Activity report
of the National Agency for Medicines and Medical Devices
(NAMMD/NAMMDR)
2019

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I. Overview of the activity performed in 2019

The National Agency for Medicines and Medical Devices of Romania (NAMMDR) has been the regulatory authority in the field of medicine in Romania for over 60 years, a field of competence to which were added, in 2010, that of medical devices, and, respectively , the evaluation of medical technologies, in 2014.

The year covered by this report was a particularly important one, both through the responsibilities entrusted to the competent national authority in the exercise of Romania's mandate as President of the EU Council and through the adoption, in June 2019, of Law no. 134/2019 on the reorganisation of the National Agency for Medicines and Medical Devices. In accordance with this law, through the reorganisation of the National Agency for Medicines and Medical Devices (NAMMD), The National Agency for Medicines and Medical Devices of Romania (NAMMDR) was established as a public institution with legal personality and specialised body of the central public administration, subordinated to the Ministry of Health, maintaining its quality of competent national authority in the field of medicinal products for human use, medical devices and health technologies assessment.

The new law was developed in response to the imperatives of developing the competent authority in the institution's specific areas, able to provide quality services in public health, predictable and anticipatory, achieved by applying effective and efficient tools, mechanisms and practices, able to meet new challenges which currently characterise the dynamics of its own field, with human resources of a high professional level.

Thus, NAMMDR is a public institution subordinated to the Ministry of Health; its scope is marketing authorisation of medicinal products for human use, authorisation of manufacturing and wholesale distribution units for medicinal products for human use, surveillance of manufacturing units and wholesale distribution as well as of the quality of medicinal products on the market and in-use control of medicinal products for human use, inspection and control of medical devices in use and inspection and control of medical equipment units.

In concrete terms, the need was felt to change the funding regime in order to ensure a revenue and expenditure budget reflecting the real needs of the Agency, which would remove any negative consequences on the whole process of conducting clinical and authorisation trials, supervision and control of medicinal products and medical devices at national level, including throughout the network of external competent authorities, in the field of medicinal products for human use and medical devices with which the Agency works. In addition, the

need to ensure a unitary and motivating salary system for NAMMDR specialists has become clear. The regulations introduced by the new regulatory act therefore aim at organising and financing the public institution, in order to strengthen and increase its capacity in fulfilling its mission to contribute to the protection and promotion of public health and to fulfil its specific tasks established by law.

Thus, according to the new law, the financing of NAMMDR is ensured from own revenues, issued from the collection of tariffs charged in accordance with the legislation as well as from state subsidy.

Another novelty introduced is the expansion of the number of allocated posts to 500, a provision designed to significantly improve the institutional capacity of the competent authority in terms of human resources, in line with the complexity and diversity of its tasks and activities arising from these.

The changes also concerned the structuring of the institution by general directions, directions, services, offices and compartments, to which are added the territorial inspection units and / or for control and supervision of the medicinal product market / surveillance of the medical devices market / use of medical devices, for the assessment of medical equipment units, as well as for control by periodic check of medical devices, considering the maximum number of approved positions.

The NAMMDR Administration Council consists of five members, appointed by order of the Minister of Health: a President, two Vice-Presidents and two representatives of the Ministry of Health. The NAMMDR President will also be the Chairman of the Administration Council. The new management structure is similar to that of the NAMMD.

In keeping with its main task of establishing the scientific policy of the NAMMDR, according to the new law, the Scientific Council is composed of eight members, the new composition signalling the concern to reflect in specific policies the issues and views of as many stakeholders as possible, regarding the scope of the national authority, namely academia, associations of health and public health professionals, and, as a novelty, patient organisations. In accordance with the established general and specific tasks, the institution's standard operating procedures of the institution have been developed / updated and approved.

The purpose of this extensive reorganisation is solely to ensure the functioning of the institution in accordance with its particularly complex role and responsibilities, in line with the expectations and requirements of national and international bodies, in all its areas of activity.

Year 2019 was an important year in the history of the Agency, considering the great responsibility that the institution had in carrying out and enforcing the actions that our country undertook on the occasion of taking over the Romanian Presidency (PRES RO) of the Council of the European Union, starting with

January 1, 2019. The NAMMD had the obligation to ensure, under the coordination of the Ministry of Health, the smooth conduct of 6 meetings focused on various issues related to medicinal products for human use, the topics on the agenda of the various meetings being determined according to the purpose of each meeting, in collaboration with the management of the working groups / scientific committees of specific European bodies (the Heads of Medicines Agencies = HMA, the European Medicines Agency = EMA).

The involvement of NAMMD in the development of the 6 specific meetings during Romania's mandate (January-June 2019), represented an opportunity to self-assess and demonstrate the maturity of the institution and, at the same time, to assume a great responsibility.

The events took place as follows:

- February 20-22, 2019, Timișoara: the first of the two meetings of HMA (Heads of Medicines Agencies). The 95th meeting of the HMA was organised by the NAMMD, under the coordination of the Ministry of Health, in collaboration with the National Sanitary Veterinary Authority and Food Safety Authority and the Institute for Control of Biological Products and Veterinary Medicines.

- April 4-5, 2019, the NAMMD hosted the Strategic Analysis and Learning Meeting (SRLM) of the Herbal Medicinal Products Committee (HMPC).

This informal meeting, of strategic analysis and learning, allowed HMPC members to collectively analyse the various challenges they face and to establish work plans for 2019, as well as priorities in support of the EU Network Strategy, until 2020 and beyond.

- May 23-24, 2019, Palace of the Parliament, Bucharest: formal meeting of the Homeopathic Medicinal Products Working Group (HMPWG).

- May 22-23, 2019, Palace of the Parliament, Bucharest: joint meeting of the Coordination Group for Mutual Recognition and Decentralized Procedures for Human Medicinal Products (CMDh) and the Pharmacovigilance Risk Assessment Committee (PRAC).

- June 13-14, 2019, Palace of the Parliament, Bucharest: Joint meeting of the Committee for Advanced Therapies (CAT) and the Clinical Trial Facilitation Group (CTFG), with the aim of strategic analysis and learning (Strategic Review and Learning Meeting = SLRM).

- June 19-21, 2019, Palace of the Parliament, Bucharest: the 96th meeting of the body of Heads of Medicines Agencies (HMA), the last event organized by the NAMMD during the Romanian Presidency of the EU Council, under the coordination of the Ministry of Health, in collaboration with the National Sanitary Veterinary and Food Safety Authority and Institute for Control of Biological Products and Veterinary Medicines.

In addition to these meetings, held in Romania, the Agency also prepared and organised, in collaboration with the National Competent Authority of Italy, AIFA, the meeting of the Committee for Orphan Medicinal Products in Rome, between 26-29 May 2019 and participated, through representatives, at the informal meeting of the Paediatric Committee (PDCO - Strategic Review and Learning Meeting), organised by the Competent Agency of Malta, which took place in Valletta, between 12.06.2019 - 14.06.2019. In the spirit of the same collaboration, between 2-5 June 2019, the competent authority of Israel hosted on behalf of Romania the meeting of the Working Group of Enforcement Officers of the HMA.

In addition, during the Romanian Presidency of the Council of the European Union, the NAMMD / NAMMDR played an extremely important role in organising 8 meetings of the Working Party for Pharmaceuticals and Medical Devices, during which negotiations on the Proposal for a Regulation for Health Technology Assessment (HTA Regulation) and amendment of Directive 2011/24 / EU continued.

On the other hand, the NAMMD / NAMMDR carried out, in 2019 as well, the same policy of equidistant partner of the representatives of the pharmaceutical industry (manufacturers, marketing authorisation holders - MAHs, importers, wholesale distributors), healthcare professionals (physicians and pharmacists), partners without whom the Agency would not be able to fulfil its mission in the three areas of competence.

Communication with all actors involved in the pharmaceutical market is a major and constant concern every year, in an attempt to propose to the Ministry of Health viable solutions for developing and implementing a policy to ensure patient access to prescribed treatments and, particularly, to treatments with new, last generation medicinal products available in other Member States of the European Union under national health insurance systems.

In terms of external communication, the NAMMD / NAMMDR has been highly visible and present, through its general communication obligations both in the EMA working groups, working in the exchange of experience in the EMA strategy until 2020, as well as in meetings organised by other European institutions, in addition to those imposed by the organisation of activities within the Romanian Presidency of the Council of the European Union. Also, the representatives of the Agency actively participated through national and international specialised presentations at numerous scientific events, congresses, conferences, workshops.

In this context, the presence in July 2019 of NAMMDR representatives at the 8th meeting of the Valletta Technical Committee Group should be noted; it was held in the capital of the Republic of Malta and it marked two years since the signing of the Declaration of Valletta and the establishment of the Group with the

same name. We remind you on this occasion that the Group is made up of 10 EU Member States (Malta, Cyprus, Greece, Ireland, Italy, Romania, Portugal, Slovenia and Croatia), representing over 160 million citizens. It was set up with the aim of working together mainly to improve the level of healthcare provided to EU citizens and access to innovative services and medicinal products under conditions of sustainability and price transparency. This meeting was all the more important as it was another opportunity for discussion and clarification in this field from the perspective of adoption at the 72nd session of the General Assembly of the World Health Organisation (held in May of the same year) of the resolution entitled "Increasing the transparency of the market for medicinal products, vaccines and other health technologies", considered the basis for future action at national and international level in this direction.

The success of organising the particularly complex process of preparing and carrying out the planned actions within PRES RO, through sustained and concentrated efforts of the entire NAMMD / NAMMDR team was thus one of the important achievements of 2019.

II. ACTIVITIES PERFORMED BY THE NAMMD/NAMMDR IN 2019

1. Activity of the Scientific Council (SC)

In line with Law 134 of 2019 Law no. 134/2019 on the reorganisation of the National Agency for Medicines and Medical Devices, as well as for amendment of some regulatory acts, the Scientific Council could not meet due to the impossibility of deciding and approving its nominal composition by Minister of Health Order, because of a legislative inaccuracy in the above-mentioned act, namely because of the specification in the Law of some structures / organisations that should have been represented in the NAMMDR Scientific Council, structures / organisations which are in fact non-existent, namely the Association of Romanian Medicine and Pharmacy Universities, the Association of Deans of Romanian Pharmacy Universities, the Association of Deans of Medicine Universities in Romania.

In order to amend the regulatory act and overcome this impediment, in December 2019, the NAMMDR submitted to the Ministry of Health a draft Emergency Ordinance to amend and supplement Law 134/2019 Law no. 134/2019 on the reorganisation of the National Agency for Medicines and Medical Devices, as well as on amendment of some regulatory acts.

2. Activity of the NAMMD Administration Council (AC)

The NAMMDR Administration Council is set up by Minister Order, and includes:

a. The NAMMDR President, who also fulfils the function of Chairman of the Administration Council;

b. Two NAMMDR vice-presidents;

c. Two representatives of the Ministry of Health.

In 2019, there were 2 meetings of the NAMMDR Administration Council, mainly focused on establishing appropriate administrative measures to apply the provisions of Law no. 134. In this respect, the diversity and complexity of the economic and administrative activities required by the transition to the Agency's new status and ensurance, at the same time, of the continuous and smooth development of NAMMDR current activities, should be noted.

3. Activity of NAMMD commissions

3.1. NAMMD Marketing authorisation commissions

Within meetings of the Commission for Marketing Authorisation, established through Decision of the NAMMD Administration Council, as established through President Decision, discussion of assessment reports was continued, for grant of the Agency's opinion concerning marketing authorisation of various medicinal products applied for in this respect, as well as other issues related to marketing authorisation of medicinal products for human use.

In 2019, 44 meetings were organised, during which a number of 1936 applications for authorisation were discussed (respectively, 1299 applications for authorisation through national procedure and 637 applications for authorisation through European procedures). Following the positive opinion of the Marketing Authorisation Commission, applications for a marketing authorisation (MAA) were approved, according to the tables and graphs in the next chapter.

A positive opinion was expressed for issuance of 1570 marketing authorisations, of which 902 for national procedure and 668 for European procedures, as follows:

- For the national procedure, the grant of 69 marketing authorisations and of 833 marketing authorisation renewals,

- For European procedures, 320 authorisations through enforcement of the decentralised procedure and of the mutual recognition procedure, 55 authorisations through enforcement of the repeat-use mutual recognition procedure and 2993 marketing authorisation renewals.

3.2 Commission for the management of crisis situations caused by medicinal product quality, safety and / or efficacy issues

The Commission for management of crisis situations operates in accordance with Decision of the NAMMD President and with its own organisational and operation rules, as approved through Administration Council Decision.

In 2019, the Commission was summoned on 13 December.

3.3 Commission for assessment and authorisation of medicinal products used for special needs

The Commission for management of crisis situations operates in accordance with Decision of the NAMMD/NAMMDR President and with its own organisational and operation rules, as approved through Administration Council Decision.

The objective of the commission is the approval / rejection following the evaluation of the applications of the authorisation of medicinal products used for special needs according to the provisions of Order no. 85/2013. In 2019, 30 meetings of this commission took place, regarding 72 medicinal products, concluded with the authorisation of 72 medicinal products for this purpose.

3.4 Commission for assessment and authorisation of the use of a medicinal product used in treatments of last resort

The Commission for management of crisis situations operates in accordance with Decision of the NAMMD/NAMMDR President and with its own organisational and operation rules, as approved through Administration Council Decision.

The objective of the commission is the approval / rejection following the evaluation of the applications of the authorisation for use of a medicinal product for human use to be available for use in last resort treatments by applying the conditions established through Order no. 1018/2014 (version updated in 2018).

In 2019, the Commission carried out its activity in 13 meetings, the commission's activity ending with the issuance of 10 authorisations for last resort treatments, especially for oncological pathology, a rare disease as well as multiple sclerosis in children.

3.5 Commission for verification of compliance of NAMMD inspection staff with the professional ethic and deontology code

The Commission operates in accordance with Decision of the NAMMD/NAMMDR President and with its own organisational and operation rules, as approved through Administration Council Decision. The goal of the Commission is verification of compliance of the Agency’s inspecting staff with

the Code of ethics and deontology, as approved through Order of the Minister of Health no. 160/2004. In 2019, there were no requests for summons of the Commission.

4. Marketing authorisation and related activities

In 2019, the main activities of the Agency, mainly the assessment of the documentation submitted to the NAMMD for marketing authorisation and marketing authorisation renewal, as well as post-authorisation surveillance of a medicinal product's safety, have been commendably performed, as imposed by high complexity standards, established through an increasingly severe European Union legislation in the field of the medicinal product for human use. These activities are specific to a competent authority in the field of the medicinal product, carried out in accordance with legal provisions on national procedure and European procedures (mutual recognition/decentralised/ repeat-use mutual recognition procedure, centralised procedure).

4.1. Marketing authorisation through national and European procedures

Last year, the specific activities carried out within the structures of the Department, respectively the European Procedures Directorate and the National Procedure Department / Directorate with the involvement of experts for biological medicinal products within the Medicinal Product Quality Control Directorate, materialised into issuance of a number of 1570 MAs for medicinal products for human use, of which for 668 (42.54%) the authorisation was granted by applying the provisions of European procedures (301 DCP, 19 MRP, 55 through MRP - Repeat Use and 293 renewals of MAs), while 902 (57.46 %) of the issued authorisations concerned applications for authorisation through national procedure (69 new MAs and 833 MA renewals).

➢ Authorisations granted through national procedures

Authorisations granted through national procedures		
Month	**Authorisations**	**Renewal**
January	**0**	**21**
February	**3**	**26**
March	**7**	**41**
April	**7**	**62**
May	**6**	**85**
June	**8**	**213**
July	**0**	**11**

August	**0**	**148**
September	**15**	**74**
October	**4**	**36**
November	**14**	**73**
December	**5**	**43**
TOTAL	**69**	**833**
	902	

National authorisations - 2019

	Jan.	Febr.	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
Authorisation	**0**	**3**	**7**	**7**	**6**	**8**	**0**	**0**	**15**	**4**	**14**	**5**
Renewal	**21**	**26**	**41**	**62**	**85**	**213**	**11**	**148**	**74**	**36**	**73**	**43**

➢ Authorisations and renewal of authorisations (R) through European procedures (decentralised procedure - DCP, mutual recognition procedure - MRP, repeat-use mutual recognition procedure – MRP- RU)

Authorisations granted through European procedures				
Month	**DCP**	**MRP**	**MRP-RU**	**R**
January	**45**	**0**	**3**	**32**
February	**7**	**0**	**4**	**11**
March	**43**	**6**	**4**	**39**
April	**40**	**0**	**12**	**26**
May	**28**	**1**	**2**	**24**
June	**27**	**3**	**4**	**45**
July	**0**	**0**	**0**	**0**
August	**18**	**0**	**12**	**13**
September	**18**	**4**	**0**	**12**
October	**27**	**2**	**5**	**23**
November	**40**	**3**	**3**	**42**
December	**8**		**6**	**26**
TOTAL	**301**	**19**	**55**	**293**
	668			

In the case of authorisations issued by applying the provisions of European procedures, a more comprehensive picture can be provided by specifying the number of authorisations granted separately with the involvement of Romania as a concerned Member State or as a reference Member State.

Thus:

- Authorisations/Renewals granted in procedures with the involvement of Romania as a concerned Member State (RO SMI):

- Authorisation through decentralised procedure (DCP): 279

- Authorisation through mutual recognition procedure (MRP): 14

- Authorisation through repeat-use mutual recognition procedure (MRP-RU (E)): 52

- MA renewal (R): 275

- Authorisations/Renewals granted in procedures with the involvement of Romania as a reference Member State (RO SMR):

- MA renewal (R): 10

Authorisations (European) - 2019

	Jan.	Febr.	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
DCP	45	7	43	40	28	27	0	18	18	27	40	8
MRP	0	0	6	0	1	3	0	0	4	2	3	
Renewal	32	11	39	26	24	45	0	13	12	23	42	26
Repeat use	3	4	4	12	2	4	0	12	0	5	3	6

Authorisations (National + European) - 2019

	Jan.	Febr.	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
National	21	29	48	69	91	221	11	148	89	40	87	48
European	80	22	92	78	55	79	0	43	34	57	88	40

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

4.2.1. Regarding the activity carried out during the post-authorisation period, undertaken in 2019, regarding the evaluation and approval of requests for

variation to MA terms by national procedure, the achievements of NAMMD / NAMMDR can be summarised in the evaluation and approval of 3706 applications, as follows:

- 3346 Type I variations;

- 138 Type II variations;

- 89 MA transfers;

- 133 changes of packaging design and imprinting;

In case of quality variations / design changes / MA transfer submitted through NP for biological medicinal products, the evaluation is performed within MPQCD; the following were evaluated and approved in 2019:

- 166 Type I variations;

- 47 Type II variations;

- 2 changes of packaging design and imprinting.

4.2.2. In 2019, as regards post-authorisation assessment of variations to MA terms granted through European procedures, the NAMMD/NAMMDR approved 4740 letters for approval for MAs and the corresponding Annexes, as follows:

4659 addresses for approval with Romania as a Concerned Member State (CMS) were issued:

- 2002 Type IA variations;

- 1546 Type IB variations;

- 424 Type II variations;

- 358 MA transfers;

- 188 notifications in accordance with Article 61(3) of Directive 2001/83/EC;

- 141 national notifications in accordance with Order of the Minister of Health no. 1205/2006

81 addresses for approval with Romania as a Reference Member State (RMS) were issued:

- 17 Type IA variations;

- 28 Type IB variations;

- 6 notifications in accordance with Article 61(3) of Directive 2001/83/EC;

- 11 national notifications in accordance with Order of the Minister of Health no. 1205/2006.

As regards biological medicinal products, the evaluation of quality variations was performed with the involvement of the experts in the field of biological medicinal products within the Medicinal Product Quality Control Directorate.

4.3. Assessment of applications and documentation for approval of clinical trials on medicinal products for human use and clinical trial sites

As in the case of the other structures of the Agency, the organisation of the profile field was marked by entry into force of Law no. 134/2019. Thus, the activity of the national competent authority in the field of clinical trials was carried out within the Clinical Trials Service (until July 2019) and, subsequently, within the Clinical Trials Directorate (CTD), with the promulgation of Law no. 134, with the same attributions, with the participation of experts for the quality documentation in the case of biological medicinal products, within the Medicinal Product Quality Control Directorate.

In accordance with the law, the main attributions of the profile structure are:

• Assessment and authorisation of clinical trials, clinical investigations and bioequivalence studies;

• Assessment and approval of amendments to approved clinical trials / clinical investigations / bioequivalence studies;

• Assessment and approval of observational studies;

• Authorisation of medical units for conducting clinical trials / clinical investigations and bioequivalence studies (activity taken over from the Legal and International Relations Directorate (DJRI) in March 2019);

• Evaluation of performance for in vitro diagnostic medical devices;

• Management of the Voluntary Harmonized Procedure (VHP);

• Receipt and management of amendments of any kind of clinical trials / clinical investigations / bioequivalence studies, various notifications, addresses with requests for different information.

