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Activity report

of the National Agency for Medicines and Medical Devices of Romania (NAMMDR)

- 2020 -

SUMMARY

I. Overview of the activity performed in 2020

Year 2020 was special, given the fact that the COVID-19 pandemic brought previously unknown challenges upon healthcare systems. The NAMMDR, in terms of its activity and responsibilities, as a key institution from the Romanian healthcare system, reacted promptly and constantly adapted to contextual requests. In spite of undersized staff and teleworking activities, the NAMMDR, through its experts, was permanently connected to the activities and decisions of the European Medicines Agency, which was the main actor in the process of centralised approval of COVID-19 vaccines, and was involved in the consultation and collaboration process at the level of the Romanian Government, with the National Coordinating Committee for Vaccination Activities and other state authorities for preparation and conduct of the COVID-19 vaccination campaign, regarding the reception, storage, transportation, monitoring and reporting of vaccines' adverse reactions.

The Agency showed transparency in its decisions and has managed to promptly respond to all requests from all its partners (industry, scientific and academic community, media, patient associations).

The global health crisis we are facing has required the performance of certain specific activities. During this period, the NAMMDR has given priority to the assessment of clinical trials for medical devices and medicinal products indicated in the treatment and prevention of infection with the new Coronavirus.

The General Directorate for Pharmaceutical Inspection (DGIF), strategic directorate within the NAMMDR, was faced with both suspension of certain activities (GMP inspections) and with the introduction of new activities in its portfolio, such as the analysis

of requests and the management of restrictions on the export and intra-community supply of medicinal products vital for the treatment of patients.

Starting with March 2020, through NAMMDR President Decision no. 332/16.03.2020, the inspection and control activity performed by the DGIF was suspended during the state of emergency.

Based on the document "Notice to stakeholders - questions and answers on regulatory expectations for medicinal products for human use during the COVID-19 pandemic", developed on 10.04.2020 by the European Commission, HMA and the EMA, the validity of GMP and BPD certificates for manufacturing sites/import and distribution of active substances and/or finished products from the EEA has been extended until the end of 2021, without the need for further action taken by the certificate holder, this being a decision taken at European level.

The experts of the Pharmacovigilance and Risk Management Directorate (DFVMR) have also played an extremely important role in management (monitoring and transmission) at national level of undesirable post-vaccination adverse reactions (RAPI), directly received by the NAMMDR, in line with the protocol in force. The DFVMR proposed the approval of Order of the Ministry of Health No. 2171 / 21.12.2020 for approval of the Reporting Sheets of Adverse Reactions in the context of the COVID-19 vaccination campaign, participated in the elaboration of the COVID-19 Vaccination Strategy in Romania through a representative within the Working Group for the COVID-19 vaccination strategy. Together with the Agency's STIC experts from the Information and Communication Technology Service (STIC), the DFVMR has developed an electronic system for reporting post-vaccination adverse reactions to COVID-19 vaccines, which is available to vaccinators and healthcare professionals, as well as reporting sheets that can be used for reporting post-vaccination adverse reactions associated with COVID-19.

In 2020, experts from the European Procedures Directorate and members of the EMA working groups participated in the extraordinary meetings of the European Medicines Agency committees where decisions on authorisation of medicinal products for treatment and prevention of COVID-19 were taken. Together with experts from the Medicines Quality

Control Directorate, they participated as Rapporteurs/Co-Rapporteurs in the evaluation of authorisation documents through centralised procedure.

The work carried out within the European Procedures Directorate has increased as a result of Brexit-related activities: marketing authorisation transfers, increasing the number of variations with Romania as Reference Member State by taking over decentralised and mutual recognition procedures from Great Britain, increasing the number of procedures for renewing marketing authorisations of medicines taken by Romania as a Reference Member State.

As regards the activities specific to the epidemiological context of another strategic direction of the NAMMDR, the General Directorate for Medical Devices, they have undergone several changes. Priority was given to actions such as: derogations, registration of medical devices of interest in combating the COVID-19 virus (masks, coveralls, gowns, rapid COVID-19 antibody tests, rapid COVID-19 antigen tests, approach to emergency donations, etc.).

In 2020, the number of requests has increased greatly, taking into account the great need for medical devices: oxygen concentrators, pulse oximeters, surgical masks, coveralls, gowns, rapid tests to determine the presence of the COVID-19 virus, etc.

The experts of the Approval Department participated in joint commissions composed of staff of the Public Health Directorate, the ISCIR, at the thematic controls in ATI sections (including those for COVID-19 patients), from healthcare units in Bucharest.

Also, at Agency level, the rapid posting of important notifications and press releases related to updates on specific pandemic activity, in order to better inform professionals and the general public, has been a priority.

II. ACTIVITIES PERFORMED BY THE NAMMD/NAMMDR IN 2020

1. Activity of the Scientific Council (SC)

In 2020, no meeting of the NAMMDR scientific council took place. Upon entry into force of Law no. 134/2019, the NAMMDR scientific council could not meet since 2019, because its composition could not be approved by minister order, due to the fact that, in Law no. 134/2019 there is a legislative inaccuracy, namely there are structures/organisations specified that should have nominated members for participation in the scientific council, and these structures/organisations do not actually exist. Thus, the amendment of Article 11 (1) is urgently needed, as the NAMMDR scientific council cannot be legally constituted as a result of the introduction into Law 134/2019 of unidentifiable entities, such as the Association of Deans of Romanian Faculties of Pharmacy, and it is necessary to return to its previous form, as regulated through Government Decision no. 734/2010. The NAMMDR submitted to the Ministry of Health the Draft Government Emergency Ordinance for amendment and supplementation of Law no. 134/2019 on the reorganisation of the National Agency for Medicines and Medical Devices of Romania.

2. Activity of the Administration Council (AC)

In 2020, there were 5 meetings of the Administration Council of the NAMMDR, focused mainly on establishing appropriate administrative measures in order to apply the provisions of Law no. 134/2019.

3. Activity of NAMMDR commissions

3.1. NAMMDR Marketing authorisation commission

In 2020, 18 meetings were organised, during which a number of 633 applications for authorisation/renewal were discussed:

- 75 applications for marketing authorisation/marketing authorisation renewal through national procedure;
- 558 applications for marketing authorisation/marketing authorisation renewal through European procedures.

Following the positive opinion of the Marketing Authorisation Commission, the grant of marketing authorisations (MAs) was approved, according to the tables and graphs in the next chapter.

743 marketing authorisations (Mas) were issued (with requests made last year as well), of which 250 were related to the national procedure and 493 to the European procedures, as follows:

• For the national procedure, the grant of 48 marketing authorisations and of 202 marketing authorisation renewals,

• For European procedures, 186 authorisations through enforcement of the decentralised procedure and of the mutual recognition procedure, 39 authorisations through enforcement of the repeat-use mutual recognition procedure and 268 marketing authorisation renewals.

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

In 2020, the Commission was summoned twice.

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

In 2020, 80 authorisations were granted for medicinal products for special needs.

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

In 2020, the Commission carried out its activity in 50 meetings, the commission's activity ending with issuance of 12 new authorisations, 5 renewals to existing authorisations and 28 amendments to the terms of authorisations/authorisation renewals for valid authorisations.

4. Marketing authorisation and related activities

In 2020, the main activities of the Agency, mainly the assessment of the documentation submitted to the NAMMDR 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 European Procedures Directorate and the National Procedure Directorate with the involvement of experts for biological medicinal products within the Medicinal Product Quality Control Directorate, materialised into issuance of 743 MAs for medicinal products for human use, of which 493 (66.35%) were granted by applying the provisions of European procedures (182 DCP, 4 MRP, 39 through MRP - Repeat Use and 268 renewals of MAs), while 250 (33.65%) of the issued authorisations concerned applications for authorisation through national procedure (48 new MAs and 202 MA renewals).

Authorisations and renewal of authorisations (R) through European procedures

2020	DCP	MRP	Reînnoire	Repeat use
ianuarie	8	0	7	1
februarie	28	0	39	4
martie	12	0	16	1
aprilie	28	1	20	5
mai	29	0	24	8
iunie	15	0	13	1
iulie	12	0	28	0
august	4	1	24	5
septembrie	13	1	38	9
octombrie	0	0	10	0
noiembrie	15	0	14	2
decembrie	18	1	35	3
TOTAL	**182**	**4**	**268**	**39**

Total: 493

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

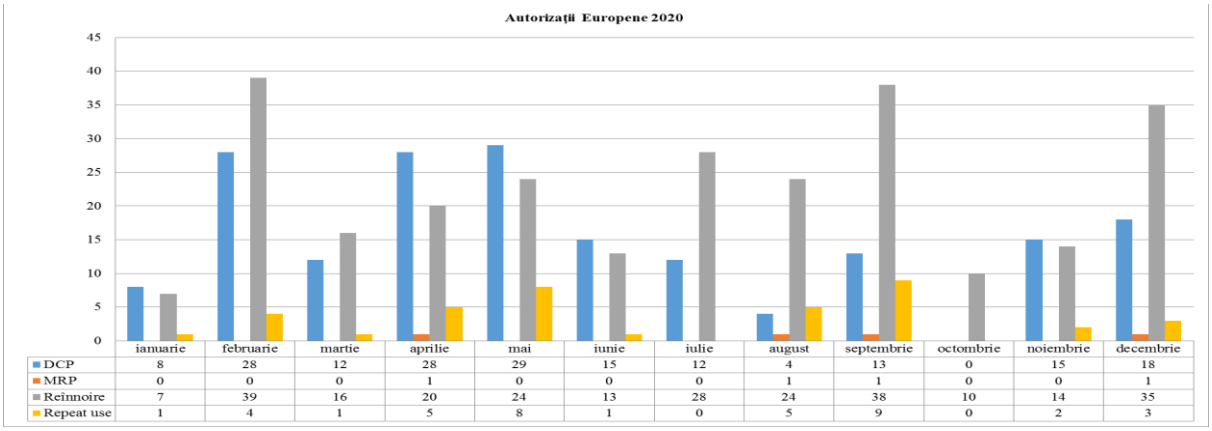
separately with the involvement of Romania as a concerned Member State or as a reference Member State.

Thus:

- Authorisations/Renewals granted in procedures with the involvement of Romania as a concerned Member State (RO SMI):
  - Authorisation through decentralised procedure (DCP): 308
  - Authorisation through mutual recognition procedure (MRP): 19
  - Authorisation through repeat-use mutual recognition procedure (MRP-RU (E)): 63
  - MA renewal (R): 244
- Authorizations/Renewals granted in procedures in which Romania has acted as a Reference Member State (RO SMR):
  - Authorisation through decentralised procedure: 1
  - MA renewal (R): 8

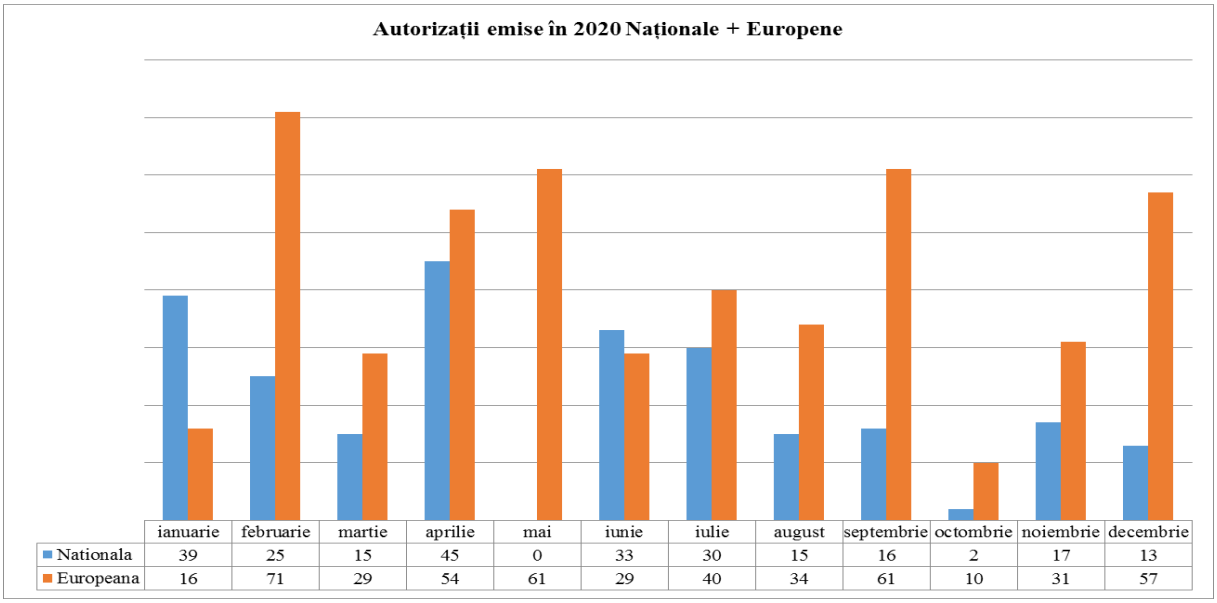
European authorisations (2020):

- DCP – Decentralised procedure
- MRP – Mutual Recognition Procedure
- Reinnoire – Renewal
- Repeat Use



	ianuarie	februarie	martie	aprilie	mai	iunie	iulie	august	septembrie	octombrie	noiembrie	decembrie
DCP	8	28	12	28	29	15	12	4	13	0	15	18
MRP	0	0	0	1	0	0	0	1	1	0	0	1
Reinnoire	7	39	16	20	24	13	28	24	38	10	14	35
Repeat use	1	4	1	5	8	1	0	5	9	0	2	3

National + European authorisations (2020):



	ianuarie	februarie	martie	aprilie	mai	iunie	iulie	august	septembrie	octombrie	noiembrie	decembrie
Nationala	39	25	15	45	0	33	30	15	16	2	17	13
Europeana	16	71	29	54	61	29	40	34	61	10	31	57

DPE together with the DCCM and the DFVMR participated as rapporteur/co-rapporteur in the evaluation of 3 applications for marketing authorisation through centralised procedure and as Peer-Reviwer for an application for authorisation through centralised procedure.

DPE experts participated as rapporteur or Peer-Reviewer in 42 procedures related to Paediatric Investigation Plans within the activity of the Paediatric Committee and in 5 scientific counselling procedures for formulation of an opinion from the Paediatric Committee on paediatric questions.

Through the expert appointed in the EMA Committee for Orphan Medicinal Products, the NAMMDR participated in the evaluation of the status of orphan medicinal product - 9 Reports (of which 6 Preliminary Reports with requests for oral explanations from the sponsor, 2 Complementary Reports with positive final resolutions for medicinal product designation as “orphan”, 1 Completion report with negative final resolutions).

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

4.2.1. As regards the activity carried out during the post-authorisation period, undertaken in 2020, concerning the evaluation and approval of requests to MA terms through

national procedure, the achievements of the NAMMDR can be summarised by the evaluation and approval of 3723 applications, as follows:

- 3335 Type I variations;
- 121 Type II variations;
- 87 MA transfers;
- 180 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 the MPQCD; the following were assessed and approved in 2020:

- 91 Type I variations;
- 49 Type II variations.

4.2.2. In 2020, as regards post-authorisation assessment of variations to MA terms granted through European procedures, the NAMMDR approved 4628 letters for approval for MAs and the corresponding Annexes, as follows:

- 1973 Type IA variations;
- 1757 Type IB variations;
- 460 Type II variations;
- 87 MA transfers;
- 98 notifications in accordance with Article 61(3) of Directive 2001/83/EC;
- 128 national notifications in accordance with Order of the Minister of Health no. 1205/2006.

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

- 50 type IA variations with Romania as Reference Member State;
- 59 type IB variations with Romania as Reference Member State;
- No notification in accordance with Article 61(3) of Directive 2001/83/EC;
- 14 national notifications in accordance with Order of the Minister of Health no. 1205/2006.

As regards biological medicinal products, the assessment 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 medical technologies

In 2020, the Medical Technologies Evaluation Directorate evaluated 102 cases related to 2019 and 2020, of which 77 new INNs and INNs with extension of indication and 25 files per request for move/addition, namely: treatment line addition, population type, age range.

Of these:

- 6 medicinal products for HIV/AIDS
- 1 medicinal product for the hepatitis C virus
- Oncology - 38 medicinal products;
- Neurology – 3 medicinal products;
- 16 medicinal products with indication in rare diseases (cystic fibrosis, mucormycosis, Fabry disease).

In 2020, HG 720/2008 was updated twice, 70 INNs - 31 INNs and subsequently 39 INNs with effect from 01.01.2021 were introduced in the list of medicinal products approved by HG 720/2008. OMS 1301/2008 has been updated 4 times, being up to date with the update of HG 720/2008.

