in 2010. At the end of the year, the NMA product index included 8168 trade names, corresponding to 1252 International Non-proprietary Names (INNs).

- "Parallel import" related activities
  - release of parallel import authorisations (PIAs) (24 PIAs)
  - request for information from other authorities in EU Member States, for PIA release (55)
  - variations to PIAs (17)
- "Parallel export" related activities
  - reply to request for information submitted by other competent authorities for PIAs release for concerned Member States (298).

The activities derived from Agency status as competent authority in an EU Member State continued as follows:

- Management of responses received in application of Art. 729 and 730 of Law no. 95/2006, i.e. notification of temporary or permanent discontinuation of manufacturing and notification of actual medicinal product marketing ("sunset clause");

- Verification of the 8168 medicinal products included in the product index at the end of 2010, of which 2100 authorised through centralised procedure, their handling concerning implementation of the "*sunset clause*" as under responsibility of the European Medicines Agency (EMA); in 2010, 3 years following Accession, the "*sunset clause"* has been applied to 177 MAs for medicinal products not actually placed on the market between 2007 and 2010.

- Management of the database related to EMA authorised medicinal products based on art. 127a of Directive 2001/83/EC and monitoring of implementation of conditions and restrictions placed on the MAH by the European Commission;

- Management of European Commission (EC) decisions related to referrals, issuing of the points to the involved MAHs, in view of requiring the transmission of variation applications for the implementation of the EC Decision.

6. **Inspection of Good Manufacturing Practice (GMP), Good Distribution Practice (GDP), Good Laboratory Practice (GLP), Good Analytical Laboratory Practice (GALP), Good Clinical Practice (GCP), Good Pharmacovigilance practice and market surveillance**

In the course of 2010, the Pharmaceutical Inspection Department (PID) continued to perform the activities mentioned in specific legislation (Law no. 95/2006, Title XVII – The medicinal product and secondary legislation thereof), in accordance with the department's *Standard Operating Procedures (SOPs)*, endeavouring to solve its tasks within deadlines stipulated by law.

The following have been prepared and issued in the pharmaceutical inspection activity:

- 62 Good Manufacturing Practice (GMP) certificates (for Romanian and foreign manufacturers);
- 54 manufacturing authorisations, annexes included;
- 65 import authorisations, annexes included;
- 7 Good Laboratory Practice (GLP) certificates;
- 29 qualified person certificates;
- 2 authorisations for independent control units;
- 163 dossiers for the inspected units, and for units requesting update of annexes to manufacturing/import authorisations have been issued and handled;
- 134 applications for waiver from legal provisions concerning medicinal product packaging/labelling have been solved;
- management of databases of inspection encoding, the list of authorised/certified manufacturing units, authorised importers, medicinal products for which the export declaration has been approved, and qualified persons.

Inspection work in the fields of Good Manufacturing Practice (GMP), Good Laboratory Practice (GLP), Good Analytical Laboratory Practice (GALP), Good Clinical Practice (GCP), and Good Pharmacovigilance in 2010 consisted of:

- 33 GMP inspections in view of manufacturing authorisation conducted in Romania,;
- 25 inspections in view of authorisation conducted at the site of medicinal product importers;
- 21 certification inspections for GMP compliance of pharmaceutical companies from third countries;
- 2 unannounced inspections for certification of GMP compliance conducted at the sites of Romanian manufacturers of medicinal products;
- 5 GLP inspections to laboratories performing bioequivalence studies;
- 4 GALP inspection at independent quality control units;
- 31 inspections for assessment of compliance with GCP rules;
- 15 pharmacovigilance inspections at MAH site, of which 9 inspections of Romanian MAHs and of Romanian MAH representatives, according to the yearly inspection plan of the Pharmaceutical Inspection Department and 6 unannounced inspections at MAH site.

In September 2010, a team of GCP inspectors was assigned to participate in the centralised procedure GCP inspection of two centres, one of the inspectors being the head of the GCP inspection team, responsible with issuing inspection reports, inspection plans, inspection related exchanges (correspondence with the EMA, the inspectors from Member States participating in the inspection).

In the context of Good Distribution Practice (GDP), inspections conducted in 2010 were as follows:

- 112 inspections for authorisation have been conducted;
- 70 wholesale distribution authorisations have been released;
- 40 unannounced inspections following which:
    - 17 authorisations were suspended;
    - 3 authorisations issued by the Ministry of Health were withdrawn, in accordance with previous legal regulations, following critical findings during inspections for authorisation;
    - the dossier for 362 applications for approval of export declarations was checked, leading to approval of export declarations for 1129 medicinal products manufactured in Romania.

As regards certification of qualified persons, the dossier containing 45 applications for issuance of the Certificate attesting the Qualified Person status was checked and assessed; 29 such certificates were released.

The surveillance activity of medicinal product quality and handling of rapid alerts consisted of:

a) Carrying out the sampling scheme for medicinal product quality monitoring:

- Of the **29** products proposed, **23** were sampled, and 6 were not found in the distribution network;

Laboratory testing results issued have been as follows:

- 22 samples have been declared compliant;

- 1 product is undergoing analysis.

In addition to the sampling scheme, the following samples were provided in 2010:

- 6 medicinal products sampled on request of the Quality Control Department, for participation in market surveillance studies proposed by the OMCL network (Official Medicines Control Laboratories); all samples of medicinal products are currently being tested;

- 10 medicinal products have been sampled for resolution of medicinal product quality complaints, of which **5** have been declared noncompliant with quality standards and have been recalled from the market;

- 4 medicinal products sampled from distribution units within the EMA/EDQM coordinated scheme for surveillance of centrally authorised medicinal products; the testing of these products has been performed by laboratories in other EU competent authorities, and the results were found compliant.

b) inspections for follow-up of medicinal product quality in the distribution network (warehouses, pharmacies):

- 373 thematic inspections were carried out in retail and wholesale distribution units.

c) inspections of the quality of oxygen used in hospitals:

- 234 inspections were carried out in hospitals across the country, to stop use of unauthorised oxygen (liquid oxygen is provided by GMP certified producers, while compressed oxygen for 17 hospitals (8%) still comes from unauthorised manufacturers. The Ministry of Health has been informed on the situation.

d) Cooperation with other bodies for resolution of issues related to legislation in the field of medicinal products and/or the quality of certain products sold in Romania:

- 14 joint actions with specialised local bodies, carried out by territorial inspectors (9 Cluj, 3 Târgu Mureş, 2 Deva).

e) Resolution of complaints relating to possible quality noncompliances of medicinal products for human use:

- of 34 resolved complaints, 18 have resulted in classification and have resulted in recall of the respective medicinal products from the market.

f) Recall from the market of medicinal products displaying quality noncompliances: in 2010, the NMA/NAMMD requested recall of 54 medicinal products, of which:

- 12 medicinal products were identified with intrinsic quality nonconformities and have therefore been proposed for destruction (3 following complaints, 5 due to rapid alert, 4 voluntary recalls performed by the manufacturers);

- 34 medicinal products had packaging/leaflet inscription nonconformities and have been proposed for remedy/destruction;

- 8 medicinal products recalled following EMA recommendation because of MA recall for centrally authorised products.

g) Rapid alert system:

- in 2010, 79 rapid alerts were received and resolved, within the EMA Rapid Alert System, the Pharmaceutical Inspection Cooperation Scheme (PIC/S).

h) Cooperation with the EMA, the EDQM, European competent authorities, concerning surveillance of the quality of raw materials/finished products manufactured in third countries:

- 21 cases reported (2 by Romania) on non-compliance with GMP rules by active substances or medicinal products manufacturers from third countries, for which the steps taken were in accordance with the joint decisions made by authorities;

- 6 certificates of conformity with the European Pharmacopoeia were suspended by the EDQM, for which steps were taken to change active substance suppliers.

i) Creating and updating the databases for all PID services, updating information on the NAMMD website and introducing in the EudraGMP database the information concerning NAMMD activities concerning manufacturing authorisation/import/GMP certification.

j) Coordination of the activities of the Territorial Inspection Units (TIU) related to surveillance of medicinal product quality.

7. **Quality control of medicinal products for human use**

Quality control of medicinal products for human use is part of the NMA/NAMMD general policy and aims at giving material form to its mission of ensuring medicinal product quality, safety and efficacy.

This activity is carried out within two departments: the Medicines quality control department (MQCD), and the Biological products control department (BPCD).

Work in both departments, main and support activities, are accomplished by a process-based approach, in line with requirements of standards SR EN ISO 9001/2001 and SR EN ISO 17025/2005.

Both NAMMD control departments are integrated into the European network of Official Medicines Control Laboratories (OMCL), coordinated by the European Directorate for the Quality of Medicines (EDQM), and participate in all related activities.

7.1. The main types of analysis performed by the **Medicines Quality Control Department (MQCD)** are: physico-chemical analysis, pharmacotoxicological analysis, immunogenetics and pathological anatomy analysis, micro-biological analysis and radio-pharmaceutics analysis.

Core activities in 2010 dealt with:

a) Quality control of non-biological (chemical) and biological medicinal products.

In 2010, 308 medicinal products were analysed, of which:

- 54 obtained through chemical synthesis; 205 laboratory analyses have been conducted to investigate their quality: cromatographic (HPLC - High Performance Liquid Chromatography and TLC – Thin Layer Cromatography), spectrophotometric (UV, IR) and potentiometric analyses, physico-chemical identifications, dissolution testing and others;

- 258 biological medicinal products (vaccines, sera), the majority of which (254) manufactured by the "Cantacuzino" Institute; 4 imported vaccines.

The analysis of the 258 medicines required 625 physico-chemical, pharmacological, immunological and microbiological determinations. To this, 900 internal analyses of environmental checks, calibration of equipment, testing of the suitability of the systems and equipment used were added.

Out of the full number of medicinal products analysed, 7 were of non-compliant quality; several non-compliances have been reported, e.g. unpleasant, persistent odour, falsified batch and manufacturing date, falsified product, with no active substance.

a) Evaluation of chemical documentation (DSSA, clinical studies, finished products).

In 2010, the MQCD assessed documentation for 921 medicinal products undergoing authorisation.

As regards assessment of the clinical trial dossier, 16 phase III clinical trial dossiers have been assessed, 1 study undergoing VHP procedure.

b) External cooperations concerning medicinal product quality.

As in previous years, in 2010 as well, the MQCD continued to collaborate with European institutions dedicated to medicines quality control, by taking part in studies initiated and coordinated by the European Directorate for the Quality of Medicines and HealthCare (EDQM):

* 3 PTS (Proficiency Testing Scheme) studies held annually and aimed at testing the capacity and professional ability of each laboratory within the European network (Official Medicines Control Laboratories = OMCL), to resolve highly difficult issues encountered in quality control of medicinal products.

** 1 study on the quality of medicinal products authorised through Mutual Recognition Procedure (MRP).

*** 1 MSS (Market Surveillance Study) for the surveillance of the European market, organised by the EDQM. Since 2010, the MSS consisted of characterisation of dissolution profile, dosage, assay of the profile of chemically-related substances (impurities) for two Romanian products, study conducted by comparison with a similar medicinal product on the European market.

7.2. The activity of the Biological Product Control Department (BPCD) in 2010 was marked and influenced by involvement in a PTS (Proficiency Testing

Scheme) study conducted at the request and under the coordination of EDQM, for which the laboratory was rated "satisfactory". The result has once again confirmed the competitive level of laboratory testing within the BPCD.

The activity of the BPCD in 2010 was influenced by the department re-location in the NAMMD headquarters; the department was relocated on the 5th floor during May-June 2010. The relocation involved complex activities concerning transportation of documents and specialised transport of the laboratory and furniture equipment, as well as start-up of the equipment required to resume laboratory work.

Activity of the department covers the following aspects:

A. Quality of medicinal products such as: vaccines, therapeutic biological products, *in vivo* diagnostic products.

a) Laboratory control:

- 196 sets of product samples have been analysed corresponding to a number of 750 laboratory tests;
- 202 test reports have been issued, including:
- 199 bulletins for finished products;
- 3 bulletins for intermediate and bulk products.

b) Official batch release for circulation in Romania of Romanian biological products for human use from third countries and EU Member States for which no official batch release was made in the EU, for various reasons.

For the purposes of official batch release procedure, product sampling is necessary to carry out product testing in the laboratory.

Finished, intermediate and bulk products were sampled in 10 sampling sessions.

For the biological products tested, 326 batch release certificates were issued and no bulletin of non-compliance.

A total number of 139 trading intentions were registered related to products for which the official batch release was performed in the EU.

c) Control of biological products for human use subject to complaint or included in the recall scheme, on PID summons.

As regards complaint solving, testing was conducted at PID request on a vaccine sample subject to complaint related to the physical aspect. Following testing, it was concluded that the sample was compliant with specifications.

Moreover, in 2010, 2 batches of biological products for human use included in the sampling plan following PID surveillance of the market were tested within BPCD Laboratories.

Throughout 2010, via the Cell culture laboratory - measurements and specific microbiology, the BPCD participated in one Proficiency Testing Scheme (PTS) study, performed at the initiative and coordinated by EDQM (PTS098: *MEASLES VACCINE POTENCY ASSAY*); the laboratory was rated „*Satisfactory"*, in the context of 16 European laboratories involved in the study receiving the same rating, while two laboratories were rated „*Unsatisfactory*".

B. As regards documentation submitted for assessment through national, mutual recognition and decentralised procedures in view of marketing authorisation/marketing authorisation renewal and variation approval:

- 33 products have been assessed through national procedure and 59 reports have been issued;
- 233 MA variations have been assessed through national procedure;
- 28 products have been assessed through mutual recognition procedure; 36 reports have been issued;
- 60 variations have been assessed through the mutual recognition/decentralised procedure; 68 reports have been issued.

Moreover, in 2010, the procedure has been initiated and the required steps have been taken for participation, as a reporting state, in the assessment of a biological product for the implementation of provisions of Article 46 of Paediatric Regulation no. 1901/2006 (a *worksharing* procedure).

C. Change of MA terms for biological products for human use, following approval of Type I/II variations or due to editing revisions:

- 26 marketing authorisations have been changed, starting with September 2010.

D. Assessment of documentation submitted for approval of application for clinical trial conduct (assessment of non-clinical and quality documentation):

- The quality and pre-clinical documentation submitted for approval of the application for conduct of clinical trials for biological products for human use has been assessed: 3 reports (2 assessment reports of the quality documentation and one assessment report for pre-clinical safety).

E. Post-authorisation surveillance of biological products for human use:

- 181 batches of authorised marketed biological products have been registered in the BPCD database.

8. **Ensuring communication and transparency**

The NMA/NAMMD pays special attention to ensuring good information transfer and communication with stakeholders and the media, in accordance with Law no. 544/2001 on free access to information of public interest and of Law no. 95/2006, Title XVII – The medicinal product on transparency in the work of EU competent authorities.

8.1. **External communication**

The agency provides good and accurate information to partner institutions on activities in all domains within its scope.