In the field of evaluation and authorisation of clinical trials, clinical investigations and bioequivalence studies, year 2019 yielded the following results:

	Interventional clinical trials	**Bioequivalence trials**	**Clinical investigations**
Applications:		-	-
Submitted	143	-	-
Withdrawn before assessment	12	-	-
Withdrawn after assessment	2	-	-
Authorisations:		-	-
Granted and issued	147 (also for applications submitted in 2018)	-	-
Rejected	18 (also for applications submitted in 2018, 2017, 2016)	-	-

As regards the assessment and approval of amendments to clinical trials / clinical investigations / bioequivalence studies, the following were registered:

Number of applications for assessment and approval of important amendments	868
Withdrawn applications	2
Approved amendments	737 approvals (also from last year)
Rejected amendments	11

The authorisation of medical units for conducting clinical trials / clinical investigations and bioequivalence studies focused on 214 applications for authorisation and ended with the issuance of 180 such authorisations.

An important activity in the field of clinical trial authorisation is the management of NAMMD / NAMMDR tasks within the Voluntary Harmonization Procedure (VHP) project conducted at the Clinical Trial Facilitation Group (HMA subgroup). In this regard, 18 applications related to clinical trials were received and evaluated, of which 1 for Romania as reference member state and 184 applications for approval of important amendments, of which 3 for Romania as reference member state.

Last year, at the level of the Clinical Trials Service / Directorate, 2351 miscellaneous notifications were received and managed (first patient, closure

notifications, temporary interruptions, non-important amendments), SUSAR, DSUR, Annual Report.

In addition, at the level of the Clinical Trials Service / Directorate, the Romsys Server / Clinical Trials database is managed by entering electronic documentation and maintenance of records of requests, notifications or any information received regarding clinical trials / investigations and bioequivalence studies.

In the field of authorisation of medical units for conducting clinical trials / clinical investigations and bioequivalence studies, activity transferred from DJRI in March 2019:

- Applications for authorisation received: 214

- Authorisations issued: 180

4.4 Assessment of medical technologies

As the main activity of the Department for Health Technology Assessment, in accordance with Law 134/2019, consisted of assessment of the support documentation of applications, according to the health technologies assessment, and of issuance of the decision on inclusion, extension of indications, non-inclusion or exclusion of medicinal products in/from the List of International Non-proprietary Names of on-prescription medicinal products as provided to insurants, irrespective of personal contribution, on prescription, in the frame of the health insurance system, as well as of International Non-proprietary Names of medicinal products provided in national health insurance programmes, 96 applications for health technologies assessment were submitted in 2019.

During the same year, 97 applications were fully assessed (8 of the applications submitted in 2017, 59 of the applications submitted in 2018 and 30 of the applications submitted in 2019).

The assessment activity performed during this year consisted of:

- 36 decisions for unconditioned inclusion for:

• Infectious diseases - 1 medicinal product

• Oncology - 13 medicinal products

• Rheumatology -1 medicinal product

• Diabetes and metabolic diseases - 2 medicinal products

• Haematology - 9 medicinal products

• Dermatovenereology: 1 medicinal product

• Endocrinology -1 medicinal product

• Pneumology -1 medicinal product

• Gastroenterology -1 medicinal product

• Neurology -1 medicinal product

In 2019, by applying a multidisciplinary approach, a number of 5 orphan medicinal products were assessed and 39 decisions were issued for conditioned inclusion by concluding the respective cost-volume contracts in the List of compensated INNs in the social health insurance system, with reference to infectious diseases, oncology, diabetes and nutrition, haematology, dermatovenereology, endocrinology, pneumology, ophthalmology, gastroenterology and neurology.

17 decisions were issued for non-inclusion in the List, regarding INNs with indication in ophthalmology, neurology, dermatology, oncology, haematology, endocrinology, rheumatology, cardiology, diabetes, gastroenterology. In 2019, within the Department, namely the Health Technologies Assessment Directorate, a number of 23 orphan medicinal products were evaluated, 14 receiving decisions for unconditioned inclusion in the List and 9 decisions for conditional inclusion in the oncology and haematology fields.

Also, in 2019, the Health Technologies Assessment (HTA) Department evaluated 15 medicinal products for rare diseases, the targeted areas being oncology, haematology, rheumatology.

Of these:

• 8 decisions for unconditioned inclusion on the List;

• 6 decisions for conditioned inclusion on the List;

• 1 decision for non-inclusion on the List for 1 medicinal product.

Following the assessment process of medical technologies carried out in 2019, the List of reimbursable medicinal products approved by Government Decision (GD) 720/2008 was updated 3 times, by GD 344 / 30.05.2019, GD 643 /27.08.2019 and GD 753 / 10.14.2019.

During the same period, WHO / NHIH 1301/500/2008 was updated 3 times respectively by WHO / NHIH no. 854/562/2019, WHO / NHIH no. 1127/669/2019 and WHO / CNAS no. 1801/1113/2019.

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

In the context of the increasing complexity of the medicinal product market and the growing need to bring the real benefit to the patient to the forefront, the

activity of approval and monitoring of advertising in the field of the medicinal product for human use is growing in importance every year.

Thus, in 2019, the specialists of the Advertising Service carried out the following activities:

In the field of Advertising:

- Evaluation of advertising materials, followed by approval: 656

- Reapproval of advertising materials: 791

- Forms for rejection of advertising materials: 10

- Evaluation of educational materials, followed by approval: 158

- Reapproval of educational materials: 140

- Forms for rejection of educational materials: 12

- Physical and electronic archiving of advertising materials and educational materials solved: 73

- Record of notifications regarding the participation of the MAH in medical events;

In the field of sponsorship, as regards the obligation of manufacturers', MAHs or their representatives in Romania, wholesale and retail distributors of medicinal products and all beneficiaries of sponsorship activities to declare all sponsorship activities to the NAMMD / NAMMDR, as well as any other expenses incurred / which benefited the year prior to reporting, for any legal or physical person with activities in the field of human health, medical or pharmaceutical care, the NAMMD / NAMMDR made public the register resulting from the receipt of 13,993 sponsorship forms from beneficiaries and 122 forms for declaring sponsorship activities performed by sponsors.

4.6. Pharmacovigilance

The main objective of the pharmacovigilance activity performed at the level of the competent authority is to know in greater depth the medicinal product's safety profile and thus to reduce the number of adverse reactions (AR) to medicinal products and to prevent their occurrence. Optimizing the collection of medicinal product data and their safe use by involvement and active participation of patients and facilitation of report of adverse reactions, increasing the level of transparency and ensuring optimal communication result in the accumulation of a significant volume of data whose prompt and consistent evaluation allows for effective regulatory actions to ensure the safety and efficacy of medicinal products.

In accordance with the procedure for adverse reaction reporting, communicated to professionals and the general public both on the NAMMD / NAMMDR website (www.anm.ro) and at any profile events and meetings, healthcare professionals and patients or caregivers can send the reports of suspected adverse reactions to NAMMD / NAMMDR by mail, fax, e-mail, by filling in the Forms or the Electronic Reporting Form available on the NAMMD website, under section Medicinal products for human use / Report an adverse reaction.

In accordance with EU pharmacovigilance requirements, ARs suspected and reported in all Member States are submitted for introduction into the European EudraVigilance Database for collection of adverse reactions. Collecting adverse reactions across Europe in a single point facilitates the monitoring at European level of the safety profile of medicinal products and thus the early detection of potential safety signals.

In this context, the Pharmacovigilance and Risk Management Service (SFMR), respectively the Pharmacovigilance and Risk Management Directorate (DFMR) carried out multiple profile activities, among which the following should be highlighted:

a. Management of reports of suspected adverse reactions to medicinal products for human use from spontaneous reporting or clinical trials. Continuing the trend of increasing the number of reported adverse reactions (ARs), following the entry into force of the new pharmacovigilance legislation in 2012 and the optimisation of specific operational procedures to adapt to requirements, 5900 AR reports were received in 2019, from all sources (patients, consumers, healthcare professionals, marketing authorisation holders, INSP / CNSCBT), of which 2014 serious adverse reaction reports.

As regards ARs to vaccines, known as undesirable post-vaccination adverse reactions (RAPI), as of 2012, there is a collaboration protocol between NAMMD / NAMMDR / Pharmacovigilance and Risk Management Service and the National Institute of Public Health / National Surveillance Centre and Control of Communicable Diseases (INSP / CNSCBT), revised in 2017 for mutual information on post-immunisation adverse reactions reported to the two institutions. The collaboration protocol in force stipulates that NAMMD / NAMMDR is responsible for the monthly transmission to INSP / CNSCBT of undesirable post-vaccination ARs received directly by the Agency; therefore, the NAMMDR transmitted to INSP / CNSCBT 21 adverse reactions to vaccines in 2019. Moreover, according to the protocol, the NAMMDR manages the RAPI transmitted by INSP / CNSCBT, so that 43 RAPI were received and processed according to the operational procedures in force, in 2019.

b. Pharmacovigilance activities in the system of European national authorities under the coordination of the EMA. This year, according to the

obligations of the NAMMD / NAMMDR as a member of the European network of competent authorities in the medicinal product field, after processing the adverse reaction reports received directly from healthcare professionals and patients, a number of 249 reports of serious adverse reactions and 641 of non-serious adverse reactions, respectively, were submitted for registration into the EudraVigilance database.

During the same period, 20 EMA press releases on medicinal product safety (translation / website posting) were managed.

Within SFMR / DFMR, 31 direct healthcare professional communications were handled, regarding safety issues of medicinal products, and 25 sets of information addresses were sent to NHIH, the Ministry of Health, the Romanian College of Physicians, the Romanian College of Pharmacists.

Regarding the specific activity of handling safety signals for the substances that Romania monitors via the EudraVigilance database, SFMR / DFMR considered 34 active substances or combinations of substances.

Regarding the responsibility of the evaluation structure of the documentation submitted by the MAH (Periodic Safety Update Report - RPAS) within the single European procedure for Assessment of the Periodic Safety Update Report (PSUSA) in which Romania is appointed Reference Member State, 2 procedures were completed during 2019.

c. Pharmacovigilance activities through the rapid alert / non-urgent information system (AR / NUI). Last year, there were 21 response situations (INUs) to requests for information received from the EMA or other authorities in EU Member States regarding information on certain medicines or classes of medicinal products. In the same area there were 2 situations involving the transmission of non-urgent information (INU) to the other EU Member States on certain medicinal products or classes of medicinal products.

d. Evaluation of the pharmacovigilance documentation in view of the authorisation and renewal of the marketing authorisation procedure. Within the centralised marketing authorization procedure, at SFMR / DFMR level, comment reports were prepared concerning the evaluation of the pharmacovigilance documentation (summary of the pharmacovigilance system - Module 1.8.1, Risk Management Plan - Module 1.8.2) in the Centralized Procedure in which Romania is appointed Rapporteur / Co-rapporteur for 2 procedures.

In order to obtain the marketing authorisation through the decentralised procedure (DCP) / mutual recognition procedure (MRP) / repeat-use mutual recognition procedure (repeat-use MRP) (with Romania as a reference member state/concerned member state), DFMR has contributed by setting up assessment reports for the pharmacovigilance documentation to all ongoing and completed procedures during 2019.

SFMR / DFMR was also involved and contributed to the verification of the documentation and its evaluation in all marketing authorisation procedures for some medicinal products for special needs and in the marketing authorisation procedures for medicinal products used in last resort treatments.

e. Assessment and approval of educational materials included in the Risk Management Plan (RMP) for medicinal products authorised in accordance with Article 127a of Directive 2001/83 / EC as subsequently amended and supplemented. In order to carry out this activity, SFMR / DFMR completed the evaluation of 105 supporting files for the applications for approval regarding approximately 180 educational materials.

f. Assessment of applications concerning the pharmacovigilance system for variations to marketing authorisation terms. As regards the responsibilities held in this field, the activities of SFMR / DFMR materialised in the completion of:

• 115 reports on variation applications submitted by the MAH for medicinal products authorised through European Procedures in which RO is a SMR / SMI - Evaluation of pharmacovigilance documentation submitted by type IA, IB and II variations for medicinal products authorised through European procedures (summary of the pharmacovigilance system - Module 1.8.1, Risk Management Plan - Module 1.8.2);

• 3 reports on variation applications submitted by the MAH for medicinal products authorised through National Procedure - PMR evaluation in type IA, IB and II variations for medicinal products authorised through national procedure;

g. Management of e-mail addresses dedicated to the pharmacovigilance activity: - roh.pharmacovigilance@ro-h.eudra.org; ro-h.ra@ro-h.eudra.org; ro-h.psur@ro-h.eudra.org;farmacovigilenta@anm.ro; variatii.farmacovigileta@anmdm.ro; psur@anmdm.ro; adr@anm.ro; contact.adr@anm.ro; signal@anm.ro

h. Collaboration with the Department / General Directorate for Pharmaceutical Inspection (DGIF)

- Development of 6 response addresses for resolution of complaints regarding medicinal product adverse reactions.

i. Participation in the meetings of the EMA Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA)

j. Participation in the elaboration / amendment of some regulatory acts in the field of activity

In this field, DFMR collaborated with other specialised NAMMD / NAMMDR structures and with the Legal and International Relations Directorate

in order to elaborate / amend regulatory acts in order to be submitted to the Ministry of Health for approval.

With the direct involvement of the Policy and Strategy Department / SCRP and the FMR Service / Directorate, the Agency organised an annual social media campaign in Romania in 2019, to promote awareness of the importance of adverse reaction reporting, along with 39 other regulatory authorities related to the medicinal product in the European Union, Australia, Canada and Norway.

Other important achievements in 2019 are the organisational responsibilities that went to the Pharmacovigilance and Risk Management Service (SFMR) during 01.01.2019-31.06.2019, when Romania held the Presidency of the Council of the European Union, especially regarding the meetings of HMA: HMA 1 (February 20-22, Timișoara), HMA 2 (June 19 - 21, Bucharest) and at the CMD (h) - PRAC meeting (May 22 - 23, Bucharest).

At the same time, as coordinator of the file "Proposal for a Regulation of the European Parliament and of the Council on the assessment of medical technologies and amendment of Directive 2011/24 / EU", the SFMR / DFMR coordinator ensured the development of specific activities of representation of Romania at the working party for pharmaceuticals and medical devices and participation in the preparatory meetings and the 3 meetings of the Group.

4.7. Miscellanea

Maintenance of the database of authorised medicinal products:

The specific activity related to this database consists of the introduction of information related to new medicinal products authorised for marketing through national, European and centralised procedures, the operation of MA amendments for already authorised medicinal products, the introduction of variations to the terms of MAs issued, the highlighting of medicinal products undergoing MA renewal procedure, MA withdrawal / discontinuation decisions.

In 2019, with the support of specialists from the Logistics, information and electronic data management (DLIGED) / Information and Communication Technology Service (STIC) regarding the operation on the Agency's website, the National Procedure Department provided:

• Maintenance of the database of authorised medicinal products:

- 2079 products authorised through: national/European/centralised procedure(s) - for those notifying effective placement on the market – information about the marketing authorisation (MA) are introduced: trade name, MAH, batch release responsible person, packaging;

- 7407 variations to MAs approved through national/European/centralised procedure (information on approved MA changes shall be introduced: trade name, MAH, person responsible for batch release, packaging etc.)

- Issue of 299 decisions for MA withdrawal/discontinuation (withdrawal of national MA when the same product is granted a marketing authorisation through European procedure; discontinuation of a valid MA on request by the company/sunset clause)/suspension in accordance with a European Commission Decision;

• Other activities related to the Index of Medicinal Products for Human Use were, among others:

- Inclusion of 310 medicinal products into the database of the Index, as "temporary/terminal marketing discontinuation";

- Introduction in the database of notifications for marketing relapse - 310 medicinal products;

- Introduction into the database of information on withdrawal of the MA / renewal procedure for - 902 medicinal products;

Operating in the database the decisions for withdrawal of MAs at the request of the company / MRR / MRR-R - 471 medicinal products or by applying the sunset clause - 7 medicinal products;

Operation in the database "Notifications for medicinal product discontinuations" on the NAMMD website - 1300 medicinal products;

Operation in the database "Medication discontinuity notifications" on the NAMMD server - 3706 medicinal products;

Identification in the Index of medicinal products for human use of therapeutic alternatives (MAs) with the same international non-proprietary name (INN), pharmaceutical form and strength as the medicinal products notified as temporarily or permanently discontinued and verification in the same database of therapeutic alternatives (MAs) identified in the Index with the same INN, pharmaceutical form and strength as the medicinal products notified as being temporarily or definitively discontinued in terms of marketing / non-commercialization on the Romanian market - 660 INN (2870 medicinal products);

As regards the activities related to the issuance of parallel import authorisations (PIAs), 123 MAs were issued in 2019, an activity that involves the evaluation of the submitted documentation, the completions sent by the applicants and the elaboration of the PIAs and their annexes.

"Parallel export" activities consisted of:

- Replies to 19 European Agencies which requested information on medicinal products authorised in Romania (the MA number of the medicinal product in Romania; the MAH; the manufacturers involved in the entire manufacturing process; details on the qualitative and quantitative composition of the product; the ATC code, manner of presentation, storage conditions) for which they received applications for issuance of parallel import authorisations in the respective member state.

5. Activity of Good Manufacturing Practice (GMP), Good Distribution Practice (GDP), Good Laboratory Practice (GLP), Good Analytic Laboratory Practice (GALP), Good Clinical Practice (GCP), pharmacovigilance and market surveillance

During 2019, the Pharmaceutical Inspection Department (PID), until entry into force of Law 134/2019 on NAMMD reorganisation, as well as amendment of certain regulatory acts and, subsequently, the Department / General Directorate for Pharmaceutical Inspection (DGIF), continued activities mentioned in specific legislation (Law 95/2006 - Title XVIII – The medicinal product, republished, and secondary legislation), in accordance with the Department's Standard Operating Procedures and according to deadlines stipulated by the law.

DGIF comprises 5 operational structures: DGIF Process Management Directorate, the Good Manufacturing Practice Inspection Directorate, Laboratory, Analytical Laboratory, Clinical Trial and Pharmacovigilance, the Good Distribution Practice Inspection Service, the Rapid Alert Service, Counterfeit Medicinal Products, the Directorate for the supervision of the quality of medicinal products and territorial units.

Inspections carried out at both national and international level are recognised by international partners. DGIF inspectors participate in joint inspections requested by the EDQM or EMA.

Through its representatives, DGIF actively participates in debates in meetings of scientific committees and working groups of specific European bodies (EMA, HMA, EDQM). DGIF is a member of the PIC / S (the Pharmaceutical Inspection Co-operation Scheme).

The following types of inspections were performed in 2019:

GMP, GLP, GALP, GCP, pharmacovigilance inspections:

- 25 GMP inspections for grant of manufacturing/import/certification authorisation have been conducted (14 GMP inspections for grant of a manufacturing authorisation/GMP certificate for starting materials – active pharmaceutical substances and 11 inspections for authorisation at the sites of medicinal product importers);

- 3 certification inspections for GMP compliance of pharmaceutical companies from third countries;

- 1 inspection at independent control units for microbiological laboratories, one unit being in the process of GMP re-authorisation / re-certification.

Specific authorisation activities of medicinal product distributors and assessment of compliance with the Good Distribution Practice

The responsibilities of the specific service consist of:

- The wholesale distribution authorisation of distribution units in Romania in accordance with the legislation in force;

- Inspections to assess compliance with the Good Wholesale Distribution Practice and issuance of certificates of compliance with the Good Wholesale Distribution Practice, in accordance with the provisions of Order of the Minister of Health no. 131/2016 (GDP recertification);

- Management of the national database with information from the wholesale distribution authorisations issued, as well as introduction of GDP authorisations and Certificates into the EudraGMDP database, including the update / suspension of the GDP authorisations;

- Evaluation of requests for amendment of Annexes to wholesale distribution authorisations;

- Management of notifications regarding the intra-community delivery of medicinal products, sent to NAMMDR in accordance with Order of the Minister of Health no. 269/2017;

- Management of databases containing wholesale distributors and medicinal products (through wholesale distribution) according to the monthly reports submitted by wholesale distributors / manufacturers / importers in accordance with Order of the Minister of Health no. 502/2013;

- Processing of information from monthly reports sent by wholesale distributors / manufacturers / importers according to Order of the Minister of Health no. 502/2013 on wholesale distribution of medicinal products, as well as processing of information from daily reporting (SER), in order to formulate responses to interested institutions and responses to complaints received by email on lipsamedicament@anm.ro;

- Coordination of local inspectors concerning local performance of inspections for authorisation of wholesale distributors;
The authorisation of GDP wholesale distribution / GDP recertification is carried out in accordance with the provisions of Order of the Minister of Health no. 131/2016; the following activities, related to the process of authorisation of the

wholesale distribution activity / assessment of GDP compliance, took place in 2019:

- Evaluation of 110 new requests for GDP inspections and continuation of 100 requests submitted in 2018;

- Issuance of 29 addresses – requests for amendment of the submitted documentation;

- Issuance of 104 tariff addresses for a GDP inspection / issuance of a GDP certificate to the General Directorate for Economics and Public Procurement, of which 87 for newly submitted applications;

- Carrying out 116 GDP inspections for authorisation (of which 52 for newly submitted applications) and 2 unexpected GDP inspections;

- Preparation of 108 lists of deficiencies, of which 8 for inspections performed in 2018;

- Request for completion of the corrective/preventive measure plan for 6 units;

- Preparation of 110 final GDP reports, of which 7 are negative;

- Issuance / update of 98 Wholesale Distribution Authorisations;

- Issuance of 136 Certificates on compliance with Good Distribution Practice;

- Periodic introduction into the EudraGMDP database and into the internal database (Access) of the issued GDP authorisations and certificates.