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

Thus, in 2020, the specialists of the Advertising Service carried out the following activities:

In the field of Advertising:

- Evaluation of advertising materials, followed by approval: 608
- Reapproval of advertising materials: 927
- Forms for rejection of advertising materials: 22
- Evaluation and approval of educational materials: 233

- Reapproval of educational materials: 200
- Forms for rejection of educational materials: 15
- Record of notifications regarding the participation of the MAH in medical events.

In the field of sponsorship, the NAMMDR updated the register resulting from the receipt of 6560 sponsorship forms from beneficiaries and 105 forms for declaring sponsorship activities performed by sponsors.

4.5. Management of the Index of medicinal products for human use Database

In 2020, the specialists from the Index Compartment provided:

4.5.1 Inclusion in the "Index" application of medicinal products authorised through national / European / centralised / special needs procedures:

- MA / MA renewal (authorized through national / European / special needs / centralised procedures, for those notifying the actual marketing in Romania) - Marketing Authorisation (MA) information is entered: trade name, MAH, responsible for batch release, packaging, etc. - 1602 medicinal products;
- correspondence with SEA in order to clarify / solve inconsistencies between MA and Annexes in case of new MAs - 415 medicinal products;

4.5.2 Maintenance of the database of medicinal products authorised for marketing: constantly updating the Index of medicinal products for human use by verifying and operating, based on the documentation received from the involved services, the resolved applications for authorisation/renewal of Marketing Authorisations, of variations/ amendments to MA terms, of cessation/expiration of MA variations/expiration/cessation, of medicinal products "with right of circulation".

- variations to MAs approved through all procedures: national / European / centralised (information on changes to the approved Marketing Authorisation: trade name, MAH, person responsible for batch release, packaging, etc. shall be entered) - 2750
- operation into the Index and Registry database of the MAs whose validity has ceased:
  - ✓ Expired MAs (for those MAs for which the applicant has not submitted the intention to initiate a renewal procedure) - 45 medicinal products;

✓ introduction of renewal positions in the Index (correlation with the Registry) - 594 medicinal products;

✓ MA termination decisions:

- cessation of the validity of a national MA when a MA is issued for the same medicinal product through a European procedure - 67 medicinal products;

- termination of the validity of a valid MA - 316 medicinal products;

- termination of the validity of an MA under SUNSET CLAUSE - 3 medicinal products;

- decisions for MA suspension - 1 medicinal product.

4.5.3. SUNSET CLAUSE enforcement

o Management of notifications for enforcement of provisions of Article 737, 738 of Law 95/2006 on healthcare reform - Title XVIII – "The medicinal product";

− assessment and management of information for compliance with the legal provisions in force regarding the "SUNSET CLAUSE" on marketing (involves MA withdrawal after 3 years if the medicinal product hasn't been marketed), drafting replies to requests for exemption from these provisions; drafting the addresses to the MAH informing on failure to meet the legal requirements and enforcement of the termination clause of the MA validity;

- notifications of temporary and permanent discontinuation of marketing - 270 medicinal products;

- notifications of resumption of marketing - 205 medicinal products;

- marketing notifications - 891 medicinal products;

- requests for exemption from the Sunset clause - 52 medicinal products;

- exemptions granted by e-mail - 35 medicinal products;

- notifications of withdrawal of MAs/MA renewal procedure - 432 medicinal products;

o permanent update of "Notifications on medicinal product discontinuations" on the NAMMDR website - 627 medicinal products;

o verification in the Index of medicinal products for human use of therapeutic alternatives (MAs) with the same INN, pharmaceutical form and strength as the medicinal products notified as temporarily or permanently discontinued by sending e-mails to all MAHs involved whenever information changes - 668 INNs (2375 medicinal products);

o providing information on the following situations: marketing, non-marketing, temporary discontinuation of marketing, permanent discontinuation of marketing, resumption of marketing to the NAMMDR Communication and Public Relations Service in order to respond to complaints received from patients/hospitals/pharmacies at lipsamedicament@anm.ro, including those redirected from http://medicamentelipsa.ms.ro/ - 265 replies sent by e-mail;

4.5.4. Monthly preparation of Annexes to the Ministry of Health in the context of the NAMMDR obligations established through Ordinance no. 8/2018 - 12 addresses + 48 Annexes.

4.5.5 Setup and technical drafting of decisions for discontinuation / suspension or lifting of suspension of MAs - 252 decisions (387 medicinal products) accompanied by 3 Annexes each (CNAS + MS + MAH / applicant).

4.5.6. Miscellanea:

o Setup of different situations based on the data contained in the NAMMDR index of medicinal products for human use:

- information processing and setup of various situations required by specialised commissions/ departments of the Ministry of Health, CNAS, the NAMMDR, others (situation of medicinal products with parallel important authorisation (API)/partial-total manufacturing/China or India; situation "Primer"/manufacturers – medicinal products manufactured in Romania; evaluation of the questions of the Competition Council, situation regarding the settlement of the applications for parallel import authorisation (PIA) required by the Government Control Body, “Brexit” situations - batch release / MAH Great Britain for DPN and DPE - 8, situations for DJRI in order to respond to some Prosecutor's Offices/Tribunals/Directorate for Investigating Organized Crime and Terrorism/ People's Advocate; other addresses and situations for NAMMDR departments;
- processing the information received from the Ministry of Health and the CNAS to ensure technical support in view of completing the Annexes to the periodic update draft or amendment of the List of International Non-proprietary Names of on-prescription medicinal products as provided to insurants, irrespective of personal contribution, in the frame of the health insurance system, as well as of International Non-proprietary Names of medicinal

products provided in national health insurance programs; permanently for the Ministry of Health and quarterly for the CNAS;

- verification on a monthly basis or whenever necessary of medicinal products recently included into the national price catalogue for medicinal products authorised for marketing in Romania (CaNaMed) –12 situations;
- evaluation and issuance of addresses regarding the status of medicinal products in CaNaMed, in accordance with Law 95/2006 and Order of the Minister of Health no. 368/2017 on approval of the Norms on the calculation method and the procedure for approving the maximum prices of medicinal products for human use - 234 addresses;
- establishing, upon request of the Ministry of Health, the classification of medicinal products from CaNaMed for enforcement of provisions of Law no. 53/2020 supplementing Government Emergency Ordinance no. 77/2011 regarding the establishment of some contributions for financing some expenses in the field of health - 8 situations;
- participation in the management of decisions of the European Commission and the Coordination Group on referrals – 1.

o Formulation of replies to the requests of the Ministry of Health and other public authorities and institutions, petitions, as well as to requests for information of public interest, directly or through the authorised organisational structure: 84 replies to the Ministry of Health, 48 to CNAS and 57 internal addresses.

o As regards the Index, the following activities related to intra-community trade were performed:

- parallel export (activity carried out between January and May 2020): receipt of requests in English from EU competent authorities (European agencies) - 139 addresses, setup and transmission of parallel export sheets (in English) by e-mail to competent EU authorities with individualised information on: MA number of the medicinal product in Romania, trade name of the medicinal product, Marketing Authorisation Holder (MAH), manufacturers involved in the entire manufacturing process, details related to the qualitative and quantitative composition of the medicinal product, pharmaceutical form, route of administration, ATC code, packaging, shelf life and storage conditions - 160 export sheets, transmission of parallel export sheets by e-mail to the EU Agencies involved - 160 export

sheets, clarifications following submission of export sheets/clarifications regarding the updating of the data from PRO, RCP and AMB on the NAMMDR website (e-mail) - 30 addresses, registration in an xls record of requested medicinal products: country where medicinal products are exported, contact, date of issue/date of dispatch of the export sheet, information for identification of the medicinal product -160 export sheets;

- parallel import (activity carried out between March and May 2020): assessment and administrative validation of applications for parallel import authorisation (PIAs) - 2 addresses, requests for completion of the authorisation documentation for issuance of PIAs to involved EU Agencies from exporting countries - 2 e-mails, issuance of parallel import authorisations - 2 PIAs, assessment and validation of requests for variations to PIA terms - 18 addresses (18 medicinal products), requests for completion of the authorisation documentation in view of issuance of variations to PIAs to involved EU Agencies in the exporting countries (7 medicinal products); setup and technical editing of PIA variations for 10 medicinal products, setup and technical editing of changes to PIA terms - 2 addresses.
  - In 2020, with the help of colleagues from the STIC, the Index of medicinal products for human use authorised for parallel import was set up, which included those PIAs (parallel import authorisations) for which the MAH requests CIM codes, in the form of an xls table and available on the NAMMDR website.

5. Assessment and authorisation of clinical trials and medical units

As regards the assessment and approval of clinical trials/clinical investigations/bioequivalence studies, the following were registered in 2020:

		Interventional clinical trials
Applications	submitted	159
	Recalled prior to assessment	11
	Recalled after assessment	2
	Granted	113 (also referring to applications submitted in 2019)

	and issued	
	rejected	2

As regards the assessment and approval of amendments to clinical trials with medicinal products for human use, the following were registered in 2020:

Number of applications for assessment and approval of important amendments	788
Withdrawn applications	1
Approved amendments	587
Rejected amendments	14

The authorisation of medical units for conduct of clinical trials focused on 206 applications for authorisation and resulted in issuance of 168 such authorisations.

In the context of the Voluntary Harmonization Procedure (VHP) project carried out at the level of Clinical Trial Facilitation Group (subgroup of the HMA), Romania participated in 27 VHP procedures for assessment of initial clinical trials and in 126 VHP procedures for assessment of substantial amendments (4 as a Reference Member State).

6. Inspection activity for supervision and quality control of medicinal products for human use in the process of manufacture, import, wholesale /retail distribution and related activities

In 2020, the General Directorate for Pharmaceutical Inspection (DGIF) continued to carry out the activities provided for by the specific legislation (Law 95/2006, republished - Title XVIII – The medicinal product, as further amended and supplemented and its secondary legislation), in accordance with the directorate's standard operating procedures, making efforts to solve specific tasks within the time limits provided by law.

The COVID-19 pandemic affected the activity of the directorate, on one hand by suspending activities (GMP inspections) and on the other hand by introducing new activities

in the DGIF portfolio (restrictions on export and intra-community supply of essential medicinal products for the treatment of patients).

The specific DGIF processes that were carried out during 2020 included: supervision of medicinal products for human use in the process of manufacturing, import, wholesale distribution through periodic inspections and planned control activities; supervisory inspections of pharmacy activity; control of clinical trials conducted for medicinal products for human use, in accordance with the guideline on Good Clinical Practice in clinical trials and the legal provisions in force in the field; issuing the certificate of Good Laboratory Practice for units that are involved in conducting non-clinical studies, respectively clinical bioequivalence studies provided by the legislation for authorisation of medicinal products for human use; control of pharmacovigilance activity; verifying the observance of the obligations incumbent on the MAH for medicinal products for human use, according to the legal provisions; quality control of medicinal products for human use in the process of manufacture, import, wholesale and retail distribution, through periodic inspections and planned control activities, as well as in all situations where there are complaints and/or alerts on their quality and effect; prevention of entry into the legal supply chain of falsified medicinal products, in accordance with the legal provisions; international collaboration for warning in case of medicinal products with major quality noncompliances; ensuring correctness of the information displayed on the NAMMDR website, regarding: manufacturers (from Romania and from third countries), authorised importers and test units, authorised wholesale distribution units, qualified persons, medicinal product recalls, authorised control laboratories and those with GLP certification, DGIF forms; ensuring the issuance and administration of manufacturing/import authorisations, GMP certificates, wholesale distribution authorisations, GDP certificates, GLP certificates, authorisations for independent control units, certificates attesting the qualified person status for batch release; ensuring transparency regarding information on the updated status of good practice compliance of manufacturing units (including import, testing)/wholesale distribution; endorsement of export declarations, following assessment of submitted documents, in accordance with the legislation in force; issuance of the certificate attesting the qualified person status to applicants who meet the conditions provided by the legislation; ascertaining

and sanctioning cases of violation of legal provisions in the field of activity of the DGIF; ensuring the provision of answers to the requests of the Ministry of Health regarding the performance of inspections and activities in its field of competence; ensuring the existence of the necessary regulatory acts; approval of donations of medicinal products for human use; issuing the agreement on the provision of free samples of medicinal products.

a) The Directorate for Administration of DGIF Processes

The following activities were carried out in 2020:

- verification of the documents submitted by applicants for performance of GMP, bioequivalence, BPLA inspections, verification of the Standard Master File (DSU), verification of the documentation submitted in order to update the Annexes to manufacturing/import authorisations - 141;

- inspections:
  - ✓ good manufacturing practice (GMP) inspections at Romanian manufacturers of medicinal products for human use: 4
  - ✓ good practice inspections for import of medicinal product for human use: 4
  - ✓ inspections of good wholesale distribution practice (GDP): 61
  - ✓ inspections for supervision of the quality of medicinal products in the distribution network (community pharmacies, hospital pharmacies, local offices, medicinal product stores): 890
- preparation and issuance of certificates/authorisations: 9 GMP certificates; 88 manufacturing authorisations, 4 import authorisations, 7 amendments/updates of the annexes of import authorisations;
- update of the EudraGMDP database;
- creation and management of the file of each inspected unit, namely of each unit which requested updates of the Annexes to the Manufacturing/Import Authorisations and GMP certificates: 86;

- administration of databases regarding the coding of inspections, the list of authorised/ certified manufacturing units, authorised importers, qualified persons;

- calculation of inspection fees and of fees for updating the annexes to manufacturing authorisations for manufacturers and importers of medicinal products and monitoring their payment;

- verification of the documentation submitted by applicants in order to issue a certificate attesting the qualified person status, correspondence with applicants for completing the documentation, drafting the documents for charging the service and supervision of payment of these fees: 52;

- preparation and issuance of qualified person certificates: 25;

- issuance of the agreement for registration as manufacturers/importers/distributors of active substances to be used as raw materials for medicinal products for human use: 1.

b) The Directorate for Good Manufacturing Practice Inspection, Laboratory, Analytical Laboratory, Clinical Trial and Pharmacovigilance (DIBPFLLASCFV)

Starting with March 2020, with the establishment of the state of emergency on Romanian territory due to the COVID-19 pandemic, by Decision 332/16.03.2020 of the NAMMDR president, the DGIF inspection and control activity was suspended during the state of emergency.

As a decision at European level, based on the document *"Notice to stakeholders questions and answers on regulatory expectations for medicinal products for human use during the COVID-19 pandemic"* prepared on 10.04.2020 by the European Commission, HMA and EMA, the validity of GMP and GDP certificates for manufacturing/import and distribution sites of active substances and/or finished products in the EEA was extended until the end of 2021, without need for further action by the certificate holder.

In the context of the COVID-19 pandemic, legal regulations were amended/issued, minister orders facilitating activities such as export to third countries and medicinal product donations, which led to the introduction of new activities in the DGIF portfolio (restrictions on intra-community exports and deliveries of medicinal products considered vital for the treatment of patients).