On its website, the NAMMD publishes bilingual Newsletters, which are a reflection of its intense regulatory activity in the area of medicines in line with European legislation and other priority activities of the Agency. The content of the NMA/NAMMD Newsletter includes:

- Laws, ordinances, Government decisions in the field of medicinal products for human use or other areas of NMA/NAMMD interest;

- Orders of the Minister of Health for approval of NMA/NAMMD Scientific Council decisions and Orders of the Minister of Health in other areas of NMA/NAMMD interest;

- Decisions of the NMA/NAMMD Scientific Council;

- Decisions of the NMA/NAMMD Administrative Council;

- Quarterly list of marketing authorisation/marketing authorisation renewal applications submitted to the NMA;

- Quarterly List of EMA newly centrally authorised medicinal products, for which the European Commission issued the decision on translation into Romanian of medicinal product information;

- Quarterly list of medicinal products authorised for marketing by the NMA/NAMMD;

- A quarterly list of medicinal product batches recalled by the NMA/NAMMD for quality defects.

The NAMMD develops the product index of medicinal products for human use, including all medicines authorised for circulation in the pharmaceutical market in Romania, with data on trade name, International Non-proprietary Name, active substance, marketing authorisation holder, pharmaceutical form, strength, route of administration, type of packaging, manner of release etc. and posts it on its website. In 2010, implementation began, for each medicine, of electronic versions of the Summary of Product Characteristics (SmPC), leaflet and information on labelling and inscription.

The NAMMD develops and keeps updated information available on the Agency's bilingual website. Hence, the NMA/ NAMMD website has published and continually updated the following information and documents:

- Press releases relating to safety of medicinal products;

- Information letters to physicians/direct healthcare professional communications;

- Notifications to Marketing Authorisation Holders (MAH) or other interested parties on issues of interest;

- Information related to medicinal products authorised through centralised procedure;

- SmPCs for medicinal products authorised in Romania through mutual recognition procedure and decentralised procedure;

- SmPCs for medicinal products authorised in Romania through national procedure;

- List of medicinal products authorised for circulation within Romania, released on medical prescription;

- List of over-the-counter (OTC) products authorised for circulation in Romania;

- List of valid orphan medicinal products;

- List of NMA/NAMMD employees assigned as full members/alternates in the Management Board, scientific committees and working groups of the European Medicines Agency (EMA);

- List of EMA experts appointed by the NMA/NAMMD.

For support of external partners involved in European procedures for the marketing authorisation of medicinal products for human use, the NMA/NAMMD website contains two sections dedicated to these procedures, which have also been posted on the new website:

- <CP> (centralised procedure)

- <MRP and DCP> (mutual recognition procedure and decentralised procedure), containing data on contact persons and useful information for the authorisation of these procedures, namely: regulatory documents, required forms, bank accounts, announcements and warnings addressed by the NMA/NAMMD to MAHs involved in European procedures.

This information has been improved and updated, in both Romanian and English, and divided by themes.

A new section related to the national procedure has been added to the new NAMMD website, under construction in 2010; just as the other two sections for the centralised/mutual recognition/decentralised procedure, it provides information about contact persons, special warnings, SmPC, leaflets and labelling. Moreover, the section "National Procedure" of the new NAMMD website provides the "List of parallel import authorisations" issued by the NMA/NAMMD since 2009.

The external users of the NMA/NAMMD found the following headings particularly interesting:

- medicinal product legislation;

- useful information on European procedures;

- Product index of medicinal products for human use authorised for marketing in Romania;

- forms and useful information.

The enhanced interest of stakeholders in the information published on the NMA/NAMMD website is reflected in the large number of website visitors, which keeps on growing, namely 271491 visitors in 2010 (an average of 22625 visitors per month).

The Agency continued to ensure transparency of work performed in accordance with provisions of Law no. 95/2006, Title XVII – The medicinal product, Art. 845 (2) and Art. 726 (4) on transparency in the activity of competent authorities in the EU medicinal product field, by:

- periodically updating the rules for organisation and operation of NAMMD commissions, approved in the Administrative Council and posted on the website;

- setting up, upon request, publicly available versions of agendas and press releases of NAMMD Commissions;

- setting up, upon request, the public versions of reports concerning assessment of the dossier submitted for authorisation through national procedure.

In 2010, the NMA/NAMMD continued to inform stakeholders about its

work through means other than its own Newsletters. Thus, the 2009 NMA Activity report continued to be posted online as a bilingual brochure; it received the appreciation of NMA partners.

Moreover, in 2010, several articles were published in Romanian professional magazines ("Farmacist.ro", "Medical Business", "Viaţa Medicală, "Pharma Business") referring to various issues concerning the Agency's activity.

The NMA/NAMMD representatives have participated with professional works in numerous scientific/professional manifestations held in Romania and abroad.

8.2. **Internal communication**

In 2010, the Agency continued to supplement and update the information (which can be found on the Intranet by NMA staff), aiming to receive the best and fastest information in the professional field and/or at organisation level.

NAMMD staff has access to the following information available on the "Intranet":

- Instructions of the NAMMD President;
- NAMMD quality-related policies;
- NAMMD regulations;
- Glossary of quality assurance;
- Activity plans of each department;
- Useful forms;
- Information provided by the Pharmacopoeia service;
- Information about training courses organised by the NAMMD or by professional companies;
- Reports issued by the employees receiving training in Romania and abroad;
- Situation of staff training;
- The outcomes of the "staff motivation" poll;
- Useful information;
- Useful addresses etc.

9. **Quality management activity**

In 2010, taking into consideration the *quality and quality objectives policy*, established by the top management, as well as processes identified and applied, the size and structure of the NAMMD and *SR EN ISO 9001* and *9004* principles in force, the Quality Assurance Bureau, together with the other organisational structures, have taken part in the implementation, development and improvement of the QMS in the context of NAMMD organisation.

Other activities have been performed, namely:

- The internal quality audit process was carried out in accordance with the *Internal Quality Audit* Program in 2010, approved by the President of the organisation.

Findings and conclusions of internal quality audits, whose objectives consisted of ensuring compliance with *Standard Operating Procedures (PSOs) applying to the audited processes,* have been mentioned in *internal quality audit reports*, submitted to the audited organisational structures and top management to improve the audited processes/products (services). *Internal quality audit reports* have been accompanied by *action plans for improvement* issued by audited departments and by reports *on the level of implementation of improvement actions* proposed due to previously conducted internal quality audits.

- Amendment (review) process of general *PSOs* (research, set up, drafting, approval, dissemination) was carried out through amendment (review) of 14 *PSOs*, in accordance with requirements of *international standards* in force and with the changed circumstances (*Government Ordinance no. 734/ 21.07.2010* and *Order of the Minister of Health no. 1275/ 30.09.2010).*
- The setup of the *"Statistical study on the release process for marketing authorisations (MAs) by the National Medicines Agency, January – February 2010"*
- The study has been issued in conjunction with the Information Logistics and Electronic Management of Data Department.
- The setup of the *documents* requested by the Ministry of Health – Secretary-general Cabinet.
- New update of the *declarations of interest, privacy commitments/ individual and general job description.*
- The set up and update of Quality Assurance Bureau *databases* (in electronic format).
- Counselling in the field of quality.

The Quality Assurance Bureau was compliant with the *2010 Activity Program*, approved by the organisation's President.

In accordance with *Order no. 43/16.04.2010*, issued by the head of the Control Department of the Prime Minister, in the context of the process for assessment of legal provisions concerning the activity performed by the NAMMD, the activity of the Quality Assurance Bureau (QAB) has also been assessed. *The control report* issued following this assessment has not detected any non-compliance of processes/activities belonging to the QAB.

Participation of NAMMD experts in specialised quality management training.

In 2010, quality assurance staff in each department participated in the training course "Elements of strategic management" provided by the qualified institution QUASARO.

10. **Medical devices**

- **Control activity through periodic update of medical devices and attempts in view of certification**

In 2010, after merging with the Technical Office for Medical Devices, the NAMMD has become the single institution assigned to assess the performances and safety of medical devices in use. The new control activity, namely periodic check-up of medical devices, was, thus, carried out for all installed and commissioned medical devices, characterised by a high risk degree, at the sites of all medical device user, both in the private and public field.

The 2010 Technical Laboratory Department staff activity was the following:

- Number of applications for registration: 1882 (1554 at the Technical Office for Medical Devices, 328 at NAMMD)
- Number of periodic check-up bulletins issued: 3325
- Number of notices for use issued: 36
- Number of notifications following periodic check-up issued: 27
- Number of medical devices assessed: 7741
- Umber of mobile intervention units assessed: 1250
- Number of reports on negative laboratory tests (rejected medical devices) issued: 56 (of which 26 rejected by the nuclear unit).

In terms of laboratory tests:

- Laboratory trials for certification: 11 papers
- Participation in technical expertise: 5 actions
- Cooperation in police enquiries: 2 actions.

- **The activity of inspection and assessment of technical-medical units**

The Technical-Medical Units Assessment Service conducts its activity in accordance with Law no. 176/2000 on medical devices, as amended and Order no. 1636/2004 on approval of the Methodological norms on implementation of Law no. 176/2000, as amended, referring to notification of medical technique units. This activity consists of assessing the ability of the organisations to perform services requiring notification from the Ministry of Health. Activities assessed deal with optics, start-up, repair and maintenance of medical devices, prosthesis manufacture (auditory/orthopaedic/other types).

Despite the reduced number of employees, the service must cover this type of activity throughout the country, having to perform not only initial assessment of the units to obtain notification and surveillance assessment every two years to maintain notification, but also to find and sanction breaches of Law no. 176/2000 implementation.

The status of projects conducted in 2010 by staff of this service is as follows:

- Number of assessment applications registered: 163
- Number of assessments and issued reports performed: 121
- Number of activities cancelled (dossier for assessment not submitted): 21
- Number of activities cancelled (the organisation only performs marketing activities): 11
- Number of ongoing projects: 10

- Number of assessment-surveillance projects: 323
- Number of conducted assessment-surveillance projects, reported: 200
- Number of ongoing assessment-surveillance projects at the end of the year: 83
- Number of assessment-surveillance projects whose activity has ceased or whose performance notice has been cancelled: 40

Several measures have been taken by the Ministry of Health to amend Order of the Minister of Health no. 842/2009 establishing the template of the findings and penalty minutes regarding Law no. 176/2000, enabling the NAMMD to apply this Order.

11. **International relations**

In 2010, NMA/NAMMD specialists continued to take part in activities of various cooperating European institutions and organisations:

11.1. **Participation in the activities of the European Medicines Agency (EMA)**

Since 2003, at the initiative of the European Medicines Agency, the NMA/NAMMD participated actively through its representatives to the initiative of the European Medicines Agency**,** as active observers to working groups, scientific committees and groups for implementation of information technology, all related to the medicinal product.

This participation represented and still represents the optimal means of keeping the Agency connected to European activities in the field of the medicinal product for human use.

Full members since 2007, participating in EMA scientific committees and working parties, NMA/NAMMD experts participated in over 100 meetings in 2010.

EMA Scientific Committees and Working Groups are the following:

- The Committee for Medicinal Products for Human Use (CHMP)
- The Committee for Orphan Medicinal Products (COMP)
- The Committee on Herbal Medicinal Products (HMPC)
- The Committee for Paediatric Medicinal Products (CPMP)
- The Committee for Advanced Therapies
- CHMP Biotechnology Working Party
- CHMP Efficacy Working Party
- CHMP Safety Working Party
- CHMP Pharmacovigilance Working Party
- CHMP Blood Products Working Party
- The Vaccines Working Party
- The common CHMP/CVMP Quality Working Party
- The CHMP Patients' and Consumers' Working Party

- The GMP/GDP Inspectors Working Group
- The Subworking Group on the EudraGMP Database
- The GCP Inspectors Working Group
- The Pharmacovigilance Inspectors Working Group
- The GLP Inspectors Working Group
- The Working Group on the database of medicinal products authorised in the EU (EudraPharm TIG)
- The Working Group on the database of adverse reactions (EudraVigilance TIG)
- The Working Group on the European database for clinical trials (EudraCT Clinical trials TIG)
- The EudraNet Working Group on the European Telecommunication Network
- The Working Group on the electronic transmission of data (e - Submission)
- The Working Group on European Union Telematics Controlled Terms (EUTCT)
- The Working Group on Product Information Management (PIM)
- The Working Group of the Quality Review of Documents
- The Invented Name Review Group.

11.2. **Participation in the activities of the "Heads of Medicines Agencies"**

NAMMD representatives are actively involved in meetings of the European body "Heads of Medicines Agencies" (HMA), as well as in meetings of the Working Groups of this body, as mentioned:

- The Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh)
- EMACOLEX (Working group on legislation)
- The Working Group of Communications Professionals
- The Working Group on Transparency
- The Working Group on Counterfeit Medicines
- The Clinical Trials Facilitation Group
- The Homeopathic Medicinal Product Working Group
- The Working Group of Quality Managers.

11.3. **Participation in activities of the European Union Council and of the European Commission (EC)**

NMA/NAMMD experts have participated in over 20 meetings of the Working Group for Medicinal Products and Medical Devices of the EU Council, where new draft directives concerning pharmacovigilance and counterfeiting have been discussed.

In the context of the meetings organised by the European Commission, NMA/NAMMD experts have participated in meetings of the Standing Committee

for Medicinal Products for Human Use and in meetings of the Pharmaceutical Committee – Notice to Applicants, as well as in the meeting of the EC ad-hoc group on development of implementation of Guidelines for application of Directive 2001/20/EC concerning clinical trials.

11.4. **Participation in World Health Organisation (WHO) activities**

The NMA is a member of the WHO Scheme on the certification of the quality of medicinal products on the international market.

In 2010, the Agency has released the Certificate of the product in WHO format for 381 medicinal products of Romanian manufacturers seeking authorisation of these products in other states.

11.5. **Participation in European Council activities**

In 2010, the NMA/NAMMD representatives participated in meetings of the Working Group on the classification for release of medicinal products for human use and the ad-hoc Committee for Counterfeit Prevention.

11.6. **Participation in European Pharmacopoeia Commission activities**

The representative assigned by the NMA/NAMMD as members of the European Pharmacopoeia Commission, has actively participated in its working sessions in 2010, as well as in the yearly meeting of the secretaries of the national Pharmacopoeia in countries belonging to the Convention for Elaboration of a European Pharmacopoeia.

The cooperation with the European Directorate for the Quality of Medicines (EDQM) was continued, in view of issuing and updating the "Romanian Standard Terms", in accordance with those adopted by the European Pharmacopoeia Commission.

11.7. **Participation in activities of the Pharmaceutical Inspection Cooperation Scheme (PIC/S)**

The activity of the NMA/NAMMD as a PIC/S member consisted of participation in the Joint-visit PIC/S program in the joint inspection of 30.05. - 04.06.2010 organised by the French inspector of Group no. 99.