108 requests for updates of wholesale distribution authorisations (amendments to the annexes) were received and assessed and 21 requests from 2018 were continued. 87 updated authorisations / annexes were issued.

The wholesale distribution authorisation inspections were carried out by inspectors from the DGIF headquarters and by some of the inspectors from territorial inspection units who, for implementation of the legislation specific to the wholesale distribution of medicinal products during inspections, received the documentation and the necessary information and transmitted the prepared documents (which were verified) to the headquarters.

As regards the inspections for assessment of compliance with the Good Wholesale Distribution Practice, 7 reports on non-compliance with BPD were prepared.

The main deficiencies found at wholesale distributors were:

- Non-compliance with the provisions of custody contracts and logistics services;

- Lack of audits for outsourced activities (e.g. delivery / transport) or formal audits;

- Non-compliances in the implementation of the quality management system (e.g. incomplete / incorrect procedures which cannot be implemented, non-application of issued system procedures – e.g. treatment of deviations, change control, risk management);

- Improper management of the transport activity, also in the situation of using the transport nodes;

- Improper implementation of the legislation in force regarding the management of serialised medicinal products (non-completion of the SNVM connection process, non-updating of operational procedures).

9 wholesale distributors were fined and the complementary measure for suspension of the wholesale distribution authorisation was applied for 2 units, due to non-compliance with the provisions of the GDP guideline on procurement, delivery and transport of medicinal products, non-compliance with public service obligations, lack of a proper implementation of the SMC created, non-compliance with the prices approved by the Minister of Health.

- Lack of training for key staff;

- Non-compliance with the GDP guideline concerning: validation of computerised systems (including the application for verification of the unique identifier), qualification of suppliers, qualification of the monitoring system of environmental conditions.

66 requests for response to various authorities and legal entities (Ministry of Health, NHIH, the Competition Council, the Ministry of Internal Affairs, the National Agency for Fiscal Administration (ANAF), MAHs, hospitals, wholesale distributors) were received, assessed and detailed.

213 complaints regarding the shortage of medicinal products were investigated, received from pharmacies and hospitals on lipsamedicament@anm.ro, for which electronic correspondence was carried out with wholesale distributors / MAH representatives / pharmacies.

Stock checks are performed on a daily basis in the SER in order to be able to respond to complaints received on the website of the Ministry of Health (http://medicamentelipsa.ms.ro/); the information in the RES is communicated to the Policy and Strategies / SCRP Department in order to draft the response to the complainant.

3059 reports sent by wholesale distributors / manufacturers / importers in accordance with Order of the Minister of Health no. 502/2013 and with Order of the Minister of Health no. 1295/2015 were recorded and managed (centralised access).

3051 notifications of intra-community deliveries sent to the NAMMDR by wholesale distributors according to Order of the Minister of Health no. 269/2017 and 115 reports of imported medicinal products in accordance with Order of the Minister of Health no. 1295/2015 were registered and managed (centralisation, verification of website posting status).

Medicinal product quality monitoring

In line with the legislation in force, this particularly complex activity carried out within the DGIF involves:

- Elaboration of the Annual Plan for Sampling and Testing;

- Establishment of thematic plans;

- Management of notifications regarding medicinal products suspected of having quality non-compliances;

- Performance of inspections for sampling of the medicinal products included in the annual sampling plan and in the additional sampling plans for finished products and starting materials from manufacturing and distribution units;

- Performance of inspections in accordance with the thematic plans established by the DGIF;

- Performance of inspections in warehouses, pharmacies, in order to solve complaints regarding medicinal products suspected of having quality non-compliances;

- Quarterly setup and update of the list of medicinal product batches recalled on the NAMMDR website;

- Setup and update of the table of fined units on the NAMMDR website;

- Administration of the setup databases detailing the activity of the service;

Both the inspectors from the headquarters and those from the 10 Territorial Inspection Units were involved in the activity of supervising the quality of the medicinal products authorised for marketing in Romania.

Thus, the medicinal product quality monitoring in 2019 consisted of:

a. Execution of the sampling plan regarding the medicinal product quality monitoring (sampling, analyses, results). In accordance with the selection criteria underlying the setup of the annual sampling plan, 44 products were proposed for sampling in order to check their quality. Sampling was performed in line with procedure DIF / S / 016 "Sampling". Of the 44 proposed products, 23 were sampled, 21 were not found in the distribution network (of these, 2 radiopharmaceuticals were not sampled since they were not available on the

market). The results obtained from the laboratory analyses performed for the 23 products were:

- 10 of the samples taken were declared appropriate;

- 13 products are under analysis.

In addition to the sampling plan, the following samples were taken in 2019:

- 6 medicinal products for laboratory testing to solve complaints regarding their quality (qualitatively appropriate);

- 1 product sampled as a result of a quality complaint (appearance of flakes in the solution after opening the vial) - could not be tested by DCCM; the respective vial was sent to the MAH for the necessary investigations on the manufacturing line; the manufacturer undertook to monitor the possibility of occurrence of this non-compliance in the case of other medicinal product batches and to inform the NAMMDR about the occurrence of a similar quality non-compliance;

- 5 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 of other EU competent authorities, and the results were found compliant;

- Quality supervision for imported products for supply in case of special needs - sampling of 2 medicinal products: 1 product with 25 imported batches (of these: 20 were qualitatively appropriate, 5 being non-compliant); 1 product suitable in terms of quality.

b. Follow-up inspections of the quality of medicinal products in the distribution network (warehouses, pharmacies, hospital pharmacies, drugstores):

These inspections follow the storage conditions, the quality documents, the advertising of the medicinal products, the compliance of the MAH of the inner and outer packaging, and of the leaflet packaging, the verification of the way in which recalls of medicinal products with quality deficiencies were carried out.

For this purpose, 1138 thematic inspections were carried out in retail distribution units (pharmacies, local dispensaries, drugstores) and the following deficiencies were found:

- Improper storage of some medicinal products, especially in terms of temperature and relative humidity conditions (not all retail distribution units have facilities to ensure the correct storage conditions; in some units, although furnished with the required equipment, the storage conditions are not monitored in all compartments of pharmacies; non-calibrated / uncertified relative temperature and humidity measuring devices; lack of (formal) records of medicinal product storage conditions);

- Improper storage of expired products, lack of arrangement of space dedicated to expired products (in some units);

- Non-compliance with the provisions of the marketing authorisations in force regarding package labelling;

- Identification of advertising materials with expired advertising visas, or materials intended for healthcare professionals available to the public in the dispensaries of some pharmacies;

- Non-compliance with the Rules of Good Pharmaceutical Practice: identification of some medicinal products / pharmaceutical substances without documents of origin / with expired validity in the merchantable stock of some pharmacies; over-the-counter release of a prescription medicinal product, in which case sanctions have been imposed;

- Identification of some medicinal products that are issued on the basis of medical prescription in the merchantable stock of some drugstores, leading to the application of sanctions;

- Identification of a pharmacy that operated without an authorisation issued by the Ministry of Health (following the registration of a notification), leading to a sanction;

- Inadequate / non-hygienised storage spaces;

- Lack of registration in the SNVM, namely non-implementation of measures for management of serialised drugs;

- Transfer of medicinal products on the basis of a delivery notification (between pharmacies / offices of the same company) without evidence regarding the assurance of temperature conditions during transport;

- Lack of records on master elaborations and preparations.

Following the finding of these deficiencies in the activity of pharmacies / drugstores inspected in 2019, NAMMDR inspectors applied sanctions and requested the inspected units to submit evidence on resolution of the deficiencies found.

d. Resolution of complaints regarding potential quality non-compliances of medicinal products for human use.

In 2019, 9 complaints were received from patients or healthcare professionals on medicinal product quality.

Of the 9 complaints, 6 ended with filing without consequences (1 of the complaints could not be resolved because the relevant information requested from the applicant was not received, and the file is to be reopened upon receipt of the

requested information), 1 proved to be substantiated and resulted in the withdrawal of the medicinal product in question; the other complaint is pending.

In order to resolve the complaints, NAMMDR inspectors took 5 product samples for laboratory testing within NAMMDR-DCCM. The received complaints came from healthcare professionals (4) or patients (5).

d. Recall from the market of noncompliant medicinal products in terms of quality:

In 2019, the NAMMDR requested recall of 30 medicinal products as follows:

- 17 medicinal products found with intrinsic quality non-compliances were proposed for recall and destruction (6 by the NAMMD, 11 voluntary recalls by manufacturers/MAHs);

- Of these, 3 medicinal products were recalled as a result of the initiation of the emergency procedure by the French regulatory authority (ANSM) at EU level, discussed in the February 2019 meeting of the Pharmacovigilance Risk Assessment Committee (PRAC), for medicinal products containing the active substance fenspiride;

- The recall measure followed by the non-destructive verification by the manufacturer was accepted for 1 medicinal product, after which the NAMMDR issued the marketing agreement of the compliant commercial units;

- 12 medicinal products were withdrawn by the MAH following cessation of the validity of the MA, for commercial reasons, exclusion from CaNaMed, change of classification upon release.

e. Coordination of activities of Territorial Inspection Units (TIUs) related to medicinal product quality surveillance

In 2019, the quarterly reported TIU activity consisted of:

- Conducting inspections monitoring the quality of medicinal product and the activity in retail distribution units (compliance with storage conditions, establishment of product traceability, identification of possible counterfeit medicinal products - how pharmacies perform decommissioning of serialised medicinal products, monitoring how retail distribution units implemented the recall of medicinal products with quality non-compliances, verification of advertising materials, verification of compliance with the requirements of the MA of the inner / outer packaging / leaflet, verification of the shelf life of medicinal products held in merchantable stock, verification of documents regarding the quality and origin of medicinal gases used in hospitals and of pharmaceutical substances / raw materials in pharmacies authorised to carry out reception and laboratory activities, checks on specialized staff - employment contracts, certificates of membership to the Romanian College of Pharmacists with a valid visa, checks on the daily reporting in the SER of medicinal product stocks);

- Resolution of punctual complaints forwarded by the DGIF on medicinal product quality and pharmacy activities;

- Assessment and transmission of outcomes of thematic plans established by the NAMMD – PID (quarterly activity reports) to the NAMMD;

- Sampling as proposed in the 2019 Annual Plan for Sampling and Testing and sample submission to the NAMMD, accompanied by documents specified in the Pharmaceutical Inspection Department Standard Operating Procedure;

- Enforcement of contraventions in accordance with the legislation in force;

- Notification of quality non-compliances to the NAMMD, found during local surveillance inspections.

In order to solve some problems related to the legislation in the field of medicinal products and / or the quality of some products sold in Romania, TIUs also collaborated with other bodies and state authorities. Thus, in 2019, upon request of the General Inspectorate of the Romanian Police, joint controls were carried out at the sites of commercial societies.

In 2019, for non-compliance with the legislation in the field, NAMMD / NAMMDR sanctioned 17 wholesale and retail distribution units / representative offices in Romania of MAHs (fines applied in a total amount of 680,000 lei).

Rapid alert system

a. Rapid alerts transmitted through the European rapid alert system

In 2019, a number of 148 rapid alerts were received (through the European rapid alert system), managed, registered, for which correspondence was carried out for investigational purposes; final reports were drafted and response addresses were developed and sent.

Thus:

- 123 alerts targeted medicinal products unauthorised for marketing in Romania;

- 21 alerts targeted products authorised for marketing in Romania but not marketed in Romania or batches not distributed in Romania;

- 4 alerts targeted batches that were distributed in Romania;

- 11 alerts concerned stolen medicinal products and medicinal products suspected of counterfeit.

The information provided this year through the rapid alert system by the EMA, EDQM, EU competent authorities, the European Economic Area (EEA) and the US Food and Drug Administration (FDA) covered:

- 14 reported cases of noncompliance with GMP rules by manufacturers, whose assessment was completed:

- Withdrawal of certificates of compliance with the European Pharmacopoeia (CEP) (10 suspensions of CEP certificates whose assessment was completed);

- 2 notifications forwarded by the FDA on GMP non-compliance (whose assessment was completed);

- 7 cases of GDP noncompliance.

In order to establish the impact of these reports of non-compliance with GMP and CEP suspensions on medicinal products authorised in Romania, 12 addresses were prepared for the MAH.

b. Non-urgent notifications from other EU member states

In 2019, there were 4 such non-urgent information on thefts and counterfeits of some medicinal products. At the request of the authorities of the Member States (Germany), traceability checks were performed on suspicions of distribution of counterfeit medicinal products in Romania (Humira Pens, Avastin, Sprycel, Herceptin, MabThera, etc.), and the outcome of the investigations carried out by the NAMMDR was sent by e-mail to the German authorities.

The Belgian Federal Agency for Medicines and Health Products sent 6 notifications on customs blockage of some packages, destined for some citizens living in Romania, which contained medicinal products unauthorised in Romania (psychoanaleptics, benzodiazepines, hyaluronic acid injections, etc.). The notifications were sent to the NAMMDR Legal Department and, subsequently, to the General Inspectorate of the Capital Police.

The representatives in Romania of some marketing authorisation holders sent to the NAMMDR-DGIF 7 notifications regarding the outcome of the investigations carried out for some product samples, suspected of counterfeiting, provided by the General Inspectorate of the Romanian Police.

c. Rapid alerts about falsified/stolen medicinal products

Such rapid alerts were transmitted through the Working Group of Enforcement Officers (WGEO), organised within the HMA. In 2019, 11 such rapid alerts on medicinal product theft and counterfeiting were registered with DGIF.

The NAMMDR issued a rapid alert through the WGEO rapid alert system for counterfeiting of Gerovital H 3 in the Philippines.

d. Alerts generated in the National Drug Verification System (SNVM)

The Romanian Organisation for Serialisation of Medicinal Products (OSMR) is responsible for the implementation and administration of the National Medicines Verification System (SNVM), the verification platform through which pharmacies or other stakeholders, such as Romanian wholesale distributors, can check the authenticity of a product.

During 2019, the OSMR extracted from the level 5 alerts and notified the authorised person from DGIF about 4 alerts generated in SNVM for which the OSMR reported the existence of a suspicion of falsification. DGIF verified the traceability of the medicinal product batches in the reports made by distributors, communicated with MAHs and the end users involved, concluding in all 4 cases that the counterfeiting is not confirmed.

e. Alerts issued by the World Health Organisation (WHO)

7 alerts issued by WHO were received this year.

f. Participation in meetings

In 2019, DGIF representatives participated in 5 meetings with the Romanian Organisation for Serialisation of Medicinal Products (OSMR):

In addition, the following have been achieved at DGIF level:

- Assessment of the documentation submitted in order to issue the certificates attesting the Qualified Person status (drafting correspondence regarding the request for qualified person certificates);

- Assessment of the documentation submitted in support of the request for approval of donations of medicinal products for human use, drafting of approvals for donation and related annexes (92 approvals for donation issued);

- Verification of the documentation for endorsement of export declarations to third countries and of 5284 export declarations drawn up for medicinal products.

6. Medicinal Product Quality Control

The main purpose of medicinal product quality control is fulfilment by the competent authority of the attribution expressly stipulated by the law to guarantee the quality, safety and efficacy of the medicinal product by performing laboratory analyses.

This activity is carried out within the Directorate for Medicinal Product Quality Control (DCCM), organised into laboratories and compartments. DCCM has the status of Official Medicines Control Laboratory (OMCL), having a role of supporting structure of the competent authority through independent testing of the medicinal product quality. The Official Medicines Control Laboratory within the NAMMDR has been audited and is officially certified (Certificate no. EDQM /

MJA-137 issued on September 20, 2018) by the European Directorate for the Quality of Medicines (EDQM).

The tasks of the DCCM concern both the assessment and control activity, the DCCM team benefiting from a vast experience in the activity of quality testing of medicinal products for human use as well as in the activity of assessment of the quality documentation submitted for assessment through national / European procedure (MRP, DCP) / centralised procedure for authorisation / renewal of MA / variations / obtaining authorisation for special needs / as a last resort treatment / exemptions / performance of clinical trials. Due to the high level of qualification, the DCCM staff with expertise is regularly requested and co-opted in centralised authorisation application assessment teams, in international audit teams, as experts / consultants by WHO and the European Directorate for Medicinal Products (EDQM), as well as in internal inspection teams, at the request of the General Directorate for Pharmaceutical Inspection (DGIF).

At the same time, as OMCL of the NAMMDR, the DCCM is part of the European network of Official Medicines Control Laboratories (OMCL), which operates under the coordination of EDQM, participating in all specific activities performed within the network. Such activities include European testing programs such as Market Surveillance Studies (MSS), analysis programmes for medicinal products authorised for marketing by the European Medicines Agency (EMA), through the centralised procedure (Europe CAP), interlaboratory studies (in which many European OMCLs participate, in order to demonstrate their competence), as well as studies on the standardisation of reference substances used in European laboratories. The DCCM obtained very good results in 2019, receiving the appreciation of the European institutions involved.

- The batch by batch laboratory control of biological medicinal products (vaccines / products derived from human blood or plasma) falling under the scope of the EU procedure for official batch release (Official Control Authority Batch Release - OCABR), together with the analysis of quality certificates and assessment of batch protocol summaries, followed by the release of test reports and of the Official Series Release Certificate (OCABR certificates), as a member of the Official Medicines Control Laboratories (OMCL) network.

- Assessment of marketing intentions and OCABR certificates issued by other OMCLs of the EU competent authorities, activity currently unpaid and for which DCCM proposed pricing; documents for marketing intention were received for 309 batches of authorised biological products from distribution companies and which are on the Romanian market (132 batches of vaccines; 174 batches of blood products; 3 batches of other types of biological products).

In this context, it should be noted that, in 2019, there were no requests for testing and laboratory analyses during the marketing authorisation / MA renewal procedure.

- The performance of laboratory analyses for medicinal products included in National Market Surveillance Programmes (in collaboration with DGIF, DPN): 33 batches of medicinal products for human use were tested (of which 6 batches of biological products and 4 batches of radiopharmaceuticals).

- The performance of laboratory analyses for medicinal products authorised through the special needs procedure, an activity that resulted in the testing of 26 batches of medicinal products for human use (including 1 biological medicinal product): 5 samples were identified as non-compliant and 21 compliant.

- Performance, in collaboration with DGIF, of laboratory analyses for medicinal products reported from the territory by healthcare units, by physical or legal persons: 6 batches of medicinal products for human use were tested.

In 2019, 296 control tests (including physical-chemical determinations, in vivo tests, serological and immunochemical determinations, microbiological determinations), 38 parameters and 40 tests for radiopharmaceuticals were performed in DCCM laboratories.

Among frequent and complex analytical techniques used in 2019, in the context of medicinal product quality control, the following are worth mentioning: High Performance Liquid Chromatography (HPLC), spectrophotometry (IR, UV-Vis), tests pharmacotechnical (dissolution, disaggregation, mechanical resistance, viability), potentiometric pH determination, Karl Fischer method, volumetric dosing, determination of melting points, determination of liquid densities, determination of refractive indices, antibiotic microbiological dosage, sterilities (parenterals) and microbiological contaminations (ophthalmic solutions, syrups and paediatric solutions, certain tablets and capsules), endotoxin determinations (LAL test), immunochemical and serological determinations, immunoelectrophoresis, ELISA determinations in vaccines, determination of impurities, of protein composition and distribution of molecular masses, of the identity and potency of biological products, specific determinations on radiopharmaceuticals, etc.

- Performance of laboratory analyses on medicinal product quality, coordinated by the European Directorate for the Quality of Medicines & HealthCare (EDQM)

7. Assuring communication and transparency

In 2009, the NAMMD/NAMMDR paid particular attention to assuring better information and communication with all stakeholders, in accordance with Law no. 544/2001 on free access to public information and Law 95/2006 - Title XVIII - The medicinal product, republished.

- Title XVIII – The medicinal product, relating to transparency and communication. The NAMMD / NAMMDR aimed at further optimizing the

activities in the field of communication, at national level and within the network by:

- Communicating its strategic objectives and communicating with stakeholders, especially in crisis situations;

- Using an efficient and collaborative communication method;

- Building and maintaining the trust of civil society as a whole in its work, by strengthening its reputation and authority with stakeholders; the medicinal product, republished as amended, relating to transparency in the work of EU drug competent authorities.

- Looking for ways to provide information on the medicinal product and the characteristics of the product that better meet the expectations and needs of stakeholders, realising that the effective and safe use of medicinal products depends to a large extent on the success of communication with relevant stakeholders, especially patients and healthcare professionals;

- Continuing to focus on a predominantly proactive approach to communication, encouraging transmission of consistent messages to stakeholders (as much as possible);

- Attaching the utmost importance to the management of health crises through prompt, consistent and effective communication to the general public.

NAMMD's communication strategy for 2017-2020 describes the framework of the internal and external communication activity carried out by the NAMMD, establishing the key actions required in view of development of the Agency's communication as a national regulatory and control authority in its areas of competence: the medicinal product for human use, medical technologies assessment, medical devices. It is a strategy based on transparency, meant to ensure:

• Internally, knowledge sharing and valorisation of activities;

• Externally, information and communication aimed at the various stakeholders;

• The interface with professional organizations and patient associations, users of the healthcare system;

• Adapting the messages to the needs and capacity of perception of the external target audience (mainly healthcare professionals and patients).