Thus, the following activities were carried out:

− GMP inspections for issuance of the Manufacturing Authorisation/GMP certificate including for raw materials -pharmaceutically active substances: 4;

- authorisation inspections at the sites of medicinal product importers: 4;

- evaluation of requests for supply of samples for authorised medicinal products: 18;

- issuing addresses with requests to complete documentation: 9;

- issuance of an agreement on provision of free medical samples: 18;

- evaluation of the reports on the situation of the samples distributed to healthcare professionals, sent by the MAH following the ending of the validity of supply agreements;

- evaluation of the documentation submitted in support of the application for approval of donations of medicinal products for human use, drafting of donation notices and related annexes: 105;

- Rejection of the request for a donation notice for noncompliance with Order of the Minister of Health no. 1032/2011 on donations of medicinal products, medical supplies, medical devices, vaccines, serums and related consumables: 1;

- issuance of NAMMDR approval notices, in accordance with Article 20 of Emergency Government Ordinance no. 70/2020 on the regulation of measures, starting with 15 May 2020, in the context of the epidemiological situation caused by the spread of the SARS-CoV-2 coronavirus, to extend deadlines, for amendment and supplementation of Law no. 227/2015 on the Fiscal Code, of the National Education Law no. 1/2011, as well as of other regulatory acts: 4;

- verification of the documentation for approval of export declarations to third countries and approval of export declarations: 5808;

- rejection of approval of export declarations, due to the lack of the wholesale export distribution authorisation of the distributor requesting the approval and to the lack of documents required in order to approve the declarations in line with Order of the Minister of Health no. 894/2006 and no. 1809/2006: 12;

- the rejection of the approval of export declarations and entrance into force of Military Ordinances, Order of the Minister of Health no. 428/2020 and Order of the Minister of Health no. 672/2020 suspending the distribution outside Romania of medicinal products included in the CANAMED (Order of the Minister of Health no. 428/2020), and of medicinal products covered by the Protocol for treatment of the SARS-Cov-2 virus infection, approved by Order of the Minister of Health no. 487/2020, and of medicinal products at increased risk of

discontinuation for chronic pathologies in the context of the SARS-Cov-2 virus pandemic, in line with Order of the Minister of Health no. 672/2020 (due to declaration of the COVID-19 pandemic): 132.

c) The Rapid Alerts and Falsified Medicinal Products Service (SARMF)

The following activities were performed in 2020:

- management of rapid alerts received through the European rapid alert system whose subject was counterfeit/suspected of counterfeit medicinal products known to circulate on the Romanian market: 125. Of these, 4 concerned authorised products and batches distributed in Romania, whose recall had been initiated, 119 targeted products unauthorised for marketing in Romania, 2 targeted clinical investigation products administered in clinical trials unauthorised by the NAMMDR;

- management of rapid alerts received through the European rapid alert system whose subject was counterfeit/suspected of counterfeit medicinal products not known to circulate on the Romanian market, who targeted products authorised for marketing in Romania but not marketed in Romania or batches undistributed in Romania: 15;

- 1 rapid alert issued by the Ukrainian authority on 02.2020;

- 1 declaration of noncompliance with GDP rules, generated by the EudraGMP system does not correspond to any report of noncompliance with GDP rules;

- management of alerts generated in the National Medicines Verification System (SNVM) notified by the Romanian Organisation for Serialisation of Medicines (OSMR), by verifying the traceability of medicinal product batches in the reports made by distributors, communication with MAHs and end users involved, for investigation of suspicions of counterfeit and confirmation/refutation of counterfeiting: the OSMR transmitted to DGIF the statistical results of the automatic processing of alerts generated in the SNVM. Following the statistical analysis of the alerts generated in the SNVM, no medicinal products with suspected falsification was reported (0);

- managing the notifications received on the e-mail address contrafacere@anm.ro;

- investigation of suspected counterfeiting on Romanian territory, under investigation: 3;

– the transmission to the DJRI and subsequently to the General Inspectorate of the Capital Police of the information regarding the result of the investigations carried out on some products suspected of being counterfeit: 1;

– registration of information issued by the Working Group of Enforcement Officers regarding thefts and falsifications of certain medicinal products: 2;

– registration of non-urgent information from EU member states on thefts and falsification of certain medicinal products: 6;

- registration of an information from the Israeli Embassy regarding the distribution in South America of a counterfeit vaccine called “Migal COVID-19 vaccine”.

In 2020, no rapid alerts were issued by the NAMMDR; the OSMR notified the NAMMDR about 1 alert generated in the SNVM for which the suspicion of counterfeit is still being investigated.

About 1 million e-mails were received in 2020 on the e-mail address where level 5 alerts generated in the SNVM are sent.

d) The Good Distribution Practice Inspection Service (SIBPD)

Starting with March 2020, due to declaration of the COVID-19 pandemic, certain Military Ordinances and regulations came into force, which have temporarily suspended the distribution (intra-community deliveries) of certain medicinal products outside Romania.

Thus, the following activities were carried out:

- issuance of addresses with requests for supplementation of the submitted documentation: 29;
- issuance of tariff addresses to the DEAP: 105 (34 from 2019 and 71 in 2020);
- carrying out GDP authorisation inspections: 61 (44 in 2019 and 17 in 2020);
- drawing up lists of deficiencies: 53 (33 in 2019 and 20 in 2020),
- issuing addresses with requests for additions to the plan of corrective/preventive measures: 3;
- preparation of final BPD inspection reports: 61 (of which 0 negative);
- issuance of Wholesale Distribution Authorisations: 126;
- issuance of Certificates of compliance with Good Distribution Practice (GDP): 61;

- introduction in EudraGMDP and in the internal database (Microsoft Access) of the issued GDP authorisations and Certificates;

- assessment of applications for update/amendment of wholesale distribution authorisations (annexed amendments): 166 (40 from 2019 and 126 from 2020);

- issuance of updated authorisations/annexes: 87;

- application of contravention sanctions for wholesale distributors, following non-compliance with the provisions of the GDP guideline on purchase and transport of medicinal products, noncompliance with the public service obligation, improper implementation of the Quality Management System created, noncompliance with prices approved through Order of the Minister of Health: 3;

- 60 complaints received from pharmacies and hospitals on lipsamedicament@anm.ro, for which electronic correspondence was carried out with wholesale distributors / MAH representatives / pharmacies, were investigated.

- checking the stocks of medicinal products and processing the information from daily reports (SER), in order to formulate the replies to the interested institutions and to the complaints received on the email address lipsamedicament@anm.ro and on the website of the Ministry of Health (www.medicamentelipsa.ro) and communication of the information to the SACR in order to draft the replies to the complainant: on a daily basis;

- processing (recording, centralisation) of information from monthly reports submitted by wholesale distributors/manufacturers/importers in accordance with Order of the Minister of Health no. 502/2013 and Order of the Minister of Health no. 1295/2015: 2820;

- processing (registration, centralisation, verification, posting on the NAMMDR website) of reports on imported medicinal products in line with Order of the Minister of Health no. 1295/2015: 81;

- processing (registration, centralisation, verification, posting on the NAMMDR website) of intra-community delivery notifications sent to the NAMMDR by wholesale distributors in line with Order of the Minister of Health no. 269/2017: 5813;

- Rejection of notifications of intra-community supply of medicinal products covered by the Protocol for the treatment of the SARS-Cov-2 virus infection, approved

through Order of the Minister of Health no. 487/2020, and of medicinal products at high risk of discontinuation for chronic pathologies in the context of the SARS-Cov-2 pandemic, as provided in the annex to Order of the Minister of Health no. 672/2020: 58;

- resolution of the appeals concerning the rejection of notifications of intra-community supply of medicinal products covered by the Protocol for the treatment of the SARS-Cov-2 infection: 5;
- collaboration with the National Vaccination Coordination Committee and other state authorities for preparation of the COVID-19 vaccination campaign, regarding the reception, storage and transport of vaccines;
- authorisation of the "**Cantacuzino**" **National Institute for Medical-Military Research and Development** for possession (storage/handling/custody) and supply of medicinal products for human use, medicinal products having a marketing authorisation in the Member States of the European Economic Area, immunological medicinal products and products distributed through the "cold" supply chain.

e) The Directorate for Quality Supervision of Medicinal Products and Territorial Units (DSCMUT)

The following activities took place in 2020:

- elaboration of the Yearly Sampling and Testing Plan on monitoring of medicinal product quality, containing 50 products proposed, based on the selection criteria, to be taken in 2020;
- sampling and transmission to the DCCM for laboratory analysis: 39; all 39 samples taken are currently being tested;
- sampling, in addition to the initial sampling plan, for laboratory analysis, in order to address medicinal product quality complaints, received from healthcare professionals or patients or at the request of the DCCM: 4; of these, 2 were compliant in terms of quality and 2 are currently being tested.
- the sampling of medicinal products within the programme coordinated by the EMA/EDQM for the supervision of centrally authorised products, which are tested by laboratories (OMCL) of other EU competent authorities; sampling is done from distribution units and is sent by parcel service to the EDQM headquarters in Strasbourg, France: 2;

– sampling of imported medicinal products for supply in case of special needs and transmission to the DCCM for laboratory analysis: 2 injectable biological products (of which 1 compliant and 1 noncompliant);

– carrying out (thematic) inspections to monitor the quality of medicinal products in the distribution network (warehouses, community pharmacies, hospital pharmacies, local offices, medicinal product stores), in which storage conditions, quality documents, advertising of medicinal products, compliance of the primary, secondary and package leaflet with the MA, verification of the manner in which withdrawals of medicinal products with quality deficiencies were carried out: 890.

– enforcement of contravention sanctions for retail distributors, following non-compliance with provisions of the Pharmacy Law no. 266/2008: 11;

– requesting inspected units to send the evidence regarding the remediation of discovered deficiencies;

– collaboration with other state authorities, in order to solve some issues related to the legislation in the medicinal product field and/or the quality of some products marketed in Romania, controls at the sites of commercial companies, carried out, in joint actions, upon request of the General Inspectorate of the Romanian Police, by UTI inspectors;

– resolving complaints about potential non-compliances in the quality of medicinal products for human use received from patients or healthcare professionals: 2

– recall from the market of medicinal products with non-compliances of quality: 27, of which:

- ordered for withdrawal and destruction by the NAMMDR: 9
- voluntary recalls of manufacturers / MAHs: 13;
- recalls following initiation of the EU emergency procedure discussed in the Pharmacovigilance Risk Assessment Committee (PRAC) for medicinal products containing ranitidine due to identification of nitrosamine impurities: 5;

– Coordination of the activity of Territorial Inspection Units (UTI) related to medicinal product quality surveillance by quarterly reporting the activity represented by:

- carrying out inspections to monitor medicinal product quality and the activity in retail distribution units;

- transmission to NAMMDR headquarters and resolution of punctual notifications regarding the medicinal product quality and the activity in pharmacies;

- performance and submission to the NAMMDR of results from the thematic plans established by the general director of the DGIF;

- performance of sampling proposed in the yearly sampling and testing plan and submission to NAMMDR headquarters of the samples taken, accompanied by the respective documents;

- application of sanctions, in line with the legislation in force;

- reporting to the NAMMDR headquarters some quality non-compliances identified during the surveillance inspections performed on the territory;

- updating the DGSCMUT database (the situation of inspections carried out to solve the thematic plan, the situation of medicinal products taken within the yearly sampling and testing plan/upon request of the EDQM/of imported medicinal products for supply in case of special needs, the situation of medicinal products sampled in order to solve quality complaints);

− updating the information on the NAMMDR website (list of withdrawals and list of sanctioned units);

In addition to the activities presented above, in 2020, the DGIF provided within the legal deadline the replies to the addresses of the Ministry of Health, other authorities and public institutions, and to the received petitions, as well as to the requests for information of public interest: 90 requests from authorities (the Ministry of Health, the CNAS, the Competition Council, the Chamber of Deputies, the Court of Accounts, the Ministry of Internal Affairs, People's Advocate, the ANAF, the DNA, the IGPR, hospitals, wholesale distributors), participated in the development and revision of guidelines and legislation in their field of activity, has formulated replies to requests of European/international authorities in the field of pharmaceutical inspection: the JAP, the MRA-EMA; it paid the fee for maintaining the membership status of the Pharmacy Inspection Convention (PIC) - the Pharmaceutical Inspection Cooperation Scheme (PIC/S) to which Romania has been affiliated since 1981, corresponded with the DEAP on the 2021 budget estimate, purchase requisitions and substantiation notes.

7. Pharmacovigilance and Risk Management

The Pharmacovigilance and Risk Management Directorate (DFVMR) is a structure within the General Directorate for Authorisation Assessment (DGEA).

The specific activities of the DFVMR include:

a. Management of reports of suspected adverse reactions to medicinal products for human use from spontaneous reporting or clinical trials.

4877 AR reports were received in 2020, from all sources (patients, consumers, healthcare professionals, marketing authorisation holders, INSP / CNSCBT), of which 1548 reports of serious adverse reactions.

As regards ARs to vaccines, known as undesirable post-vaccination adverse reactions (RAPI), as of 2012, there is a collaboration protocol between the NAMMDR / Pharmacovigilance and Risk Management Directorate and the National Institute of Public Health / National Surveillance Centre and Control of Communicable Diseases (INSP / CNSCBT), for mutual information on post-immunisation adverse reactions reported to the two institutions. The collaboration protocol in force stipulates that the NAMMDR is responsible for the monthly transmission of undesirable post-vaccination ARs received directly by the Agency to the INSP / CNSCBT; therefore, in 2020, the NAMMDR transmitted to the INSP/CNSCBT a number of 30 adverse reactions to vaccines. Moreover, according to the protocol, the NAMMDR manages the RAPI transmitted by the INSP/CNSCBT, so that 41 RAPI were received and processed according to the operational procedures in force.

Quarterly information addresses sent to the Romanian College of Physicians/Romanian College of Pharmacists in order to grant EMC/EFC (Medical Education/Continuing Pharmaceutical) credits to physicians/pharmacists who reported adverse reactions to the NAMMDR - 4 addresses to the CMR and 4 addresses to the CFR.

Information addresses sent to healthcare professionals who reported adverse reactions, concerning the number of EMC/EFC credits obtained - 397 addresses.

b. Pharmacovigilance activities in the system of European national authorities under the coordination of the EMA.

✓ This year, according to the obligations of the NAMMDR as a member of the European network of competent authorities in the medicinal product field, after processing of adverse reaction reports received directly from healthcare professionals and patients, 192 reports of serious side effects and 540 reports of non-serious side effects were submitted for registration into the EudraVigilance database.

✓ Within the DFVMR, 30 documents such as Direct Communications to healthcare professionals were managed, regarding safety issues of medicinal products, and 30 sets of information addresses were sent to the CNAS, the Ministry of Health, the Romanian College of Physicians, the Romanian College of Pharmacists.

✓ As regards the specific activity of management of safety signals for the substances monitored by Romania into the EudraVigilance database, the DFVMR considered 40 active substances or combinations of substances.

✓ As regards the responsibility of the evaluation structure of the documentation submitted by the MAH (Periodic Safety Update Report - RPAS) within the single European procedure for evaluation of the periodic safety update report (PSUSA) in which Romania was appointed Reference Member State, 2 procedures were completed during 2020.

✓ Pharmacovigilance activities through the rapid alert / non-urgent information system (AR / NUI). Last year, there were 12 response situations (INUs) to requests for information received from the EMA or other authorities in EU Member States regarding information on certain medicinal products or classes of medicinal products.

✓ Monitoring and verifying the implementation by the MAH of European Commission decisions for medicines authorised for being placed on the market in Romania.

c. Assessment of the pharmacovigilance documentation in view of authorisation and renewal of the marketing authorisation procedures:

✓ Within the centralised marketing authorisation procedure, at SFMR/DFMR level, assessment reports were prepared for the pharmacovigilance documentation in the Centralised Procedure in which Romania is appointed Rapporteur / Co-rapporteur for 2 procedures.

✓ In order to obtain the marketing authorisation through decentralised procedure (DCP) / mutual recognition procedure (MRP) / repeat-use mutual recognition procedure (repeat-use MRP) (with Romania as a reference member state - RMS/concerned member state - CMS), the DFVMR has contributed by setting up assessment reports for the pharmacovigilance documentation to all ongoing and completed procedures during 2020.

✓ As part of the procedure for marketing authorisation renewal in European procedures (RO as SMR/SMI), the DFVMR submitted evaluation reports on the assessment of pharmacovigilance documentation to all European procedures in progress and completed during 2020.

✓ The DFVMR established specific pharmacovigilance authorisation conditions for 41 medicinal products authorised through European/national procedure(s).

✓ Within the marketing authorisation procedure through national procedure, the DFVMR submitted 81 pharmacovigilance documentation assessment reports. Also, the DFVMR was involved in the validation stage of the pharmacovigilance documentation submitted by the applicants in the authorisation procedure through National Procedure - 24 procedures.

✓ As part of the procedure for marketing authorisation renewal in the national procedure, the DFVMR submitted 139 assessment reports of the pharmacovigilance documentation (final evaluation reports or upon request). Moreover, the DFVMR was involved in the the process of validation of the pharmacovigilance documentation submitted by the applicants in the MA renewal procedure through National Procedure - 33 procedures.

✓ The DFVMR was also involved and contributed to the verification of the documentation and its assessment 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.

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

✓ The DFVMR contributed by setup of assessment reports of pharmacovigilance documentation to all variations submitted by the MAH for medicinal

products authorised through European Procedures with RO as SMR/SMI, ongoing and completed by 2020.