11.8. **Participation in activities of Official Medicines Control Laboratories (OMCL)**

In 2010, in the context of the cooperation with European institutions in the field of medicinal product control, NAMMD laboratory experts participated in 5 trials:

- 3 analytical Proficiency Testing Scheme (PTS) studies performed at the initiative and under the coordination of the EDQM;

- 1 study of surveillance of medicinal product quality authorised through mutual recognition procedure (MRP);

- 1 study of surveillance of medicinal product quality (MSS).

These activities are described under section 7.1 c).

12. The Information, Logistics and Electronic Management of Data

The Information, Logistics and Electronic Management of Data Department is structured as follows:

- Information and Logistics Service
- Data and Document Management Service
    - Registry – Document Distribution and Release Service
    - Inter/Intra-Departmental Communications Office.

In 2010 as well, the Logistics and Information Service managed to maintain optimum parameters of communication channels with the EMA and provide real-time information exchange between the agency and its external collaborators (MAHs, distributors, healthcare professionals, patients, organisations and associations).

In 2010, the database applications programming was continued, namely amendments to the structure of the Product Index of medicinal products for human use, designed to optimize the work in the field and meet the new requirements arising from its use; moreover, statistical data reports were extracted periodically at the request of the Minister of Health, the National Health Insurance, the NMA/NAMMD President and various departments of the Agency.

Throughout the year, continued connection to the European EudraNet network (EudraCT, EudraLink, EudraMail, EudraPharm, EudraVigilance, PIM, CTS, EPITT) was monitored.

The maintenance of the NMA website (*www.anm.ro*) and other software applications has been ensured throughout the year (the new NAMMD website has been set up – ongoing project; the NEWCADREAC (*www.newcadreac.org*), the Agency's new intranet website has been maintained, modified and updated.

Maintenance and administration of NMA/NAMMD servers (folder servers, web-intranet servers, internet servers for several services, accounting servers) have been ensured.

Also, maintenance and troubleshooting of software and hardware of existing computers was performed, as well as the installation and configuration of new computers purchased in 2010.

The NOD 32 antivirus program and other security programs have been maintained and administered on the Agency's servers.

The Data and Document Management Service ensures receipt of documents in the Agency and their distribution to the concerned offices, release of all documents in the Agency to external collaborators to facilitate swift movement of

documents among Agency departments.

The Documents release bureau provided the drafting of Marketing Authorisations (MA), of annex 4 "qualitative and quantitative data on the composition of the medicinal product" and annex 5 "drug manufacturing data" for the 813 drugs approved for authorisation.

Also, the writing of:

- 42 President Decisions on MA discontinuation of 177 medicinal products, following implementation of the "*sunset clause"*.
- 84 Decisions on withdrawal/discontinuation of MAs issued for 202 medicinal products (MA withdrawal for medicinal products authorised through national procedure, replaced by MAs issued through European procedure; discontinuation of a valid MA at the request of the company).

381 product certificates in WHO format for Romanian medicinal products have been released upon request.

860 payment confirmations have been received for marketing authorisation/renewal applications.

47 meetings of the Marketing Authorisation Commission(s) have been organised and 1172 product dossiers have been assessed.

13. **Ensurance of setup and implementation of NMA/NAMMD policies and strategies**

The Department for policies and strategies (DPS), resulting from reorganisation and renaming of the NMA structures, is composed of:

- The European Affairs Service
- The Communication, institutional relations and pharmacopoeia service.

In 2010, the Policies and Strategies Department contributed to fulfilment of the NAMMD mission, among others, by drafting policies and strategies of the Agency in its fields of activity, namely:

- *The organisational strategy:*
- establishes the strategic objectives and guidelines for Agency work, in accordance with the legal framework in force;
- establishes the relationship between the NAMMD and the Ministry of Health, as well as the relationship between the NAMMD and stakeholders;
- covers a 5-year period and is updated yearly.
- *The Communication strategy:*
- establishes the Agency's objectives concerning internal and external communication for a 5-year period;
- is updated yearly.

Together with the other professional departments, the PSD participated in the proper functioning of the NAMMD within the European network of competent authorities in the field of the medicinal product, acting as connection between the Agency and the European and international authorities in this field, through:

- handling and monitoring the participation of NAMMD staff assigned as

full members or alternates in scientific committees and working groups of the EMA, HMA, EDQM, European Council, EU Council, European Commission, the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S);

- ensuring communication with the EMA for assignment of NAMMD experts as full members/alternates;

- communicating with the secretariats of working groups/scientific committees of the cited bodies for transmission of forms, as well as through:

- acting as connector among the various NAMMD departments, through monthly monitoring/centralisation of the attendance of assigned NAMMD experts in the meetings of working groups/committees to the attention of the Economic Department.

The same as in the previous year, the PSD managed to ensure secretariat activity of the NAMMD Scientific Council (SC) and organise (in accordance with interdepartmental SOP) the 5 SC meetings through:

- centralisation and check-up of 33 SC draft decisions, setup of the SC agenda, forwarding of documents to SC members in electronic format or on paper;

- handling of electronic versions of SCDs from draft to publication (both in the Official Gazette of Romania, Part I, for SCDs approved through Order of the Minister Health, as well as on the NAMMD website, under the headings "Legislation" and "Newsletters") in the directories for Scientific Council meetings;

- dispatch of the assessed documents in electronic format/on paper to SC members;

- updating the record of contact coordinates of SC members;

- elaborating the minutes of SC meetings;

- of the 33 SCDs approved in 2010, 31 have been posted on the NAMMD website and published in the Agency's bilingual Newsletters

The Policies and Strategies Department prepared, issued/ensured the final check-up for publication on the Agency's website for:

- 121 regulatory documents, in Romanian and English;

- 65 amendments, supplementations, withdrawal of legislative documents published on the website;

- the form and editorial style of applications and forms to be posted under the heading <Forms> on the website;

- NAMMD Newsletters in English and Romanian;

- the bilingual brochure containing NAMMD's annual report.

Development of the NMA Newsletters was continued; these were posted on the NMA/NAMMD website, namely: 3 issues in Romanian (No.: 4/2009, 1/2010, 2/2010).

Delays, for objective reasons, of newsletter translation into English were recovered and 7 issues issues were completed (No.: 2/2008, 3/2008, 4/2008, 1/2009, 2/2009, 4/2009, 1/2010).

In collaboration with NMA departments, the PSD participated to update and improve information contained on the Agency's website as well as the NAMMD

intranet.

The brochure containing the NMA Annual Report for 2009 was developed and presented bilingually and with enhanced graphic and illustrative material.

In 2010, the PSD helped to ensure transparency of NAMMD activity in accordance with provisions of Law no. 95/2006, Title XVII – The medicinal product, Art. 845 (2) and 726 (4) on transparency in the activity of EU competent authorities in the medicinal product field, through:

- The setup, upon request, of the publicly available version for one assessment report for a medicinal product authorised through national procedure and

- The verification of the translation into English of public versions of 31 European Public Assessment Reports (EPARs) through mutual recognition procedure and decentralised procedure, with Romania as interested member state.

The European Affairs Service ensured, via its trained staff:

- translation of Directive 2009/102/EC on amendment of Directive 2001/83/EC of the European Parliament and of the Council on the community code relating to medicinal products for human use concerning advanced therapy products;

- translation/verification of the translation of 6 European Guidelines;

- Checking translation into English of 31 evaluation reports and documents, the mutual recognition procedures and decentralised procedures;

- Checking / translating into English of 110 EMA press releases, questions and answers documents and DHPCs from the EMA as well as action lines proposed by the EMA ("Lines to take") etc.

- Providing advice for verification of translation of SmPCs and leaflets, mail exchanges in English with European bodies;

- Linguistic assessment of EMA's proposals of translation into Romanian of various specialised legislative terms related to the medicinal product and proposal of terms agreed by the NAMMD.

In line with the NMA/NAMMD Communication Strategy, the following activities have been performed in 2010:

- Internal and external communication, namely statements, communication with the written media and the television (by telephone, e-mail, broadcast interviews), relationships with other Romanian and foreign institutions specialised in this field;

- Free access was ensured to public information in accordance with Law 544/2001, *ex officio* and/or upon request, both to the media, and to the general public, providing information on NAMMD activities or information on the safety of medicinal products for human use;

- Cooperation with all NAMMD departments to ensure transparency of the Agency's activity by providing public accessibility/availability, namely passive transparency by ensuring reactive information upon request;

- Notification of media representatives and/or other applicants according to

the deadlines imposed by the norms in force, if the required information is already communicated *ex officio* as per Art. 5 of Law no. 544/2001, also stating where the required information can be found;

- Notification of the applicant, according to deadlines imposed by the norms in force, if the required information is identified as exempt from free access;

- Cooperation with all NAMMD departments in order to gather and organise information required by the media and/or the stakeholders, for drafting the required answer;

- The set up/verification and broadcast of official NAMMD communications and statements to the media;

- Participation in the drafting and submission of mail exchanges with internal and external partners, related to issues specific to NAMMD activity;

- Daily monitoring of the mass-media (TV press and written press) in the field of healthcare.

The first steps have been taken to set up a strategy to attract and involve patients and the public for enhanced communication and information, by counselling and cooperation, namely:

- Identification of the NMA need to provide general information on generic versus original/innovator medicinal product, as well as on counterfeiting-related issues, following the frequent misperception of patients related to generic and counterfeit medicinal products;

- Organisation of a meeting of the Agency's management with the representatives of the Romanian Coalition of Patients with Chronic Diseases (COPAC), to identify patients' needs and expectations and possibilities of cooperation in the context of the Agency's activities;

- Forwarding (in the context of the COPAC meeting in June 2010) the dossier related to generic versus original medicinal product, as well as to counterfeiting-related issues, emphasising that generics are therapeutic equivalents of original medicinal products, with the advantage of a cheaper price, thus representing a «crisis» solution for social health insurance systems.

More than 550 e-mails received from permanent representatives of Romania to the EU and / or Ministry of Health were monitored / handled in electronic records, regarding participation of NMA/NAMMD experts assigned to working groups of the European Council, to the Pharmaceutical Committee and the Standing Committee of the European Commission and redirecting them to experts appointed by the NMA/NAMMD.

The electronic theme database of documents under debate received from the Permanent Representation of Romania to the EU and/or from the Ministry of Health, set up in 2009, has been maintained in 2010.

E-mails received from the Representation referring to European Commission (EC) Decisions concerning medicinal products authorised conditionally (according to Art. 127a of Directive 2001/83/EC), MA suspension/withdrawal/amendment (according to Art. 107 of Directive 2001/83/EC) and decisions issued following referrals (according to Art. 29, Art. 30, 31, 32, 33, 34 and 35 of Directive

2001/83/EC) have been monitored/handled into an electronic database and forwarded to NMA/NAMMD specialists assigned for their implementation.

Electronic records have been set up for 25 European Commission Decisions, received on paper version from the Ministry of Foreign Affairs / Ministry of Health in 2010.

Secretariat work was provided for activities of the commission for crisis situations; 9 minutes of the commission meetings have been prepared.

The minutes of Agency management operation meetings have been set up upon request.

14. **Legal work of the NMA/NAMMD**

In 2010, from the organisational of view, the Legal Department functioned during the first 4 months, in the following structure:

- The European Legislation Service;
- The National Legislation Service;
- The Administrative Legal Service.

Subsequently, following reorganisation measures imposed by the chief credit accountant, namely the Ministry of Health, the three services were merged; the structure has been maintained even after the institution's reorganisation by merger with the TOMD.

The legal department has covered a wide range of legal relationships, both in terms of legal relations within the institution and those of the NMA and other legal entities, public or private.

Regarding the areas addressed, these were aimed at activities and actions related to all branches of positive law - mainly labour law, civil law, civil procedure, administrative law, financial law, tax law, administrative etc.

Via activities conducted in 2010, the Legal Department cooperated with all departments of the institution.

Thus, the following have been performed:

a) Various mail exchanges – 305 documents;
b) President Decisions – 324, 136 – NMA and 188 - NAMMD;
c) Solved administrative enquiries – 3;
d) Minutes of Administrative Council meetings – 6, of which 4 of the NMA Administrative Council and 2 of the NAMMD Administrative Council;
e) Administrative Council Decisions – 42, 27 of the NMA and 15 of the NAMMD.

Thematically speaking, AC Decisions managed to cover various issues related to current activities; due to the given circumstances, the main weight rested with orders whose regulatory scope were organisational issues – gradual changes in the institution's structure, in the collective labour contract at unit level, approval of the job list and of the organisational structure, other aspects of current work.

In the context of the activity performed, the Legal Department set up the documentation concerning the institution's regulatory initiatives, promoted through

the main credit accountant, namely the Ministry of Health. Thus, documentation has been prepared to promote a ruling document for supplementation of Law 95/2006 on healthcare reform, of a Government Decision (regulatory scope: the organisation and operation of the NAMMD – Romanian Government Decision no. 734/2010), and of 5 Orders of the Minister of Health.

At the same time, documentation has been prepared concerning the addendum to the collective labour contract at unit level, submitted to the Territorial Labour Inspectorate of Bucharest.

The institution was also represented within law courts; there have been 4 litigations in 2010, one of which is still under appeal. As in previous years, the institution has not suffered patrimonial or financial losses following litigations solved in 2010.

Together with other departments, the Legal Department too contributed to prevention of medicinal product counterfeiting and of illegal marketing of counterfeit medicinal products; it informed and warned the public and also developed cooperation with other institutions and bodies involved in this activity.

For better information of the public this year, the NMA/NAMMD website heading "Counterfeiting" contained notifications of counterfeiting reported via the rapid alert system.

The NAMMD has continued cooperation, initiated through a protocol in 2009, with the Directorate for Investigation of Organised Crime and Terrorism (DIICOT) in view of combating counterfeit medicinal products and their illegal trade.

This step ensured continued setup of the implementation framework for the provisions of the future European Directive concerning entry into the legal supply chain of falsified medicinal products in terms of identity, history or source, now a draft under EU Council debate including the NMA/NAMMD appointed representative presenting and supporting the views of Romania.

15. **Management of human resources**

15.1. **Human resources policy**

In 2010, the dynamic of main activities included as key objectives of the Human Resources and Payroll Department managed to:

- Ensure the human resources at the level of NAMMD structures, especially in those sectors where a lack of qualified staff with higher education (particularly medico-pharmaceutical) has been detected, to properly ensure coverage of poorly staffed positions in specialised departments, which practically ensure accomplishment of the Agency's main work.
- Develop human resources through employee training, i.e.:
  - Training and improvement of existing specialised personnel, to benefit from highly qualified specialists, able to deal with the entire range of assignments and tasks in the NAMMD scope of work;

- Training and improvement of NAMMD personnel, performed in accordance with yearly plans fully established at department level, depending on each employee's activity and training. Training has been performed for newly hired employees and has been constantly performed both inside and outside the NAMMD by institutions specialised in various fields of activity, such as: quality assurance management (ISO 9001:2000), training specific to pharmaceutical inspection, financial-accounting legislation etc. Moreover, there has been active participation with studies at various symposia, congresses in the medicinal product field, as well as the remarkable participation of NAMMD experts to working groups of international bodies in the medicinal product field.