7.1. External communication

Among other specific objectives, one of the NAMMD / NAMMDR communication strategy objectives was the constant pursuance of the

consolidation of the communication impact on the NAMMD / NAMMDR partners by ensuring a wide availability of information and their immediate accessibility. Ensuring quality, bilateral communication with the various stakeholders (by exchanging messages, asking questions) and analysing stakeholders were important elements in setting the specific objectives of the communication strategy.

For effective communication, the NAMMD / NAMMDR has always sought to clearly identify what and to whom it should convey and what the expected results are. It was essential that the NAMMD / NAMMDR be aware of the differences between different stakeholders and adapt their communication to the specifics of the target party.

Maintaining trust in the NAMMD / NAMMDR is a key objective of the institution's external communication. In order to achieve this goal, the NAMMD has assumed new responsibilities in recent years. Thus, it is worth mentioning that, given shortage of medicinal products on the market observed since 2015, a constant topic for the media both nationally and internationally, the NAMMD/NAMMDR handles the e-mail address lipsamedicament@anm.ro, established upon Ministry of Health request in February 2015. Daily coordination of the activity consisting of providing answers to complaints received on lipsamedicament@anm.ro, directly from patients, carers, hospitals, open circuit pharmacies and hospital pharmacies, patient associations, pharmaceutical warehouses, medical associations, physicians, as well as those redirected by the Ministry of Health from the website signalling medicinal product shortages (http://medicamentelipsa.ms.ro/), is based upon interdepartmental collaboration within the Agency, as well as, in certain cases, on contact of C.N. Unifarm S.A. representatives and/or wholesale distributors of medicinal products, in order to effectively help patients with updated information.

The NAMMD/NAMMDR has permanently updated the specific website section, posting information about notifications received from marketing authorisation holders concerning temporary or permanent discontinuation of medicinal product availability in the Romanian supply chain.

Administration of the NAMMD/NAMMDR Facebook page (setup of notifications and NAMMD press releases, posting EMA press releases on review of the safety profile of certain medicinal products/classes of medicinal products, replying to messages sent via the social network site) was integrated into the institution’s communication activity in 2019.

The NAMMD/NAMMDR has continued to organise/host meetings, round tables with associations of patients, healthcare professionals and pharmaceutical industry on topics of interest.

The NAMMD/NAMMDR has posted its quarterly bilingual newsletter (IB) on its website, mirroring the Agency's regulatory work in the medicinal product and medical device field, in line with European legislation, as well as other priority activities of its own. The Agency's Newsletter includes:

- Laws, Ordinances, Government Decisions in the field of human medicines or other areas of NAMMD interest;

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

- Decisions of the NAMMD Scientific Council;

- Quarterly list of applications for marketing authorisation/ marketing authorisation renewal;

- Quarterly list of medicinal products authorised through centralised procedure by the EMA, for which a price has been established for marketing in Romania;

- Quarterly list of medicinal products authorised for marketing by the NAMMD.

The NAMMD has constantly updated and developed its website information. Accordingly, the following information and documents have been constantly posted and updated:

- EMA and NAMMD Press releases on medicinal product safety;

- NAMMD important notifications, opinions about certain issues from the written press/TV on the Agency's medicinal product policy, to the attention of interested persons;

- Direct healthcare professional communications;

- Notifications to marketing authorisation holders (MAHs) or other stakeholders on issues of interest;

- List of employees assigned as NAMMD full/alternate representatives to the EMA Management Board, EMA Scientific Committees and working groups, Heads of Medicines Agencies – HMA, the European Directorate for the Quality of Medicines & HealthCare – EDQM, the Council of Europe, the Council of the European Union, the Pharmaceutical Inspection Cooperation Scheme (PIC/S) and of the European Commission.

- information on marketing authorisation procedures (centralised procedure, European and national procedure (s)): information on contact persons, special warnings, SmPCs, leaflet and labelling information; the „National procedure" section will continue to make available the List of parallel import authorisations, issued by the Agency since 2009.

As of particular interest to external NAMMD website users, the following sections have been updated:

- Laws, Ordinances, Government Decisions;

- Orders of the Minister of Health;

- Decisions of the NAMMD Scientific Council;

- Decisions of the NAMMD Administration Council.

- The Index of medicinal products for human use authorised for marketing in Romania, which contains all medicinal products with the right to circulate on the pharmaceutical market in Romania, with data on the trade name, international non-proprietary name (INN), marketing authorisation holder, pharmaceutical form, strength, route of administration, packaging form, manner of release etc. The implementation of electronic versions of the Summary of Product Characteristics (SPC), package leaflet and labelling information for each medicinal product was also ensured.

- forms, useful information.

- Information related to:

  - Clinical trials,
  - pharmacovigilance,
  - pharmaceutical inspection,
  - medical technologies assessment
  - advertising
  - falsified medicinal products

Under the heading "Pharmaceutical Inspection" the following information was published and constantly updated:

- List of Romanian manufacturers of medicinal products and active pharmaceutical substances;

- List of NAMMD/NAMMDR certified manufacturers in third countries;

- List of Romanian medicinal product importers;

- List of Romanian medicinal product distributors;

- List of medicinal product control laboratories;

- List of medicinal product batches recalled/withdrawn;

- List of NAMMD/NAMMDR certified qualified persons and contact details for submission of medicinal product quality complaints.

The section referring to NAMMD/NAMMDR activity as a national competent authority in the field of medical devices has been periodically developed and updated.

The NAMMD/NAMMDR has continued to inform stakeholders about its activity via other publications, apart from its own Newsletter. Thus, posting of the NAMMD Activity report for the previous year (also available in English) has been continued.

In 2019, the Agency has provided for:

- Internal and external communication, i.e. official statements, communication with print and TV media (by phone, e-mail, television interviews, participation in TV programmes), relations with other Romanian and foreign institutions specialised in this area;

- Free access to public information in accordance with Law 544/2001, by rule and/or request for both media representatives and anyone interested, providing information on NAMMD/NAMMDR work or the safety of medicinal products for human use;

- Collaboration of all departments for proactive and reactive communication, i.e. assuring transparency/accessibility/public availability of information on medicinal products for human use, medical devices and health technology assessment.

The Department for Policies and Strategies (DPS) has provided:

- Collection of data from scientific departments and organisation of information required for development and draft of responses requested by stakeholders;

- Notification of media representatives and/or other stakeholders within the timeframes allowed by existing rules, when the information requested has already been transmitted by rule as one communication form as mentioned in Article 5 of Law no. 544/2001, also indicating the location of the requested information;

- Notification of enquirers, within time limits provided in current rules, when the information requested is found exempt from free access;

- Dissemination to the media of official NAMMD/NAMMDR press releases and statements.

NAMMD/NAMMDR representatives continued to make presentations in various scientific events organised in Romania and abroad.

7.2. Internal communication

In 2019, for better and prompter information on professional and/or organisational issues, data available to Agency employees on the intranet was further supplemented and updated.

Thus, the following information was found by NAMMD employees on the NAMMD intranet:

- NAMMD quality policies;

- NAMMD regulations;

- Glossary of quality assurance terms;

- Work plans of NAMMD departments;

- Useful forms;

- Information about the Pharmacopoeia;

- Reports by staff attending training sessions both at home and abroad;

- Useful information;

- Useful addresses etc.

8. Quality management

In 2019, the following activity was also included among the attributions of the Human Resources and Quality Management Directorate:

- Ensurance of implementation of the quality management strategies and objectives declared by the NAMMD / NAMMDR management;

- Coordination of the design, documentation, implementation, maintenance, improvement and reporting of the Quality Management System, in accordance with the requirements of the ISO 9001: 2015 standard and with the objectives established by the NAMMD / NAMMDR management;

- Promotion at NAMMD / NAMMDR level of the Quality Management System according to the requirements of the ISO 9001: 2015 standard in order to achieve compliant services by the staff involved;

- Collaboration with all NAMMD / NAMMDR structures in order to permanently optimise the quality management system;

- Provision of advisory activities on quality management system (QMS) issues;

- Provision of support to all requests of the NAMMD / NAMMDR management in the quality management field;

- Consistent reporting to the NAMMD / NAMMDR management regarding the functioning of the Quality Management System and the formulation of proposals for its improvement;

- Representation of NAMMD / NAMMDR in external relations in the field of quality management;

- Coordination and monitoring of the preparation, review, controlled distribution, maintenance of revisions of the Quality Manual, system procedures, operational procedures, general instructions, work instructions specific to each activity, structure and of other specific documents for quality assurance;

- Update of all quality assurance documents, depending on the dynamics of the organisational and functional structure and the specific requirements.

Thus, in 2019, corrective and preventive actions were initiated for the development and improvement of the quality management system, whose enforcement was monitored.

Within the specialised structure, the annual analysis of the Quality Management System, carried out by the management of the NAMMD / NAMMDR, was initiated; proposals for improvement of the documents of the Quality Management System were made.

Based on the exchange of information and collaboration with staff from all NAMMD / NAMMDR structures, in order to permanently improve the quality management system, the specialised staff developed and analysed the Annual Quality Management Plan, ensuring permanent application of effective tools for quality assurance and for evaluation of services offered in order to implement and maintain compliance of the quality management system with the specific requirements of the ISO 9001: 2015 standard. Following the profile verifications performed, the specialised structure transmitted for implementation in the documents related to quality management, the changes proposed following the quality audits performed, and coordinated the analyses performed by the management regarding the efficacy of the quality management system and the conclusion of the corrective actions recommended by the various internal and external audits.

At the level of this structure, records of the training of the management staff, execution staff and internal auditors for improvement of the quality management system is kept. This year, necessary activities were carried out in order to assess compliance of the Quality Management System with the requirements established through ISO 9001: 2015 and specific documents were drawn up in order to

participate in the management analysis on the operation, effectiveness and efficiency of the Quality Management System.

9. Medical devices

In accordance with Law no. 134/2019 Law no. 134/2019 on the reorganisation of the National Agency for Medicines and Medical Devices, as well as for amendment of some regulatory acts and of previous legislation, the NAMMDR is also a competent authority in the field of medical devices.

In this capacity, the Agency's scope includes regulation of the field of medical devices, supervision of the medical devices market, approval of units with marketing activities and provision of services in the field of medical devices, registration of medical devices placed on the market or commissioned in Romania, of authorised representatives, importers and distributors of medical devices as well as inspection and control of medical devices in use.

In accordance with Order no. 1.412 / September 2019 on approval of the organisational structure of the NAMMDR, the Medical Devices Department became the General Directorate for Medical Devices and the Technical-Laboratories Department was transformed into the Technical-Laboratories Directorate. The technical structure of the General Directorate for Medical Devices comprises the operational structure of the Technical-Laboratories Directorate, which carries out its activity through the Tests and Verifications Service and the Nuclear Unit Service.

9.1 Control by periodic check of medical devices

This is the main activity of the Tests and Verifications Service and is carried out based on the requests sent by the health units. In 2019, the controls performed by both public and private health units, yielded the following results:

- Total periodic check bulletins issued: 1960

- Total user opinions issued: 213

- Total negative test reports (medical devices rejected): 220

- Total medical devices checked: 5797

- Total mobile intervention units checked: 592

- Total positive test reports issued: 4770

This year, the processing of 764 applications was completed, 52 being cancelled for various reasons (lack of payment of the tariff, incomplete file, etc.), 379 being in progress, cumulated with those received in the previous year. 220 negative test

reports were issued, prohibiting the use of potential incident-causing medical devices. In order to perform this activity, trips were made to private health units, public hospitals and county ambulance services; in case of large hospitals, several trips were needed, since it is possible to check 30-60 devices / week during a delegation.

Due to the large number of requests, insufficient staff and lack of equipment, there are delays in carrying out the works / in this context, the following measure was taken and communicated on the institution's website, ever since the first quarter of 2019: in order to avoid discontinuities on the validity of the periodic check bulletins for medical devices, it is recommended to submit the requests for issuance of a new periodic inspection bulletin 6 months before its expiry date.

Given the fact that the endowment with measuring equipment for monitoring of medical devices must keep up with technological progress in the field, the lack of acquisition of such equipment in the last 4 years represents a significant impediment.

This year, the specialists of the Technical-Laboratories Directorate (DTL) participated upon request of the DGPMB – "CRIME INVESTIGATION" SERVICE in the technical evaluation of two medical devices (vital functions monitor and pulse oximeter, involved in the incident registered at the SANADOR hospital); 2 technical expertise reports were issued in this regard.

At the same time, the specialists of the same directorate, upon request of the Regulatory, Market Surveillance Directorate (DRSP) within the NAMMD / NAMMDR performed a technical assessment of the medical device involved in the incident at the Sfânta Maria Hospital (Bucharest) (burns caused to a patient during electrosurgery); a technical assessment report was issued.

Also in collaboration with the DRSP, DTL technical experts participated in performing the technical verification control of the medical device, triggered by the incident at the Emergency Clinical Hospital (Bucharest – Floreasca) (burns caused to a patient during electrosurgery). The electrosurgical unit was sealed and taken over by the DGPMB – "CRIME INVESTIGATION" SERVICE, which subsequently requested the performance of a technical-scientific inspection of the respective medical device, completed with the issuance of a technical-scientific inspection report.

In this context, in order to understand the complexity of the process completed by issuance of periodic verification bulletins / approvals for use of the medical devices, the multiple related activities must be highlighted: registration and analysis of applications, charging (in case of requests from private health units), scheduling of inspections (depending on several criteria, such as the application registration number, date of payment confirmation, number and specialty of staff,

equipment and means of transport required, approval of the travel order for the concerned county / area), travel and technical checks, elaboration of travel documents, drafting of documents and endorsement, approval and transmission to beneficiaries, archiving of these documents, their introduction on the server of the institution, database administration, etc.

Tests and verifications were carried out within the DTL nuclear unit at the request of third parties, through periodic inspections and the issuance of periodic check bulletins, for medical devices with ionizing radiation, magnetic resonance imaging equipment and radiological protection equipment, or for performance and safety for approval and inspections of devices in use.

Thus, in 2019, 633 applications were registered at the level of the profile unit, these, as well as a small number of applications from the previous year, were completed.

At the same time, 685 periodic check bulletins and approvals for use were issued, as well as 534 test reports issued for medical devices with radiation generators and 1125 test reports for radiation protection equipment.

This year, 83 negative test reports were issued, banning the use of medical devices whose use could generate incidents.

9.2 Inspection of technical and medical-assessment units

This activity is performed in line with provisions of Title XX of Law 95/2006, republished as amended, and with Order of the Minister of Health no. 1008/2016, within the Technical-Medical Units Assessment Department (DEUTM) – The Directorate for endorsement (DA).

The 2019 activity was carried out procedurally, in line with Order of the Minister of Health no. 1008/2016 on approval of the Methodological Norms for the enforcement of Title XX of Law no. 95/2006 on healthcare reform, concerning the approval of activities in the field of medical devices. The activities related to marketing and service provision in the field of medical devices, subject to control by approval, were:

a) import of medical devices;

b) storage and distribution of medical devices;

c) repair, maintenance and commissioning / installation of medical devices;

d) medical optics - assembly / repair of glasses according to the prescription of a specialist;

e) prosthesis.

In this respect, it is illustrative to present a centralised situation of the applications received during the last four years:

Year	Total number of applications	Average number of activities/month	Average number of activities/employee/month	Number of employee assessments
2016	395	33	4	8
2017	1049	87	10.8	8
2018	2223	185	20.5	9
2019	1817	151, 4	16.8	9

According to the table, it can be seen that in 2019, despite the slight decrease compared to 2018, when applications were submitted for the change of all operation approvals, the number of applications is almost double compared to 2017, as in the case of number of works per employee, given the fact that staff employment has been blocked.

In 2019, 1150 assessment reports were prepared; there were delays in processing the works, also due to the significant increase in the number of works by enforcement of provisions of Article 18 of Order of the Minister of Health no. 1008/2016 on approval of the Methodological Norms for the enforcement of Title XX of Law no. 95/2006 on healthcare reform, concerning the approval of activities in the field of medical devices. Thus, according to the law, the operation approvals issued or changed until entry into force of these methodological norms are changed in stages, until December 31, 2018, upon request of the respective unit.

In accordance with Article 19 of Order of the Minister of Health no. 1.008/2016, „Operation approvals issued until the date of entry into force of these methodological norms, as stipulated in Order of the Minister of Health no. 309/2015 on approval of methodological norms for enforcement of Title XIX of Law no. 95/2006 on healthcare reform, concerning approval of medical device related activities, are available until the date of their change, but no later than the date stipulated under Article 18 (1) – 31.12.2018."

Given the high volume of work and insufficient time for the timely exchange of all the notices of the applicants who submitted a request for change, Order of the Minister of Health no. 3/2019 on amendment of the Annex to Order of the Minister of Health no. 1008/2016 on approval of the Methodological Norms for the enforcement of Title XX of Law no. 95/2006 on healthcare reform, concerning the approval of activities in the field of medical devices, was drawn up and promoted; under Article 191, it provides that:

"(1) In order to ensure the continuity of the activities provided in art. 3, the NAMMDR issues temporary operation approvals, valid until the date of issuance of the operating approval provided in art. 4, but no later than 30.06.2019.

(2) Temporary operation approvals provided in par. (1) shall be issued only for the holders who have submitted to NAMMDR the documentation provided in art. 18 (3), in order to change them.

(3) Temporary operation approvals provided in par. (1) shall be issued on the basis of the information provided in the request for change.

(4) For the holders of the operating permit for which NAMMDR has issued a favourable report until the date of entry into force of this Order, the operating approval shall be issued according to the provisions of art. 10 par. (2).

(5) The model of temporary operation approval is provided in Annex 6.

(6) Temporary operation approvals shall be issued within a maximum of 7 days following entry into force of this Order. "

In this context, a number of 525 temporary approvals were issued, completed by 30.06.2019.

9.3 Regulation, authorisation and market surveillance of medical devices

The activities in this field allow the fulfilment by NAMMDR of the attributions incumbent on it by law as a national market surveillance authority and a competent authority in the field of medical devices. Through the market surveillance activity, the implementation by the medical devices of the requirements of the applicable technical regulations as well as the observance by economic operators of the obligations incumbent on them is controlled.

These activities are the responsibility of the Medical Devices Market Regulation and Surveillance Department (DRSP), through its specialised services, namely the Regulatory Service (SR) and the Medical Devices Market Surveillance (SP) Service. Both services are in coordination / collaboration with all other departments operating in the field of medical devices.

At the same time, in the conditions of the increasingly strong shaping of the European regulatory network in this field, the NAMMDR is represented in the working groups for medical devices, of the European Commission, as well as in the technical committees of the National Standardization Body (ASRO).

In terms of regulatory activity, it is organised on several levels, as follows:

- Internally (within the NAMMDR):

1. Registration of medical devices placed on the market or commissioned in Romania, of domestic manufacturers, authorised representatives, importers and distributors of medical devices, according to the regulations in force. Currently, there are 9745 medical devices introduced on the market by responsible economic operators (domestic manufacturers, authorised representatives living in Romania)

and 8093 medical devices operated by these economic operators, increasing by 340 and 1645 compared to the year previous year;

2. Permanent setup and update of the national database in accordance with provisions of the national legislation transposing European directives;

3. Authorisation of the programme on enforcement of the clinical investigation procedure/assessment of the performance with medical devices for clinical investigations; thus, until halfway throughout the year, upon entry into force of Law 134/2019, when the clinical investigation activity was taken over by another NAMMDR structure, 3 authorisations and 4 amendments were issued for conducting clinical investigations with medical devices and 75 dossiers related to requests for approval of amendments or reports on ongoing clinical investigations were assessed;

4. Issuance of approvals, notifications and registration certificates, in line with the specific legal provisions in force, in this field being issued 2 customs approvals, 22 approvals for donation as well as notifications and certificates;

5. Carrying out permanent documentation, implementation, research and development activities in the specific field of activity;

6. Elaboration and transmission of responses to requests for information; 570 such responses were made in 2019.

7. Participation in scientific events and training programmes according to the Annual Staff Training Programme, 4 self-training courses were organised within the NAMMDR in 2019.

- At national level (in relation to Romanian authorities / bodies):

1. Elaboration of norms in the field of medical devices, for the harmonisation of the national legislation with the European directives and regulations, which are submitted for approval to the Minister of Health. In this field, the draft for amendment of WHO 1009/2016 was elaborated this year and it was published in the Official Gazette, Order no. 1778 / 25.11.2019 in November 2019.

At the same time: participation in the elaboration of the project in order to issue Law no. 134/2019 on the reorganisation of the National Agency for Medicines and Medical Devices, as well as for amendment of some regulatory acts.

2. Participation, within the inter-ministerial working groups, in the elaboration of documents for harmonisation and implementation of regulations in the field of medical devices and / or provision of services, upon request of the Ministry of Health.

This activity consisted of:

-Translation of the ISO 9999-2016 standard and data processing for the Order on assistive technologies and devices;

- A meeting with the representatives of the National Authority for Quality Management in Health (ANMCS) regarding the enforcement of the European legislation in the medical devices field in Romania.

3. Drafting of methodological norms regarding the organisation and operation of the medical devices sector and their submission for approval to the Minister of Health.

Thus, in 2019, the following were drafted and proposed for approval:

- Amendment of Order of the Minister of Health no. 1356/2013 on approval of fees of the National Agency for Medicines and Medical Devices for medical devices-related activities;

- Amendment of Order of the Minister of Health no. 1009/2016;

- Participation in the elaboration of the Minister of health Order proposal on the nomination of bodies for assessment of compliance with the provisions of Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices (NDR);

- The draft of a regulatory act for implementation of Regulation (EU) 2017/745.