✓ 89 variation requests submitted by the MAH for medicinal products authorised through National Procedure were completed;

e. Evaluation and approval of educational materials included in the Risk Management Plan for authorised medicinal products in line with Art. 127a of Directive 2001/83/EC with subsequent amendments and completions. In order to carry out this activity, the DFVMR completed the evaluation of 75 files in support of the applications for approval of approximately 202 educational materials.

f. Management of e-mail addresses dedicated to the pharmacovigilance activity: ro-h.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, RA.Vaccinare.covid@anm.ro;

g. Miscellanea:

- DFVMR collaboration with all organisational structures of the NAMMDR: elaboration and transmission of replies to internal requests/petitions received from the Legal and Administrative Litigation Directorate, collaboration with the General Directorate of Pharmaceutical Inspection (DGIF) in order to solve complaints regarding adverse reactions to medicinal products, communication with the NAMMDR spokesperson on pharmacovigilance issues and provision of requested information.
- Collaboration with other public institutions: in 2020, replies were provided within the legal deadline to the addresses of the Ministry of Health, other authorities and public institutions, as well as to requests for information of public interest. Addresses were forwarded to the specialised commissions of the Ministry of Health in order to request views on safety issues for certain medicinal products for human use.
- An information note was prepared for the NAMMDR President and the Ministry of Health on regulation of the parallel import of medicinal products in Romania and the potential to contribute to increasing patients' access to treatment.

- The DFVMR maintains and manages the adverse reaction database, by recording and archiving adverse reactions reported in Romania, ensuring local management and entering information from spontaneous adverse reaction reports received by the NAMMDR from all sources in the adverse reaction database, managing the pharmacovigilance databases of the DFVMR, updating the information available on the NAMMDR website under the "pharmacovigilance" sections.

- Participation of the DFVMR director or his deputies in meetings within or outside the NAMMDR:

- Participation of DFVMR members appointed by the NAMMDR President in the EMA Committee for Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA), in PRAC meetings, monthly meetings, meetings of PRAC - ORGAM Teleconference. The PRAC strategic review and learning meeting (SRLM) took place between 22-24 April 2020 under the Croatian presidency of the Council of the European Union and, on 22 October 2020, the PRAC strategic review and learning meeting took place under the German presidency of the Council of the European Union (EU).

- Participation of the members appointed by the NAMMDR President in the monthly meetings of the Authorisation Commissions for the marketing of medicinal products authorised through national procedure/European procedures/special needs/last resort treatments.

- Meetings with the MAH in order to address pharmacovigilance issues.

- Participation of the DFVMR member appointed by the NAMMDR president in the meetings of the National Coordinating Committee for activities on vaccination against COVID-19 (CNCAV).

- Participation of the appointed member in the working group for the collaborative registration procedure of the World Health Organisation.

- Participation of 2 persons from the DFVMR in the meeting with the representatives of the Medicines Agency of the Republic of Moldova on August 12, 2020.

- The representatives of the Directorate have elaborated and presented papers at specialised scientific events - 7 events/conferences.

- The DFVMR participated in the elaboration/amendment of some regulatory acts in the field of activity:

- submitted a proposal to amend Order 1018/2014 on approval of Conditions for authorisation of human medicinal products for compassionate use, in accordance with provisions of Article 83 of Regulation (EC) no. 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency;
- proposed for approval the Order of the Minister of Health on Adverse Reaction Fact Sheets;
- participated in the elaboration of the COVID-19 vaccination strategy in Romania through a representative in the Working Group for the COVID-19 vaccination strategy;

- through DFVMR, the NAMMDR, together with the press officer, participated in the organisation and development of an annual social media campaign in Romania, to promote awareness of the importance of reporting suspected adverse medicinal product reactions - #MedSafetyWeek 2020 campaign entitled "Each adverse reaction counts" - encouraging the general public and healthcare professionals to report adverse reactions, 02-08 November 2020;

- Together with the STIC, the DFVMR has developed an electronic system for reporting post-vaccination adverse reactions to COVID-19 vaccines available to persons to be vaccinated and healthcare professionals, as well as reporting sheets to be used in order to report post-vaccination adverse reactions.

8. Medicinal Product Quality Control

As regards the assessment activity in 2020, the DCCM showed an active participation, through its representatives, in the EMA Biologics Working Party (BWP). Representation by assigned persons was ensured through both physical (January and February 2020) and virtual participation (the rest of the monthly meetings in 2020) in EMA meetings, in the CHMP Biologics Working Party (BWP) and in the Committee for Advanced Therapies (CAT). In 2020,

similar to previous years, the DCCM participated again through its assessors in the assessment of quality documentation in centralised procedures, as co-rapporteurs/peer reviewers.

Starting with 01.10.2019, in line with Order no. 1412 of 13 September 2019 on approval of the NAMMDR Organisational structure and with Order No. 1522 of 9 October 2019 on approval of the Regulation on the Organisation and operation of the NAMMDR, the Department of Evaluation and Quality Control of Medicines has become the Directorate for Medicinal Product Quality Control, with the following structure:

- Laboratory for Physical, Chemical and Instrumental Determinations for Synthetic Medicinal Products (LDFCIMS);
- Laboratory for Physical, Chemical, Immunochemical and Serological Determinations for Biological Medicinal products and Pharmacotoxicology (LDFCISMBFT);
- Laboratory for Determinations on Cell Cultures and Microbiology (LDCCM);
- Radiopharmaceutical control department (CCPR);
- Medicinal Product Quality Control Procedures Administration Department (CAPCCM).

a. Laboratory for Physical-Chemical and Instrumental Determinations in Synthetic Medicinal Products (LDFCIMS)

Within the laboratory, 131 physical-chemical parameters were analysed for 24 medicinal products, of which 18 medicinal products were coded as “SN”, 2 as “RI”, 2 as “SE” and 2 as “NS”.

The LDFCIMS participated in 2020 in the following PTS (Proficiency Testing Study) programs for the analysis of laboratory competence, interlaboratory comparisons and competence tests, organised by the EDQM:

1) PTS197: Assay - Liquid Cromatography;

2) PTS204: Potentiometric determination of pH;

3) PTS205: Proficiency Testing Scheme on Water: semi-micro determination;

4) PTS206: Proficiency Testing Study: Loss on drying;

The LDFCIMS also participated in the European program for analysis of medicinal products authorised through centralised procedure (CAP) in accordance with the

PA/PH/CAP (05) 96 DEF procedure - "Ad-HOC testing procedure for centrally authorised products", in which a product containing temozolomide was analysed.

Market Surveillance Studies - MSS - studies initiated by the EDQM in order to monitor the quality of generic medicinal products on the European market compared to the reference product authorised through the "Common Testing Sample-CTS" centralised procedure were performed by the LDFCIMS." Market Surveillance Study MSS 058 - tablets containing "sildenafil citrate"; in addition to the CTS test, two other medicinal products taken from the market were analysed.

At the same time, the laboratory carries out the evaluation of the ASMF-DPN/DPE documentation by evaluation of the ASMF documentation and elaboration of reports for European procedures, upon request of the DPE:

- European decentralised procedure: 45 initial reports + 20 additions
- European repeat-use procedure: 8 initial reports
- European procedure - variations: 120 initial reports

Total number: 193 reports (173 initial reports + 20 additions);

Upon punctual request of the Variations Service/DPN, the evaluation of the documentation supporting some requests for variations regarding medicinal product quality was performed: 9 evaluation requests.

Also, the ASMF documentation was evaluated and reports were prepared for European centralised procedures or with Ro-SMR upon request of the DPE.

b. Laboratory for Physical, Chemical, Immunochemical and Serological Determinations for Biological Medicinal products and Pharmacotoxicology

The laboratory control activity for checking the quality of biological medicinal products for human use consists of:

−the scientific evaluation of the manufacturing documentation and the control methods included in the authorisation documentation; the accompanying documentation was analysed and studied and 6 analytical files were prepared for the biological products tested in 2020;

−performing laboratory analyses attesting the quality of biological medicinal products for human use (37 control tests for 6 batches of biological medicinal products for human use, of which 2 were coded "SN", 2 "BR", 2 "NS".;

- issuing analysis bulletins (5 analysis bulletins);

- analysis of trend data of laboratory results for batches of biological medicinal products submitted for batch release.

The LDFCSMBFT participated in 2020 in the following PTS (Proficiency Testing Study) programs for the analysis of laboratory competence, interlaboratory comparisons and competence tests, organised by the EDQM:

1) PTS204: Potentiometric determination of pH PA/PH/PTS (20) 11

2) PTS205: Water: semi-micro determination (PA/PH/PTS (20) 17)

3) PTS207: UV-Vis Spectrophotometry (PA/PH/PTS (20) 16)

4) PTS 212 determination of seasonal influenza vaccine potency (haemagglutinin content) (FE 2.7.1) PA / PH / PTS (20) 5

In the EDQM Report evaluating the results of PTS studies, the LDFCISMBFT had good and very good results.

The LDFCSMBFT also participated in the European program for analysis of authorised medicinal products through centralised procedure (CAP) in accordance with the PA/PH/ CAP (05) 96 DEF procedure - "Ad-HOC testing procedure for centrally authorised products", which included the analysis of a product containing teriparatides.

During evaluation and centralisation of the batches officially released by another control authority from another Member State, the distribution companies received documents regarding the intention for marketing for 450 batches of authorised biological products marketed in Romania (139 batches of vaccines, 311 batches of blood products). Starting with 01.09.2020, marketing agreements are issued, a number of 114 marketing agreement addresses for 156 medicines being issued.

Within the Laboratory of Physico-Chemical, Immunochemical and Serological Determinations for Biological Medicinal Products and Pharmacotoxicology, the following assessment activities are performed:

- validation of variation requests (112 validations of type IB and type II variation requests, 12 invalidations of type IB and type II variation requests);

- evaluation, preparation and issuance of evaluation reports for biological medicinal products;

- evaluation of applications submitted by national procedure (evaluation and drafting of 6 quality assessment reports for products under authorisation/renewal, evaluation and elaboration of 33 reports supporting type II post-authorisation variations, evaluation of type IA and IB variations/design changes/MA transfer/Braille imprinting and issuance of 57 requests for completion of documentation approval sent to the applicant);
- evaluation of applications submitted through European procedures (MRP, DCP, centralised) (evaluation and drafting of 5 quality assessment reports for products under authorisation/renewal through the mutual recognition procedure, evaluation and elaboration of 84 reports and 84 annexes/addresses for variations submitted by mutual procedure, evaluation of quality documentation for biological/biosimilar medicinal products under authorisation by centralised procedure, as Co-rapporteur for 1 procedure for adalimumab and as Peer Reviewer for another pegfilgrastim product;

- evaluation of the quality documentation submitted for 8 clinical trial protocols for 5 investigational biological medicinal products and elaboration of 12 evaluation reports;

- the activity of evaluation, preparation and issuance of evaluation reports for the ASMF within the European procedures;

- 25 amendments were made to the marketing authorisations for biological medicinal products.

c. Laboratory for Determinations on Cell Cultures and Microbiology

The control activity of the LDCCM consists in performing laboratory microbiological analyses for medicinal products for human use, as well as assessing the quality of biological medicinal products by tests on cell cultures. In 2020, 23 such analyses were performed for 19 medicinal products:

- for the official batch release, in accordance with the provisions of HCS no. 3/14.02.2012 (the OCABR procedure), for the circulation on the Romanian territory of Romanian biological products for human use, imported from third countries and EU member states, for which the official batch release in the EU has not been performed for 2 batches of biological medicinal products;

- for 17 medicinal products included in the national market surveillance program.

In 2020, the LDCCM participated in the following PTS (Proficiency Testing Study) programmes for laboratory competency analysis, interlaboratory comparisons and proficiency testing, organised by the EDQM: *PTS 203 Bacterial endotoxins (vaccine samples).* According to the EDQM Assessment Report of the outcomes of the PTS 203 study, the LDCCM had good and very good results.

The LDCCM also participated in the CRS 5 Streptomycin Sulfate Study, coordinated by the EDQM, in order to establish a new batch of chemical reference standard, namely the 5-streptomycin sulfate batch. Participation in the CRS 5 collaborative study was highly appreciated by the EDQM and the European Pharmacopoeia Commission.

Assessment activity of the documentation submitted for marketing authorisation (MA) / marketing authorisation renewal / approval of type I / II variations to MA terms / approval of applications for conduct of clinical trials, through national/European procedure(s) (mutual recognition procedure, decentralised and centralised procedure), materialised through assessment reports and related documents:

- Assessment of the documentation submitted through national procedure: a Report was issued requesting supplementation of the quality documentation and 93 addresses, 7 annexes and 16 assessment reports for variations of type IA, IB and II were elaborated for 1 medicinal product.
- Assessment of the documentation submitted through the mutual recognition procedure: Quality Assessment Reports were prepared for 10 medicinal products (with a proposal for MA renewal, including the conditions for renewal) and the corresponding annexes (14 Annexes), and 46 annexes and 38 assessment reports were prepared for type IB and II variations.
- Assessment of the documentation submitted through decentralised procedure was performed for 3 medicinal products: Quality evaluation reports and the corresponding annexes (4 Annexes) were prepared for 3 medicinal products (and a proposal for approval).
- Assessment of the quality documentation submitted for authorisation of the conduct of clinical trials for investigational medicinal products of biological origin: the quality documentation submitted for authorisation of conduct of clinical trials was evaluated for 7

investigational medicinal products of biological origin and 14 Assessment Reports were prepared.

− Other requirements related to the assessment activity: the information on microbiological dosage of active substances was assessed (from 2 variations).

− Assessment of the quality documentation for biological/biosimilar medicinal products under authorisation through centralised procedure, as Co-rapporteur for a product containing adalimumab, as Peer Reviewer for a medicinal product containing pegfilgrastim, proposed for authorisation through centralised procedure.

− Evaluation of the documentation submitted through centralised procedure for sections S.4.1., S.4.2., S.4.3, S.4.5., P.5.1., P.5.2., P.5.3., concerning the microbiological methods of control of active substance and finished product, as co-rapporteur for the centralised procedure for a medicinal product containing teriparatide.

d. Radiopharmaceutical control compartment

Within this compartment, tests are performed for radiopharmaceutical medicinal products, as well as activities related to monthly radiation protection training of the staff, performing radioactivity measurements for work areas, in accordance with radiation protection rules, conducting dosimetric surveillance of staff with photodimimetric films, in line with the legal provisions, the record of the doses received by the staff, based on the weekly results acquired by individual dosimeters with direct reading, monitoring the rhythmic supply with reagents and required materials, including liquid nitrogen supply, in order to ensure optimal conditions for proper operation of laboratory activity, metrological verification and calibration of laboratory devices, as well as ensuring technical assessment.

At the same time, the evaluation-expertise of the authorisation/re-authorisation documentation of pharmaceutical products is carried out: 74 ASMF evaluation reports for the European Procedure Department, 74 ASMF variation evaluation reports.

e. The Compartment for Medicinal product quality control procedures administration

− Receipt of medicinal product samples for laboratory testing, verification of data and sample integrity and their registration into the medicinal product register and in specific

databases, namely 50 batches of medicinal products for human, Romanian and foreign use in 2020;

- The receipt, verification and registration into the database of 16 batches of medicinal products received for analysis at the proposal of the EDQM within the international participation in conducting interlaboratory PTS, CRS, CAP studies; receipt, verification and registration into databases of reference substances required for laboratory testing, reagents and accompanying documentation, and their distribution in testing laboratories of the DCCM: 105.
- Distribution of samples according to the distribution made by the DCCM director; storage of samples and references in appropriate conditions and ensurance of their monitoring, security and traceability.
- Registration of Certificates of Analysis issued by all laboratories involved in testing and their centralisation into the register of analyses and databases: 35 certificates and 243 parameters.

9. Assuring communication and transparency

In 2020, the 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, concerning transparency and communication.

The Communication and Public Relations Service (SCRP) of the NAMMDR ensured both the internal communication, with the Agency's experts, and the external one, with the stakeholders, acting as an interface with professional organisations, patient associations, beneficiaries of the healthcare system, but also with the media.

In 2020, the List of employees assigned, through decision of the President, 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 the European Commission, was updated.

The SCRP has updated the NAMMDR database on Server-romsys, regarding European Commission (EC) Decisions and consensus agreements of the Coordination Group for Mutual and Decentralised Procedures for Medicinal Products for Human Use (CMDh), on medicinal products authorised in Romania, in order to implement them by the persons assigned for this purpose in the NAMMDR, 15 decisions concerning medicinal products having marketing authorisations in Romania.

The SCRP has also coordinated the monitoring on the Community Register and the management in electronic records within the department and on the Romsys Server / anm / EC Decisions, namely 22 Decisions of the European Commission (EC) (periodically received from the PR of Romania to the EU / MFA on paper), regarding: medicinal products with conditional marketing authorisations, maintenance / suspension / withdrawal / amendment of MAs following completion of referral procedures on safety, quality, efficacy, these being forwarded to NAMMDR specialists assigned to ensure their implementation in Romania (in the case of the 15 EC Decisions referring to medicinal products in Romania as well, the remaining 7 EC decisions referring to medicinal products unauthorised in Romania).