- Career administration, aiming to ensure long-term agreement between the employees' career improvement needs and jobs available in the Agency;

- Organisational development, aiming to train employees in terms of anticipation, change initiation and management.

Throughout 2010, staff motivation could not be performed by wage-related compensations (bonuses, pay rises etc.) for special professional merits.

- A motivational endeavour consisted of stimulating the assigned persons to show their ability in performing tasks and responsibilities required by management jobs.

- Another motivational endeavour consisted of setting up an adequate system for assessment of performances;

- The organisational structure substantially altered in 2010 following Government Emergency Ordinance no. 72/2010 on the set up of the NAMMD by merger of the National Medicines Agency with the Technical Office for Medical Devices; the new organisational structure has been approved through Order of the Minister of Health no. 1275/2010. The new structure aimed to:

- Ensure smooth communication between organisational structures, cooperation, task accomplishment, supply distribution and decision making in the most effective manner.

15.2. **Ensuring Human Resources within NMA/NAMMD structures**

As regards accomplishment of the goal of the Human Resources Department, reorganised in 2010 into the Human Resources and Payroll Department**,** concerning securing of qualified personnel, it is worth mentioning that, starting with April 2009 and throughout 2010, this was obviously hampered by the legal framework set up through Government Emergency Ordinance no. 34/2009 on the rectification of the budget for 2009 and regulating certain financial-fiscal measures. This refers particularly to provisions of Art. 22 of Chapter II "Measures on public expenditure" providing for "suspension of employment proceedings by examination or contest for vacant positions in public institutions".

Moreover, the negative impact on the management of human resources was doubled by the unfavourable economic circumstances at legislative level by Law

118/2010 on certain measures necessary to restore the budgetary balance, stating that wages were diminished by 25%. The implementation of the respective legislative-economic measures led to leave of 38 employees from the NAMMD.

As a consequence, following legal provisions in force in 2009 and 2010, the lack of staff recorded as of 2009 was enhanced by termination of many individual labour contracts. Specification should be made however that the only positions allowed for temporary use by the Ministry of Health, have been those with individual labour contracts suspended for strictly determined periods.

15.3. **Development of human resources through employee training and improvement**

Apart from participation in activities organised by various European institutions and bodies, the best manner to maintain the NMA/NAMMD connected to European activities in the medicinal product field was for the Agency's specialised personnel to yearly benefit from both an ongoing training program, specific to professional development, at the site of the Agency, and from training organised nationally and internationally by various authorities and bodies in the field:

- participating in a GMP course organised by the Centre for Professional Advancement in Bucharest, June 2010;
- participating in the course "Reference standards, impurities, pharmacopoeias and solvents" organised by the LGC Standards, Bucharest, November 2010;
- participating in the course "PK Assessors Training on a New Bioequivalence Guideline" organised by the EMA, June 2010;
- participating in the course for pharmacovigilance inspectors organised by the EMA, Belgium, November 2010;
- participating in the course for EMA GCP inspectors, London, November 2010;
- participating in the course concerning the 7th edition of the European Pharmacopoeia, - Istanbul, Turkey, December 2010.

16. **Financial activity**

In 2010, the Economic Department developed and managed a balanced budget of revenues and expenses from the state budget, as follows:

- NMA 10,455,000 lei
- TOMD 1,560,000 lei
- NAMMD 9,676,000 lei

TOTAL 21,691,000 LEI

The expenditure amounted to the following sums:

- NMA 10,148,973 lei
- TOMD 1,559,658 lei

- NAMMD 8,847,084 lei
TOTAL 20,555,715 LEI

of which:

staff costs.

- NMA 8,741,858 lei
- TOMD 1,044,031 lei
- NAMMD 4,676,058 lei
TOTAL 14,461,947 LEI

to cover goods and services.

- NMA 1,407,115 lei
- TOMD 515,627 lei
- NAMMD 1,632,662 lei
TOTAL 3,555,404 LEI

capital expenditure.

- NAMMD 2,538,364 lei
TOTAL 2,538,364 LEI

All expenses were within the approved budget for 2010 in accordance with the legal provisions on economic and financial discipline.

The data reveals a balance between NMA/NAMMD revenue and expenditure, held in compliance with the budgetary principles and rules according to Law 500/2002 on public finance and in conjunction with specific legislation in force.

From an organisational perspective, in 2010, the Economic department has undergone several transformations and modifications in terms of management of the department and personnel, as well as in terms of the activities performed (NMA/TOMD closing balance, assuming balance accounts in accordance with the protocols and set up of NAMMD opening balance, merging of inventories in accordance with the protocols, establishment of the new NAMMD budget, closure of NMA accounts and opening of new accounts for the NAMMD).

All financial activities were conducted in the Economic Department, ensuring optimal and efficient performance of payments and receipts in the business.

In 2010, through its financial-accounting activities, the Economic Department provided proper performance of their objectives.

17. **General administration**

In 2010, the General Administration Department (GAD – set up in 2010 through reorganisation of the former General Administration and Payroll Department - GAPD) managed to fulfil its objectives and deal in a prompt and efficient manner with requests submitted by NMA/NAMMD structures. Thus, GAD most substantial achievements consisted of performance and completion of activities related to the endowment and refurbishment of the NAMMD building.

The most important acquisitions have been:

- **The controlled access system in the building of NAMMD headquarters;**
- **Video surveillance systems (for both the headquarters and 20, Demostene Street), purchased to ensure safe and effective measures to protect the location, by eliminating the possibility of unauthorised persons entering areas** containing secret or confidential documents.

Due to the department's structure, namely to the diversity of assignments of services/departments located in its structure, GAD employees were directly involved in the reorganisation of the NMA/NAMMD:

- the GAD took part in the rearrangement of organisational structures in the NMA/NAMMD headquarters;
- In 2010, the DGAH initiated and completed the relocation of the Biological Product Evaluation and Control Department from its headquarters located in Demostene street to the NMA headquarters; this move resulted in creation of an optimal environment for laboratory work, and resolution of the problem of biological samples transportation from the former location to the NMA headquarters. The area vacated in Demostene street is used to expand the NMA/NAMMD archive.

The Public Acquisitions Service organised and tracked the planning, performance and acquisition of products, services and works needed for proper functioning of the NMA/NAMMD activity, consistent with its needs and objectives and with the approved budget, developing documents needed for all types of procurement.

Throughout 2010, 133 public acquisition contracts and 165 additional documents were signed; utility contracts, rental of areas, various services (for all NMA/NAMMD sites – 63 contracts) were handled.

18. **Internal audit**

The internal audit structure set up at NAMMD level is subordinated to the NAMMD president, thus ensuring the freedom needed to perform internal audit activities, in view of objective assessment of deficiencies detected at the Agency's audited departments and provision of adequate recommendations.

In 2010, 2 audit missions were conducted in accordance with the yearly internal audit plan.

The risks of potential impact upon the activity performed by the NMA/NAMMD throughout the period under assessment were organisational, operational, juridical and financial in nature.

Pursuant to legal requirements, a report on activities of the Internal Audit Office last year was submitted to the Ministry of Health.

19. **Difficulties encountered**

- Lack of higher education staff, employed full time, increased by the doubled assessment work due to Romania's accession to the European Union and initiation of authorisation of medicinal products through decentralised, mutual recognition and/or “repeat use“ procedure with Romania as a Reference member state.

- Lack of specialised literature needed in view of assessing clinical documentation and specialised training courses.

- Difficult archiving system and insufficient archiving space.

20. **Priorities for 2011**

As every year, the NAMMD formulated its priorities in the end of 2010 for the coming year, 2011:

- Ensuring proper performance of NAMMD objectives, as stipulated in the Regulation on the organisation and operation, supplemented with other tasks related to the field of medical devices, such as:

- Maintaining a high level of performance and security of medical devices when using healthcare networks throughout the country, regardless of the property right upon them;

- Exigent assessment of technical – medical units dealing with medical devices, so that any type of stenting or fixing and maintenance services for medical devices can be performed at optimal quality and competence level;

- The set up of specific technical procedures in the field of medical devices.

- Permanent contribution to the elaboration of secondary legislation in the field of medical devices.

- Strengthening the prestige acquired domestically and internationally through high quality performance with both internal and external partners;

- Meeting of all obligations in relation with internal and external partners, working closely with the specialist directorate of the Ministry of Health, the National Health Insurance House, other state competent authorities, active participation in actions and activities of the EMA, PIC/S and other specialised bodies to which the NAMMD is affiliated;

- Ensuring adequate human and financial resources for sound operation;

- Supplying NAMMD employees with efficient and reliable computers with intranet and internet connection;

- Producing a complete integrated software that is versatile, multitasking, to manage medicinal product information throughout their lifecycle;

- Attracting young specialised personnel for training and specialisation;

- Continuation of personnel training at the workplace, in Romania and abroad, in view of professional improvement and thorough operation according to the European system;

- Strict adherence to the law in all fields of activity and implementation of medicinal products legislation, in accordance with Law no. 95/2006 on healthcare reform, as amended;

- Continuous improvement of the quality management system;

- Ensuring proper communication with all partners in the pharmaceutical field (manufacturers of innovative and generic medicinal products, importers, distributors), with patient organisations, associations of companies which coordinate clinical trials etc., in view of ensuring transparency;

- Continuation of preparations on institution level for the audit concerning quality management system to be conducted by EMA experts in May 2011 - Benchmarking European Medicines Agencies (BEMA), a complex activity requiring accurate, realistic self-assessment.

Moreover, year 2011 will involve:

- Initiation of transposition into Romanian legislation of two new European directives, one referring to a new approach of pharmacovigilance and the other to the prevention of the entry of falsified medicinal products into the supply chain, both amending the community code of the medicinal product for human use (Directive 2001/83/EC).

The NAMMD shall also consider:

- Update of its strategies (organisational and communicational);

- Set up of new Regulations on advertising of medicinal products for human use in line with provisions of Directive 2001/83, of the Guideline on evaluation of advertising of medicinal products for human use (approved through NAMMD SCD) and, simultaneously, to settle all aspects for correct, non-misleading advertising, whether it addresses the general public or healthcare professionals.

- Organisation of meetings with representatives of all stakeholders (manufacturers, distributors) to establish regulatory measures for implementation of a tracking system for a medicinal product, identification of all elements which can represent a starting point in finding reliable solutions for implementation in Romania;

- Revision of the Medical Devices List for periodic control, so that it solely contains devices with maximum risk for patients and users.

- Revision of Order of the Minister of Health no. 1636/2004 on approval of Methodological Norms for implementation of Law no. 176/2000 concerning medical devices, as amended, referring to medical technical units, in order to explain certain issues leading to various interpretations of this Order and the performance of steps, determining the main credit accountant to understand the need to hire more staff for more efficient management of implementation of Law 176/2000 at national level.

- Revision of Government Decision no. 734/2010 so as to exclude the Technical Office for Medical Devices (Certification of medical devices and management systems which no longer meet the accreditation requirements and cannot maintain their status as accredited body) from the NMA; a legally enforced entity, with a documented structure able to grant equity in fulfilling accreditation conditions is required.

CONCLUSIONS

In 2010, the NMA/NAMMD managed to dutifully fulfil its tasks and duties as a national competent authority in the medicinal product field, even in the context of the international financial crisis.

It is a well-known fact that the institution suffered major transformation throughout the past two years.

Several changes were made in 2009 in the internal structure of the Agency, starting from the manner of structuring and functioning of the European Medicines Agency (EMA), to optimise its activity.

If, by the end of 2009, the National Medicines Agency (NMA) was reorganised as a public institution wholly financed from state budget, in accordance with Law 329/2009 on reorganisation of certain public authorities and institutions, in 2010, in line with Emergency Government Ordinance no. 72 of June 2010, the NAMMD was founded by merging the NMA with the Technical Office for Medical Devices. The organisation and functioning of the NAMMD was subsequently established through Government Decision no. 734 of July 2010.

As a consequence, the Agency managed to accomplish its mission, supplemented with other tasks related to the field of medical devices, even under the circumstances of the reorganisation imposed by the severe financial crisis.

In 2010, through management's permanent availability for cooperation and communication, in view of creating the conditions required for the manifestation of its human resources at full professional capacity, through the efforts undertaken by the Agency's staff (experts and auxiliary staff), the NMA/NAMMD managed to maintain its status as regulatory, competent European authority, entirely in line with community requirements, active member in committees and working groups related to the medicinal product for human use.

The activity of the Agency continued at the same pace in line with current requirements: assessment and marketing authorisation of medicinal products, Good Manufacturing Practice (GMP) inspections, Good Distribution Practice (GDP) inspections, Good Clinical Practice (GCP) inspections, **Good Analytical Laboratory Practice** (GALP) inspections, pharmacovigilance, providing stakeholders (healthcare professionals, media, patients and, last but not least, the general public) with the latest and most accurate information concerning medicinal products.

In 2010, after merging with the Technical Office for Medical Devices, the NAMMD became the single institution able to assess performance and safety of medical devices in use. The new control activity, namely periodic check-up of medical devices, was, thus, carried out for all installed and commissioned medical devices, characterised by a high risk degree, at the sites of all medical device users, both in the private and public field.

The organisations' ability to perform the services requiring approval of the Ministry of Health was also assessed; activities related to optics, operation, fixing, maintenance and stenting (auditory, orthopaedic, and other) of medical devices

were assessed.

The NAMMD has a solid Quality Management System (QMS), based on international standards *9001*, *9004*, *17025* etc. in force. The Agency's top management showed particular interest in QMS-related activities, being preoccupied with the implementation of the process-based approach.

In 2010, the NAMMD and the Competition Council continued their cooperation in accordance with the cooperation protocol signed to ensure and promote competition in the field of the medicinal product for human use, in accordance with provisions of Law no. 21/1996 on Competition, forbidding competition limitation, prevention or adulteration on the Romanian pharmaceutical market. This document aimed to establish ways to enforce and maintain a balanced pharmaceutical market, without prejudice to any of the participants, be it manufacturer (of innovative/generic medicinal products), importer or supplier.

The Agency is one of the decision factors in the field of the medicinal products for human use and this status intends to promote the involvement in all regulatory to attain balance on the medicinal product market, in accordance with the European Commission recommendation, for the good of the final consumer: the patient.