4. Elaboration and submission for approval of the lists containing the Romanian standards that adopt the European standards harmonised with the European directives (in the field of medical devices) to the Minister of Health.

In this field, in 2019:

- Collaboration with ASRO in order to translate some necessary standards, according to a contract concluded in this regard;

- A NAMMDR expert participated in the 377th ASRO Technical Committee, for adoption of European standards harmonised with European directives as well as in the 22nd Technical Committee of the same body.

6. Registration and assessment of information about incidents and corrective actions reported in connection with medical devices and implementation of the vigilance procedure according to the harmonised legislation in force; investigations through the Market Surveillance Service in case of 2 reported incidents were conducted in this respect.

7. Formulation of answers to requests addressed by other ministries, public authorities and other physical and legal persons in the field of medical devices.

- At international level:

1. Participation in meetings of the European Network of Competent Authority for Medical Devices (CAMD), designed to strengthen collaboration, communication and market surveillance across the EU.

At the same time, participation in 6 meetings of the European Commission working groups in the field of medical devices was ensured, namely the Working Group on Standards, the Clinical Investigation & Evaluation subgroup of the Medical Devices Coordination Group (MDCG). The documents concerning the NAMMDR experts nominated in working groups in this field were transmitted to the European Commission.

2. Elaboration from a technical viewpoint of Romania's position and the mandate of representation towards the proposals of community legislative acts and topics for discussion within the working groups at European Union level, in the field of medical devices, and their transmission to the Ministry of Health. In this sense, 12 representation mandates were drawn up and sent in 2019.

An important event for the competent authority in the field of medical devices in Romania was the organisation, with the help of Denmark, of the 44th meeting of the CAMD within the Romanian Presidency of the Council of Europe.

3. Assessment and designation of certification bodies in the field of medical devices, submission for approval to the Minister of Health of the list of nominated bodies and notification of those bodies through the electronic procedure managed by the European Commission. Within this activity, the application and the dossier submitted at the end of 2018 for nomination as a notified body in line with Regulation 745/2017 for medical devices (MDR), on behalf of GMDC INTERNATIONAL CERTIFICATION SRL, were assessed, and a request for supplementation was sent.

4. Surveillance of notified bodies and provision of appropriate measures was not necessary, as in 2019 there were no notified bodies in Romania under surveillance.

5. Ensurance of the permanent introduction into the European Eudamed database of data from the national database, in accordance with the provisions of Commission Decision 2010/227 / EU of 19 April 2010 on the European Medical Device Database (Eudamed).

6. Permanent ensurance of administrative cooperation with competent authorities of EU Member States regarding the provision of services in the field of medical devices, through the Ministry of Health and the internal market information system - IMI, established by the European Commission;

7. Registration and evaluation of information on reported incidents and proposed corrective actions in relation to medical devices and implementation of the vigilance procedure in line with the harmonised legislation in force.

In this regard, requests for information have been made and they were addressed to:

- Competent Authorities (minimum 10 cases),

- Notified Bodies (minimum 12 cases),

- Authorised representatives (minimum 9 cases),

- Manufacturers (minimum 2 cases).

At the same time, the Competent Authorities for sanctioned non-compliant products (COEF) were contacted, namely:

- COEF information evaluation - minimum 31 cases;

- COEF response assessment and response forms - minimum 9 cases;

- COEF RO initialisation - 7 cases.

- elaboration and posting of announcements on the NAMMDR website - minimum 2 cases (non-sterile thread, contaminated disinfectants). In this regard, following the investigations launched in hospitals after the AURA case, a ban was issued for the non-sterile thread Aspide Sutures, France;

Data were recorded and evaluated for at least 150 reported incidents, Corrective Action Reports on Safety in Operation (FSCA), Warning Notes (FSN) taken in relation to medical devices and the vigilance procedure was implemented in accordance with the harmonised legislation in force.

As far as market surveillance is concerned, this is a complex process, which involves the following steps:

a) monitoring of medical devices placed on the market and / or commissioned as well as those presented at fairs, exhibitions, demonstrations and other such actions;

b) establishment of measures to be taken by the economic operator, as the case may be, to ensure product compliance;

c) following the enforcement of the established measures.

The staff of the specific service carried out control actions aimed at verifying compliance with European and national legislation in the field of medical devices (including in vitro medical devices and active implantable medical devices).

In 2019, the activity in the field materialised in the organisation and performance of 248 thematic control actions and 31 additional control actions regarding the verification of compliance of medical devices placed on the Romanian market (regarding registration, notification, compliance with the requirements in Government Decision no. 54 / 2009, Government Decision no. 55 / 2009,

Government Decision no. 798 / 2003), in-use control and observance of the legislation in force by economic agents, in this case Law 95/2006 on health care reform, republished as amended.

Thus, controls were performed at the sites of 202 importers / distributors, 5 manufacturers, 27 medical optics units, 6 sanitary units, 3 medical equipment stores and 5 retail stores.

Of the 248 controls performed, 35 controls were proactive, 92 reactive, 156 unannounced and 2 were controls following reported incidents. Minutes and final control reports were drawn up for all these inspections where appropriate.

In 2019, 30 warnings, 40 fines of which 39 were paid, and 1 address (sent to ANAF) were applied; minutes were drawn up for these in order to ascertain and apply the sanctions, accompanied by the related payment notices; points of view, objections, addresses were prepared and sent to the legal department of the NAMMDR for the 94 notifications / complaints received for resolution within the market surveillance service in order to complete the responses and send them to the petitioners within the legal deadline.

In 2019, the market surveillance activity consisted of the investigation of 2 incidents reported by users regarding medical devices. As a result of this activity, 3 types of medical devices were temporarily / permanently discontinued from sale / use.

Surveillance activities also resulted in the posting on the NAMMD / NAMMDR website of some warnings about non-compliant medical devices identified on the Romanian market and the periodic update of the tables with the sanctioned companies.

Another mandatory activity for the competent authority in the field of medical devices is registration of medical devices commissioned in Romania into the national database. On the one hand, due to the legislation in force in the field of medical devices (WHO 1009/2016), which led to an increase in the volume of notifications submitted by economic operators for registration and, on the other hand, due to the shortage of staff at NAMMD / NAMMDR, the staff of the Market Surveillance Service was also co-opted for the registration in the national database.

In accordance with the provisions of Order of the Minister of Health no. 1009/2016, the activity in the field of market surveillance required verification of 250 notification files for the commissioning of a medical device in view of registration into the national database.

In 2019, 49 free sale certificates were issued at DRSP level.

The issuance of periodic verification bulletins / approvals for use of medical devices involves: registration and analysis of applications, charging (in case of

requests from private healthcare units), scheduling of trips according to the registration number of the application, date of payment confirmation, staff, equipment and necessary means of transportation, drafting, endorsement, approval and transmission of the documents to the beneficiaries, archiving the documents, uploading them on the institution's server, management of the database.

10. International relations

The following activities involved in organising, together with the Ministry of Health, the Ministry of Foreign Affairs and all other government institutions with attributions in this field, as well as the participation in the events performed in the context of the Romanian Presidency at the Council of Europe, were particularly important in this field for the activity and evolution of the Agency, as a member of the European network of competent authorities in the medicinal product field, namely:

- 20-22 February 2019, Timișoara, the 95th meeting of the Heads of Medicines Agencies (HMA), at whose organisation, given the quality of this network entity of national competent authorities in the European Economic Area in the field of both human and veterinary medicinal products, it has also collaborated with the National Sanitary Veterinary and Food Safety Authority and with the Institute for the Control of Biological Products and Veterinary Medicinal Products.

- April 4-5, 2019, Meeting of Strategic Analysis and Learning of the Herbal Medicinal Products Committee (HMPC).

- May 23-24, 2019, Bucharest, Palace of the Parliament: formal meeting of the Working Group for Homeopathic Medicines (HMPWG).

- 22-23 May 2019, Bucharest, Palace of the Parliament: joint meeting of the Coordination Group for Mutual Recognition and Decentralised Procedures for Human Medicinal Products (CMDh) and the Pharmacovigilance Risk Assessment Committee (PRAC).

- 13-14 June 2019, Bucharest, Palace of the Parliament: Joint meeting of the Committee for Advanced Therapies (CAT) and the Clinical Trial Facilitation Group (CTFG),

- June 19-21, 2019, Bucharest, Palace of the Parliament: the 96th meeting of the Heads of Medicines Agencies (HMA), organised in collaboration with the National Sanitary Veterinary and Food Safety Authority and the Institute for Control of Biological Products and Medicinal Products for Veterinary Use.

Both HMA meetings took place with the participation, in addition to the participation of the heads of regulatory and control authorities in the field of the medicinal product for human and veterinary use, and of the representatives of the European Medicines Agency (EMA), the European Directorate for Medicinal

Products Quality and Health Care (EDQM) and the European Commission - General Directorate for Health and Food Safety (DG-Santé). These meetings were of particular significance for EU experts in the field, with the aim of addressing issues of strategic importance in current and future aspects in the specific field (such as, for example, identification of solutions in view of monitoring the supply with medicinal products aimed at preventing and combating medicinal product shortages across the EU, optimisation of the transparency of the medicinal product and vaccine markets in order to expand public access to existing treatment options), making decisions on the operation and optimisation of the network activity, ensuring its coherence through exchange of information and good practices in the field of regulation of medicinal products for human and veterinary use.

The success of these events was largely due to the increased involvement of NAMMDR specialists in the activities of scientific committees and working groups, especially of those operating under the auspices of the European Medicines Agency (EMA) and of the Head of Medicines Agencies (HMA), the various European institutions and bodies with which the Agency maintains collaborative relations and in whose actions NAMMDR representatives participate in an active manner.

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

As a full member of the European Network of National Competent Authorities in the medicinal product field, through its representative specialists, the NAMMDR participated in 2019 in all activities of the EMA scientific committees and working groups:

- The Committee for Medicinal Products for Human Use (CHMP);
- The Committee for Orphan Medicinal Products (COMP);
- The Committee for Herbal Medicinal Products (HMPC);
- The Paediatric Committee (PDCO);
- The Committee for Advanced Therapies (CAT);
- The CHMP Safety Working Party;
- The Pharmacovigilance Risk Assessment Committee (PRAC);
- The CHMP Blood Products Working Party;
- The CHMP Biologics Working Party;
- The CHMP Vaccines Working Party;
- The CHMP/CVMP Quality Working Party;
- The GMP/GDP Inspectors Working Group;

- The EudraGMP database sub-working group;

- The GCP Inspectors Working Group;

- The GLP Inspectors Working Group;

- The Pharmacovigilance Inspectors Working Group;

- The EudraPharm TIG;

- The EudraVigilance TIG;

- The EudraCT Clinical trials TIG;

- The IT Directors Group;

- The EudraNet TIG;

- The e-Submission TIG;

- The European Union Telematics Controlled Terms (EUTCT);

- The Product Information Management (PIM) group;

- The Quality Review Documents (QRD) group;

- The Invented Name Review Group.

- The Working Group for the clinical trials portal and database provided by the Clinical Trials Regulation.

10.2. Participation in activities of the Heads of Medicines Agencies (HMA)

NAMMD/NAMMDR representatives also actively participate in meetings of the Heads of Medicines Agencies (HMA) European body, as members of the working groups coordinated by the HMA, i.e.:

• Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human - CMD-h;

• HMA Working Group of Quality Managers;

• EMACOLEX - European Medicines Agencies Cooperation on Legal Issues;

• Working Group of Communication Professionals - WGCP;

• Working Group of Enforcement Officers - WGEO;

• Clinical Trials Facilitation Group - CTFG;

• The subgroup organised within the Working Group for the facilitation of clinical trials, in the draft of harmonised evaluation of clinical trials: VHP procedure;

• Homeopathic Medicinal Products Working Group - HMPWG.

10.3. Participation in the activities of the EU Council and the European Commission (EC)

In 2019, nominated NAMMD experts attended meetings of the EU Council and of the European Commission, i.e.:

➢ in the field of medical devices:

• The Medical Device Vigilance Experts Group;

• The IVD Technical Group;

• The Compliance and Enforcement Group (COEN);

• The Classification and Borderline Work Group;

• The European Union Competent Authorities for Medical Devices (CAMD);

• The Medical Device Coordination Group (MDCG).

➢ in the field of human medicinal products:

 The Standing Committee;

 The Pharmaceutical Committee;

 The Expert Group on the Delegated Act on safety features on the packaging of medicinal products for human use;

 Notice to Applicants.

10.4. Participation in activities of the World Health Organisation (WHO)

The NAMMD is a member of the WHO scheme for certification of the quality of medicinal products on the international market. In 2019, the Agency granted the medicinal product certificate in WHO format for 387 medicinal products of Romanian manufacturers in view of authorisation in third countries.

10.5. Participation in activities of the Council of Europe

In this field, the collaboration with the European Directorate of the Quality of medicines (EDQM) in view of updating the Standard Terms (ST) in Romanian, which represent the translation of the ST adopted by the European Pharmacopoeia Commission, was continued. At the same time, the representative appointed by NAMMDR as a member of the European Pharmacopoeia Commission, participated in one of its Working Sessions organised this year, as well as in the annual meeting of national pharmacopoeia secretariats of member countries of the Convention for the elaboration of the European Pharmacopoeia.

10.6. Participation in Official Medicines Control Laboratories (OMCL) activities

A representative of the specialised structure of the NAMMDR, which is part of the Official Medicines Control Laboratories (OMCLs), participated in the Annual Meeting of the OMCL Network, organised in 2019 by the European Directorate of the Quality of medicines (EDQM) and the national competent authority in the United Kingdom (see section 6).

11. Logistics, information and electronic data management-related activity

The Information and Communication Technology Service (STIC) also met its assignments in 2019 related to achievement of effective communication with the EMA and provision of real time information exchange between the Agency and its external collaborators (MAHs, distributors, healthcare professionals, patient organisations and associations).

In order to respond to these diverse and complex tasks, the specific service acted in the following areas:

• administration of servers and of the NAMMDR network

This activity involves performing various tasks, such as:

• elaboration of the regulation for use of the Computer Network of the Romanian National Agency for Medicines and Medical Devices

• configuration and optimisation of the network work mode for the staff of the Medical Devices General Directorate/Department;

• implementation and updating of the Quality Assurance information system - Standard Info necessary for the quality assurance structure

• maintenance and administration of ANMDM servers (file server, web-intranet server, multi-service internet server, accounting server) were ensured

• allocating unlimited internet access according to the reports

• creating e-mail accounts according to the reports

• reallocation of rights to directories and files stored on NAMMDR servers at the request of the departments / services / offices involved

• design and administration of databases;

Particularly important activities were carried out for the accomplishment of NAMMDR's attributions as competent authority in the field of medicinal products, medical devices and evaluation of medical technologies through direct involvement of the specialised service in the activities associated with specific databases, which are absolutely necessary.

Thus, in addition to the input and support provided in connection with external databases, STIC ensures the administration of the INDEX, Registry and Variations databases.

Thus, the maintenance, amendment and update of the database of the Index of medicinal products for human use as well as the update of the automatic periodic update system for posting on the website of the Index of medicinal products for human use continued in 2019. At the same time, the STIC ensures/participates in the extraction of data from the Index of medicinal products for human use and in their communication to the directly involved NAMMDR structures in view of preparation of statistical reports.

• managing together with NAMMDR experts the Database with experts involved in EMA and HMA activities and updating their information through the application provided by EM

• participation in the management of the database of declarations submitted by sponsors / beneficiaries;

• elaboration of reports from the databases at the request of the management or of the collaborating institutions (weekly or upon request);

• update of a series of integrated electronic forms (submission of large documents, forms for submission of petitions and registration for audience), sponsorships at the NAMMDR registry or sent by email (introduction into the database, update of the WEB application for submission of the declarations of sponsorship beneficiaries for 2019).

• maintenance and updating of the NAMMDR internet / intranet pages;

As regards implementation of the Interface between the competent authority and stakeholders, the Service has carried out the following activities:

➢ permanent ensurance of daily maintenance and update of the NAMMD/NAMMDR website (www.anm.ro) and of other software applications, involving:

- website maintenance, change and update of search engines (Medicinal Product Index, management of recalled medicinal products, management of GMP sites);

- updating the online platform for the Newsletter and the various sections (Newsletters, Forms, Legislation, Press Releases, Questions and Answers, Important Announcements, Direct Healthcare Professional Communications (DHPC), sponsorship declarations of Sponsors for 2019, etc.),

- maintenance, amendment and update of the NAMMD / NAMMDR intranet website, particularly in the context of the changes regarding the status and organisation of the Agency introduced by publication of Law no. 134/2019 on the reorganisation of the NAMMD/NAMMDR

➢ ensuring the setup, configuration and service of hardware and software for computing equipment within the NAMMD / NAMMDR network;

For proper running of the Agency's activities, the IT team was involved or directly responsible for fulfilling its responsibilities in terms of software installation required to perform the activity as required, equipment maintenance operations, inventory management of IT&C equipment and of NAMMDR software licenses and setup of specifications, the technical evaluation of the offers in view of purchase of IT services and equipment, the transfer and setup of computers according to the organisation of the departments.

The specific service provided ongoing and adapted support to all other Agency structures through various routine interventions regarding the operation of both hardware and software, through reinstallations and reconfigurations of Windows 7 Professional, Windows 8.1, Windows 10;

- performing reinstallations and reconfigurations for the Office range (Office 2010, Office 2013, Office 2016);

- fixing software issues (system crashes, malfunctions of options in various installed applications, data / email recovery, defragmentation and hard disk scanning);

NAMMDR servers have been maintained and managed through routine activities such as configuring security, network and service policies. There were also activities for remediation of some critical situations of malfunction of the @ anm.ro e-mail server in the context of using equipment worn both morally and physically. Workstations were configured for use in webinars using the Adobe Connect / WEBEX service, and the specifications and market prospecting were developed in order to establish a NAMMD / NAMMDR Data Centre (containing several servers and data storage equipment).

➢ ensurance of the antivirus and anti-spam protection of the NAMMDR computer network;

The STIC, having important responsibilities related to ensurance of a safe use of media and electronic tools, has carried out specific activities such as:

• configuration, testing, administration and updating as well as maintenance of the antivirus software and security programs on NAMMDR servers;

• update of the security system based on limiting the nominal access of NAMMDR users to various services and electronic devices;

• integration of the Security system with the NAMMDR Domain Controller;

• implementation and updating for NAMMDR domains of digital SSL (Secure Sockets Layer) certificates used to establish a secure connection between achieving a secure mutual communication between the user and the web server;

➢ ensuring connectivity

One of the responsibilities of the specific NAMMDR structure is to ensure and monitor the connectivity to the telecommunications network in the pharmaceutical field entitled European Union Drug Regulatory Authorities Network (EudraNet), an IT platform created in order to facilitate the exchange of information under superior safety conditions both between regulatory partners and between national competent authorities and industry in the process of submitting and evaluating various applications. The respective network includes:

- EudraCT, the European database of all interventional clinical trials conducted with medicinal products authorised in the European Union, the EEA and outside the EU / EEA, in case of their inclusion in a Paediatric Investigation Plan;

- EudraLink, a secure file transfer system designed for the safe electronic transmission of large amounts of information;

- EudraMail, a dedicated system for safe transmission of electronic messages, using mailboxes, which allows working groups to exchange messages of importance to that group;

- EudraPharm, an electronic database for EU authorised medicinal products for human use, abolished in June 2019 and replaced with an Excel document available on the EMA website, which provides the same information (https://www.ema.europa. eu / en / humanregulatory / post-Authorization / date medicines ISO-standards-based idmp / public-data-article-57-database);

- EudraVigilance, the system for the management and analysis of information on suspected adverse reactions to medicinal products authorised or subject to clinical trials carried out within the European Economic Area (EEA). The European Medicines Agency (EMA) operates the system on behalf of the European Union (EU) Medicines Regulatory Network; in this regard, the SSL digital certificates of the portal were updated in order to report adverse reactions;

- PIM (Product Information Management), the platform for managing medicinal product information submitted in electronic format;

- CTS (Communication and Tracking System), the communication and tracking system used by national competent authorities in the field of the medicinal product with regard to authorisation through mutual recognition and decentralised procedure;

- maintenance of connection with the CTS service through setup of access accounts, according to the primacy reports and communication with the CTS helpdesk service for signalling malfunctions in provision of services;

- EPITT (European Pharmacovigilance Issues Tracking Tool), the European pharmacovigilance tracking tool for signal detection.

Other activities permanently carried out by the profile service:

• ensurance of the NAMMD / NAMMDR connection to the Common Repository (Centralized Procedure Submissions) database;

• facilitation of daily access to BP, PhEur, USP, CTS;

• ensurance of the connection of NAMMDR to the CESP (Common European Submission Portal) database and daily download of documentation submitted in electronic format through CESP;

• management of the Learning Management System portal;

• ensurance of maintenance of the BGP (Border Gateway Protocol) system to ensure the redundancy of internet connections provided by internet service providers;

➢ development of software and applications at NAMMD / NAMMDR level, through setup of internal programmes / applications (software for technical support and assistance, analysis and design of registry software, creation of an electronic time stamping system for NAMMD / NAMMDR employees based on the data provided by the magnetic card access system;

NAMMD / NAMMDR Informatisation Strategies and Standard Operating Procedures and proposals for amendment of some regulatory acts have been developed; the NAMMD / NAMMDR logo and other image elements have been updated, in view of permanent update of the NAMMD / NAMMDR image in accordance with the latest legislative developments.