The SCRP has collaborated with NAMMDR experts to issue replies to requests from media representatives and/or other applicants, within the timeframes provided for by the rules in force, if the requested information is already communicated ex officio in one of the manners specified in Art. 5 of Law no. 544/2001, also indicating the location where the requested information can be found;

The DPS has prepared the NAMMDR annual activity report for 2019 by corroborating data from activity reports of NAMMDR structures and monitored the new information available in the public space, regarding the NAMMDR and the healthcare system, on a daily basis.

The SCRP has ensured preparation of the NAMMDR newsletters, which have been posted on the Agency's website:

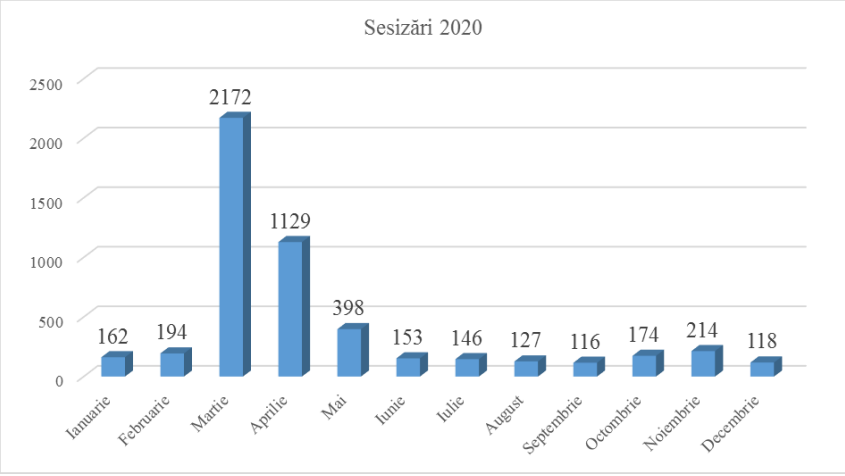
- Newsletters issued in Romanian: 4/2019; 1/2020; 2/2020.
- Newsletters issued in English: 1/2020 and 2/2020.

The SCRP has organised and/or participated in various meetings/working meetings with representatives of the Ministry of Health, of other institutions, at NAMMDR audiences together with other structures. In August 2020, the SCRP initiated and organised the working visit of the delegation of the Agency for Medicines and Medical Devices of the Republic of Moldova, ensuring the signing of a new collaboration protocol.

The SCRP prepared and / or verified the dissemination to the media of all official releases and positions of the NAMMDR management and managed the NAMMDR Facebook page.

In 2020, the SCRP continued to manage the e-mail address lipsamedicament@anm.ro. As regards the documentation, drafting and transmission of replies to notifications received during January-December 2020 on the e-mail address of the NAMMDR (lipsamedicament@anm.ro), it consisted of 5103 notifications from patients, owners, hospitals, open circuit and hospital pharmacies, patient associations, pharmaceutical warehouses, medical companies, physicians.

The monthly situation of received notifications is as follows:



In 2020, the activity of documenting and formulating replies to the notifications redirected from the e-mail address of the Ministry of Health, noreply@medicamentelipsa.ro, which refers to the notifications posted at http://medicamentelipsa.ms.ro/, was continued. Between January - October 2020 (since the end of October 2020 - the platform of the

Ministry of Health was no longer functional) at lipsamedicament@anm.ro were automatically redirected by the Ministry of Health: 1986 notifications out of 5103. In these cases, as well, the employed documentation/assessment procedure was the one used in the case of notifications received directly by the NAMMDR, on its own e-mail address.

The SCRP coordinated the interdepartmental collaboration regarding the activity of providing support upon request of colleagues from the Pharmaceutical Inspection and National Procedure departments, namely the elaboration of documents for the Ministry of Health, the National Health Insurance House, etc. In this context, we hereby mention:

- preparation of monthly statements according to OUG 8/22 February 2018 on regulation of certain measures in the field of health, which were sent to the National Procedure Directorate of – the Index of medicinal products Compartment;
- the setup and permanent update of a database meant for internal use, which in 2020 consisted of a number of 108 complaints received from pharmacists and specifying the manner in which these should be dealt with by the General Directorate for Pharmaceutical Inspection, in line with OMS 269/March 2017 on the obligation to provide adequate and continuous stocks of medicinal products;
- weekly preparation, under the headings of the SCRP, of the summary of intra-community delivery notifications sent to the NAMMDR according to OMS 672/April 2020 on approval of the List of medical devices required in order to ensure the prevention and treatment of the SARS-CoV-2 infection, whose distribution is temporarily suspended, as well as measures to ensure the supply of medicinal products at high risk of discontinuation on the national market.

In managing the situations, the NAMMDR organised numerous meetings by videoconference both with the representatives of marketing authorisation holders and with those of wholesale distributors, of the Ministry of Health and of the Romanian College of Pharmacists. Following those discussions, certain measures were agreed which led to restoration of market balance. For example, in the case of Euthyrox, the measures taken included: intensifying control of the release of the medicinal product in pharmacies, identifying alternative market supply solutions (parallel import authorisation, special needs authorisation), sending joint press releases, requesting supplementation of the quantity of the

medicinal product placed on the market by the marketing authorisation holder.

At the same time, in 2020, patients reported the lack of other medicinal products, such as: Siofor, Novothyral, Plaquenil, Venter, Gastrofait, Colchicine, Amitriptyline, Cupripen, Glucobay, Tamoxifen.

The SCRP provided consultancy/translation into English of profile documents and verification of the translation performed by other NAMMDR specialists:

- translation of the NAMMDR Activity Report for 2019;
- translation of NAMMDR Newsletters no. 1 and 2/2020;
- translation of EMA press releases and NAMMDR important notifications and press releases;
- translation of documents requested by the internal departments of NAMMD;
- Proofreading of all the works translated into English, presented abroad by the NAMMDR;
- providing advice on correspondence and communication with European and international bodies and representatives of the pharmaceutical industry.

The SCRP actively participated in the weekly meetings of the Working Group of Communication Professionals (WGCP) of the Heads of Medicines Agencies (HMA).

In 2020, the SCRP continued to supplement and update the information available online to the Agency's employees (on the intranet), in order to provide the best and fastest information in the professional and/or organisational field.

10. Quality management

In 2020, the quality management activity, responsibility of the Human Resources and Quality Management Directorate consisted of:

- Ensurance of implementation of quality management strategies and objectives declared by the NAMMDR management;
- Coordination of the design, documentation, implementation, maintenance, improvement and reporting of the Quality Management System;
- Collaboration with all NAMMDR structures in order to permanently optimise the

quality management system;

- Provision of counselling on quality management issues to Agency staff;
- Provision of support to all requests of the NAMMDR management related to quality management;
- Consistent reporting to the NAMMDR management regarding the functioning of the Quality Management System and the formulation of proposals for its improvement;
- Representation of the 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 other specific documents in view of ensuring quality assurance;
- Update of all quality assurance documents, depending on the dynamics of the organisational and functional structure and specific requirements.

All quality-related documents were checked and, whenever necessary, revised, depending on the evolution of the quality management system/changes in the structure or field of activity of the NAMMDR organisational structures, to ensure continued adequacy and compliance with applicable requirements. If the verification did not identify the need for amendments, they were not revised.

In order to ensure a unitary and coherent system of documentation of all procedures at organisation level, the NAMMDR management decided to integrate the two quality management systems and the SCIM (internal management control system) by developing a single procedure pattern (PS-09/01-Management of the procedure, in force).

In 2020, the review/update of the procedures for transposing the procedures into the new unitary format in force was continued.

11. Medical devices

Considering the epidemiological context from the beginning of 2020, the activity within the Directorate for Regulation and Surveillance of the Medical Devices Market has undergone several changes, focusing on various specific activities: derogations, registration of medical

devices of interest in combating the COVID-19 virus (masks, coveralls, gowns, COVID-19 antibody rapid tests, COVID-19 antigen rapid tests, emergency donation approach, etc.).

Posting important notifications on pandemic-related activity updates has been a priority.

On 23.04.2020, in the context of the pandemic, the European Commission announced the adoption at the level of the Council of Europe and the European Parliament of the proposal to postpone, by 1 year, the deadline for full implementation 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 - MDR, until 26 May 2021, in order to prioritise the fight against Coronavirus.

11.1. Control by periodic check of commissioned and in-use medical devices

In 2020, following the controls performed by both public and private healthcare units, the following results were obtained:

- Total periodic check bulletins issued: 943;
- Total user opinions issued: 150;
- Total test reports issued: 2627.

This year, 764 applications were processed, 52 being cancelled for various reasons (failure to pay the tariff, incomplete dossier etc.), 428 being in progress. In order to perform this activity, inspections were made to private healthcare units, public hospitals and county ambulance services; in case of large hospitals, several inspections were needed, since it is possible to check 30-60 devices / week during a delegation.

Given the fact that the endowment with measuring equipment for monitoring of medical devices must keep up with the technological progress in the field, measurement and control equipment was purchased at the end of 2020.

In November and December 2020, all NAMMDR staff from the DGDM-DTL structure performed thematic control in ATI sections according to the address of the Ministry of Health - State Health Inspection no. 563/16.11.2020, in order to identify non-compliances and draw up the measure plan.

Interventions were made to remedy some issues occurred with the measuring and

monitoring equipment in order to be able to further perform measurements of the technical parameters of medical devices.

In this context, in order to understand the complexity of the process completed with issuance of periodic verification bulletins / approvals for use of medical devices, it is necessary to highlight the multiple related activities, involving registration and analysis of applications, charging (in case of requests from private healthcare units) depending on several criteria, such as application registration number, date of payment confirmation, number and specialty of staff, equipment and means of transportation required, approval of the travel order for the concerned county/area), travel and technical checks, elaboration of travel-related documents, drafting of documents, endorsement, approval and transmission to beneficiaries, archiving of documents and upload on the institution's server, database administration, etc.

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

Thus, in 2020, 532 applications were registered at the level of the profile unit, and 487 of them were completed.

At the same time, 460 periodic check bulletins and approvals for use were issued, as well as 507 test reports issued for medical devices with radiation generators and 1120 test reports for radiation protection equipment.

11.2. Inspection and assessment of technical-medical units

The activity performed in 2020 was performed in line with Order of the Minister of Health no. 1008/2016 on approval of Methodological Rules for implementation of Title XX of Law no. 95/2006 on healthcare reform, regarding approval of medical device-related activities.

The activities related to marketing and service provision in the field of medical devices,

subject to control by approval, until 03.04.2020, were as follows:

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.

Following publication of Order 566 of 2020, the activities subject to control by approval were:

a) import of medical devices;

b) distribution of medical devices;

c) installation and/or maintenance of medical devices.

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

Year	Total number of applications	Average number of activities/months	Average number of activities/employee/months	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
2020	2986	248.8	24.8	10

In 2020, 420 documents were prepared (registered in 2019), as follows:

Type	**Number**
Functioning authorisations	120
Annexes to authorisations	206

Surveillance	67
Classification	25
Various notifications	2

In line with Order of the minister of Health no. 566/2020, 71 Temporary Operating Approvals were issued during the state of emergency, with a validity period of only 6 months.

Type	Number of requests	Number of analysed requests	Number of unsolved requests	Number of classified requests	Number of solved requests
Functioning authorisations and annexes to the functioning authorisations	2986	262	87	315	2322
Documents received in 2019 and finished in 2020	1817	276	125	6	395
Total	4803	538	212	321	2717

In 2020, 978 functioning authorisations and 1739 Annexes to functioning authorisations were issued. The 978 functioning authorisations issued are:

Type	Number
Temporary functioning authorisations	71
Renewed functioning authorisations	98
New functioning authorisations	597
Surveillance	51

Starting with 16.11.2020, the staff of the Directorate for Approval participated in joint commissions formed by staff from the DSP, the ISCIR, the IGSU in accordance with the provisions of notification no. 563/16.11.2020 issued by the Ministry of Health - State Sanitary Inspection at the thematic controls in ATI sections (including those intended for COVID-19 patients) from health units of Bucharest.

At the same time, the Directorate for Approval also participated in auction and evaluation commissions of the dossiers submitted in auctions organised by the Ministry of Health, ONAC.

11.3. Regulation, authorisation and market surveillance of medical devices

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

Internally (within the NAMMDR):

1. Participation in scientific events and training programmes according to the Annual Staff Training Programme: 4 self-training courses were organised within the NAMMDR in 2020.

2. Registration of medical devices placed on the market or put into operation in Romania by domestic manufacturers, authorised representatives, importers and distributors of medical devices, according to the regulations in force - 607 (from 9746 to 10353) medical devices placed on the market by responsible economic operators (domestic manufacturers, authorised representatives residing in Romania) + 170 (from 8094 to 8264) medical devices put into operation by responsible economic operators (all types mentioned above);

3. Setup and update of the national database in accordance with the provisions of the national legislation transposing the European directives;

4. Authorisation of the programme for enforcement of the clinical investigation procedure / assessment of performance with medical devices intended for clinical investigations - starting with 21.09.2020, the following were issued: 1 substantial amendment for conduct of the clinical investigation and 8 files were assessed, representing amendments or reports to ongoing clinical investigations;

5. Documentation, implementation, research and development in its field of activity;

6. Issuance of approvals, notifications and registration certificates, in line with the specific legal provisions in force: 3 customs approvals, 22 approvals, 98 refusals for donation as well as notifications and certificates in accordance with point 2 above.

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

1. Elaboration of norms for medical devices, for harmonisation of the national legislation with the European directives and regulations, which are submitted for approval to the Minister of Health;

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

3. Elaboration of methodological norms regarding the organisation and operation of the medical devices sector and submits them to the approval of the Minister of Health. In this sense, it was proposed to amend Order no. 1356/2013 on approval of the tariffs practiced by NAMMD, during the meeting of 24.08.2020;

4. Elaboration and submission for approval of the lists containing the Romanian standards adopting the European standards harmonised with the European directives in the field of medical devices to the Minister of Health. Thus, we collaborated with the ASRO in order to translate some necessary standards. In the same context, the NAMMD expert participated in a virtual meeting of the CT 374 organized by the ASRO (September 2020).

5. Authorisation, in duly justified cases, of placing on the market and commissioning of single medical devices, where this is in the interest of the health protection policy.

6. Formulation of replies 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 and working groups in the field of medical devices at European Union level.

In the context of the pandemic, participation in the meetings of the working groups in the field of medical devices at European Union level was carried out remotely (online).

- online participation in the meetings of the working groups: the MDCG (Medical Device Coordination Group) MD + IVD, working group on Standards, the MDCG - Working Group NBO, the MDCG - Working Group on Market Surveillance, working group on IVD, -Vigilance expert group, the EUDAMED, the UDI, ANNEX XVI.

- transmission of the documents regarding the requested updates concerning the NAMMD experts nominated in the working groups: the UDI, the EUDAMED and the MDCG, to the European Commission.

- online participation in teleconferences of the Competent Authorities for Medical Devices (CAMD).

- online participation in the CAMD - Operational Working Group teleconference (07/02/2020) and submission of RO comments to the MDR/IVDR Roadmap document (17/01/2020; 04/11/2020).

- online participation in specific COVID-19 related meetings.

- Sending (on 01.04.2020) Romania's reply to the European Commission (to an e-mail related to "JRC offer positive control material SARS-CoV-2 RNA").

2. Elaboration from a technical viewpoint of Romania's position and mandate of representation concerning the proposals of community legislative acts and the themes of the working groups at European Union level, in the field of medical devices, and their transmission to the Ministry of Health.

3. Evaluation and designation of certification bodies in the field of medical devices, submission for approval of the list of designated bodies to the Minister of Health and notification of these bodies through the electronic procedure managed by the European Commission.

4. Surveillance of notified bodies and provision of appropriate measures.

5. Ensuring the entry of data from the national database into the European Eudamed database, in accordance with the provisions of Commission Decision 2010/227/EU of 19 April 2010 on the European Medical Device Database (Eudamed 2): viewing records from the European Database data on medical devices (Eudamed 2).

The voluntary registration of Economic Operators in EUDAMED began on 01.12.2020, this being an operation managed by the DRSP and the DGDM.

6. Making a decision on classification of a medical device in the event of a dispute between the manufacturer and the body responsible for assessing its compliance.