Medicinal product batches recalled during the 4th quarter of 2012

Crt. No.	Product recalled	Pharmaceutical form	Strength	INN	Manufacturer/ MAH	Batch	Grounds for recall	Action proposed	Date of withdrawal
1	OSPAMOX	powder for oral suspension	125mg/ 5ml	amoxicillinum	Sandoz GmbH Austria	BF2270, AS1471, AV4734, AW6821, AW6822, BD4674, BD4675, BG4921, BG4923, BH8487, BL4054, BL4055, BP4428, BP4427, BT1320, BT1321, BW4711, BY1061, BY1060, BY9528, BZ2292, CD2772, CG9691	Out-of-specification results obtained during stability studies (water content, amoxicillin dimer impurity, impurity 2, unknown impurities)	Recall and destruction	26.10.2012
2	RUTINOSCORBIN	film-coated tablets	25 mg/ 100 mg	rutozidum+ acidum ascorbicum	GlaxoSmithKline Pharmaceuticals S.A., Poland	PC1608	Voluntary recall by MAH in accordance with Order of the Minister of Health no. 279/ 30.03.2005	Voluntary recall and destruction	05.11.2012
3	CAELYX 2 mg/ml	concentrate for solution for infusion, 1 vial x 25 ml	2 mg/ml	doxorubicinum	SP Labo NV, BELGIUM/Janssen Cilag Internationali NV, Belgium	BDZ0100, BDZ0101, BFZ0G00, BHZ1900	Recall at wholesale distributor level, following EMA (CHMP) decision	Recall at wholesale distribution level and destruction	28.11.2012
4	CAELYX 2 mg/ml	concentrate for solution for infusion, 1 vial x 10 ml	2 mg/ml	doxorubicinum	SP Labo NV, BELGIUM/Janssen Cilag Internationali NV, BELGIUM	BFZ0Y00, BFZ1300, BHZ1B00, BIZ0800,	Recall at wholesale distributor level, following EMA	Recall at wholesale distribution level and	28.11.2012

Crt. No.	Product recalled	Pharmaceutical form	Strength	INN	Manufacturer/ MAH	Batch	Grounds for recall	Action proposed	Date of withdrawal
						BIZ0A00,	(CHMP) decision	destruction	
5	LERPIN	film-coated tablets	10 mg	lercanidipinum	Torrent Pharma GmbH, GERMANY/ Torrent Pharma S.R.L.	BM392025	Inconsistency between the approved leaflet (Annex 1 to MA no. 319/2010/08) and secondary packaging leaflet)	Voluntary recall and destruction	29.11.2012
6	LIPANOR	capsules	100mg	ciprofibrate	Sanofi-aventis Romania	all	Marketing authorisation withdrawal on MAH request	Voluntary recall and destruction	17.12.2012
7	TICLID	film-coated tablets	250mg	ticlopidine	Sanofi-Aventis Romania	all	Marketing authorisation withdrawal on MAH request	Voluntary recall and destruction	17.12.2012
8	BENGAY GREASESALESS	cream	-	combinations	Mcneil Products Limited C/O Johnson&Johnson - Great Britain	0971V A.1, 1031V A.1, 1241V B.2, 1821V A.1, 3220V A.1, 3220V B.3, 3221V A.1, 3420V A.1	Product manufactured prior to the expiry of the one-year period after approval of Marketing Authorisation transfer	Voluntary recall and destruction	19.12.2012
9	SUDAFED	film-coated tablets	60mg	pseudoephedrine	Mcneil Products Limited C/O Johnson&Johnson - Great Britain	PK0655, RB0372, RB0373, RE1038	Product manufactured prior to expiry of the one-year period after approval of Marketing Authorisation transfer	Voluntary recall and destruction	19.12.2012
10	PROCTO-GLYVENOL	cream	5%/2%	tribenozidum/ lidocainum HCL	Recordati Romania S.R.L.	K01738A, K02536A, L01245B, L01654A, K02537A, K02560A, K02914A, K02561A,	Product manufactured prior to approval of MA transfer no. 6055/2005/01 from Novartis Consumer Health GmbH to Artmed	Voluntary recall and destruction	27.12.2012

Crt. No.	Product recalled	Pharmaceutical form	Strength	INN	Manufacturer/ MAH	Batch	Grounds for recall	Action proposed	Date of withdrawal
						K02562A, K02914A, K02953A, K00771A, K01737B, K01995A	International S.R.L. (currently Recordati Romania S.R.L).		
11	PROCTO-GLYVENOL	suppository	400mg+ 40mg	tribenozidum/ lidocainum	Recordati Romania S.R.L.	H5090, H5089, H5084, H5095, H5087, H5091, H5093, H5094, K02269A	Product manufactured prior to approval of MA transfer no. 6054/2005/01 from Novartis Consumer Health GmbH to Artmed International S.R.L. (currently Recordati Romania S.R.L).	Voluntary recall and destruction	27.12.2012

Applications for marketing authorisation/marketing authorisation renewal submitted to the NAMMD during the 3rd quarter of 2012

During the 3rd quarter of 2012, 397 marketing authorisation/renewal applications for medicinal products corresponding to the following therapeutic groups have been received:

A01 – Stomatological preparations
A02 – Drugs for acid related disorders
A05 – Bile and liver therapy
A07 – Antidiarrheals, intestinal anti-inflammatory – anti-infective agents
A11 – Vitamins
B01 – Antithrombotic agents
B03 – Antianemic preparations
B05 – Blood substitutes and perfusion solutions
C01 – Cardiac therapy
C03 – Diuretics
C04 – Peripheral vasodilators
C05 – Vasoprotectives
C07 – Beta blocking agents
C09 – Agents acting on the renin-angiotensin system
C10 – Lipid modifying agents
D01 – Antifungals for dermatological use
D07 – Corticosteroids, dermatological preparations
D11 – Other dermatological preparations
G02 – Other gynecologicals
G03 – Sex hormones and modulators of the genital system
G04 – Urologicals
H02 – Corticosteroids for systemic use
H05 – Calcium homeostasis
J01 – Antibacterials for systemic use
J05 – Antivirals for systemic use
L01 – Antineoplastic agents
L02 – Endocrine therapy
M01 – Anti-inflammatory and antirheumatic products
M05 – Drugs for treatment of bone diseases
N01 – Anesthetics
N02 – Analgesics
N03 – Antiepileptics
N04 – Anti-parkinsonian drugs
N05 – Psycholeptics

N06 - Psychoanaleptics
N07 - Other nervous system drugs
R03 – Drugs for obstructive airway diseases
R05 – Cough and cold preparations
R06 – Antihistamines for systemic use
S01 - Ophthalmologicals
V01 – Allergens
V03 - All other therapeutic products
V09 - Diagnostic radiopharmaceuticals

Medicinal products authorised for marketing by the NAMMD during the 3rd quarter of 2012

INN	Invented name	Pharmaceutical form	Strength	Manufacturer	Country	MA Number		
OMEGA-3-ACID ETHYL ESTER	OMEGA 3 SANDOZ 1000mg	soft capsules	1000 mg	SANDOZ S.R.L.	ROMANIA	5016	2012	16
OMEGA-3-ACID ETHYL ESTER	OMLIPEX 1000 mg	soft capsules	1000 mg	SANDOZ S.R.L.	ROMANIA	5009	2012	10
ACIDUM ASCORBICUM	VITAMEDI 750 mg/5 ml	solution for injection	750 mg/5ml	PROMOMED S.R.L.	ROMANIA	4907	2012	03
ACIDUM IBANDRONICUM	IBANDRONIC ACID TEVA 3 mg	solution for injection in pre-filled syringe	3 mg	TEVA PHARMACEUTICALS S.R.L.	ROMANIA	4811	2012	01
ACIDUM IBANDRONICUM	IBANDRONIC ACID TEVA 2 mg	concentrate for solution for infusion	2 mg	TEVA PHARMACEUTICALS S.R.L.	ROMANIA	4809	2012	01
ACIDUM IBANDRONICUM	IBANDRONIC ACID TEVA 6 mg	concentrate for solution for infusion	6 mg	TEVA PHARMACEUTICALS S.R.L.	ROMANIA	4810	2012	02
ACIDUM IBANDRONICUM	IBANDRONAT BLUEFISH 150 mg	film-coated tablets	150 mg	BLUEFISH PHARMACEUTICALS AB	SWEDEN	4819	2012	02
ACIDUM IBANDRONICUM	IBANDRONIC ACID POLPHARMA 3 mg	solution for injection in pre-filled syringe	3 mg	PHARMACEUTICAL WORKS POLPHARMA SA	POLAND	5008	2012	01
ACIDUM RISEDRONICUM	RISEDRONAT ARENA 5 mg	film-coated tablets	5 mg	ARENA GROUP S.A.	ROMANIA	4930	2012	03
ACIDUM RISEDRONICUM	RISEDRONAT ARENA 30 mg	film-coated tablets	30 mg	ARENA GROUP S.A.	ROMANIA	4931	2012	03
ACIDUM RISEDRONICUM	RISEDRONAT ARENA 35 mg	film-coated tablets	35 mg	ARENA GROUP S.A.	ROMANIA	4932	2012	03
ACIDUM ZOLEDRONICUM	ZYOLIX 4 mg/5 ml	concentrate for solution for infusion	4 mg/5 ml	ROMASTRU TRADING S.R.L.	ROMANIA	4951	2012	03
ACIDUM ZOLEDRONICUM	ZACIDATE 4 mg/5 ml	concentrate for solution for infusion	4 mg/5 ml	MEDICO UNO WORLDWIDE (CYPRUS) LTD.	CYPRUS	4878	2012	03
ACIDUM ZOLEDRONICUM	ZALEOST 4 mg/5 ml	concentrate for solution for infusion in pre-filled single dose syringe	4 m/5 ml	ITALFARMACO S.P.A.	ITALY	4917	2012	04
ACIDUM ZOLEDRONICUM	RICHTER, ZOLEDRONIC ACID 4 mg/5 ml	concentrate for solution for infusion	4 mg/5 ml	GEDEON RICHTER ROMANIA S.A.	ROMANIA	4937	2012	03
ACIDUM ZOLEDRONICUM	FRESENIUS KANI,	concentrate for solution	4 mg/5 ml	FRESENIUS KABI	ROMANIA	5022	2012	03

	ZOLEDRONIC ACID 4mg/5ml	for infusion		ROMANIA S.R.L.				
ACIDUM ZOLEDRONICUM	SANDOZ, ZOLEDRONIC ACID 4 mg/5 ml	concentrate for solution for infusion	4 mg/5 ml	SANDOZ S.R.L.	ROMANIA	5010	2012	03
ACIDUM ZOLEDRONICUM	SANDOZ, ZOLEDRONIC ACID 4 mg/100 ml	concentrate for solution for infusion	4 mg/100 ml	SANDOZ S.R.L.	ROMANIA	5011	2012	03
ACIDUM ZOLEDRONICUM	SANDOZ, ZOLEDRONIC ACID 5 mg/100 ml	concentrate for solution for infusion	5 mg/100 ml	SANDOZ S.R.L.	ROMANIA	5012	2012	04
ALBUMINUM HUMANUM	KEDRION, HUMAN ALBUMIN 500g/l	solution for infusion	200 g/l	KEDRION S.P.A.	ITALY	5024	2012	02
ALMOTRIPTANUM	ALMOZEN 12.5 mg	film-coated tablets	12.5 mg	ZENTIVA, K.S.	CZECH REPUBLIC	4835	2012	05
AMLODIPINUM	AMLODIPINA ACTAVIS 5 mg	tablets	5 mg	ACTAVIS GROUP PTC EHF.	ICELAND	4826	2012	12
AMLODIPINUM	AMLODIPINA ACTAVIS 10 mg	tablets	10 mg	ACTAVIS GROUP PTC EHF.	ICELAND	4827	2012	12
AMLODIPINUM	AMLODIPINA CIPLA 5 mg	tablets	5 mg	CIPLA UK LIMITED	GREAT BRITAIN	4970	2012	01
AMLODIPINUM	AMLODIPINA CIPLA 10 mg	tablets	10 mg	CIPLA UK LIMITED	GREAT BRITAIN	4977	2012	01
AMPICILLINUM + SULBACTAM	AMPIPLUS 1000mg/500mg	powder for solution for injection/infusion	1000 mg/ 500 mg	ANTIBIOTICE S.A.	ROMANIA	4772	2012	02
ANASTROZOLUM	ANASTROZOL DR. REDDY'S 1 mg	film-coated tablets	1 mg	DR. REDDY'S LABORATORIES ROMANIA S.R.L.	ROMANIA	4824	2012	06
ATORVASTATINUM	TULIP 30 mg	film-coated tablets	30mg	SANDOZ S.R.L.	ROMANIA	4780	2012	07
ATORVASTATINUM	TULIP 60 mg	film-coated tablets	60 mg	SANDOZ S.R.L.	ROMANIA	4781	2012	07
AZITHROMYCINUM	AZITROMICINA SANDOZ 500 mg	granules for oral suspension in dosage spoon	500 mg	SANDOZ S.R.L.	ROMANIA	4814	2012	01
BENAZEPRILUM	BENAZEPRIL AUROBINDO 10 mg	film-coated tablets	10 mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	4784	2012	11
BENAZEPRILUM	BENAZEPRIL AUROBINDO 20 mg	film-coated tablets	20 mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	4785	2012	11
CAPECITABINUM	CAPECITABINA GLENMARK 150 mg	film-coated tablets	150 mg	GLENMARK PHARMACEUTICALS S.R.O.	CZECH REPUBLIC	4798	2012	06
CAPECITABINUM	CAPECITABINA	film-coated tablets	500 mg	GLENMARK	CZECH	4799	2012	06

	GLENMARK 500 mg			PHARMACEUTICALS S.R.O.	REPUBLIC			
CAPECITABINUM	BINODA 150 mg	film-coated tablets	150 mg	GLAXOSMITHKLIE (GSK) S.R.L.	ROMANIA	4882	2012	01
CAPECITABINUM	BINODA 500 mg	film-coated tablets	500 mg	GLAXOSMITHKLIE (GSK) S.R.L.	ROMANIA	4883	2012	01
CAPECITABINUM	CAPECITABINA INTAS 150 mg	film-coated tablets	150 mg	INTAS PHARMACEUTICAS LIMITED	GREAT BRITAIN	4876	2012	06
CAPECITABINUM	CAPECITABINA INTAS 500 mg	film-coated tablets	500 mg	INTAS PHARMACEUTICAS LIMITED	GREAT BRITAIN	4877	2012	06
CAPECITABINUM	COLOXET 150 mg	film-coated tablets	150 mg	EGIS PHARMACEUTICAS PLC	HUNGARY	4942	2012	06
CAPECITABINUM	COLOXET 300 mg	film-coated tablets	300 mg	EGIS PHARMACEUTICAS PLC	HUNGARY	4943	2012	06
CAPECITABINUM	COLOXET 500 mg	film-coated tablets	500mg	EGIS PHARMACEUTICAS PLC	HUNGARY	4944	2012	06
CAPECITABINUM	CAPECITABINA MEDANA 150 mg	film-coated tablets	150 mg	MEDANA PHARMA SA	POLAND	4945	2012	06
CAPECITABINUM	CAPECITABINA MEDANA 500 mg	film-coated tablets	500 mg	MEDANA PHARMA SA	POLAND	4946	2012	06
CAPECITABINUM	CAPECITABINA FRESENIUS KABI 150 mg	film-coated tablets	150 mg	FRESENIUS KABI ONCOLOGY PLC.	GREAT BRITAIN	5018	2012	02
CAPECITABINUM	CAPECITABINA FRESENIUS KABI 500 mg	film-coated tablets	500 mg	FRESENIUS KABI ONCOLOGY PLC.	GREAT BRITAIN	5019	2012	02
CARVEDILOLUM	CARVEDILOL AUROBINDO 3.125 mg	film-coated tablets	3.125 mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	4836	2012	30
CARVEDILOLUM	CARVEDILOL AUROBINDO 6.25 mg	film-coated tablets	6.25 mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	4837	2012	30
CARVEDILOLUM	CARVEDILOL AUROBINDO 12.5 mg	film-coated tablets	12.5 mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	4838	2012	30
CARVEDILOLUM	CARVEDILOL AUROBINDO 25 mg	film-coated tablets	25mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	4839	2012	30