The STIC was directly involved in organising all the events that focused the Agency's concern during its presidency of the EU Council. The team of the Information and Communications Technology Service ensured the following, in close collaboration with STS throughout this period as well as with the administrators of various locations where the events took place:

• Endowment of meeting rooms allocated with portable laptop devices, printing equipment, power strips, peripheral equipment (presenter / laser pointer - role in remote control of presentations - PowerPoint);

• The connection between participants / readers and administrator of the conference room – person responsible for the hardware equipment - sound, projection and lights;

• Configuration and testing of sound and projection systems.

12. Assuring implementation of NAMMD/NAMMDR policies and strategies

In 2019, the Department for Policies and Strategies (DPS), until entry into force of Law no. 134/2019 on the reorganisation of the National Agency for Medicines and Medical Devices, as well as for the amendment of some regulatory acts and,

subsequently, the Service for Communication and Public Relations (SCRP), conducted the following activities:

- Development by collaboration with all NAMMDR structures and under coordination of the NAMMDR management, of the NAMMD/NAMMDR Organisational Strategy 2018-2020, particularly by:

• Strengthening of the Agency's status of reference national authority in the field of the medicinal product for human use in its specific sector;

• Strengthening of the Agency's status of expert and reliable source of accurate and timely information in the field of the medicinal product for human use, provided to stakeholders, by active and priority participation in implementation of the NAMMDR Communication Strategy, internally and externally, permanently pursuing the improvement of its strategy and finding ways for its adjustment to new demands and changes in the legislative and socio-economic area.

The specific activities conducted by the DPS / SCRP in 2019 were:

- Preparation of responses to media queries and NAMMD/NAMMDR top management decision making by:

- TV interviews, including live broadcasts;

- Written responses for TV and print media;

- Telephone interviews for print, TV and radio media;

- Press releases and important announcements posted on the NAMMD site;

- Collaboration with all NAMMD/NAMMDR departments for gathering and organisation of information requested by the media in view of elaboration and drafting of the required reply.

In line with the NAMMDR Communication Strategy, as the NAMMDR spokesperson, the DPS representative has provided for:

- Participation in the internal and external communication, i.e. official statements, communication with print and TV media (by telephone, e-mail, television interviews, participation in TV programmes), relations with other Romanian and foreign institutions specialised in this area;

- Setup / verification and dissemination to the media of the official releases and the official statements of the NAMMDR management;

- Participation in drafting and transmission of the correspondence with internal and external partners, on issues specific to the NAMMDR activity;

- Daily monitoring of the health media (TV press, print media and online press);

- Participation in scientific events, with papers presenting the NAMMD / NAMMDR viewpoint in various issues related to the institution's areas of competence;

- Communication with other specialised institutions in the field, in Romania and abroad;

- Free access to public information in accordance with Law 544/2001, by rule and/or request, for both media representatives and anyone interested, providing information on NAMMD work or on the safety of medicinal products for human use;

- Notification of media representatives and/or other stakeholders within time limits provided in current rules, when the information requested has already been transmitted by rule as mentioned in Article 5 of Law no. 544/2001, also indicating the location of the requested information;

- Notification of the applicant, within time limits provided in current rules, when the information requested is found exempt from free access;

Together with other professional departments, the DPS/SCRP took part in assuring proper NAMMD/NAMMDR operations within the European network of competent authorities in the field of the medicinal product, acting as an interface between the Agency and European and international authorities, by:

- Managing and monitoring participation of Agency employees appointed as full or alternate members in scientific committees and working groups of the EMA, the HMA, the EDQM, the Council of Europe, the EU Council, the European Commission, the Pharmaceutical Inspection Cooperation Scheme (PIC/S): communication with the Permanent Representation of Romania to the European Union;

- Ensuring communication with the EMA for the nomination of the Agency's representatives as members / alternates, an activity which consists of:

- Checking / centralising the forms filled in by NAMMD / NAMMDR specialists;

- Communication with the secretariats of the working groups / scientific committees of the aforementioned specific European bodies in view of submission of nomination forms, or on other topics;

- Periodic update of the List of employees assigned as NAMMD/NAMMDR as full members or alternates in scientific committees and working groups of the European Medicines Agency (EMA), the Heads of Medicines Agencies (HMA), the European Directorate of the Quality of medicines (EDQM), the Council of Europe, The Council of the European Union, the Pharmaceutical Inspection Cooperation Scheme (PIC/S) and of the European Commission in accordance with the President's decision and posting on the NAMMD/NAMMDR website;

- Permanent monitoring of the Community Register and handling on paper and electronically (within the DPS/SCRP and on the Romsys/anm/Decizii CE Server) and update of the NAMMDR database of European Commission (EC) decisions and consensus agreement of the CMDh, referring to medicinal products authorised in Romania as well, for implementation by NAMMDR assigned specialists (26 decisions referring to medicinal products authorised in Romania);

- Electronic record of paper documents received from the Ministry of External Affairs via the Ministry of Health concerning issuance of EC Decisions for medicinal products authorised in Romania as well.

The DPS has prepared the NAMMD annual activity report for 2018 by corroborating data from activity reports of NAMMD structures.

In accordance with the Regulation on the operation and organisation of the structure, the DPS / SCRP coordinates the training and ensures the scientific secretariat of the Scientific Council (SC) of the NAMMD / NAMMDR. In 2019, given the context determined by the busy schedule imposed by the role played by the NAMMDR in carrying out the activities involved in exercising the mandate of the Presidency of the EU Council and, after July, the implementation of organisational changes provided by Law 134 / 209, the Scientific Council was not summoned.

The DPS/SCP has ensured preparation of the NAMMD/NAMMDR newsletters, which have been posted on the Agency's website:

- 4 Newsletter issues in Romanian (4/2018; 1/2019; 2/2019; 3/2019);

- 5 Newsletter issues in English (3/2018, 4/2018, 1/ 2019; 2/2019; 3/ 2019).

The DPS / SCRP participated and provided the secretariat for the NAMMDR Crisis Committee meeting.

The DPS/SCRP has also contributed to setup of an interface between the NAMMD/NAMMDR and its stakeholders by updating and improving information on the NAMMDR website in collaboration with other internal departments, by managing the posting of the following:

- Legislative documents, notifications in Romanian and English;

- NAMMD/NAMMDR Newsletters in Romanian and English;

- The NAMMD Annual Activity Report (2018);

- The List of NAMMD/NAMMDR employees assigned as representatives or alternates in the Administration Council, scientific committees and working groups of the European Medicines Agency (EMA), the Heads of Medicines Agencies (HMA), the European Directorate for the Quality of Medicines

(EDQM), the Council of Europe, the EU Council, the Pharmaceutical Inspection Cooperation Scheme (PIC/S) and the European Commission.

The DPS/SCRP also provided:

- Translation of EMA press releases, EMA Q & A documents;

- Monitoring of the terminology in order to ensure compliance with the European terminology, especially of the EMA and EUDRA websites;

- Ensuring upon request of the various NAMMD/NAMMDR structures of advice/translation of specific mail and communication with various international bodies and/or representatives of pharmaceutical companies;

- Update of the English version of the NAMMD/NAMMDR website by translation of NAMMD/NAMMDR legal documents, notifications and press releases.

Ensurance of communication with the Permanent Representation of Romania to the European Union/Brussels was achieved by:

- Monitoring/managing electronic records of all e-mails (about 800 e-mails) received from the Permanent Representation of Romania to the European Union to the EU and/or the Ministry of Health regarding:

• Participation of NAMMD/NAMMDR employees assigned as representatives or alternates in Administration Council, scientific committees and working groups of the EMA, the HMA, the EDQM, the Council of Europe, the Council of the European Union, the PIC/S and the European Commission;

• Regulatory papers/documents concerning NAMMDR's field of competence, in various debate stages/approved at EU level.

In 2019, the DPS/SCRP has continued:

- Administration of the NAMMD/NAMMDR Facebook page, started in 2015 (setup of notifications and NAMMD/NAMMDR releases, posting EMA press releases on review of the safety profile of certain medicinal products/classes of medicinal products, replying to messages sent via this social network site).

- Handling of the lipsamedicament@anm.ro e-mail, setup upon request of the Ministry of Health in February 2015. The daily coordination of answers to complaints received on lipsamedicament@anm.ro is based on interdepartmental cooperation (DPS//SCRP – DIF/DGIF – DPN – DECCM). In some cases, this activity has also involved contacting (by e-mail or telephone) the representatives of C.N. Unifarm S.A. and/or wholesalers of medicinal products, in order to be able to help the patient with updated information.

As regards documenting, setup and transmission of feedback to complaints received on NAMMD's e-mail address, lipsamedicament@anm.ro, these refer to

389 complaints received from patients, kin, hospitals, open circuit and hospital pharmacies, patient associations, pharmaceutical storehouses, medical societies, physicians. Apart from lipsamedicament@anm.ro, the Ministry of Health has developed and applied another manner of signalling the lack of certain medicinal products from the market, namely posting them on http://medicamentelipsa.ms.ro/ in September 2016. Thus, the 903 complaints sent on lipsamedicament@anm.ro were also handled by the DPS/SCRP. In such cases as well, the employed documentation/assessment was the one used for complaints received directly by the NAMMD on its already functional address.

Other DPS/SCRP activities:

- Coordinating interdepartmental collaboration regarding provision of support at the request of colleagues from the Pharmaceutical Inspection and National Procedure departments, for elaboration of works for the Ministry of Health, the National Health Insurance House, etc. In this context, we mention:

• Preparation and permanent updating of a database for internal use, which contains, for 2019, a number of 211 complaints received from pharmacists and a manner of resolution in this respect, by the Pharmaceutical Inspection Department, based on Order of the Minister of Health no. 269 / March 2017 on the obligation to ensure adequate and continuous stocks of medicinal products;

- Organisation of activities planned to be carried out in Romania during the Romanian Presidency of the EU Council (namely two of the quarterly meetings of the Heads of Medicines Agencies (HMA)), the Strategic Analysis and Learning Meeting (SRLM) of the Committee for Herbal Medicinal Products (HMPC), Formal Meeting of the Homeopathic Medicinal Products Working Group (HMPWG), the joint meeting of the Coordination Group for Mutual Recognition and Decentralised Procedures - Human, the joint meeting of the Committee for Advanced Therapies (CAT) and of the Clinical Trial Facilitation Group (CTFG);

- Activity within the Marketing and Public Communication Working Group of the Romanian Organisation for Serializing Medicines (OSMR);

- Coordination of materials for posting on the NAMMD / NAMMDR bilingual website, namely: the NAMMDR newsletters, the NAMMDR annual activity report, laws, decisions of the Romanian Government (GD), emergency ordinances, orders of the Minister of Health);

- Monitoring of European / national websites in order to update the information on European / national legislation in the field of the medicinal product for human use;

- Updating of the NAMMD / NAMMDR website as regards the amendments, supplementations, repeals of the regulatory acts;

- Monitoring of new information in the public space to ensure a constant flow of information: articles and press news; press releases issued by the Ministry of Health, the National Health Insurance House, patients' associations, etc.; legislative acts subject to public debate by the Ministry of Health or other information of interest for the activity of the NAMMD / NAMMDR;

- Maintenance and update of the "INFO- Serviciul Farmacopee" intranet database containing electronic versions of records of documentation provided, of issued FR X Supplements, of Standard Terms in Romanian and other useful information;

- Correspondence management for the appointment of NAMMD / NAMMDR employees in EMA working groups, etc. (59 documents);

- Participation in the NAMMD / NAMMDR group of employees, delegated to the Ministry of Health, in order to annually correct the maximum prices of medicinal products for human use;

- Maintenance and update of the database with contact details for state institutions, European and international organisations, EU counterparts, personalities, collaborators, etc. .;

- Ensuring the interpreting activity during the Presidency of the EU Council 1.01.2019-1.07.2019;

- Elaboration and translation into English of the minutes of all meetings organised by the NAMMD / NAMMDR during PRES-RO (6 documents)

- Elaboration of draft press releases related to the meetings organised by the NAMMD / NAMMDR within PRES-RO (6 documents)

- Translation (upon request) of forms for completion of the English version of the NAMMD / NAMMDR website (40 documents);

- Translation of documents requested by the Evaluation-Authorisation, Legal, Economic departments (52 documents);

- Translation of the NAMMD Annual Activity Report (2018);

- Translation of EMA press releases and of the NAMMD/NAMMDR communications and important notifications (92 documents);

- Translation of a Good Pharmacovigilance Practice guideline and of a guideline for the activity of the Assessment-Authorisation Department (2 documents);

- Provision of specialist advice for correspondence and communication with European and international bodies and representatives of the pharmaceutical industry;

- Checking the translation into Romanian of direct healthcare professional communications, posted on the website;

- Checking the translation of assessment reports and documents into English, under the mutual recognition procedure (7 documents);

- Providing consultancy for verifying the English translation of Summaries of Product Characteristics and leaflets (12 documents);

- Checking all papers translated into English presented outside the NAMMDR by NAMMD/NAMMDR specialists (27 documents).

13. Legal issues

13.1 NAMMD/NAMMDR legal issues

The main tasks of the NAMMD Legal and International Relations Directorate (DJRI) is Agency representation in court, comprising in January-December 2019 of 171 litigations, in which requests for summons, objections, written conclusions, requests for evidence, expertise, written notes, requests for legalisation, addresses to the courts regarding pending cases were drafted; the representation and defence of NAMMD interests in court were also provided.

Thus, in 2019, the legal issues in which the authority was involved were constantly growing, doubled in number compared to 2018, and in terms of scope and subject of the file, they diversified, targeting most branches of law (labour law, civil law, civil procedure, administrative law, contentious proceedings etc.); at the end of the year, there were 60 files solved and 111 still pending.

In most of the legal issues, the solutions pronounced by the courts were in favour of the NAMMD.

Moreover, any request addressed by the courts, by other institutions with administrative-jurisdictional activity, by criminal investigation bodies, as well as by other bodies, both from Bucharest and from the territory, related to the communication of information or documents, also in cases where the NAMMD / NAMMDR was not a party, were promptly answered.

13.2 Regulatory activity

The Legal and International Relations Directorate and other NAMMD/NAMMDR professional departments have set up documentation (drafts of regulatory documents, substantiation notes, approval reports) for promotion via the Ministry of Health of and proposed amendments of the following drafts of regulatory documents:

I) 3 drafts for Government ordinance/ Government ordinance/Government Decision, namely:

1) The draft of Government ordinance for amendment and supplementation of Law no. 95/2006 on healthcare reform, as well as for amendment and supplementation of some regulatory acts, of some regulations regarding the national governmental programs and the fiscal-budgetary measures approved through Government Ordinance no. 9/2019 on amendment and supplementation of Law no. 95/2006 on healthcare reform, as well as for amendment and supplementation of some regulatory acts, of some regulations regarding the national governmental programs and the fiscal-budgetary measures published in the Official Gazette no. 692 / 21.08.2019, which provides in the field of activity of the NAMMDR the following:

- Amendment of provisions of Article 893 justified by provisions of Article 17 (2) of Law 134/2019, so that "upon submission of the documentation in order to obtain the marketing authorisation, the applicants pay to the NAMMDR a marketing authorisation fee of 5000 euros or the equivalent in lei at the exchange rate of the National Bank of Romania, which constitutes NAMMDR's own revenue";

- After Article 875, four new articles have been introduced, Articles 8751–8754, which regulate complementary measures for confiscation and retention of medicinal products for human use or documents issued in connection therewith, if necessary, where legal requirements and / or the good manufacturing practice or good distribution practice principles provided for by national legislation are not complied with and if they represent a potential threat to public health.

– In accordance with which the revenues generated from tariffs related to performance of the specific NAMMDR activities represent own revenues.

The issuance of the marketing authorisation represents a specific activity of the NAMMDR according to the provisions of Article 4 (3) point 2 of Law 134/2019 and therefore that any activity and marketing authorisation activity involves certain costs related to: the remuneration of the staff involved in the authorisation flow; ensurance of the space in which the activity takes place; expenses related to the provision of the communication system and the information system; expenses related to the provision of office supplies and internal services.

2) The draft of Government emergency ordinance for amendment and supplementation of Law no. 134/2019 Law no. 134/2019 on the reorganisation of the National Agency for Medicines and Medical Devices, as well as on amendment of some regulatory acts, is currently awaiting approval.

The project was mainly proposed in order to:

- Correlating the NAMMDR scope with its tasks (i.e. supplementation of the Agency's scope with activities related to authorisation of clinical investigations for medical devices, evaluation of performance of in vitro diagnostic medical devices, authorisation of clinical trials on medicinal products for human use and

monitoring of medicinal product safety through pharmacovigilance activity), in accordance with Law no. 134/2019;

- Amendment of provisions regarding the composition of the NAMMDR Scientific Council, in order to ensure its functionality;

- Regulation of advertising for medical devices:

- Urgent regulation of sanctioning measures regarding medical devices in order to safeguard the health and safety of the patient / user and advertising in the field of medicinal products for human use and medical devices;

- Streamlining the activity by delegating the attribution of tertiary credit ordinator, executive status and representation to one of the two NAMMDR vice-presidents;

- Supplementation and clarification of certain aspects related to the NAMMDR organisational structure, all in accordance with Law no. 134/2019;

- Adoption of a measure on remuneration of the NAMMDR staff, enabling it to become an institution which provides quality services in the field of public health, predictable and anticipatory, supported by efficient and effective tools, mechanisms and skills, able to respond to new challenges, with professional and adequately motivated human resources.

3) The draft of a Government decision establishing measures for ensurance of application of certain provisions of (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83 / EC, Regulation (EC) no. 178/2002 and Regulation (EC) no. 1223/2009 and repealing Council Directives 90/385 / EEC and 93/42 / EEC, currently being endorsed, providing the necessary legal framework for the application of the provisions of Regulation (EU) 2017/745 in this field and aligning the rules applicable to medical devices with the new European legislative framework.

The proposals submitted by this legislative project intend to:

- Regulate the manufacturing of medical devices in health facilities, for their own use;

- Establish measures for advertising of medical devices;

- Regulation of contraventions and sanctions applicable in case of non-compliance with provisions of Regulation (EU) 2017/745 and of this regulatory act once it has entered into force;

- Introduction of provisions regarding the issuance of the free sale certificate;

- Elimination of the obligation to make available, together with the medical device, the instructions for use in Romanian and to clarify the aspect regarding the language in which the information provided by the equipment interface with the user must be written, within a software system;

- Regulation of the obligation of health units regarding the implant card;

- Ensuring the transparency and traceability of medical devices, in order to improve the effectiveness and safety of users.

II) 9 Minister of Health Order drafts:

1. The draft of the Minister of Health Order on the registration of manufacturers, importers and distributors of active substances to be used as raw materials for medicinal products for human use, approved through Order of the Minister of Health no. 775/2019 on the registration of manufacturers, importers and distributors of active substances that will be used as raw materials for medicinal products for human use, published in the Official Gazette, Part I no. 473 of June 11, 2019.

This regulatory act mainly regulates aspects regarding the manner of registration of the activity at NAMMDR by manufacturers, importers and distributors of active substances used in the manufacture of medicinal products for human use, established in Romania, the obligation to submit the registration form even in case of possession by the manufacturer / importer of a Good Manufacturing Practice certificate issued by the NAMMDR, the necessary administrative and technical documents in the file submitted to the NAMMDR together with the registration form, the procedures for issuance by the NAMMDR of the agreement on registration of the manufacturer / importer or distributor of active substances used as raw materials for medicinal products for human use, the Good Manufacturing Practice certificate or the Good Distribution Practice certificate and the frequency of inspections at the premises of manufacturers, importers or distributors of active substances and the manner of conducting inspections.

2. The draft for amendment of the Annex to Order of the Minister of Health no. 85/07.02.2013 on approval of the Norms for implementation of provisions of Article 703 (1) and (2) of Law No. 95/2006 on healthcare reform concerning medicinal products for special needs, undergoing approval, with express regulations regarding:

- The possibility of issuance, for safety reasons, in respect of a medicinal product authorised in a third country, of an authorisation for supply of medicinal products for special needs, only if the medicinal product is not available in the EEA;

- Clarification of the concept of "medicinal product for special needs", in the sense of excluding from this category medicinal products which are the pharmaceutical equivalent of medicinal products already authorised for marketing and which are already in the therapeutic circuit;

- The deadlines for the NAMMDR to solve the requests for authorisation for supply of medicinal products for special needs, currently unregulated;

- Clarification of certain issues related to the documentation required to obtain the authorisation for supply of medicinal products for special needs;

- Detailing the issues related to the obligations regarding pharmacovigilance activities of the wholesale distributor of medicinal products for special needs and of the NAMMD;

- Elimination of the provision regarding termination of validity of the authorisation for supply of medicinal products for special needs in case of resumption of the marketing of the medicinal product via the usual distribution channels;

- The manner of distribution on the Romanian territory of the medicinal products for which an authorisation was obtained regarding the supply of medicinal products for special needs, by direct distribution to the final beneficiaries or through other wholesale contract partners.