7. Ensures administrative cooperation with the 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.

8. Records and assesses information on reported incidents and proposed corrective actions in relation to medical devices, implements the vigilance procedure according to the

harmonised legislation in force: incidents (MIR) - from 26 manufacturers, FSCA + NCAR - from 95 manufacturers, FSN - 5:

- requests for information were sent to 4 Competent Authorities, 6 Notified Bodies, 2 authorised representatives in the EU, 2 manufacturers;

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

- COEF information evaluation - minimum 91 cases;
- COEF response assessment and response forms - minimum 9 cases;
- COEF RO initialisation - 11 cases.
- at least 20 COVID-19 rapid tests were verified in the Eudamed (especially at the beginning of the pandemic, before publication by the European Commission of the Database containing in vitro diagnostic medical devices);
- the information on falsified EC Certificates of compliance found on the EU market was analysed, with announcements posted on the NAMMDR website - minimum 84;

- 3 marketing ban decisions were issued;

- in accordance with Art. 8 (3) of Directives 93/42/EEC and 98/79/EC and Art. 7 (3) of 90/385/EEC, we are in a state of permanent exchange of information with the other authorities of Member States, regarding compliance of medicinal products - Active participation in the meetings of the Compliance and Enforcement Group - COEN.

• Eu Market Surveillance Conference - Facing the challenges (04-05/11/2020).

• MDCG - Market Surveillance (18/06/2020; 04-05/11/2020; 26/11/2020).

In 2020, the Market Surveillance Service organised and performed 109 thematic control actions and 11 additional control actions on verifying compliance of medical devices placed on the Romanian market, control in use and compliance with the legislation in force by economic agents (Law 95/2006).

73 importers/distributors, 2 manufacturers, 3 medical optical units, 21 sanitary units, 10 retail stores were controlled. Of the 109 controls, 63 were reactive controls, 45 unannounced controls, 1 incident involving a medical device in use. The service staff prepared minutes for the 109 controls and, where appropriate, final control reports. In 2020, 20 fines were applied, of which 19 were paid and 9 warnings were drawn up, for which

minutes were drawn up for finding and enforcement of contraventions. For the 590 notifications/complaints received for resolution within the market surveillance service, points of view, objections and addresses were prepared, which were sent to the NAMMDR DJRI in order to finish the reply and send it to the petitioners within the legal term. Opinions were sent to other state authorities: Customs - 50, Prosecutor's Office - 15, ANANPC - 31, DSP - 17, Police - 33.

As regards the market surveillance activity, 9 types of medical devices were temporarily / permanently halted from marketing / use and 3 decisions were issued.

Between 28.05.2020 - 06.06.2020, employees from the DRSP participated in the elaboration of the tender book and as members in the technical commission for evaluation within the auction for protection masks organised by the Ministry of Health - Order 950/28.05.2020.

During 09.06.2020-30.06.2020 we have participated in the elaboration of the tender book and as members in the technical commission for evaluation of the offers within the public procurement of surgical masks organised by the Ministry of Health - Order 1027/09.06.2020.

Between 10-25.05.2020, a participant was appointed on behalf of the NAMMDR as a co-opted member of the procurement procedure for various types of equipment: facial masks for medical use organised by the Ministry of Education and Research in order to properly conduct the entrance exams that took place between 02.06 - 10.06.2020.

Between 08.09 - 02.10.2020, participants from the NAMMDR were designated in the process of acquisition of medical devices - surgical masks and disposable medical gloves organised by the Ministry of Health (Order no. 151010/02.09.2020).

During 23.11-04.12.2020: participation in the elaboration of the tender book and as co-opted experts for public procurement for award of the supply contract “Rapid tests for determination of the SARS-CoV-2 antigen” for ensurance of emergency medical stocks, CPV: 33141625-7 - Diagnostic kits (Rev.2), organised by the ONAC (National Office for Centralised Procurement).

10 controls were performed based on notification of the Ministry of Health no. 563/16.11.2020 regarding observance of provisions of Minister of Health Order no.

1500/2009 and of Minister of Health Order no. 914/2006 -participation in controls in ATI sections in hospitals from Bucharest together with the DSP, the ISU, the ISCIR - and action plans were set up for the 10 controls.

In 2020, in addition to the core activities, the Regulatory Service also carried out multiple activities specific to the period affected by the pandemic: 5 derogations regarding medical devices in the context of COVID-19, participation in CTs of the ASRO, 223 certificates of free sale, inventory activities, DRSP database update, participation in work meetings organised by top management were issued.

12. International relations

Particularly important in this field were, for the activity and evolution of the Agency, as a member of the European network of competent authorities in the field of the medicinal product, the activities it carried out, together with the Ministry of Health, the Ministry of Foreign Affairs and all other governmental institutions in this field.

Instructions and negotiating mandates in the field of the medicinal product for human use, assessment of medical technologies and medical devices were prepared in 2020 for regulations of:

- the proposal for a Regulation of the European Parliament and of the Council amending Regulation (EU) 2017/745 on medical devices as regards the dates of application of certain provisions thereof;
- the proposal for a Regulation of the European Parliament and of the Council on the conduct of clinical trials and the supply of medicinal products for human use containing genetically modified organisms or consisting of genetically modified organisms and intended for treatment or prevention of COVID-19;
- the proposal for a Regulation of the European Parliament and of the Council on assessment of medical technologies in the field of health, amending Directive 2011/24/ EU;
- the draft of the Pharmaceutical Strategy for Europe, actively participating in the discussions addressing the Strategy's initiatives, and supported ensuring the availability of innovative and affordable medicines for patients, as well as supporting competitiveness,

innovation capacity and sustainability of the pharmaceutical industry in Romania and the European Union.

The table of training measures/communication measures at NAMMDR level, specific to its field of activity, was sent to the Ministry of Health and included:

- the action plan in the context of the end of the transitional period in relation to the United Kingdom. When drawing up the plan, the COM Communication "Preparing for change", as well as the preparation opinions issued by the European Commission, on the sectoral areas falling within the competence of the NAMMDR, were taken into account;

- the public communication plan by the NAMMDR, according to the competencies and the target audience, in order to ensure a proactive information;

- the inclusion of a Brexit (readiness) section as visible as possible on the institution's official website.

The possibility of creating levers similar to the mechanisms implemented by EU Member States, following a unitary and common approach, in the context of a no-deal scenario and without an agreed transition period, was also examined. In this regard, the NAMMDR approach to minimizing the negative impact on medicinal products, plus avoiding the issues related to the availability of medicinal products on the market, as well as on medical devices, was sent to the Ministries of Foreign Affairs, through the Ministry of Health.

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

The Information and Communication Technology Service (STIC) has also met its assignments in 2020 related to optimal maintenance of effective communication with the EMA and provision of real time information exchange between the Agency and its external collaborators (MAHs, distributors, healthcare professionals, patients and associations).

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

- issuance of replies regarding various questionnaires regarding information technology upon request of the EMA and the working groups;

− database administration together with NAMMDR experts and update of their information; administration of the Learning Management System portal;

− administration of the database with experts from the NAMMDR assigned in EMA working groups;

− managing the database with "IRIS Competent Authority Users" experts within the EMA Account Management Portal acting as local administrator;

- ensuring NAMMDR connection to the Common Repository database (Centralised Procedure Submissions);

- ensuring NAMMDR connection to the CESP database (Common European Submission Portal); participation in IT Directors working groups;

- participation in the E.U.T.C.T working groups.

At the same time, the programme for online reporting of post-vaccination adverse reactions was developed, as well as programmes / applications for internal use; the regulation on use of the NAMMDR Computer Network was updated. Specific applications were installed for performance of the activity within the NAMMDR (European Pharmacopoeia, United States Pharmacopeia, etc.); the sponsorship statements for 2020 were published on the NAMMDR website, the Index of Medicinal Products, Registry and Variations databases were administered and access to PHEur, USP, CTS, etc. was facilitated.

The STIC ensured the administration, configuration and restoration of local equipment, by monitoring EudraNet connectivity (EudraCT, EudraLink, EudraMail, EudraPharm, EudraVigilance, CTS, Citryx, EPITT), software and hardware interventions, as well as ensuring maintenance of the NAMMDR website (www.anm.ro) and other software applications.

The STIC activity included maintenance, amendment and update of the following website sections: search engine (The Index of Medicinal Products for Human Use), search engine (Administration of recalled medicinal products), search engine (Administration of GMP units), The "Intranet" website of the National Agency for Medicines and Medical Devices of Romania and other sites under administration. It elaborated strategies for computerisation of the NAMMDR and the Standard Operating Procedures, as well as proposals for amendment of certain regulatory acts.

14. Legal activity

14.1. NAMMDR legal issues in 2020

In January - December 2020, the activity of the Directorate for Legal and International Relations, namely representation in court of the institution, consisted of 262 litigations, dealing with requests for summons, objections, written conclusions, requests for evidence, expertise, written notes, requests for legalisation, addresses to the courts regarding pending files; the representation and defence in court of NAMMDR interests was ensured.

Thus, in 2020, the legal issues in which the authority was involved were constantly growing, compared to 2019, when 170 litigations were pending, and in terms of scope and subject of the file, these have 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 77 files solved and 185 still pending.

Moreover, any request addressed by the courts, by other institutions with administrative-jurisdictional activity, by criminal investigation bodies, related to the communication of information or documents, also in cases where the NAMMDR was not a stakeholder, were promptly answered.

14.2. Legal activity

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

14.2.1 3 drafts for Law/Government emergency ordinance/ Government Decision, namely:

1) Draft Government Emergency Ordinance for amendment and supplementation of Law 134/2019 on reorganisation of the National Agency for Medicines and Medical Devices and

amendment of further ruling provisions, as well as for amendment and supplementation of certain ruling provisions, pending approval, which was elaborated considering the fact that:

- Amendment and supplementation of some provisions of Law 134/2019 were proposed, namely by completion of the field of activity with the activities regarding the authorisation of clinical investigations for medical devices, the evaluation of performance of in vitro diagnostic medical devices, the authorisation of clinical trials for medicinal products for human use and the monitoring of the safety of medicinal products for human use through pharmacovigilance, as well as the clarification of some aspects regarding the organisational structure;

- it is necessary to complete the field of activity of the NAMMDR regarding issuance of the free sale certificate for medical devices, in accordance with the provisions 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) 178/2002 and Regulation (EC) 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC, which apply from May 26, 2021;

- Article 4 (3) point 7 of Law 134/2019 must be correlated with the provisions of Chapter X of Law 95/2006, which regulates the field of pharmacovigilance;

- Under Article 4 (2) of Law no. 134/2019, new attributions were introduced in the field of pharmaceutical inspection, for correlation with provisions of Order of the Minister of Health no. 775/2019 on the registration of manufacturers, importers and distributors of active substances to be used as raw materials for medicinal products for human use, Order of the Minister of Health no. 1032/2011 regarding the approval of the "Norms regarding the donations of medicines, medical equipment, medical devices, vaccine, serums and corresponding supplies and of Article 875 of Law 95/2006;

- The NAMMDR does not have the status of wholesale distributor of medicinal products and does not intervene in the commercial activity in the pharmaceutical industry and it is necessary to amend Article 804 (23) of Law 95/2006 and accordingly of Article 4 (3) point 34 of Law 134/2019;

- The NAMMDR is one of the actors registered in the internal market information system – IMI established by the European Commission at national level with responsibilities in the field of medicinal products for human use and it is necessary to complete the attributions

regarding administrative cooperation with competent authorities of the Member States, concerning provision of services in the field of the medicinal product for human use, through the Ministry of Health and the IMI system;

- the advertising of medical devices is not currently regulated in the national legislation, and it is regulated by the provisions of Article 7 of Regulation (EU) 2017/745 on medical devices, at community level, therefore this activity must be introduced in Law 134/2019 and correlated with the provisions of the Regulation for organisation and operation of the NAMMDR approved by Order of the Minister of Health no. 1522/2019;

- As regards the appropriate measures that the NAMMDR may take in line with Article 5 of Law 134/2019, the correlation of these provisions with the NAMMDR field of activity (which is exclusively in the field of medicinal products for human use and medical devices and does not consider any product intended for human consumption) is required;

- In order to streamline the activity, an important aspect to be regulated by this draft regulatory act is the possibility of delegating the attribution of tertiary credit accountant, executive powers and representation for one of the two NAMMDR vice-presidents;

- Upon entry into force of Law 134/2019, the NAMMDR scientific council could not meet since 2019, because its composition could not be approved through Order of the Minister of Health, due to the fact that Law 134/2019 contains a legislative inadvertence, namely certain structures/organisations mentioned in it should have appointed members for the Scientific Council, however these structures/organisations do not actually exist. Thus, amendment of Article 11 (1) is urgently needed, as the NAMMDR Scientific Council cannot be legally constituted following introduction of unidentifiable entities in Law 134/2019, such as the Association of Deans of Romanian Faculties of Pharmacy, and it is necessary to return to the previous form regulated by Government Decision no. 734/2010.

- Amendment and supplementation of Article 18 (3) of Law 134/2019 is required in order to ensure clarity and fairness of the legal norm and in order to be able to establish the way of establishing and granting financial incentives in a concrete, objective, non-discriminatory and transparent manner.

- It is necessary to repeal Article 20 of Law 134/2019 on medicinal products for human use, given the fact that Law no. 95/2006 already contains regulations in this sense. The main

safety monitoring activities are: reporting/management/assessment of adverse reactions, PSUR assessment, detection of safety signals, PASS assessment. Following assessment of pharmacovigilance data, the marketing authorisation may be suspended or withdrawn; the use of medicinal products with an unfavourable benefit-risk balance which may compromise patients' health and/or safety may be prohibited.

As regards medical devices, the legislation in force allows "appropriate measures for the withdrawal, prohibition and/or restriction of placement on the market of any product intended for human consumption which may compromise the health and / or safety of consumers" (namely Law 95/2006, Government Decision no. 54/2009 on the conditions for placing on the market medical devices, Government Decision no. 55/2009 on active implantable medical devices and Government Decision no. 798/2003 establishing the conditions for marketing and use of in vitro diagnostic medical devices.

- in order to fulfil the NAMMDR mission, namely authorisation, supervision and control of the medicinal product and medical device market, emergency legislative intervention is needed in order to clarify the terms used in Romania by returning to "medical devices" and replacing "medical devices, technologies and assistive devices" of Title XX of Law 95/2006 with "medical devices".

The amendment is required to align with the definition of medical devices regulated by the provisions of Article 2 (1) of Regulation (EU) 2017/745 of the European Parliament and of the Council.

- Marketing Authorisation Holders cannot be sanctioned for noncompliance with Art. 823 of Law 95/2006 when it is found that they distribute advertising materials intended for the general public without prior approval of the NAMMDR. This sanction was regulated until 22.02.2018, when it was abrogated by provisions of Emergency Ordinance no. 8/2018 on regulation of certain health measures.

Moreover, numerous cases of breaches of the legal provisions on advertising presented through social networks or mobile applications to the general public have been identified, which cannot be sanctioned in the absence of a regulated legal framework.

- the draft law proposes to regulate the approval of the activity of marketing a medical device offered through the services of the information society, a situation which is not currently regulated by a normative act.

2) The Draft Government Decision laying down measures to ensure the 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, which provides the necessary legal framework for application of provisions of Regulation (EU) 2017/745 and aligns the rules applicable to medical devices with the the new European legislative framework, so that, by repealing Government Decision no. 54/2009 and the Government Decision no. 55/2009:

- provisions have been introduced in order to ensure transparency and traceability of medical devices, in order to improve health and safety;

- there will no longer be the obligation to make available the instructions for use in Romanian, together with the medical device;

- the aspect regarding the language in which the information provided by the equipment interface with the user is clarified, as part of a software system;

- the obligation of healthcare units regarding the implant card is regulated;

- the issuance of the free sale certificate is regulated;

- the manufacturing process of medical devices in healthcare facilities, for personal use, is regulated;

- the advertising of medical devices is regulated;

- the contraventions and sanctions applicable in case of noncompliance with the provisions of Regulation (EU) 2017/745 and of this normative act are regulated.

3) Draft Government Emergency Ordinance to amend and supplement Law 287/2009 regarding the Civil Code, which was taken over at the Article of Government Emergency Ordinance no. 70/2020 regarding the regulation of some measures, starting with 15 May 2020, in the context of the epidemiological situation determined by the spread of the SARS-CoV-2 coronavirus, for extension of some deadlines, amendment and completion of Law 227/2015

regarding the Fiscal Code, National Education Law 1/2011, and of other normative acts, by which it was proposed that:

- the donation of medicinal products, healthcare supplies, medical devices, vaccines, serums and related consumables should no longer end in an authentic document, so that they can be immediately made available to those who need them most, at minimal costs, in the context of the COVID-19 pandemic.