CARVEDILOLUM	CARVEDILOL ALVOGEN 6.25 mg	tablets	6.25 mg	ALVOGEN IPCO S.A.R.L.	LUXEMBURG	4939	2012	01
CARVEDILOLUM	CARVEDILOL ALVOGEN 12.5 mg	tablets	12.5 mg	ALVOGEN IPCO S.A.R.L.	LUXEMBURG	4940	2012	01
CARVEDILOLUM	CARVEDILOL ALVOGEN 25 mg	tablets	25 mg	ALVOGEN IPCO S.A.R.L.	LUXEMBURG	4941	2012	01
CEFUROXIMUM	APROKAM 50 mg	powder for solution for injection	50 mg	LABORATOIRES THEA	FRANCE	5000	2012	03
CELECOXIBUM	CELECOXIB 100 mg	capsules	100 mg	TEVA PHARMACEUTICALS S.R.L.	ROMANIA	4880	2012	19
CELECOXIBUM	CELECOXIB 200 mg	capsules	200 mg	TEVA PHARMACEUTICALS S.R.L.	ROMANIA	4881	2012	19
CLARITHROMYCINUM	CLARITROMICINA TEVA 250 mg	film-coated tablets	250 mg	TEVA PHARMACEUTICALS S.R.L.	ROMANIA	4918	2012	20
CLARITHROMYCINUM	CLARITROMICINA TEVA 500 mg	film-coated tablets	500 mg	TEVA PHARMACEUTICALS S.R.L.	ROMANIA	4919	2012	20
CLARITHROMYCINUM	CLARITROMICINA TEVA 500 mg	prolonged-release tablets	500 mg	TEVA PHARMACEUTICALS S.R.L.	ROMANIA	4920	2012	12
CLOPIDOGRELUM	CLOPIDOGREL RANBAXY 75 mg	film-coated tablets	75 mg	RANBAXY (U.K.) LIMITED	GREAT BRITAIN	4853	2012	16
CLOPIDOGRELUM	CLOPIDOGREL USV EUROPE 75 mg	film-coated tablets	75 mg	USV EUROPE LIMITED	GREAT BRITAIN	5007	2012	12
COMBINATIONS	PARALEN GRIP	film-coated tablets		ZENTIVA K.S.	CZECH REPUBLIC	4870	2012	04
COMBINATIONS	REHYDRON	powder for oral solution		ORION CORPORATION	FINLAND	4906	2012	05
COMBINATIONS	MOVIPREP	powder for oral solution		NORGINE LIMITED	GREAT BRITAIN	4965	2012	06
COMBINATIONS	INFLUBENE 500mg/12.2mg	powder for solution for infusion	500 mg/ 12.2 mg	TEVA PHARMA-CEUTICALS S.R.L.	ROMANIA	4994	2012	07
COMBINATIONS (ETONOGESTRELUM+ ETINILESTRADIOLUM)	NUVARING 0.120 mg/ 0.015mg per day	vaginal delivery system	0.120 mg/ 0.015mg	NV ORGANON	HOLLAND	4823	2012	02
COMBINATIONS (LATANOPROSTUM+	LATANOPROST/TIMOLOL VELKA 50 micrograms/ml +	eye drops, solution	50 micro-grams/ml+	VELKA HELLAS S.A.	GREECE	4904	2012	03

TIMOLOLUM)	5 mg/ml		5 mg/ml					
COMBINATIONS (LISINOPRILUM+ HYDROCHLOROTHIAZIDUM)	SKOPRYL PLUS 20mg/12.5mg	tablets	20 mg/ 12.5 mg	ALKALOID-INT D.O.O.	SLOVENIA	4900	2012	01
COMBINATIONS (OLMESARTANUM+HCT)	OLMICOMBI 40 mg/12.5 mg	film-coated tablets	40 mg/ 12.5 mg	KRKA D.D., NOVO MESTO	SLOVENIA	4891	2012	09
COMBINATIONS (OLMESARTANUM+HCT)	OLMICOMBI 40 mg/25 mg	film-coated tablets	40 mg/ 25 mg	KRKA D.D., NOVO MESTO	SLOVENIA	4892	2012	09
COMBINATIONS (OLMESARTANUM+HCT)	OLMICOMBI 20 mg/12.5 mg	film-coated tablets	20 mg/ 12.5 mg	KRKA D.D., NOVO MESTO	SLOVENIA	4889	2012	09
COMBINATIONS (OLMESARTANUM+HCT)	OLMICOMBI 20 mg/25 mg	film-coated tablets	20 mg/ 25 mg	KRKA D.D., NOVO MESTO	SLOVENIA	4890	2012	09
COMBINATIONS (PERINDOPRILUM+ INDAPAMIDUM)	PRESTARIUM ARG PLUS 5 mg/1.25 mg	film-coated tablets	5 mg/ 1.25 mg	LES LABORATOIRES SERVIER	FRANCE	4830	2012	10
COMBINATIONS (PERINDOPRILUM+ INDAPAMIDUM)	NOLIPREL ARG 2.5 mg/0.625 mg	film-coated tablets	2.5 mg/ 0.625 mg	LES LABORATOIRES SERVIER	FRANCE	4828	2012	10
COMBINATIONS (PERINDOPRILUM+ INDAPAMIDUM)	NOLIPREL ARG FORTE 5 mg/1.25 mg	film-coated tablets	5 mg/ 1.25 mg	LES LABORATOIRES SERVIER	FRANCE	4829	2012	11
COMBINATIONS (ACIDUM ACETYLSALICYLICUM+ PSEUDOEPHEDRINE)	SANDOZ, **ACETYLSALICYLIC ACID** /PSEUDOEPHEDRINE	granules for oral suspension in single-dose sachets	500 mg/ 30 mg	SANDOZ S.R.L.	ROMANIA	5017	2012	08
CYTARABINUM	CITARABINA KABI 100 mg/ml	solution for injection or infusion	100mg/ml	FRESENIUS KABI ONCOLOGY PLC.	GREAT BRITAIN	4910	2012	04
DAPOXETINUM	PRILIGY 30 mg	film-coated tablets	30 mg	JANSSEN PHARMACEUTICA N.V.	BELGIUM	4864	2012	04
DAPOXETINUM	PRILIGY 60 mg	film-coated tablets	60 mg	JANSSEN PHARMACEUTICA N.V.	BELGIUM	4865	2012	04
DESLORATADINUM	DESLORATADINA IBERMEDGEN 0.5 mg/ml	oral solution	0.5 mg/ml	IBERMEDGEN SA	SPAIN	4787	2012	04
DESLORATADINUM	DESLORATADINA IBERMEDGEN 5 mg	film-coated tablets	5 mg	IBERMEDGEN SA	SPAIN	4786	2012	05
DESLORATADINUM	DESLORATADINA PMCS 5mg	tablets	5 mg	PRO. MED. CS PRAHA A.S.	CZECH REPUBLIC	4915	2012	08
DIHYDROCODEINUM	DHC CONTINUS 60 mg	prolonged-release tablets	60 mg	MUNDIPHARMA	AUSTRIA	4896	2012	02

				GES.M.B.H				
DIHYDROCODEINUM	DHC CONTINUS 90 mg	prolonged-release tablets	90 mg	MUNDIPHARMA GES.M.B.H	AUSTRIA	4897	2012	02
DIHYDROCODEINUM	DHC CONTINUS 120 mg	prolonged-release tablets	120 mg	MUNDIPHARMA GES.M.B.H	AUSTRIA	4898	2012	02
DILTIAZEMUM	ADOH, **DILTIAZEM CLORHYDRATE** 200 mg	prolonged-release capsules	200 mg	ADOH B.V.	HOLLAND	4913	2012	02
DILTIAZEMUM	ADOH, **DILTIAZEM CLORHYDRATE** 300 mg	prolonged-release capsules	300 mg	ADOH B.V.	HOLLAND	4914	2012	02
DOCETAXELUM	DOCETAXEL STRIDES ARCOLAB INTERNATIONAL 40 mg/ml	concentrate and solvent for solution for infusion	40 mg/ml	STRIDES ARCOLAB INTERNAȚIONAL LTD.	GREAT BRITAIN	4860	2012	02
DOCETAXELUM	DOCETAXEL LEK 10 mg/ml	concentrate for solution for infusion	10 mg/ml	SANDOZ S.R.L.	ROMANIA	4884	2012	02
DOCETAXELUM	DOCETAXEL PFIZER 10 mg/ml	concentrate for solution for infusion	10 mg/ml	PFIZER EUROPE MA EEIG	GREAT BRITAIN	4968	2012	08
DOCUSATE SODIUM	KLYXIT 120 mg	rectal gel	120 mg	FERRING GMBH	GERMANY	4783	2012	01
DONEPEZILUM	DONENERTON 5 mg	film-coated tablets	5 mg	DOLORGIET GMBH & CO. KG	GERMANY	4821	2012	10
DONEPEZILUM	DONENERTON 10 mg	film-coated tablets	10 mg	DOLORGIET GMBH & CO. KG	GERMANY	4822	2012	10
DONEPEZILUM	COGITON 5 mg	orodispersible tablets	5 mg	BIOFARM SP. ZO.O.	POLAND	5005	2012	08
DONEPEZILUM	COGITON 10 mg	orodispersible tablets	10 mg	BIOFARM SP. ZO.O.	POLAND	5006	2012	08
ENOXAPARINUM	CLEXANE 2000 IU anti-Xa/0.2 ml	solution for injection	2000IU anti-Xa/0.2ml	LABORATOIRE AVENTIS	FRANCE	4926	2012	02
ENOXAPARINUM	CLEXANE 4000 IU anti-Xa/0.4 ml	solution for injection	4000IU anti-Xa/0.4 ml	LABORATOIRE AVENTIS	FRANCE	4927	2012	02
ENOXAPARINUM	CLEXANE 6000 IU anti-Xa/0.6 ml	solution for injection	6000IU anti-Xa/0.6 ml	LABORATOIRE AVENTIS	FRANCE	4928	2012	02
ENOXAPARINUM	CLEXANE 8000 IU anti-Xa/0.8 ml	solution for injection	8000IU anti-Xa/0.8 ml	LABORATOIRE AVENTIS	FRANCE	4929	2012	01
EPIRUBICINUM	EPIRUBICINA STRIDES ARCOLAB INTERNATIONAL 2 mg/ml	solution for injection/infusion	2 mg/ml	STRIDES ARCOLAB INTERNAȚIONAL LTD.	GREAT BRITAIN	4859	2012	02
EPLERENONUM	HARTESIN 25 mg	film-coated tablets	25 mg	PHARMACEUTICAL WORKS POLPHARMA SA	POLAND	4922	2012	06
EPLERENONUM	HARTESIN 50 mg	film-coated tablets	50 mg	PHARMACEUTICAL WORKS POLPHARMA	POLAND	4923	2012	06

				SA				
EPROSARTANUM	EPROSARTAN GENERICS 300 mg	film-coated tablets	300 mg	GENERICS (UK) LTD T/A MYLAN	GREAT BRITAIN	4845	2012	08
EPROSARTANUM	EPROSARTAN GENERICS 400 mg	film-coated tablets	400 mg	GENERICS (UK) LTD T/A MYLAN	GREAT BRITAIN	4846	2012	08
EPROSARTANUM	EPROSARTAN GENERICS 600 mg	film-coated tablets	600 mg	GENERICS (UK) LTD T/A MYLAN	GREAT BRITAIN	4847	2012	08
ESOMEPRAZOLUM	REMESOLIN 20 mg	gastroresistant capsules	20 mg	ACTAVIS GROUP PTC EHF.	ICELAND	4979	2012	18
ESOMEPRAZOLUM	REMESOLIN 40 mg	gastroresistant capsules	40 mg	ACTAVIS GROUP PTC EHF.	ICELAND	4980	2012	18
FINASTERIDUM	FINASTERIDE TEVA 5 mg	film-coated tablets	5 mg	TEVA PHARMACEUTICAL S.R.L.	ROMANIA	4875	2012	14
FLURBIPROFEN	STREPSILS INTENSIV 8.75 mg	granules	8.75 mg	RECKITT BENCKISER HEALTHCARE INTERNATIONAL LIMITED	GREAT BRITAIN	4873	2012	32
FLURBIPROFEN	STREPFEN 8.75 mg	granules	8.75 mg	RECKITT BENCKISER HEALTHCARE INTERNATIONAL LIMITED	GREAT BRITAIN	4874	2012	32
SUCCINILATE GELATIN	GELOFUSINE 4 g/100 ml	solution for infusion	4 g/100 ml	B. BRAUN MELSUNGEN AG	GERMANY	4899	2012	01
GEMCITABINUM	GEMCITABINA PHARMA RESOURCES 200 mg	powder for solution for infusion	200 mg	PHARMA RESOURCES GMBH	GERMANY	4908	2012	01
GEMCITABINUM	GEMCITABINA PHARMA RESOURCES 1000 mg	powder for solution for infusion	1000 mg	PHARMA RESOURCES GMBH	GERMANY	4909	2012	01
GLIMEPIRIDUM	GLIMEPIRIDA AUROBINDO 1 mg	tablets	1 mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	4789	2012	16
GLIMEPIRIDUM	GLIMEPIRIDA AUROBINDO 2 mg	tablets	2 mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	4790	2012	16
GLIMEPIRIDUM	GLIMEPIRIDA AUROBINDO 3 mg	tablets	3 mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	4791	2012	16
GLIMEPIRIDUM	GLIMEPIRIDA AUROBINDO 4 mg	tablets	4 mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	4792	2012	16