3. The draft Order for approval of conditions for authorisation of the use of an unauthorised medicinal product for human use in order to make it accessible to a group of patients for last resort use or to facilitate the patient's access to last resort treatment, pending endorsement, with regulated issues referring to:

- Nomination of the NAMMDR as the competent authority for assessment and authorisation of an unauthorised medicinal product for human use in order to make it accessible to a group of patients for last resort use or to facilitate the patient's access to last resort treatment;

- Establishment of a requirement stating that the medicinal product for which authorisation is sought for use in last resort treatments for a group of patients should be subject to an application for marketing authorisation through centralised procedure or to being in the clinical trial stage, where evidence was accumulated to support the effectiveness and safety of its administration in the proposed use, in at least one of the EU Member States or in a member country of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH);

4. The draft of the Order on amendment of the Annexes to Order of the Minister of Health no. 373/2015 on approval of the special regime form of the report of finding and application of minor sanctions regarding non-compliance with legal provisions regarding medical devices and related activities, whose adoption is necessary given the setup of the NAMMDR by entry into force of Law no. 134/2019 as well as the amendment, pursuant to Law no. 203/2018 on measures to streamline the payment of fines, of the provisions of Government Ordinance no. 2/2001 regarding the legal regime of contraventions, as amended by Law no. 180/2002.

The main provisions of this draft order refer to:

- The possibility to pay, regardless of the provision or not of this aspect in the act regulating the contravention fine, within 15 days from the date of submission / communication of the minute, half of the minimum fine as provided by the regulatory act; this possibility should be mentioned by the ascertaining agent in the minute;

- The abrogation of the provisions from regulatory acts in force that establish the payment of half of the minimum contravention fine, in a shorter term than the one provided in Government Ordinance no. 2/2001 on the legal regime of contraventions, approved as amended by Law no. 180/2002, with subsequent amendments and supplementations;

- The character of debt title and payment notification of the minute for contravention finding.

5. The draft of the Order regarding the amendment and supplementation of the annex to Order of the Minister of Health no. 895/2006 on approval of Regulations regarding marketing authorisation and supervision of medicinal products for human use, undergoing approval, which proposes measures to streamline the evaluation of applications for authorisation and renewal of marketing authorisations submitted for authorisation through national procedure as follows:

- Harmonisation of the renewal process of the marketing authorisation through the national procedure with the mutual / decentralised recognition procedure, by applying the Coordination Group Guideline for renewal procedures through MRP / DCP procedures (edition in force at the time of application evaluation) for renewal applications submitted within the national procedure, in order to reduce the duration of their evaluation as a result of the possibility of submitting a reduced clinical documentation for medicinal products authorised in line with Article 709, 718 of Law no. 95/2006, for medicinal products for which there is no obligation to submit PSURs (Periodic Safety Update Reports) and for the possibility of renewal by applying a short-term procedure, for medicinal products authorised in line with Article 708 (1) of Law no. 95/2006, for medicinal products for which there is no obligation to submit PSURs (Periodic Safety Update Reports), in the situations provided in the Guideline;

- Reduction of the duration of the evaluation of marketing authorisation applications submitted for authorisation through national procedure by introducing deadlines for responding to NAMMDR requests similar to those applied via decentralised authorisation procedure.

6. The draft of the Order on approval of the Methodological Norms for the application of Title XX of Law no. 95/2006 on healthcare reform, regarding approval of the activities in the field of medical devices, undergoing approval, regarding approval of the activities in the field of medical devices, which regulates aspects related to:

- The definition of economic operators, namely manufacturers, distributors and importers, their obligations, as well as supply and maintenance activities, in accordance with the definitions set out in Regulation (EU) 2017/745, in order to clearly set out the general obligations of different operators to improve the degree of compliance with the regulations for relevant operators, as proof of Romania taking, as an EU Member State, all the necessary measures to ensure the implementation of provisions of this Regulation;

- Introduction of the validity term of 3 years for the operating approvals, in favour of the economic operators and for facilitation of maintenance of the records of the units approved by the NAMMDR;

- Increasing the effectiveness of the market surveillance service, reflected in ensuring a higher level of protection of public health interests, overall security, occupational health and safety and consumer protection.

7) The draft of order for supplementation of Order of the Minister of Health no. 1009/2016 on registration of medical devices into the national database, approved by Order of the Minister of Health no. 1778/2019 for supplementation of Order of the Minister of Health no. 1009 / 2016 on registration of medical devices into the national database and published in the Official Gazette no. 963 of November 29, 2019, which regulates aspects related to registration of data with the NAMMDR by the manufacturer, the manufacturer's authorised representative, importer or distributor, in situations where the medical device is made available to the end user taking into account the definitions in line with Article 2 points 27 and 29 of Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385 / EEC and 93/42 / EEC, in force since 25 May 2017.

8) The draft order for approval of the Methodological Norms regarding the evaluation, notification and monitoring of the bodies assessing compliance of medical devices, undergoing approval, proposed in view of implementation of provisions of Government Ordinance no. 20/2010 on establishment of measures for unitary application of the EU legislation for harmonisation of the conditions for marketing of the products, approved as amended by Law no. 50/2015, with subsequent amendments. The proposal is justified by entry into force of provisions of Regulation (EU) 2017/745 on medical devices, according to which, from 26 November 2017 and "until 26 May 2020, the obligations of the bodies notified in line with Articles 35 - 50 shall apply only to those bodies that submit an application for designation in accordance with Article 38 "as well as the registration at the NAMMDR of an application for designation for notification by a body assessing compliance of medical devices, for operation in Romania, which would support Romanian manufacturers of medical devices, given the fact that, currently, no notified body carries out its activity in Romania.

9) The draft of the Order for approval of the Norms regarding the taking over, evaluation, free transmission, liquidation or destruction of medicinal products for human use, project awaiting approval. The proposals contained in this project have been elaborated taking into account provisions of Law no. 95/2006 on healthcare reform, republished, which stipulates the application of the complementary measure of confiscation and retention of medicinal products for human use by NAMMDR inspectors, as well as the provisions of Government Ordinance no. 14/2007 for regulation of the manner and conditions of capitalisation of the goods entered, in accordance with the law, into the private property of the state and those of the Annex to Government Decision no. 731/2007 on approval of the Methodological Norms for enforcement of Government Ordinance no. 14/2007 for regulation of the manner and conditions of capitalisation of the goods entered, in accordance with the law, in the private property of the state, republished, with the subsequent amendments and supplementations.

10) The draft of order regarding the amendment of Order of the Minister of Health no. 1297 / 2010 on the manner and conditions of taking over, evaluating, transmitting free of charge, capitalising or, as the case may be, liquidation or destruction of consumable materials of medical utility, materials such as medical inventory items, medicinal products and medical devices which have become, according to the law, the private property of the state, awaiting approval. The project was elaborated considering the current way of transferring the medicinal products to the state property through county public health directorates, according to provisions of Order of the Minister of Health no. 1297 / 2010, as well as the need to correlate the provisions of the respective Order of the Minister of Health with those stipulated in the draft order for approval of the Norms on how to take, evaluate, transmit free of charge, liquidate or destroy medicinal products for human use.

At the same time, during 2019, about 167 petitions, 41 requests for information of public interest and 206 external addresses were analysed and resolved within the Legal and International Relations Department.

14. Management of human resources and quality management

The Human Resources and Quality Management Directorate carries out its activity in accordance with the attributions provided in Order no. 1522 of October 9, 2019 for approval of the Regulation on the organisation and operation of the NAMMDR (ROF-NAMMDR).

14.1. Assuring human resources to NAMMD structures

This activity is performed by the Payroll Service - NAMMDR, which carries out its activity in accordance with the attributions stipulated in Order no. 1522 of October 9, 2019 on approval of the Regulation for organisation and operation of

the NAMMDR. In order to achieve the specific objectives in this field, consultancy was provided during 2019, concerning the application of specific legislation; the secretariat and participation in commissions for examination and appeal for competitions for filling vacant and temporarily vacant positions of civil servants and contract staff was ensured. In this sense, the necessary documentation was elaborated according to the NAMMDR ROF (Regulation for organisation and operation).

1. Staff-related activities carried out in 2019 were performed within a continuous process of analysis of the institution's required human resources, of elaboration of staff strategies and policies, in accordance with the organisation's long-term objectives and efficiency.

In this respect, particularly in the context created by entry into force of Law no. 134/2019, a better provision of the institution's structures with qualified specialised staff, maintenance and efficient use of the existing staff were considered. In connection with this aspect, following approval of the head of the Ministry of Health, the organisation of competitions for temporarily vacant and vacant positions of contract staff within the NAMMDR was carried out, resulting in 8 contracts for candidates admitted to the competition for occupation of contractual executive functions and management functions. Thus, 610 additional documents attached to the individual employment contracts were forwarded and submitted for approval, twice as many as in 2018.

In 2019, as a result of entry into force of the law on reorganisation of the NAMMD and setup of the NAMMDR, the unit's job title list and documentation / correspondence to the Ministry of Health and the National Agency of Civil Servants were drawn, regarding the change of status, transformation of the structure jobs, together with all the required documentation. Decisions have been made regarding the nomination, release / termination, suspension, promotion, secondment, reassignment, transfer, relocation and modification of service / employment relationships for the NAMMD / NAMMDR staff.

By acquiring the status of self-funded institution, achieved from the collection of tariffs according to the legislation in force and the subsidy granted from the state budget, the Agency was required to elaborate decisions for establishing / increasing the amount of basic monthly gross salaries, as well as certificates regarding the completion of the employees' accumulated service after 01.01.2011.

At the same time, in order to carry out the remuneration activity, the application of indexations, increases, seniority raises and changes regarding staff remuneration was followed and the IT procedures regarding the Remuneration application within the Softech programme were updated, in line with the legislation in force. Also in terms of ensuring the rights of NAMMDR employees according to the law, the necessary documentation for issuance of holiday vouchers for its staff was drawn up.

In the field of employee performance evaluation, advice was provided concerning the evaluation of professional performances of the NAMMD/NAMMDR contract staff. The records of the job descriptions and individual professional performance evaluation sheets of the employed staff and of the job descriptions prepared, were monitored according to the law, by the responsible persons; structures were advised in view of elaboration of these documents.

In accordance with the law, the Human Resources and Quality Management Department had a consistent contribution, in line with the deadlines established for transparency of NAMMDR activities, by registration and preparation for publication of 250 wealth declarations and 250 declarations of interests of employees with managerial positions on the institution's website.

14.2. Development of human resource through employee training and retraining

The development of human resources refers to the improvement of the quality of professional training of the workforce, given the fact that quality is a function of both basic and higher education and of vocational training programmes. The quality and adaptability of the workforce is a key factor in creating a favourable environment for rapid adaptation to the dynamics of the regulation of the medicinal product issue. In the context of a knowledge-based economy, where the application of knowledge is a major factor in all sectors, not only of economy-related ones but also of the administration, the essential component of activities is the balance between knowledge and the comprehension skill, accumulation of information, generation and dissemination of new knowledge, and particularly the application of knowledge for the purpose of superior performance, thus becoming the key to organisational success. In this context, considering the particularly rapid dynamics in the medicinal product field, generally speaking, and the need to regulate medicinal product development, authorisation and monitoring of its evolution on the market in terms of efficacy and safety, a high level of competence is essential for NAMMDR specialists, whose attainment and maintenance cannot be achieved in the absence of a sustained continuing training programme specific to the requirements of professional development in this field, oriented both towards in-house training to trainings (within the Agency) and towards participation in trainings organised at national or international level by different authorities and specific bodies.

To the extent of the availability of funds in this respect, there have been numerous reference participations of the staff in scientific/professional events, at some of them, with presentation of specialised works, such as:

• "EU approach to nitrosamine impurities in synthetic medicinal products", National Pharmacy Conference, 14 November 2019, Bucharest

• "Molecules with therapeutic benefit in urothelial cancer, evaluated by the NAMMDR in view of reimbursement proposal", National Pharmacy Conference, 14 November 2019, Bucharest

• "The medicinal product shortage: major challenge for the EU regulators network - Steps to improve reporting and communication", National Pharmacy Conference, 14 November 2019, Bucharest

• "Medication errors from the pharmacovigilance perspective", National Pharmacy Conference, 14 November 2019, Bucharest

• "Safety of phenobarbital administration in children with febrile seizures", National Pharmacy Conference, 14 November 2019, Bucharest

• "National legislation on shortage of medicinal products in Romania", the 95th meeting of the HMA, February 21-24, 2019, Timișoara

• „CAT case study: Post-authorisation efficiency study of an ATMP, Simona Badoi, CAT member, Joint CAT / CTFG meeting for strategic analysis and learning, 13 - 14 June 2019, Bucharest

• „The Vaccine safety communication Strategic Review and Learning Meeting, PRAC-CMDh Joint Meeting on Strategic Analysis and Learning, 22 - 23 May 2019, Bucharest

• Collaboration between NCAs and the Academy / Clinical Experts PRAC-CMDh Joint Meeting on Strategic Analysis and Learning, Joint PRAC and CMDh meeting 22 - 23 May 2019, Bucharest

• "Structured approach to reflect extrapolation in the development of medicinal products for paediatric use", Informal PDCO meeting on strategic analysis and learning, Valletta, Malta, 12 - 14 June 2019.

• "Pharmacist involvement in pharmacovigilance activity", event organised by the Buzau College of Pharmacists in partnership with the NAMMDR.

Participation in congresses / conferences in the field:

• The Congress of the Carol Davila University of Medicine and Pharmacy Bucharest, 10-12 October 2019, Bucharest;

• The National Conference of Clinical Pharmacy, 19 - 21 September 2019, Bucharest;

• The National Pharmacy Conference, the 12th Edition, 14-16 November 2019, Bucharest;

• The National Conference of the College of Physicians of Bucharest, 14-16 March 2019, Bucharest;

• The Congress of the Carol Davila University of Medicine and Pharmacy - Bucharest, the 7th edition, 10-12 October 2019, Bucharest;

• The International Conference "From Science to Guidance and Practice", October 31, November 1, 2019, Bucharest;

• The National Conference of Family Medicine, 23-26 October 2019, Bucharest;

Participation in training courses:

• "QWP Seminar - Learn to develop and draft regulatory documents on quality", organised by the State Institute for Drug Control (SUKL), Czech Republic, under the auspices of the European Medicines Agency (EMA), 14-15 March 2019, Prague

• The "Urinary tract infection in children" online course, organised by the Romanian College of Physicians, 11 March 2019;

• The "Chronic pelvic pain" course, organized by the Society of Endometriosis and Infertility Eastern Europe, 19-20 April 2019, Bucharest;

• The "Excellence in personalized medicine" course, organised by the Romanian Academy of Medical Sciences, 5-7 June 2019, Bucharest;

• The "News in the diagnosis and treatment of ENT diseases" course, organised by the Romanian Society of Rhinology, 21-22 November 2019, Bucharest;

• The "New perspectives in approaching the patient with hypertension" course, organised by the Romanian Society of Cardiology, 2 November 2019, Bucharest;

• An online course for clinical assessors on final evaluation objectives in clinical trials in the field of oncology and interpretation of survival curves, organised by the EU NTC;

• Preclinical Assessors Meeting (PAM), 8-9 May 2019, Oslo.

• A course for clinical assessors on practical information from the Summary of Product Characteristics and Package Leaflet, obtained from the scientific evaluation and concerning safety information, organised by the European Medicines Agency (EMA).

• A course related to quality management, SR EN ISO 9001: 2015, organised within the project "Strengthening the administrative capacity of the Ministry of Health and of subordinated units, coordinated through the unitary sanitary implementation of the SR EN ISO 9001: 2015 Quality Management System".

The setup of individual employment contracts and additional documents for the contract staff within the institution was drawn up and monitored in accordance with the law and registered in the register of employees according to the directions in force.

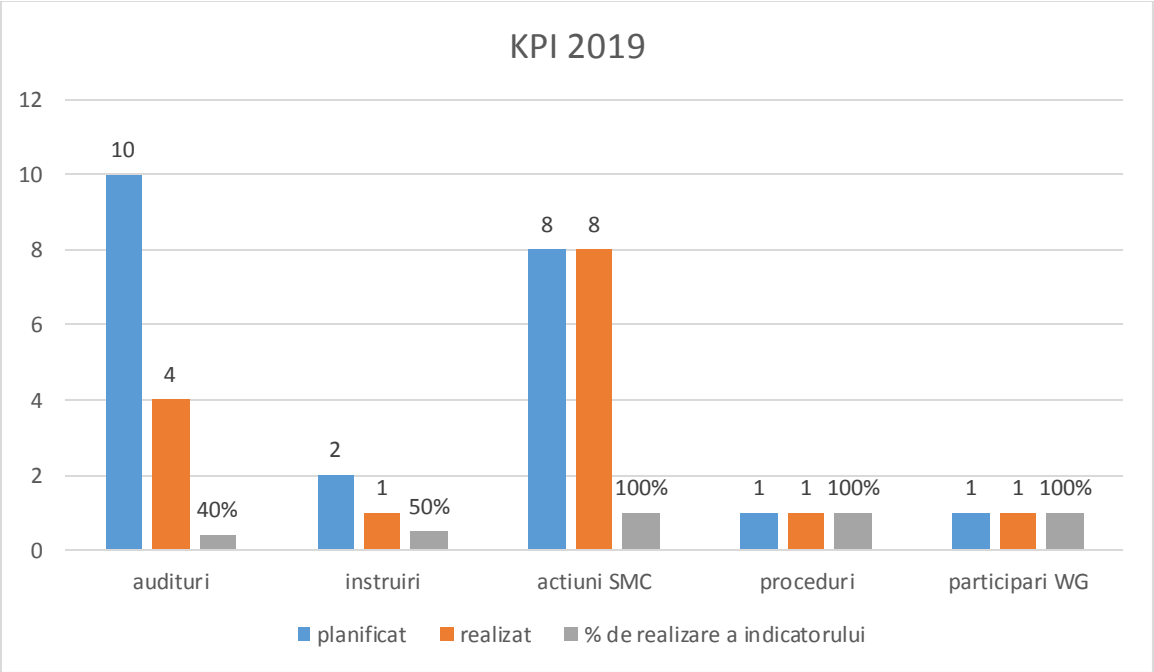
Regarding other activities of the Human Resources Department Payroll / Payroll Service, its permanent activity consisted of preparing the documentation in order to terminate the individual employment contract / secondment / retirement / promotion, drafting 610 additional documents to individual employment contracts in this respect.

14.3 Quality Assurance and Registry Service

Until 12.09.2019, this Service was named Quality Assurance Bureau (QAB); after this date, as a result of the provisions of Law no.134 / 2019 on reorganisation of the National Agency for Medicines and Medical Devices, as well as for amendment of some regulatory acts, of the provisions of Order of the Minister of Health no. 1522 / 09.10.2019 for approval of the Regulation on the organisation and operation of the National Agency for Medicines and Medical Devices in Romania, as well as of the provisions of Order of the Minister of Health no. 1412 / 13.09.2019 for the approval of the organisational structure of the NAMMDR, the Bureau was reorganised as the Quality Assurance and Registry Service (SACR), subordinated to the Human Resources and Quality Management (DRUMC).

In 2019, the specific objectives of BAC were updated, derived from the general objectives of the NAMMD. In order to achieve the specific objectives, the actions and activities of the BAC were identified by drawing up the Activity Program of the BAC for 2019 and its periodic updating.

At the same time, the performance indicators of the BAC were identified, monitored and reported. The situation of performance indicators for 2019 is as follows:



The partial performance of specific BAC activities planned for 2019 was caused, first of all, by the small number of BAC staff in relation to the large number of planned audits and the time required to perform them, but also by the lack of financial resources for staff training.

In 2019, specialized assistance was provided to persons responsible for quality assurance in the NAMMD organisational structures, in order to comply with quality management requirements by methodologically coordination of their activities in the field of SMC.

Seeing the need for update of the nominations of persons responsible for quality assurance in NAMMD departments, the proposals submitted by the departments were centralised, a report was prepared for issuing a decision in this regard and collaboration with the DRUS was ensured, in order to prepare the decision. The contact details of the persons responsible for quality assurance and of their alternates of all NAMMD structures have been updated.

The "Quality Management System" section was organised on the intranet server, with the support of the SLI (IT Logistics Service). The internal quality audit programme for 2019 was developed by the audit program coordinator (head of BAC) based on the strategy and approved by the NAMMD President in December 2018.

Subsequently, in January 2019, there was a change in the 2019 Internal Quality Audit Programme caused by moving the planned audit to the DIF in November and performing the internal quality audit at the Registry and Archives Department (CRA) within the IT logistics and electronic data management Department (DLIGED), in February, following notification of the Pharmaceutical Inspection Department (DIF), showing the fact that the department was in a transition period due to significant changes in the staff structure of the DIF, through departure of a large number of experienced inspectors and transfer of their duties to newly hired persons who needed a period of preparation and training in order to take over those duties and responsibilities; these aspects affect the main activities of the department and the achievement of its specific objectives, preventing its response to the request regarding conduct of an internal quality audit involving the availability of adequate time and staff resources.

10 structures were audited in 2019.

Following the (internal and external) audits performed, non-compliances and opportunities for improvement were identified for which the auditors made recommendations. For each detected non-compliance or opportunity for improvement, a Monitoring Sheet for non-compliances / recommendations was prepared. These were forwarded to the audited structures which proposed actions to address each non-compliance or improvement action and implementation

deadlines. The effective implementation of the proposed actions has been carried out or is being carried out by the audited department.

The application of corrective and preventive actions for the resolutions established by NAMMD / NAMMDR departments / structures was followed, as a result of internal audits performed by BAC.