14.2.2. 7 Minister of Health Order drafts:

1) The draft Order on approval of Methodological norms for enforcement of Title XX of Law. 95/2006 on healthcare reform regarding approval of activities in the field of medical devices, published in the Official Gazette, Part I no. 293 of 8 April 2020 (Order of the Minister of Health no. 566/2020), which regulates issues related to:

- the general criteria for evaluating the competence and capacity of economic operators to carry out the activities for which they request the approval provided in Article 926 (2) of Law 95/2006 on healthcare reform, republished, as amended;

- the definition of economic operators, i.e. producers, distributors and importers, their obligations, as well as supply and maintenance, in accordance with the definitions set out in Regulation (EU) 2017/745 of the European Parliament and of the Council, in order to make clear the general obligations of various economic operators, in order to improve in accordance with the regulations among relevant operators and to prove that Romania, as an EU Member State, has taken all necessary measures to ensure that the provisions of the Regulation are implemented;

- the introduction of the 3-year validity period for operation approvals, in favour of the economic operators and in order to facilitate the keeping of records of the units approved by the NAMMDR;

- elimination of assessment at the economic operator's premises, as the economic operator is not active at the time of approval. The assessment for approval will be carried out on the basis of the documents and declarations submitted, following which these economic operators will be subject to unannounced controls. Thus, operation approvals will be granted within a reasonable time and we demonstrate compliance with provisions of Article 114 of the Treaty

on the Functioning of the European Union (TFEU), by implementing the provisions of the two Regulations harmonising the rules for placing on the market and commissioning of medical devices and related accessories on the EU market, enabling them to benefit from the principle of free movement of goods;

- strengthening the market surveillance service, which will lead to an increase in the amounts to be paid to the state budget as fines and at the same time ensure a high level of protection of public interests, such as general health and safety, health and safety in the workplace, consumer protection;

- issuance of a temporary emergency operating notice valid for a maximum period of 6 months.

2) The draft order regarding the amendment and supplementation of the Annex to Order of the Minister of Health no. 85/2013 on approval of the Norms for application of the provisions of Article 703 (1) and (2) of Law 95/2006 on healthcare reform regarding medicinal products used to solve special needs published in the Official Gazette no. 286 of April 6, 2020 (Order of the Minister of Health no. 561/2020), with express regulations regarding:

- issuance of a special needs authorisation under derogating conditions, for the situation provided under Article 703 (2) of Law 95/2006 on healthcare reform, republished, with subsequent amendments and completions, taking into account the pandemic declared by the World Health Organisation on March 11, 2020, for medicinal products without a marketing authorisation in Romania and which are necessary in the event of a suspicion of an epidemic or in case of a confirmed epidemic with pathogens, toxins, as well as in case of a suspicion of spread or confirmed spread of chemical agents or nuclear radiation that could endanger the health of the population;

- Issuance of a special needs authorisation for a medicinal product in addition to the approved therapeutic indications for that medicinal product, in its country of origin.

3) The draft order regarding the amendment and supplementation of Order of the Minister of Health no. 1032/2011 on approval of the Norms regarding the donations of medicinal products, sanitary materials, medical devices, vaccines, serums and related consumables, published in the Official Gazette no. 306 of 13 April 2020 (Order of the Minister of Health no. 615/2020), which regulated issues related to:

- the possibility of accepting as donations in healthcare facilities: medicinal products, vaccines and sera required for the treatment of COVID-19, authorised for marketing in third countries with which the European Union has concluded mutual recognition agreements (MRAs) and Canada, Australia, Switzerland, New Zealand, Israel and Japan;

- acceptance of waiver from the shelf life of donated medicinal products, vaccines and sera for the treatment of COVID-19, which may be less than 8 months from the date of request of an approval for donation, provided that these are used within the shelf life of the product;

- exemption of donated medicinal products from assessment of safety features in accordance with Commission Delegated Regulation (EU) 2016/161 of 2 October 2015 supplementing Directive 2001/83/EC of the European Parliament and of the Council by laying down detailed rules for safety features printed on the packaging of medicinal products for human use;

- acceptance as donations in healthcare facilities of medical devices used in the context of the COVID-19 epidemic for which compliance assessment procedures, including affixing of the CE marking, have not been fully completed in accordance with the applicable regulations, provided that these offer an adequate level of safeguard of health and safety of users, and that their compliance assessment procedures do not involve the intervention of a body carrying out compliance assessment activities as a third party, based on the donor's statutory declaration.

4) The draft order for supplementation of Order of the Minister of Health no. 1009/2016 regarding the registration of medical devices into the national database, published in the Official Gazette no. 267 of 31 March 2020 (Order of the Minister of Health no. 537/2020), whose adoption was necessary in view of the following aspects:

- making available to healthcare facilities, medical staff, patients, users of medical devices ensuring prevention and treatment of diseases triggered in the context of the state of emergency (masks, gowns, filter suits, fans);

- the exemption from the obligation to register in the national database at the time of placement on the market of the aforementioned medical devices, during the state of emergency, and from the obligation to register them into the national database after commissioning, during the state of emergency.

5) The draft order regarding the amendment and supplementation of Order of the Minister of Health no. 861/2014 for approval of criteria and methodology for assessment of health technologies, of documentation to be submitted by applicants, methodological means used in the assessment for inclusion, extension of indications, non-inclusion into or exclusion from the List of International Non-proprietary Names of on-prescription medicinal products as provided to insurants, irrespective of personal contribution, 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, as well as the means for appeal thereof, published in the Official Gazette No. 687 of July 31, 2020 (Order of the Minister of Health No. 1353/2020), which regulated the following issues:

- the phrase "comparator" has been changed by removal of the criterion of "the same pharmacodynamic properties" from the definition of the comparator;

- in order to ensure that patients have access to as many therapeutic alternatives as possible and to enable marketing authorisation holders to submit evaluation dossiers for medicinal products comparing medicinal products corresponding to Ω-rated INNs performed on the basis of concluded cost-volume contracts, the possibility to use as a comparator a medicinal product in cost-volume/cost-volume-result, which at the end of the evaluation will be able to obtain a conditional inclusion at most, was introduced. Thus, a product already reimbursed on the basis of cost-volume or cost-volume-result contracts can be considered as a comparator exclusively by comparing the prices available in CANAMED at the time of submission of the evaluation file. If the comparator is a product compensated on the basis of a cost-volume or cost-volume-result contract, the medicinal product subject to evaluation will be able to benefit from conditional compensation at most, even if the final score obtained as a result of the evaluation process would allow unconditional inclusion;

- the notation with (**) in point p) of Article 1 of Annex 1 to the Order, as it was missing from the previous regulatory act;

- a separate evaluation procedure has been introduced for generics without an INN reimbursed in the List, and for biosimilars without an INN reimbursed in the List and for which the holder of the original marketing authorisation has not shown the intention to submit the documentation for evaluation on inclusion, extension of indications, non-inclusion or exclusion

of medicinal products in/from the List. This criterion is beneficial in order to facilitate the access of patients in Romania to innovative therapies to an equal extent with patients in the European Union;

- if a medicinal product is already reimbursed on a strength, a new strength / pharmaceutical form has been added to the List, which is the most accessible and eloquent comparator;

- the withdrawal of the INN from the List is regulated in case a decision has been received to withdraw the marketing authorisation or for which the specialised commissions from the Ministry of Health have informed the NAMMDR that there is no therapeutic benefit based on the analysis of the existing documentation at European level or the INN is no longer recommended in international or national clinical guidelines, as appropriate;

- the possibility of obtaining the 45 points was added, if the clinical studies related to the medicinal product to be evaluated were carried out in Romania or if the proof of notification of a non-interventional study for the collection of real data on the indication submitted for evaluation is brought to the NAMMDR. From a financial viewpoint, it was considered in this respect that the free access of patients to the medicinal product under evaluation for a certain period of time can be equivalent to the cumulative score of the evaluation reports related to the 3 countries present in the regulatory act;

- the advanced therapy medicinal product was introduced, in addition to the orphan designation medicinal product and, as defined in Article 2 of Regulation (EC) no. 1394/2007 of the European Parliament and of the Council of 13 November 2007 on advanced therapy medicinal products, amending Directive 2001/83/EC and Regulation (EC) no. 726/2004 and the Directive of the European Parliament and of the Council of 6 November 2001 establishing a Community code relating to medicinal products for human use, as they constitute one of the most relevant therapeutic progresses in recent years which provide Romanian patients access to a treatment similar to the treatment received by patients from other European Union countries;

- the possibility of accumulating the 10 points and granting the unconditional inclusion resolution was introduced, in order to stimulate the pharmaceutical industry to access the procedures for medicinal product donations, last resort treatments and clinical trials, only if the

marketing authorisation holder proves the ensurance of a treatment with a medicinal product donated for a period of at least 12 months, on the indication submitted for at least 50% of the population eligible for treatment;

- under point 4.1 of Table no. 7, the phrase "paediatric patients aged between 0 and 12 months" was added. Thus, by introducing this criterion, 10 points are obtained by this population segment, so as to allow faster access to innovative treatments to the paediatric population segment when there is no therapeutic alternative in the evaluated indication;

- under point 4.2 Table no. 7, the score was introduced both for increasing the survival by 3 months as well as for inducing remission or stopping the evolution of the disease for a period longer than 3 months. This criterion will also facilitate access to treatment for categories of patients who, although not suffering from a cancerous condition, suffering from a rare pathology or causing irreducible deterioration of life with a single therapeutic alternative;

- point 4.3 of Annex no. 1 to the Order was amended so that a medicinal product enters unconditional inclusion only when it meets 2 or 3 cumulative criteria in line with Table no. 7 point 4;

- point 21 was introduced in Annex 2 section I letter A, after point 2, because the methodology in force does not stipulate what happens to generics/biosimilars after expiry of the patent/data exclusivity/certificate of protection of the innovating medicinal product; since these meet the conditions for marketing in Romania, the authorities must ensure the continuity of patients' treatment;

- the phrase “medical technology assessment report” has been replaced with “notification” motivated by the fact that, at this stage of the assessment, the issuance of a report is not justified, only a notification on completion of documents being required;

- two new points, points 8 and 9, are introduced in Annex 2 to the Order, after point 7 of letter B of Section I, regulating the case where, for the same indication mentioned in the SmPC, at the time of submission of the documentation for assessment, a medicinal product for a new INN or a medicinal product extension of indication, for which the documentation has been submitted for assessment in Table no. 4, 41 or 7, is administered in two or more therapeutic schemes or in two or more treatment lines on the same indication and the same population segment/subgroup, in which case the decision of unconditional inclusion is issued only if for

all therapeutic schemes/treatment lines corresponding to that indication obtain the necessary score for unconditional admission in the List;

- In order to ensure adequate protection of patients' right to life, for assessment applications submitted before entry into force of the new regulatory act, unresolved by issuance of a decision on the inclusion, non-inclusion, addition, removal or exclusion of medicinal products in/from the List, if the provisions of this Order are more favourable, the MAH may opt, by submitting a request to the NAMMDR, for the resolution of the respective application according to the provisions of the new regulatory act.

6) The draft Order on 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 and on repeal of Order of the Minister of Health no. 1203/2006 on approval of the National Medicines Agency procedure for cancellation of marketing authorisation applications for medicinal products for human use, in decision-making transparency on 24.09.2020 on the website of the Ministry of Health, pending approval, proposing the following amendments:

- harmonisation of the marketing authorisation renewal through national procedure with the mutual recognition/decentralised procedure, by applying the Coordination Group Guideline for renewal procedures through MRP/DCP (edition in force at the time of evaluation of the application) for the submitted renewal applications in the national procedure, which will allow the shortening of their evaluation periods as a result of:

a) the possibility of submitting a reduced clinical documentation in the case of medicinal products authorised in line with Articles 709, 718 of Law no. 95/2006, for medicinal products for which there is no obligation to submit PSURs (Periodic Safety Update Reports);

b) the possibility of renewal through a short 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), under the circumstances stipulated by this Guideline;

- shortening the evaluation period for marketing authorisation applications submitted through national procedure by introducing deadlines for responding to NAMMDR requests in line with the decentralised procedure.

7) Draft Order on approval of the Conditions for authorisation for use of an unauthorised medicinal product for human use in order to be made available to a group of patients for use in last resort treatments or to facilitate patients' access to last resort treatments, submitted by the Ministry of Health through notifications no. 42875E/21.04.2020, no. 42875E/12.06.2020 and 43875 23.06.2020, currently undergoing approval, in which issues related to the following have been regulated:

- the designation of the NAMMDR as the competent authority for evaluation and authorisation of an unauthorised medicinal product for human use in order to be made available to a group of patients for use in last resort treatments or to facilitate patients' access to last resort treatments;
- the medicinal product for which an authorisation for use in last resort treatments is requested, for a group of patients, must be subject to a marketing authorisation application through centralised procedure or to be included in the clinical trial stage, where the effectiveness and safety of administration according to the proposed use in at least one of the EU Member States or in the United States of America have been demonstrated;
- the information and documents to be submitted by the manufacturing company to the NAMMDR headquarters for authorisation of the medicinal product for which the authorisation is requested for use in last resort treatments are specified, as well as the obligations of the manufacturing company after the authorisation was issued;
- the procedure for issuance of a recommendation from the specialised commission of the Ministry of Health on appropriateness of using the medicinal product for which an authorisation is sought as a last resort (when there is no CHMP approval for use of that product as a last resort treatment or positive opinion for its marketing authorisation) was issued;
- the validity of the authorisation for use of a medicinal product for human use as a last resort treatment from date of issuance to completion of the treatment of the last patient or until its effective marketing in Romania is mentioned.

In 2020, the Directorate for Legal, European affairs and international relations prepared, together with the specialised technical directorates of the NAMMDR, the instructions and negotiating mandates in the field of medicinal products for human use, the assessment of medical technologies and medical devices for regulations concerning:

- the proposal for a Regulation of the European Parliament and of the Council amending Regulation (EU) 2017/745 on medical devices as regards the dates of application of certain provisions thereof;

- the proposal for a Regulation of the European Parliament and of the Council on conduct of clinical trials and supply of medicinal products for human use containing genetically modified organisms or consisting of genetically modified organisms intended for treatment/prevention of COVID-19;

- the proposal for a Regulation of the European Parliament and of the Council on the assessment of medical technologies in the field of health, amending Directive 2011/24 EU;

- the draft Pharmaceutical Strategy for Europe, actively participating in the discussions addressed by the Strategy's initiatives, supported the ensurance of the availability of innovative and affordable medicinal products for patients, as well as the competitiveness, innovation capacity and sustainability of the pharmaceutical industry in Romania and the European Union.

The possibility of creating levers similar to the mechanisms implemented by EU Member States, following a unitary and common approach, in the context of a no-deal scenario, and without an agreed transition period, was also examined. In this regard, the NAMMDR approach to minimising the negative impact on the field of medicinal products, including avoidance of issues related to the availability of medicinal products on the market, as well as on the field of medical devices, was sent to the Ministry of Foreign Affairs, through the Ministry of Health.

At the same time, an approximate number of: 511 petitions, 156 requests for information of public interest and 366 external addresses were analysed and resolved by the Legal and International Relations Directorate.

15. Management of human resources and quality management

15.1. Assuring human resources to NAMMD structures

Staff-related activities carried out in 2020 were carried out within a continuous process of analysis of the institution’s human resources needs, of elaboration of staff strategies and policies, in accordance with long-term objectives and efficiency of the organisation. The NAMMDR job title list was drawn up and the documentation/correspondence to the Ministry

of Health regarding amendment of the job title list, transformation of the job structure, 24 Decisions on appointment, release/termination, suspension, promotion, secondment, reassignment, transfer, relocation and to modify the service/work relations for the NAMMDR staff, Decisions for appointment and dismissal of the members of the commissions were drawn up, professional files of the employees were drawn up and the NAMMDR Code of Conduct was updated.

As a result of the epidemiological context declared at national level, preventive measures were taken within the NAMMDR in order to eliminate the risks and vulnerabilities generated by the COVID-19 coronavirus epidemic.

Thus, the competition for filling the vacant contractual positions was postponed, for an indefinite period of time, in accordance with the provisions of Government Ordinance no. 286/2011 with further amendments and completions, according to the announcement published in the Official Gazette, Part II, of 02.03.2020.