PORK-BRAIN **PROTEIN HYDROLYSATE**	CEREBROLYSIN 215.2 mg/ml	solution for injection/concentrate for solution for infusion	215.2mg/ml	EVER NEURO PHARMA GMBH	AUSTRIA	4804	2012	03
HOMEOPATHIC MEDICINAL PRODUCTS	GALSTENA	sublingual tablets		RICHARD BITTNER AG	AUSTRIA	4894	2012	04
IBUPROFENUM	IBUPROFEN LIDERFARM 100 mg/5 ml	oral suspension	100 mg/ 5 ml	FARMALIDER S.A.	SPAIN	4933	2012	03
IBUPROFENUM	IBUPROFEN LIDERFARM 200 mg/5 ml	oral suspension	200 mg/ 5 ml	FARMALIDER S.A.	SPAIN	4934	2012	04
IBUPROFENUM	IBUPROFEN FARMALIDER 100 mg/5 ml	oral suspension	100 mg/ 5 ml	FARMALIDER S.A.	SPAIN	4935	2012	03
IBUPROFENUM	IBUPROFEN FARMALIDER 200 mg/5 ml	oral suspension	200 mg/ 5 ml	FARMALIDER S.A.	SPAIN	4936	2012	04
IMIPENEMUM + CILASTATINUM	TIENAM I.V. 500 mg/500 mg	powder for solution for infusion	500 mg/ 500 mg	MERCK SHARP & DOHME ROMANIA S.R.L.	ROMANIA	4955	2012	03
ANTI-D IMMUNOGLOBULIN	RHOPHYLAC 300 micrograms/2 ml	solution for injection in pre-filled syringe	300 micro-grams/2 ml	CSL BEHRING GMBH	GERMANY	5031	2012	01
RABIES IMMUNOGLOBULIN OF EQUINE ORIGIN	FAVIRAB 200-400 IU/ml	solution for injection	200-400IU/ ml	SANOFI PASTEUR S.A.	FRANCE	5025	2012	02
HUMAN NORMAL IMMUNOGLOBULIN	INTRATECT 50 g/l	solution for infusion	50g/l	BIOTEST PHARMA GMBH	GERMANY	4995	2012	04
KALII CHLORIDUM	POTASSIUM IODIDE G.L. PHARMA 65 mg	tablets	65 mg	G.L. PHARMA GMBH	AUSTRIA	4825	2012	04
KETOPROFENUM	RUBIFEN 100 mg	suppositories	100 mg	ANTIBIOTICE SA	ROMANIA	4843	2012	02
LACTULOSUM	LACTULADE 650 mg/ml	oral gel	650 mg/ml	MIP PHARMA GMBH	GERMANY	4818	2012	03
LETROZOLUM	LETROZOL TEVA 2.5 mg	film-coated tablets	2.5 mg	TEVA PHARMACEUTICALS S.R.L.	ROMANIA	4879	2012	05
LETROZOLUM	FEMARA 2.5 mg	film-coated tablets	2.5 mg	NOVARTIS PHARMA GMBH	GERMANY	5026	2012	02
LETROZOLUM	FALVAX 2.5 mg	film-coated tablets	2.5 mg	DR. REDDY'S LABORATORIES ROMANIA S.R.L.	ROMANIA	4771	2012	06
LETROZOLUM	LETROZOL POLIPHARMA 2.5 mg	film-coated tablets	2.5 mg	POLIPHARMA INDUSTRIES S.R.L.	ROMANIA	4802	2012	06
LEVETIRACETAMUM	LEVELANZ 250 mg	film-coated tablets	250 mg	ABBOTT LABORATORIES LTD.	GREAT BRITAIN	4996	2012	06

LEVETIRACETAMUM	LEVELANZ 500 mg	film-coated tablets	500 mg	ABBOTT LABORATORIES LTD.	GREAT BRITAIN	4997	2012	06
LEVETIRACETAMUM	LEVELANZ 750 mg	film-coated tablets	750 mg	ABBOTT LABORATORIES LTD.	GREAT BRITAIN	4998	2012	06
LEVETIRACETAMUM	LEVELANZ 1000 mg	film-coated tablets	1000 mg	ABBOTT LABORATORIES LTD.	GREAT BRITAIN	4999	2012	06
LEVOFLOXACINUM	MACLEODS LEVOFLOXACIN 250 mg	film-coated tablets	250 mg	MACLEODS PHARMA UK LIMITED	GREAT BRITAIN	4924	2012	02
LEVOFLOXACINUM	MACLEODS LEVOFLOXACIN 500 mg	film-coated tablets	500 mg	MACLEODS PHARMA UK LIMITED	GREAT BRITAIN	4925	2012	02
LOSARTANUM	LOSARTAN JENSON 12.5 mg	film-coated tablets	12.5 mg	JENSON PHARMACEUTICAL SERVICES LTD	GREAT BRITAIN	4794	2012	16
LOSARTANUM	LOSARTAN JENSON 25 mg	film-coated tablets	25 mg	JENSON PHARMACEUTICAL SERVICES LTD	GREAT BRITAIN	4795	2012	16
LOSARTANUM	LOSARTAN JENSON 50 mg	film-coated tablets	50 mg	JENSON PHARMACEUTICAL SERVICES LTD	GREAT BRITAIN	4796	2012	16
LOSARTANUM	LOSARTAN JENSON 100mg	film-coated tablets	100 mg	JENSON PHARMACEUTICAL SERVICES LTD	GREAT BRITAIN	4797	2012	16
MEROPENEMUM	MEROPENEM ATB 500 mg	powder for solution for injection/infusion	500 mg	ANTIBIOTICE S.A.	ROMANIA	4871	2012	03
MEROPENEMUM	MEROPENEM ATB 1000 mg	powder for solution for injection/infusion	1000 mg	ANTIBIOTICE S.A.	ROMANIA	4872	2012	03
MESALAZINUM	MEZAVANT 1200 mg	prolonged-release gastroresistant tablets	1200 mg	SHIRE PHARMACEUTICAL CONTRACTS LTD	GREAT BRITAIN	4793	2012	02
METHOTREXATUM	ANTIFOLAN 25 mg/ml	solution for injection/infusion	25 mg/ml	ACTAVIS GROUP PTC EHF.	ICELAND	5023	2012	04
METOPROLOLUM	EGILOK EP 25 mg	prolonged-release tablets	25 mg	EGIS PHARMACEUTICALS PLC	HUNGARY	4885	2012	11
METOPROLOLUM	EGILOK EP 50 mg	prolonged-release tablets	50 mg	EGIS PHARMACEUTICALS PLC	HUNGARY	4886	2012	11

METOPROLOLUM	EGILOK EP 100 mg	prolonged-release tablets	100 mg	EGIS PHARMACEUTICALS PLC	HUNGARY	4887	2012	11
METOPROLOLUM	EGILOK EP 200 mg	prolonged-release tablets	200 mg	EGIS PHARMACEUTICALS PLC	HUNGARY	4888	2012	11
MONTELUKASTUM	MONTELUKAST AUROBINDO 5 mg	chewable tablets	5 mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	4868	2012	19
MONTELUKASTUM	MONTELUKAST AUROBINDO 4 mg	chewable tablets	4 mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	4867	2012	19
MONTELUKASTUM	MONTELUKAST AUROBINDO 10 mg	film-coated tablets	10 mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	4869	2012	17
NAPROXENUM	NALDOREX 275 mg	film-coated tablets	275 mg	KRKA, D.D., NOVO MESTO	SLOVENIA	4952	2012	04
NAPROXENUM	NALDOREX 550 mg	film-coated tablets	550 mg	KRKA, D.D., NOVO MESTO	SLOVENIA	4953	2012	05
NATRII CHLORIDUM	KABI, PHYSIOLOGICAL SERUM 9 mg/ml	solvent for parenteral use	9 mg/ml	FRESENIUS KABI ROMANIA S.R.L.	ROMANIA	4969	2012	05
NATRII FLUORIDUM	DURAPHAT, FLUORIDE 5mg/g	toothpaste	5 mg/g	COLGATE - PALMOLIVE (ROMANIA) S.R.L.	ROMANIA	4911	2012	02
NICOTINUM	NICORETTE FRESHMINT 1 mg/spray	oromucosal spray, solution	1 mg/spray	MCNEIL AB	SWEDEN	4848	2012	02
OLANZAPINUM	OLANZAPINA JENSON PHARMACEUTICAL SERVICES LIMITED 5 mg	orodispersible tablets	5 mg	JENSON PHARMACEUTICAL SERVICES LTD.	GREAT BRITAIN	4767	2012	32
OLANZAPINUM	OLANZAPINA JENSON PHARMACEUTICAL SERVICES LIMITED 10 mg	orodispersible tablets	10 mg	JENSON PHARMACEUTICAL SERVICES LTD.	GREAT BRITAIN	4768	2012	32
OLANZAPINUM	OLANZAPINA JENSON PHARMACEUTICAL SERVICES LIMITED 15 mg	orodispersible tablets	15 mg	JENSON PHARMACEUTICAL SERVICES LTD.	GREAT BRITAIN	4769	2012	32
OLANZAPINUM	OLANZAPINA JENSON PHARMACEUTICAL SERVICES LIMITED 20 mg	orodispersible tablets	20 mg	JENSON PHARMACEUTICAL SERVICES LTD.	GREAT BRITAIN	4770	2012	32
OLANZAPINUM	ZOLAFREN 5 mg	tablets	5 mg	LABORATORIOS ADAMED SP. Z O.O	POLAND	4960	2012	02

OLANZAPINUM	ZOLAFREN 10 mg	tablets	10 mg	LABORATORIOS ADAMED SP. Z O.O	POLAND	4961	2012	02
OXALIPLATINUM	OXALIPLATINA STRIDES ARCOLAB INTERNATIONAL 5 mg/ml	powder for solution for injection	5 mg/ml	STRIDES ARCOLAB INTERNAȚIONAL LTD.	GREAT BRITAIN	4849	2012	02
OXIGENUM	MEDICAL OXYGEN (COMPRESSED GAS)	medicinal gas, compressed		SIAD ROMANIA S.R.L.	ROMANIA	4800	2012	16
OXIGENUM	MEDICAL OXYGEN (LIQUEFIED GAS)	medicinal gas, liquefied		SIAD ROMANIA S.R.L.	ROMANIA	4801	2012	01
OXIGENUM	OXIGEN MEDICINAL GAS AIR LIGUIDE	medicinal gas for inhalation		AIR LIQUIDE ROMANIA SRL	ROMANIA	4854	2012	11
OXIGENUM	OXYGEN SOLUTION 100%	medicinal gas, compressed	100 %	SOL S.P.A.	ITALY	5032	2012	19
OXIGENUM	OXYGEN SOLUTION 100%	cryogenic medicinal gas	100 %	SOL S.P.A.	ITALY	5033	2012	02
OXIGENUM	OXYGEN SOLUTION 100%	cryogenic medicinal gas, cylinder	100 %	SOL S.P.A.	ITALY	5034	2012	01
OXYBUTYNINUM	INTAS, **OXYBUTYNIN HYDROCHLORIDE** 5 mg	tablets	5 mg	INTAS PHARMACEUTICALS LIMITED	GREAT BRITAIN	4893	2012	18
PANCREATINUM	KREON 40000	gastroresistant capsules	400 mg	ABBOTT PRODUCTS GMBH	GERMANY	4974	2012	03
PERINDOPRILUM	PRENESSA 4 mg	orodispersible tablets	4 mg	KRKA, D.D., NOVO MESTO	SLOVENIA	5020	2012	08
PERINDOPRILUM	PRENESSA 8 mg	orodispersible tablets	8 mg	KRKA, D.D., NOVO MESTO	SLOVENIA	5021	2012	08
HERBS	VALBEN 112.5mg/125mg/80mg	lozenges	112.5 mg/ 125mg/80mg	WALMARK, A.S.	CZECH REPUBLIC	4895	2012	05
HERBS	VEREGEN 100mg/g	ointment	100mg/g	MEDITRINA PHARMACEUTICALS LTD	GREECE	4916	2012	02
QUETIAPINUM	SETININ 50 mg	prolonged-release tablets	50 mg	ACTAVIS GROUP PTC EHF.	ICELAND	4805	2012	06
QUETIAPINUM	SETININ 200 mg	prolonged-release tablets	200 mg	ACTAVIS GROUP PTC EHF.	ICELAND	4806	2012	06
QUETIAPINUM	SETININ 300 mg	prolonged-release tablets	300 mg	ACTAVIS GROUP PTC EHF.	ICELAND	4807	2012	06
QUETIAPINUM	SETININ 400 mg	prolonged-release tablets	400 mg	ACTAVIS GROUP PTC EHF.	ICELAND	4808	2012	06
QUETIAPINUM	SETININ 50 mg	film-coated tablets	50 mg	ACTAVIS GROUP PTC	ICELAND	4834	2012	08

				EHF.				
RABEPRAZOLUM	RABEPRAZOL TERAPIA 10 mg	gastroresistant tablets	10 mg	TERAPIA S.A.	ROMANIA	4990	2012	03
RABEPRAZOLUM	RABEPRAZOL TERAPIA 20 mg	gastroresistant tablets	20 mg	TERAPIA S.A.	ROMANIA	4991	2012	03
RAMIPRILUM	RAMIPRIL CIPLA 2.5 mg	tablets	2.5 mg	CIPLA UK LIMITED	GREAT BRITAIN	4981	2012	01
RAMIPRILUM	RAMIPRIL CIPLA 5 mg	tablets	5 mg	CIPLA UK LIMITED	GREAT BRITAIN	4982	2012	01
RAMIPRILUM	RAMIPRIL CIPLA 10 mg	tablets	10 mg	CIPLA UK LIMITED	GREAT BRITAIN	4983	2012	01
REPAGLINIDUM	REPAGLINIDA CHANELLE MEDICAL 0.5 mg	tablets	0.5 mg	CHANELLE MEDICAL	IRELAND	4901	2012	09
REPAGLINIDUM	REPAGLINIDA CHANELLE MEDICAL 1 mg	tablets	1 mg	CHANELLE MEDICAL	IRELAND	4902	2012	09
REPAGLINIDUM	REPAGLINIDA CHANELLE MEDICAL 2 mg	tablets	2 mg	CHANELLE MEDICAL	IRELAND	4903	2012	09
RIBAVIRINUM	RIBAVIRIN AUROBINDO 200 mg	capsules	200 mg	AUROBINDO PHARMA (MALTA) LIMITED	MALTA	4921	2012	06
RIVASTIGMINUM	RESYMTIA 1,5 mg	capsules	1,5 mg	ABBOTT LABORATORIES LTD.	GREAT BRITAIN	5027	2012	03
RIVASTIGMINUM	RESYMTIA 3 mg	capsules	3 mg	ABBOTT LABORATORIES LTD.	GREAT BRITAIN	5028	2012	03
RIVASTIGMINUM	RESYMTIA 4.5 mg	capsules	4.5 mg	ABBOTT LABORATORIES LTD.	GREAT BRITAIN	5029	2012	03
RIVASTIGMINUM	RESYMTIA 6 mg	capsules	6 mg	ABBOTT LABORATORIES LTD.	GREAT BRITAIN	5030	2012	03
ROPINIROLUM	ROPINIROL ACTAVIS 2 mg	prolonged-release tablets	2 mg	ACTAVIS GROUP PTC EHF.	ICELAND	4777	2012	07
ROPINIROLUM	ROPINIROL ACTAVIS 4 mg	prolonged-release tablets	4 mg	ACTAVIS GROUP PTC EHF.	ICELAND	4778	2012	07
ROPINIROLUM	ROPINIROL ACTAVIS 8 mg	prolonged-release tablets	8 mg	ACTAVIS GROUP PTC EHF.	ICELAND	4779	2012	07
ROPINIROLUM	NERVAMAT 2 mg	prolonged-release tablets	2 mg	EGIS PHARMACEUTICALS PLC	HUNGARY	4773	2012	15
ROPINIROLUM	NERVAMAT 4 mg	prolonged-release tablets	4 mg	EGIS PHARMACEUTICALS PLC	HUNGARY	4775	2012	15