In 2019, no complaints were received about the activity of BAC or other NAMMD / NAMMDR departments / structures that would determine the transfer of corrective or improvement actions established as a result of dealing with a complaint in the SMC action system.

In 2019, the BAC undertook steps for acquisition of pharmacopoeias relevant to the activity of NAMMD departments: USP-NF Online and BP Online, by preparation of purchase requisitions and substantiation notes to the Economic Department.

The NAMMD Quality Manual developed by BAC in 2018 and the Quality Policy and quality objectives in NAMMD were maintained in force, as annexes of the quality manual. These were forwarded to the staff by posting on the NAMMD / NAMMDR intranet server; the quality policy and objectives were also posted on the ANMDM / NAMMDR website, in order to make sure that all stakeholders are informed.

The process of keeping under control (elaboration, revision, amendment, dissemination / withdrawal) of system and operational procedures was integrated into the activity of the Technical Secretariat of the SCIM Monitoring Commission provided by the BAC staff. Thus, the following activities were carried out:

- allocation of system procedure codes and coordination of the allocation of operational procedure codes within organisational structures;

- analysis of the documented procedures, considering observance of compliance with the minimum structure provided in the model presented in SGG Order no. 600/2018 supplemented with the requirements of NAMMD's own system procedure regarding procedure management;

- Submission for analysis of the system procedures to commission members;

- Maintenance of original copies of system procedures: 39 standard procedures at the end of 2019;

- Dissemination of existing versions of system procedures to all NAMMD employees and ensuring that they are available or easily accessible on the intranet server;

- Withdrawal of cancelled versions and archiving in order to prevent unintentional use of obsolete version procedures;

- Keeping updated records of all system and operational procedures within the NAMMD / NAMMDR. In 2019, the process of keeping the records / information documented in the BAC under control was significantly improved by moving from paper records (paper registers) to electronic records (Excel registers).

In 2019, BAC coordinated and carried out the standardisation activity through:

- Collaboration with DM departments in order to establish the list of European standards in the field of medical devices selected to be included in the National Standardisation Programme for 2019 for which the Ministry of Health finances the elaboration of the Romanian version and the correspondence with the Ministry of Health;

- Collaboration with the Legal Department for conclusion of the Contract for the translation of 19 standards for 2019 between the NAMMDR and the ASRO;

- Elaboration of the updated List of NAMMD persons appointed as representatives in the national standardisation technical committees of the ASRO.

- Preparation of the Substantiation Note to the Economic Department regarding payment of the NAMMD membership fee to ASRO and update of the WEB Info Standard application used as a tool for documentation, information and management of Romanian standards for the entire NAMMD / NAMMDR staff;

- Collaboration with the SLI for administration of the application on the NAMMD / NAMMDR intranet server, granting access rights and uploading the purchased standards;

- Preparation of purchase requisitions for acquisition of Romanian standards;

- Following the ASRO Newsletter and informing the interested persons from NAMMD / NAMMDR (about standards, training courses, etc.).

- Free access to ASRO publications: the Standardisation newsletter and the Standardisation magazine.

In 2019, the BAC participated in the organisational meetings, helping with the preparation of the meetings organised by the NAMMD / NAMMDR during Romania's Presidency of the Council of the European Union, in the first half of 2019, as well as in the half-yearly meeting organised by the State Institute for Drug Control (SUKL) in the Czech Republic, at its headquarters in Prague, in the context of the Romanian Presidency of the Council of the European Union, from 6 to 7 June 2019.

Technical Secretariat of the SCIM Monitoring Commission

The BAC ensures the attributions of the Technical Secretariat of the Monitoring Commission (CM) of SCIM established in accordance with OSGG 600/2018,

according to the decision of the NAMMD President regarding the establishment of the Monitoring Commission of SCIM and the ROF of the commission.

The main task of the secretariat is to assist the chair of the Monitoring Commission in coordinating the activity of the commission and managing the documents that are the responsibility of the commission.

Thus, the following activities took place in 2019:

- Preparation of reports for update of the Decision establishing the Monitoring Commission - 4 decisions (216/02.2019, 533/04.2019, 252/09.2019, 422/10.2019);

- Preparation of support documents, organisation of commission meetings and elaboration of their minutes: 2 meetings;

- Drafting the definition of the general objectives of the NAMMDR and presenting the members of the commission for debate;

- Centralisation of the specific objectives of the NAMMD / NAMMDR structures defined by them, in the form of Annex no. 2 to the Register of Risks;

- Keeping system and operational procedures under control through:

- Allocation of system procedure codes and coordination of allocation of operational procedure codes within organisational structures;

- Analysis of the documented procedures, from the viewpoint of the observance of compliance with the minimum structure provided in the model presented in SGG Order no. 600/2018 supplemented with the requirements of the NAMMD / NAMMDR own system procedure regarding the management of procedures;

- Submission for analysis of system procedures to commission members;

- Keeping the original copies of the system procedures;

- Dissemination of existing versions of the system procedures to all NAMMD / NAMMDR employees, ensuring that they are available or can be easily accessed on the intranet server;

- Withdrawal of cancelled versions and archiving in order to prevent unintentional use of obsolete version procedures;

- Maintaining an updated record of all system and operational procedures within the NAMMD / NAMMDR, on the intranet server under the section specially created with SLI support;

- Centralisation of self-evaluation questionnaires of the implementation stage of internal / managerial control standards completed by each structure from the NAMMD / NAMMDR organisation chart in order to prepare the Synthetic Situation of self-evaluation results elaborated in line with Annex no. 4.2 to the

code approved through OSGG 600/2018 and of the Centralising Situation regarding the stage of implementation and development of the internal managerial control system on December 31, elaborated in accordance with Annex no. 3 to the code approved through OSGG 600/2018;

- Preparation of the Report on the internal managerial control system on December 31, elaborated according to Annex no. 4.3 to the Instructions from OSGG 600/2018 and the transmission to the Ministry of Health, upon its request, together with the Centralising Situation regarding the stage of implementation and development of the internal managerial control system on December 31, elaborated according to Annex no. 3 to the code approved through OSGG 600/2018;

- Drafting the SCIM Development Program for the NAMMD and the NAMMDR and presenting the members of the committee for debate;

- Elaboration of the project of the Business Continuity Plan based on the information partially received from some organisational structures;

- Preparation of reports updating the Decision on the nomination of responsible individuals for risks at the level of NAMMD/NAMMDR structures and establishing their attributions - 3 decisions (612 / 05.2019, 695 / 06.2019, 610 / 11.2019).

In 2019, the BAC was the subject of an internal public audit by BAI (Internal Audit Office).

THE QUALITY MANAGEMENT SYSTEM

The quality management system implemented within the NAMMDR and implicitly, in each of its departments is a mature one, based on the SR EN ISO 9001 standard for all activities and on the SR EN ISO / CEI 17025 standard for laboratory activities, implementing the process-based approach for all activities.

Operational management at the level of departments / structures and the top management are involved in quality management activities by demonstrating leadership and commitment. The NAMMD / NAMMDR staff knows and complies with the specific requirements of the SMC, is familiar with the quality documentation and implements the procedures into the current activity.

In order to ensure a unitary and coherent system of documentation of all procedures at the level of the entire organisation, the NAMMD management decided to integrate the two SMC (quality management systems) and SCIM (internal managerial control system) by developing a single model procedure.

In 2019, the review of the procedures for transposition of all procedures into the new unitary format was continued, but the achievement of this objective was affected by a number of internal and external factors. Following this activity, the

importance of improving the quality of activities and making each employee responsible for their work, increasing the efficiency of human resources through continuous training and streamlining the activity by developing formalised procedures for all activities, simplifying information flows by computerising the processes, was confirmed.

15. Economic activity

After publication of Law no. 134/2019 on reorganisation of the NAMMD, as well as for amendment of some regulatory acts, in the Official Gazette of Romania no. 587 of 17 July 2019, the NAMMDR is a newly established institution, which has taken over all rights and obligations, as well as all other assets in the patrimony of the NAMMD.

In accordance with the law, the Economic Department has taken all steps in order to prepare the handover protocol between the NAMMD and all documents for the organisation and operation of the NAMMDR, and in order to obtain new fiscal identification data for the newly created institution, currently the NAMMDR, having the unique fiscal registration code 41433222, of 23.07.2019.

Since the entry into force of Law no. 134/2019, the financing of NAMMDR is ensured from NAMMDR's own revenues, obtained from collection of tariffs charged according to the legislation in force, and from subsidy granted from the state budget. In this respect, the financial budget accounting service was mainly concerned with substantiating and implementing the draft budget, managing the approved budget with payments within the stipulated limits as well as rectifying budget appropriations according to the institution’s needs.

The provisions for classification of the requested amounts by categories of budgetary expenditures were observed, with their detailing by titles, articles and paragraphs; the documentation related to the 3 phases of the budgetary execution of expenditures, namely the commitment, liquidation and ordering of expenses, were correctly registered in the "ALOP” computer system.

In 2019, the approved budget, as well as all subsequent changes made in line with the corrections approved by the chief credit ordinator, as well as all budgetary and legal commitments approved within the institution, were entered into the Forexebug IT system.

This year, in the field of financial budget accounting, the organisational framework for the administration and use of funds approved through budget was ensured, in accordance with the law. Following reorganisation of the NAMMD, capital expenditures amounting to 1,300,000 lei were approved. From the approved budget, NAMMDR made capital expenditures, as follows:

The budget approved for 2019 was below the level requested by the NAMMD / NAMMDR, so there were some inconsistencies with the real needs of the institution.

In 2019, the NAMMD / NAMMDR did not have a budget for capital expenditures.

The approved NAMMD / NAMMDR budget also included capital expenditures.

Cars, equipment and means of transportation - 24,081.54 lei.

Other fixed assets - 54,164.04 lei.

BUDGET, NAMMD/NAMMDR incomes

Between 01.01.2019 and 22.07.2019, the NAMMD was fully financed from the state budget, receiving a sum of 16.673.406 lei, of which:

• Budget credits for staff expenses, including the fund for non-disabled persons: 15,485,095 lei.

• Budget credits for expenses with goods and services: 1,188,310.7 lei.

As regards the revenues collected by the NAMMD until 09.08.2019, the date of entry into force of Law no. 134/2019, during 2019, it collected 48,329,653.16 lei, of which tariffs and fees, amounting to 2,256,871.9 lei, were transferred to the state budget. As an effect of the entry into force of Law no. 134/2019, the NAMMDR is currently financed from its own revenues and state subsidies from source G. The subsidy approved according to the budget on 09.08.2019 was of 3,218,000 lei and was returned to the Ministry of Health. The NAMMDR final budget (excluding the subsidies approved for 2019) was of 17,782,000 lei.

Since entry into force of the law on reorganisation of the NAMMD and the establishment of the NAMMDR, the Agency has collected from various sources revenues amounting to 35,012,585.29 lei, revenues from differences between exchange rates amounting to 869,739.62 lei and an interest income of 0.29 lei. At the end of 2019, the NAMMDR had a surplus of 20,648,470.21 lei.

Regarding the effective budget execution, until reorganisation of the Agency, the value of NAMMD budget expenditures, according to those published in December 2019, was of 16,254,816.68 lei, of which actual staff expenses represented 15,485,095.34 lei, the effective expenditures for goods and services being of 1,188,310.7 lei and the payments made during the previous years and recovered during the current year related to the current expenses and financial operations representing 418,589.36 lei.

Since the establishment of the NAMMDR, the budget execution of the agency was: the NAMMDR budget approved for 2019 was 17,782,000 lei, the value of actual budget expenditures in 2019 according to the budget execution published

in December 2019 being 12,822,334.41 lei (11,649,792.42 lei, actual staff expenses, 1,094,296 lei, actual expenses for goods and services, and 78,245.58 lei, actual capital expenses).

These numbers allow us to conclude that, from the budget execution for 2019, the total value of budget expenditures represents 72.10% of the approved budget, of which staff expenditures represent 65.1%, expenditures for goods and services represent 6.15%, and capital expenditures 0.44% of the respective budgets approved for each of these categories.

16. General administration

As regards public procurement, in 2019, current activities such as the elaboration, amendment and update of the "Annual Public Procurement Program - 2019" at institution level were carried out, based on the requirements specified in the necessity reports, prepared by NAMMDR departments, as well as the elaboration of the necessary documentation for concluding public procurement contracts for products / services / works and direct acquisitions from the SEAP / SICAP catalogue. In addition, the structure collaborated with all organisational structures within the NAMMDR depending on the specifics and complexity of the procurement object as well as with external suppliers on the requested procurements. Public procurement procedures have been established in accordance with the results of the analysis of purchase requisitions for public procurement of products / services / works. Legal commitments (public procurement contracts / additional documents or firm orders required in order to verify and sign the legal commitments) concluded within the Compartment as well as public utility contracts and rents concluded within the specific department, were verified and signed. The structure handled the organisation and provision of support services (secretariat, transportation of goods and people, courier, telephone communication) as well as the implementation of Standard Operating Procedures (PSO) regarding the activities carried out within the DAG in the implementation, maintaining and improving the quality system in the activities within the department, etc.

The entire structure carried out a sustained activity to support the organisation and conduct of events during the period in which Romania held the Presidency of the EU Council.

In the first part of 2019, the general administration activity was marked by the imperatives of organising events that represented Romania's organisational responsibility, when taking over the Presidency of the EU Council. As regards the activities carried out in order to ensure smooth running of the events organised by the NAMMDR in the context of the Presidency of the EU Council, the General Administration Directorate coordinated at institution level and was directly involved in:

- Providing transport for participants;

- Collaboration and permanent exchange of information with the Ministry of Foreign Affairs in matters of budget and organisation;

- Identification of locations and related services for performance of events and ensurance of smooth running of events in the identified spaces (the Palace of the Palace, the NAMMDR and the Timiș County Council);

- Ensuring connection with the Security and Protection Service;

- Provision of the required logistics materials.

- Analysis of the purchase requisitions for public procurement of products / services / works and establishment of the public procurement procedure;

- Verification and signing of legal commitments (public utility contracts and rents / additional documents) concluded within the DAG;

- Management of rental contracts, invoices and reports for Romanian territorial inspection units (UTI);

- Organising and providing support services (secretariat, transport of goods and people, courier, telephone communication, cleaning, security) necessary for the proper conduct of the activity within the organisation;

- We have permanently pursued the implementation, maintenance and improvement of the quality system in the activities within the DAG;

- An adequate level of competence was ensured through regular training of staff;

- Responsible for the implementation of the Standard Operating Procedures (PSO) regarding the activities carried out within the DAG;

- Responsible for archiving the documents within the department in accordance with the legislation in force.

17. Internal audit

The internal audit operates through its own structure within the NAMMDR and is organised as an office according to the NAMMDR organisation chart; it is directly subordinated to the NAMMDR president.

In 2019, the NAMMD / NAMMDR President did not involve the Internal Audit Bureau in carrying out auditable activities. During the year, in accordance with the established Audit Plan, 5 insurance audit missions were performed; 6 of its missions were rescheduled, out of which 5 were insurance audit missions and 1 mission from another category.

Informal advisory missions, consultancy, facilitation of understanding certain aspects related to the activities of the NAMMD / NAMMDR structures were granted within planned audit missions as well as outside of them. Assurance / counselling missions covered NAMMD / NAMMDR structures in fields such as quality assurance, policies and strategies, general administration, corruption prevention, clinical trials, pharmacovigilance and risk management and specific NAMMDR functions.

The degree of accomplishment of the public internal audit plan within the NAMMD / NAMMDR for 2019 was fully achieved.

The findings following internal public audit missions carried out according to the Annual Public Internal Audit Plan established for 2019 are recorded in the audit reports prepared for each mission and are signed by the auditors participating in the mission, representatives of the audited structure and NAMMD / NAMMDR management.

According to the provisions of Government Decision no. 1086/2013, the Internal Audit Bureau within the NAMMD / NAMMDR developed the Quality Assurance and Improvement Programme (PAIC), regarding all aspects related to internal audit, thus allowing a continuous control of its effectiveness.

The programme for ensuring and improving the quality of the internal audit activity allows the evaluation of:

- Compliance with the legal basis in force;

- The contribution of internal audit to processes of governance, risk management and control of the organisation;

- The degree of coverage of the auditable sphere;

- The level of compliance with the laws, regulations and procedures that the internal audit activity must comply with;

- The risks affecting the operation of the internal audit.

Thus, the Programme for Ensurance and Improvement of the Quality of the Internal Audit Activity helps to express conclusions regarding the quality of the internal audit activity and leads to recommendations for implementation of appropriate improvements of this activity. Currently, this program is fully operational and ensures permanent monitoring of the internal audit activity as well as its regular self-assessment in order to ensure compliance with the applicable legal and procedural framework.

Regarding the external evaluation in 2019, the Internal Audit Office within the NAMMD / NAMMDR, was neither evaluated by the hierarchically superior body - the Ministry of Health, nor by the Romanian Court of Accounts.

At the end of 2018 and the beginning of 2019, the Internal Audit Office, together with NAMMD structures, was evaluated by the Prime Minister's control body, an evaluation completed with a specific report.

The contribution of the Internal Audit Office to the addition of value to the NAMMD / NAMMDR was achieved by:

- Internal public audit missions and recommendations made to the audited structures.

- Participation in the risk management process that was achieved by identifying and tracking risks in order to minimise / eliminate them.

- Informal counselling of the structures from the NAMMD / NAMMDR Organisation Chart.

- Improvement of internal control quality- carried out every six months through counseling and evaluation, in accordance with the provisions of OSGG annexes no. 600/2018.

- Improving the activity of the audited structures, materialised through recommendations of internal auditors systematised on the main audited fields.

- Evaluation activities of the managerial internal control system and analysis of the risks associated with auditable activities, as well as through recommendations contained in public internal audit reports prepared and transmitted in order to ensure the achievement of the objectives of the audited structures.

- Monitoring and application of the specific legislation applicable in force.

- Monitoring and achieving the performance indicators established at BAI level.

- Carrying out the activities included in the Work Program for 2019.

- Execution of the Activity Plan for 2019.

- Monitoring the implementation of the measures proposed through Public Internal Audit Reports.

- Auditing all NAMMD / NAMMDR activities and structures every three years.

18. Activity of the Prevention and Protection Service in the field of occupational safety and health (SPPSSM)

In 2019, the SPPSSM carried out the following types of activities:

- Identification of hazards and risk assessment materialised by elaboration of:

• Training topics in the field of occupational safety and health;

• Planning regular occupational safety and health training;

• Its own instructions on training SSM employees;

• Occupational risk exposure sheets;

• Materials on regular training for staff in laboratories and nuclear units, respectively for staff with office activities;

-Additional and introductory training – general training;

- Verification of periodic trainings;

- Managing the archive containing individual files on occupational safety and health, in electronic and letter format, of the temporarily or definitively inactive persons, or their renewals;

- Testing the knowledge of the employees regarding the prevention and protection measures incumbent on them in the field of occupational safety and health;

- Periodic SSM training within the service;

- Periodic PSI training within the service;

- Ensuring first aid services whenever requested.

With regard to staff training, in order to meet the requirements of job descriptions, the SPPSSM carried out:

- Training in the field of emergencies - aimed at preventing and extinguishing fires as well as civil protection;

- Training in the field of occupational safety and health - with the aim of preventing occupational risks, protection of staff health and safety, eliminating risk factors and injury;

- Work-related training - knowledge and compliance with regulatory requirements specific to the field (laws, decisions, PSO in force, etc.).

- The incomplete nature or the presence of errors in the documentation submitted in the national procedure or in the replies received to the requests made by NAMMD / NAMMDR assessors (for approximately 70% of the medicinal products proposed for authorisation, renewal).

III. Priorities envisaged for 2020

All NAMMDR structures have self-assessed their activity in 2019 and have formulated proposals and priorities for the next period.

Fulfilment of the current mission of the NAMMDR, the national competent authority for medicinal products for human use, medical devices and medical technology assessment, is confirmed as the institution's primary goal.

Thus, the proposals made for streamlining the activity, by different NAMMDR structures, are identified in several priorities for 2020, among which can be listed:

- Supplementation of the staff of the structures with specialised staff in order to fulfil the proposed objectives;

- Participation of staff in professional development courses specific to the activities they perform, even if online;

- Allocating the necessary funds for endowment / purchase of equipment specific to the structures of the institution;

- Modernisation and development of the endowment of medical device testing laboratories in order to keep up with the medical-hospital technique in continuous development;

- Allocating the necessary funds and carrying out the steps for setup of a functional computer system, similar to a database, with adequate capacity, able to keep all information reported monthly on the distribution of medicinal products and to allow the interrogation according to the established criteria;

- Development of a computer application with adequate capacity and multiple facilities for querying data on medicinal products manufactured, imported, wholesale distributed, according to daily reports from the Electronic Reporting System (SER) (in collaboration with the Ministry of Health and the Special Telecommunications Service (STS);

- Continuing investments in laboratory equipment to supplement the necessary equipment, aiming to better cover medicinal products on the Romanian market by post-marketing testing and by increasing involvement in European testing projects;

- Setup of an electronic platform for those interested in registering / notifying their medical devices and document download;

- Endowment with equipment for measuring and monitoring medical devices, in line with the technological progress in the field;

- Strengthening pharmacovigilance and pharmaceutical inspections;

- Improving the evaluation activity of medical technologies through the contribution brought to the amendment and completion of the legal evaluation criteria.