ROPINIROLUM	NERVAMAT 8 mg	prolonged-release tablets	8 mg	EGIS PHARMACEUTICALS PLC	HUNGARY	4776	2012	15
ROPINIROLUM	NERVAMAT 3 mg	prolonged-release tablets	3 mg	EGIS PHARMACEUTICALS PLC	HUNGARY	4774	2012	15
SEVOFLURANUM	SOJOURN	liquid for inhalation vapours		PIRAMAL HEALTHCARE UK LIMITED	GREAT BRITAIN	4788	2012	01
SILDENAFILUM	GEDENA 25 mg	chewable tablets	25 mg	ALVOGEN IPCO S.A.R.L	LUXEMBURG	4850	2012	03
SILDENAFILUM	GEDENA 50 mg	chewable tablets	50 mg	ALVOGEN IPCO S.A.R.L	LUXEMBURG	4851	2012	03
SILDENAFILUM	GEDENA 100 mg	chewable tablets	100 mg	ALVOGEN IPCO S.A.R.L	LUXEMBURG	4852	2012	03
SILDENAFILUM	SILDENAFIL DR. REDDY'S 25 mg	film-coated tablets	25 mg	DR. REDDY'S LABORATORIES ROMANIA S.R.L.	ROMANIA	4957	2012	05
SILDENAFILUM	SILDENAFIL DR. REDDY'S 50 mg	film-coated tablets	50 mg	DR. REDDY'S LABORATORIES ROMANIA S.R.L.	ROMANIA	4958	2012	05
SILDENAFILUM	SILDENAFIL DR. REDDY'S 100 mg	film-coated tablets	100 mg	DR. REDDY'S LABORATORIES ROMANIA S.R.L.	ROMANIA	4959	2012	05
SILDENAFILUM	SILDENAFIL TORRENT 25 mg	film-coated tablets	25 mg	TORRENT PHARMA S.R.L.	ROMANIA	4962	2012	03
SILDENAFILUM	SILDENAFIL TORRENT 50 mg	film-coated tablets	50 mg	TORRENT PHARMA S.R.L.	ROMANIA	4963	2012	03
SILDENAFILUM	SILDENAFIL TORRENT 100 mg	film-coated tablets	100 mg	TORRENT PHARMA S.R.L.	ROMANIA	4964	2012	03
SIMVASTATINUM	SIMVASTATIN BLUEFISH 10 mg	film-coated tablets	10 mg	BLUEFISH PHARMACEUTICALS AB	SWEDEN	4815	2012	09
SIMVASTATINUM	SIMVASTATIN BLUEFISH 20 mg	film-coated tablets	20 mg	BLUEFISH PHARMACEUTICALS AB	SWEDEN	4816	2012	09
SIMVASTATINUM	SIMVASTATIN BLUEFISH 40 mg	film-coated tablets	40 mg	BLUEFISH PHARMACEUTICALS AB	SWEDEN	4817	2012	09
SIMVASTATINUM	SIMVASTATIN AUROBINDO 10 mg	film-coated tablets	10 mg	AUROBINDO PHARMA LIMITED	GREAT BRITAIN	4840	2012	12

SIMVASTATINUM	SIMVASTATIN AUROBINDO 20 mg	film-coated tablets	20 mg	AUROBINDO PHARMA LIMITED	GREAT BRITAIN	4841	2012	12
SIMVASTATINUM	SIMVASTATIN AUROBINDO 40 mg	film-coated tablets	40 mg	AUROBINDO PHARMA LIMITED	GREAT BRITAIN	4842	2012	12
SIMVASTATINUM	SIMVASTATIN ACCORD 10 mg	film-coated tablets	10 mg	ACCORD HEALTHCARE LIMITED	GREAT BRITAIN	4855	2012	18
SIMVASTATINUM	SIMVASTATIN ACCORD 20 mg	film-coated tablets	20 mg	ACCORD HEALTHCARE LIMITED	GREAT BRITAIN	4856	2012	18
SIMVASTATINUM	SIMVASTATIN ACCORD 40 mg	film-coated tablets	40 mg	ACCORD HEALTHCARE LIMITED	GREAT BRITAIN	4857	2012	18
SIMVASTATINUM	SIMVASTATIN ACCORD 80 mg	film-coated tablets	80 mg	ACCORD HEALTHCARE LIMITED	GREAT BRITAIN	4858	2012	18
SIMVASTATINUM	SIMVASTATIN ACTAVIS 10 mg	film-coated tablets	10 mg	ACTAVIS GROUP PTC EHF	ICELAND	5013	2012	07
SIMVASTATINUM	SIMVASTATIN ACTAVIS 20 mg	film-coated tablets	20 mg	ACTAVIS GROUP PTC EHF	ICELAND	5014	2012	07
SIMVASTATINUM	SIMVASTATIN ACTAVIS 40 mg	film-coated tablets	40 mg	ACTAVIS GROUP PTC EHF	ICELAND	5015	2012	07
SULFADIAZINUM	REGEN-AG 10 mg/g	cream	10 mg/g	FITERMAN PHARMA S.R.L.	ROMANIA	4844	2012	01
SUMATRIPTANUM	SUMACTA 50 mg	film-coated tablets	50 mg	ACTAVIS GROUP PTC EHF.	ICELAND	4992	2012	21
SUMATRIPTANUM	SUMACTA 100 mg	film-coated tablets	100 mg	ACTAVIS GROUP PTC EHF.	ICELAND	4993	2012	21
TACROLIMUSUM	TRACSUS 0.5 mg	capsules	0.5 mg	ALVOGEN IPCO S.AR.L	LUXEMBUG	4976	2012	01
TACROLIMUSUM	TRACSUS 1 mg	capsules	1 mg	ALVOGEN IPCO S.AR.L	LUXEMBUG	4977	2012	01
TACROLIMUSUM	TRACSUS 5 mg	capsules	5 mg	ALVOGEN IPCO S.AR.L	LUXEMBUG	4978	2012	01
TAMSULOSINUM	TAMSUNORM 0.4 mg	prolonged-release capsules	0.4 mg	ICN POLFA RZESZOW S.A.	POLAND	4912	2012	02
TAPENTADOLUM	PALEXIA RETARD 25 mg	prolonged-release tablets	25 mg	GRUNENTHAL GMBH	GERMANY	4905	2012	22
TELMISARTANUM	TELMISARTAN EGIS 20 mg	film-coated tablets	20 mg	EGIS PHARMACEUTICALS PLC	HUNGARY	4984	2012	09

TELMISARTANUM	TELMISARTAN EGIS 40 mg	film-coated tablets	40 mg	EGIS PHARMACEUTICALS PLC	HUNGARY	4985	2012	09
TELMISARTANUM	TELMISARTAN EGIS 80 mg	film-coated tablets	80 mg	EGIS PHARMACEUTICALS PLC	HUNGARY	4986	2012	09
TELMISARTANUM	TELMISARTAN RENANTOS 20 mg	tablets	20 mg	RENANTOS PHARMAVERTRIEBS GESSELLSCHAFT GMBH	GERMANY	4989	2012	09
TIANEPTINUM	ATINEPTE 12.5 mg	film-coated tablets	12.5 mg	PHARMACEUTICAL WORKS POLPHARMA SA	ROMANIA	4954	2012	04
TIAPRIDUM	TIAPRIDA PHARMAGEN 100 mg	tablets	100 mg	PHARMAGEN S.R.O.	SLOVAKIA	4782	2012	07
TOLTERODINUM	UROFLOW SR 2 mg	prolonged-release capsules	2 mg	ZENTIVA K.S.	CZECH REPUBLIC	4812	2012	06
TOLTERODINUM	UROFLOW SR 4 mg	prolonged-release capsules	4 mg	ZENTIVA K.S.	CZECH REPUBLIC	4813	2012	09
TOLTERODINUM	TOLTERODINA GENERICS 2 mg	prolonged-release capsules	2 mg	GENERICS (UK) LTD	GREAT BRITAIN	4987	2012	14
TOLTERODINUM	TOLTERODINA GENERICS 4 mg	prolonged-release capsules	4 mg	GENERICS (UK) LTD	GREAT BRITAIN	4988	2012	17
TOPOTECAMUM	TOPOTECAN ACCORD 1 mg/ml	concentrate for solution for infusion	1 mg/ml	ACCORD HEALTHCARE LIMITED	GREAT BRITAIN	4866	2012	04
TRAMADOLUM	TRADOLAN RETARD 150 mg	prolonged-release tablets	150 mg	LANNACHER HEILMITTEL GES.M.B.H	AUSTRIA	4765	2012	02
TRAMADOLUM	TRADOLAN RETARD 200 mg	prolonged-release tablets	200 mg	LANNACHER HEILMITTEL GES.M.B.H	AUSTRIA	4766	2012	02
TRIMETAZIDINUM	TRIMETACOR 35 mg	prolonged-release tablets	35 mg	ATTIC PHARMA EHF.	ICELAND	4803	2012	02
TRIMETAZIDINUM	ELCOROL 35 mg	prolonged-release tablets	35 mg	IVOWEN LIMITED	IRELAND	4967	2012	02
TRIMETAZIDINUM	VELTIANG 35 mg	prolonged-release tablets	35 mg	IVOWEN LIMITED	IRELAND	4966	2012	02
COMBINED DTPA-IPV/HIB VACCINE	PENTAXIM	powder and suspension for injection in pre-filled syringe		SANOFI PASTEUR SA	FRANCE	4956	2012	05
INACTIVATED INFLUENZA VACCINE	INFLEXAL V	suspension for injection		CRUCELL ITALY S.R.L.	ITALY	4975	2012	02

HEPATITIS A VACCINE (INACTIVATED, ADSORBED)	AVAXIM 160 U	suspension for injection	160 U	SANOFI PASTEUR SA	FRANCE	4938	2012	04
RUBEOLA, RUBELLA, URLIAN, LIVE ATTENUATED VACCINE	PRIORIX, RUBEOLA, RUBELLA, URLIAN, LIVE ATTENUATED VACCINE	powder and solvent for solution for injection		GLAXOSMITHKLINE BIOLOGICALS S.A.	BELGIUM	4820	2012	19
VALSARTANUM	VAPRESS 40 mg	film-coated tablets	40 mg	MEDOCHEMIE LTD.	CYPRUS	4831	2012	20
VALSARTANUM	VAPRESS 80 mg	film-coated tablets	80 mg	MEDOCHEMIE LTD.	CYPRUS	4832	2012	20
VALSARTANUM	VAPRESS 160 mg	film-coated tablets	160 mg	MEDOCHEMIE LTD.	CYPRUS	4833	2012	20
VALSARTANUM	WAROTA 40 mg	film-coated tablets	40 mg	ALKALOID – INT D.O.O.	SLOVENIA	4861	2012	12
VALSARTANUM	WAROTA 80 mg	film-coated tablets	80 mg	ALKALOID - INT D.O.O.	SLOVENIA	4862	2012	12
VALSARTANUM	WAROTA 160 mg	film-coated tablets	160 mg	ALKALOID - INT D.O.O.	SLOVENIA	4863	2012	12
VALSARTANUM	VALSARTAN KRKA 40 mg	film-coated tablets	40 mg	KRKA, D.D., NOVO MESTO	SLOVENIA	5001	2012	13
VALSARTANUM	VALSARTAN KRKA 80 mg	film-coated tablets	80 mg	KRKA, D.D., NOVO MESTO	SLOVENIA	5002	2012	13
VALSARTANUM	VALSARTAN KRKA 160 mg	film-coated tablets	160 mg	KRKA, D.D., NOVO MESTO	SLOVENIA	5003	2012	13
VALSARTANUM	VALSARTAN KRKA 320 mg	film-coated tablets	320 mg	KRKA, D.D., NOVO MESTO	SLOVENIA	5004	2012	11
VERAPAMILUM	CORDAMIL 40 mg	film-coated tablets	40 mg	AC HELCOR S.R.L.	ROMANIA	4972	2012	01
VERAPAMILUM	CORDAMIL 80 mg	film-coated tablets	80 mg	AC HELCOR S.R.L.	ROMANIA	4973	2012	01
ZIPRASIDONUM	ZIPRASIDONA MYLAN 20 mg	capsules	20 mg	MYLAN S.A.S	FRANCE	4947	2012	11
ZIPRASIDONUM	ZIPRASIDONA MYLAN 40 mg	capsules	40 mg	MYLAN S.A.S	FRANCE	4948	2012	11
ZIPRASIDONUM	ZIPRASIDONA MYLAN 60 mg	capsules	60 mg	MYLAN S.A.S	FRANCE	4949	2012	11
ZIPRASIDONUM	ZIPRASIDONA MYLAN 80 mg	capsules	80 mg	MYLAN S.A.S	FRANCE	4950	2012	11

EMA centrally authorised medicinal products for which a marketing price was established in Romania during the 3rd quarter of 2012

INN	Invented name	Pharm. form	Strength	Manufacturer	Country	MA Number		
ACLIDINIUM BROMIDUM	BRETARIS GENUAIR 322 micrograms	inhalation powder	322 µg	ALMIRALL S.A.	SPAIN	781	2012	03
AXITINIBUM	INLYTA	film-coated tablets	1 mg	PFIZER LIMITED	GREAT BRITAIN	777	2012	03
AXITINIBUM	INLYTA	film-coated tablets	5 mg	PFIZER LIMITED	GREAT BRITAIN	777	2012	03
CEFTAROLINUM FOSMIL	ZINFORO	powder for concentrate for solution for infusion	600 mg	ASTRA ZENECA AB	SWEDEN	785	2012	01
COMBINATIONS (LINAGLIPTINUM+ METFORMINUM)	JENTADUETO 2.5 mg/850 mg	film-coated tablets	2.5 mg/ 850 mg	BOEHRINGER INGELHEIM INTERNAȚIONAL GMBH	GERMANY	780	2012	14
COMBINATIONS (LINAGLIPTINUM+ METFORMINUM)	JENTADUETO 2.5 mg/1000 mg	film-coated tablets	2.5 mg/ 1000 mg	BOEHRINGER INGELHEIM INTERNATIONAL GMBH	GERMANY	780	2012	14
RUXOLITINIBUM	JAKAVI	tablets	5 mg	NOVARTIS EUROPHARM LIMITED	GREAT BRITAIN	773	2012	01
RUXOLITINIBUM	JAKAVI	tablets	15 mg	NOVARTIS EUROPHARM LIMITED	GREAT BRITAIN	773	2012	01
RUXOLITINIBUM	JAKAVI	tablets	20 mg	NOVARTIS EUROPHARM LIMITED	GREAT BRITAIN	773	2012	01
TAFAMIDIS	VYNDAQEL	soft capsules	20mg	PFIZER LIMITED	GREAT BRITAIN	717	2012	01