Jobs issued according to Emergency Government Ordinance no. 40 of 2 April 2020, for a determined period - April 2020:

Total number of jobs	Total number of candidates	Selection of dossiers		
		Admitted	Rejected	Withdrawn
39	43	29	13	1
Total number of candidates for interview	Admitted	Employment denied	Rejected	Absentees
29	18	1	7	3
Total number of employed candidates	17			

Occupation without exam of vacant or temporarily vacant positions for the period determined in line with Order of the Minister of Health no. 905/26.05.2020 based on Article 11 of Law 55/2020:

Total number of jobs	Registered candidates	Candidates rejected following the selection of files	Candidates admitted following the selection of files	Candidates rejected following the interview	Candidates admitted following the interview	Total number of admitted candidates
33	20	9	11	1	1	10 (1 has resigned)

Occupation without exam of vacant or temporarily vacant positions for a period determined according to the provisions of Art. 9 of Order of the Minister of Health no. 1839/30.10.2021 regarding the amendments of Order of the Minister of Health no. 905/26.05.2020 based on Art. 11 of Law 55/2020:

Total number of jobs	Registered candidates	Candidates rejected following the selection of files	Candidates admitted following the selection of files	Candidates rejected following the interview	Candidates admitted following the interview	Total number of admitted candidates
5	10	4	6	3	1	3

In 2020, decisions were drawn up regarding the appointment, release/termination, suspension, promotion, secondment, reassignment, transfer, relocation and amendment of service/work relationships of the NAMMDR staff. 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 performed and the IT procedures regarding the Remuneration application within the Softech programme were updated, according to the legislation in force. Also concerning the assurance of the rights of NAMMDR employees according to the law, the documentation required for issuance of holiday vouchers for its staff was prepared.

As regards the evaluation of employee performance, advice was provided on the evaluation of the professional performance of the NAMMDR contract staff. The records of job descriptions and the individual professional performance evaluation sheets of the employed staff and of the job descriptions prepared, in line with the law, were monitored by the responsible persons and the NAMMDR structures received advice on how to prepare

these documents.

In accordance with its obligations by law, the DRUMC has contributed to achievement of transparency of NAMMDR activities, by registering and preparing 79 wealth declarations and 77 declarations of interests of employees with positions of responsibility for publication on the institution's website, in a consistent manner and in line with the deadlines established.

15.2. Human resources development through training and improvement of employees

Considering the particularly rapid dynamics of the medicinal product field, in general, and the need to regulate the scope of medicinal product development, its authorisation and monitoring its evolution on the market in terms of efficacy and safety, a high level of competence is required from NAMMDR specialists, whose realization 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 internal training nationally or internationally by various authorities and bodies.

Moreover, in the field of professional training of the staff, in addition to stimulating, facilitating and monitoring staff participation in identified training opportunities, documentation was prepared for acquisition of training services, services on training programmes for employees. The development of individual employment contracts and additional documents for contract staff of the institution was prepared and monitored in line with the law and was registered in the register of employees according to the provisions in force.

As regards other activities of the Human Resources and Payroll Department/The Payroll Service, the department was permanently concerned with preparation of documentation for termination of individual employment contract/ secondment/retirement/ promotion, drafting 490 addenda to individual employment contracts.

15.3. Quality Assurance and Registry Service

In 2020, the specific objectives of the SACR were maintained, derived from the general objectives of the NAMMDR. In order to achieve the specific objectives, the actions and activities of the SACR were identified through elaboration of the SACR Activity Programme for 2020 and its periodical update.

Specialized assistance was provided to the persons responsible for quality assurance in the NAMMDR organisational structures, in order to comply with quality management requirements, by methodological coordination of their activities in the field of the SMC.

Considering the pharmacovigilance legislation establishing the legal obligation for competent authorities of Member States to carry out audits of their own pharmacovigilance systems [Law 95/2006 on healthcare reform, transposing Directive 2001/83/EC (L 95/2006) Art. 812 (2), Art. 815 (2), Regulation (EC) 726/2004 (REG) Art. 28f], including risk-based audits of the respective quality systems (European Commission Implementing Regulation (EU) No. 520/2012 (IR) Art. 13(1), Art. 17(1)), as well as the obligation of competent authorities of the Member States to report the outcomes of audits of their pharmacovigilance systems to the Commission on 21 September 2013 at the latest, and every two years thereafter (Law 95/2006 Art. 812(2)), upon written request of the DFVMR Coordinator, the decision for appointment of an internal auditor to meet the specified requirements and to perform audits of the NAMMDR pharmacovigilance system was issued, an activity which has been planned for year 2020. In this regard, the report was sent to the European Commission (Health and Food Safety Directorate-General, Health systems, medical products and innovations Medicines: policy, authorisation and monitoring, Pharmaceutical Committee).

In 2020, no complaints were received related to the activity of the SACR or other NAMMDR structures to determine the transfer of corrective or improvement actions established as a result of dealing with a complaint within the SMC action system.

External documents relevant to the activity of the SACR and the implementation of the SMC at NAMMDR level, such as guidelines of certain organisations/authorities (the ISO, WHO, EMA, EDQM etc.) and publications (books, etc.) are kept under control within the SACR.

In 2020, the NAMMDR Quality Manual (MC) elaborated in 2018, together with the NAMMDR Quality Policy and quality objectives, as annexes to the quality manual, remained in force.

In order to ensure a unitary and coherent system for documentation of all procedures throughout the entire institution, the NAMMDR management maintained and supported the

integration of the two systems, SMC (quality management system) and SCIM (internal management control system), by elaboration of a single template of procedure (PS-09/01-Management of procedures, in force).

The model was developed by the SACR and endorsed by the SCIM Monitoring Commission. After approval, it became mandatory for all system procedures (PS) and operational procedures (OP) developed within the NAMMDR.

The process of keeping under control (elaboration, revision, amendment, distribution) of system and operational procedures was integrated into the activity of the Technical Secretariat of the SCIM Monitoring Commission provided by the SACR staff. Thus, the following activities were performed:

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

- the analysis of the documented procedures, from the viewpoint of observance of compliance with the minimal structure provided in the model presented in SGG Order no. 600/2018 supplemented with the requirements from the NAMMDR system procedure regarding procedure management, the version in force (109-PO/2020);

- submission for analysis of system procedures to commission members;

- keeping the original copies of system procedures (37 PS at the end of 2020);

- dissemination of existing versions of system procedures to NAMMDR employees, making sure that these are available or can be easily accessed on the intranet server;

- withdrawal of cancelled versions of the SP and archiving in order to prevent unintentional use of obsolete procedures (3);

- keeping up to date records of all PS and PO within the NAMMDR.

At the level of organisational structures, the NAMMDR continued the process of reviewing/updating the procedures for transposition of all procedures into the new unitary format, however, the achievement of this objective was affected by several internal and external factors (specificity/complexity of each organisational structure, large volume of specific procedures dedicated to each organisational structure, atypical review mode, risk of delaying main/current activities by blocking the staff involved in reviewing procedures, lack/fluctuation of human resources).

236 procedures (37 PS and 199 PO + IL) were transposed according to the new unitary model in 2020.

In 2020, 3 PS were withdrawn and transformed into PO (PO-DEAP/20; PO-DEAP-21; PO-DEAP-22), namely 111 PO were transposed according to the new unitary model.

The SACR-CACEI staff participated in updating the operational procedures (PO) and transposing the related forms/annexes/flow charts for NAMMDR departments according to the new model.

In 2020, keeping records/information documented in the SACR under control has been significantly maintained and improved by transition from written records (paper records) to electronic records. The issuance, storage and archiving of documents prepared within the SACR is performed according to a system procedure. Within the Registry and Archive Department, numerous activities were carried out, such as receipt, registration, distribution and archiving of documents/records received or sent.

In 2020, within the SACR, the record of all NAMMDR standards was updated.

In 2020, only self-training was conducted.

In 2020, the SACR made sure that the record of all standards within the NAMMDR was updated.

Self-training was the only type of training conducted in 2020.

Regarding the participations in the HMA Working Group of Quality Managers (WGQM), 2 online trainings took place, with the participation of the head of the SACR.

No external audits took place in 2020, but non-compliances and recommendations following the external audits carried out in previous years remained in the SMC's action system.

The specific risk management activities were carried out, in coordination with the SCIM Monitoring Commission, according to OSGG 600/2018, by nominating a responsible person for risk identification, assessment and management and for updating the Risk Register and associated annexes for 2020.

The assessment of the SCIM implementation stage was performed by completion of the Self-assessment Questionnaire, according to OSGG 600/2018.

The SACR ensures the attributions of the Technical Secretariat of the SCIM Monitoring Commission (CM), established in line with OSGG 600/2018, according to the decision of the NAMMDR President regarding the setup of the SCIM Monitoring Commission and the Commission's ROF.

Thus, in 2020, activities were carried out related to: updating the Decision for setup of the Monitoring Commission, following vacancy, with the support of the DRUMC-SPS; preparation of documents for support, organisation and elaboration of the minutes of the commission meetings; keeping under control the system (PS) and operational (PO) procedures by allocating PS codes, as well as coordination of allocation of PO codes within all NAMMDR organisational structures; analysis of the documented procedures, from viewpoint of the observance of compliance with the minimal structure provided in the model shown in OSGG no. 600/2018, supplemented with the requirements of the NAMMDR system procedure (PS-09/01-Management of procedures) in force; dissemination of existing versions of the PS and ensuring that these are available or can be easily accessed on the intranet server; keeping up to date the record of all PS and PO within the NAMMDR, on the intranet server in the special section created with the support of the STIC; centralisation of the self-assessment questionnaires of the implementation stage of the internal managerial control standards completed by each structure from the NAMMDR organisation chart in order to prepare the Synthetic situation of self-assessment results elaborated according to Annex 4.2 to the code approved through OSGG 600/2018 and the Centralising Situation regarding the stage of implementation and development of the internal managerial control system on December 31, elaborated according to Annex 3 to the code approved through OSGG 600/2018; drafting of the Report on the internal managerial control system on December 31, elaborated in line with Annex 4.3 to the Instructions of OSGG 600/2018 and transmission to the Ministry of Health, upon request, together with the Centralising Situation regarding the stage of implementation and development of the internal managerial control system on December 31, elaborated in line with Annex 3 to the code approved through OSGG 600/2018; participation in the elaboration of the project of the SCIM Development Programme for the NAMMDR in order to present the members of the commission for debate; participation in the elaboration of the draft Plan of

continuity of activities based on the information partially received from some organisational structures, in order to present the members of the commission for debate.

In 2020, the BAI request was answered by completion of the measures in the document entitled "Status of implementation of proposals for measures to take in order to optimise the activity", developed by the Quality Assurance and Registry Service (SACR) within the Directorate of Human Resources and Quality Management (DRUMC).

At the same time, the NAMMDR Register of sensitive positions for year 2020 was elaborated, namely the NAMMDR List of high-risk sensitive positions for year 2020 (for 270 positions/persons employed/2020).

The legal attributions specific to Occupational Safety and Health (OSH) have been fulfilled by:

- conducting regular training for the SACR staff, based on the OSH (Semestrial) Training Topic and training/self-training according to the measures imposed at the workplace on combating the COVID-19 pandemic (disinfection of premises, wearing a mask, physical distancing, postponement of the program, working from home, restricting direct contact with the public, etc.).

The legal attributions specific to PSI and emergency situations (SU) were fulfilled by conducting regular training for the SACR staff.

16. Economic activity

The Directorate for Economy and Public Procurement operates under the direct subordination of the NAMMDR President, being composed of the Economic and Public Procurement Directorate, the Procurement Department and the Financial Budget Accounting Service.

The activity of the Financial Budget Accounting Service mainly consisted of substantiation and implementation of draft budget, management of the approved budget with payments situated within the stipulated limits as well as in transferring budget credits according to the needs of the institution. In 2020, the approved budget was also entered in the Forexebug IT system, and all subsequent changes were made based on the transfers

approved by the chief credit ordinator, as well as all budgetary and legal commitments approved within the institution.

Following reorganisation of the NAMMDR, capital expenses amounting to 7,413,000 lei were approved.

Out of the approved budget, the NAMMDR has made capital expenses, as follows:

Machines, equipment required for the control and inspection activity	1,272,532.44
Other fixed assets software	15,363.58
Access control and video surveillance system, for access into laboratories at the NAMMDR headquarters	36,402.10
Total general	**1,324,298.12**

The execution of 2020 was below the level requested by the NAMMDR, mainly due to the existing epidemiological context at national and international level which has limited external travel, employment and the inability of external suppliers to deliver the requested goods.

The NAMMDR final budget without subsidies, approved for 2020, amounted to 69,413,000 lei.

- Budget credits for staff expenses: 54,459,000 lei;
- Budget credits for expenses for goods and services: 7,121,000 lei;
- Budget credits for investment expenses: 7,413,000 lei.

On 31.12.2020, the balance sheet ends with a surplus amounting to 105,940,913.75 lei, the actual expenses amounting to 34,636,000.92 lei and the total revenues to 140,576,914.67 lei, of which: income from exchange rate differences - 6,006,942.16 lei, operating income - 92,888,043.55 lei and income, goods and services received free of charge - 2,470 lei, interest income - 0.33 lei and income from provisions - 41,679. 458.63 lei.

At the end of 2020, the NAMMDR had a surplus of 63,402,176.20 lei.

Receipts: 93,983,524.94 lei.

The value of the actual budgetary expenses of 2020, according to the published budget execution, amounted to 30,581,348.74 lei, of which:

Actual staff costs	27.347.451,75
Amounts for disabled persons not included who have not been granted a disability degree	233.240
Actual expenditure for goods and services	1.865.107,35
Actual capital expenses	1.324.29,12

According to the budget execution for 2020, the total amount of budget expenditure represents 44% of the approved budget, of which:

- the value of staff expenses represents 50.21% of the budget approved for this category;

- the value of expenses for goods and services represents 26.19% of the budget approved for this category;

- the value of capital expenses represents 17.86% of the budget approved for this category.

All expenses were included in the budget approved for 2020, in compliance with legal economic and financial provisions.

In 2020, the following attributions and responsibilities were fulfilled within the Public procurement Department: elaboration, amendment and updating of the “Annual Public Procurement Program - 2020” based on the requirements specified in purchase requisitions, prepared by NAMMDR directorates; centralisation of annual purchase requisitions elaborated and transmitted by NAMMDR directorates; elaboration of the “Annual program of public procurements - year 2021” project; preparation of the required documentation for conclusion of public procurement contracts for products/services/works; direct purchases from the SEAP/SICAP catalog; ensurance, setup and storage of public procurement files for products, services and works; fulfilment of the obligations regarding advertising (publication in SEAP of initiation of acquisitions by direct purchase from the SEAP electronic catalogue, designation notifications, advertisements, market consultation notifications); market

prospecting and consultation of the SEAP/SICAP catalogue in order to determine the estimated value and make purchases; undertaking the necessary steps in order to make the acquisitions related to internal and external travel requested by NAMMDR employees; preparation of the documents required for the return of participation/good execution guarantees; preparation of reports for appointment of assessment commissions and commissions for receipt of purchased services /works, collaboration with all NAMMDR organisational structures depending on the type and complexity of the procurement object and collaboration with external suppliers on procurement requested.

17. General administration

In 2020, the General Administration Directorate fulfilled its specific attributions as provided in the Regulation for Organisation and Operation and in the specific Job Description for each employee:

- administrative activities (organisation and provision of support services required for proper performance of the activity within the Organisation, maintenance of the NAMMDR infrastructure, cleaning, carrying out handling and transport of goods from the NAMMDR, insurance of transport, monitoring of (motor vehicle) fleet, monitoring the execution of works performed according to public procurement contracts and their reception, monitoring the execution of works performed on their own, preparation of lease contracts, utility contracts, preparation and updating of operational and system procedures of the department, completion of the register of inventory numbers);

- Setting up (according to the PSI line) the documents for appointment of responsible persons;
- updating procedures;
- ensuring safety of the NAMMDR movable and immovable property;
- courier activity;
- maintenance and repair activity;
- initiation and achievement of the public procurement.

18. Internal audit

In 2020, the Internal Audit Office performed assurance missions that involved objective assessment of evidence by the audit team, in order to formulate opinions or conclusions on the audited structures and activities. The NAMMDR President did not involve the Internal Audit Bureau in carrying out auditable activities.

In 2020, according to the established Audit Plan, 6 assurance audit missions and one ad hoc mission were performed. The degree of accomplishment of the public internal audit plan within the NAMMDR for 2020 was fully achieved.

The findings from internal public audit missions carried out in line with the yearly public internal audit plan established for 2020 can be found in the audit reports prepared for each mission and are signed by the auditors of the audit team and by the NAMMDR management.

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

Thus, the PAIC guarantees the performance of the internal audit activity in accordance with the norms, instructions and the Code on the ethical conduct of the internal auditor, contributes to improvement of the activity of the public internal audit structure, helps to express conclusions on the quality of the internal audit activity, leading to making recommendations for appropriate improvements brought to this activity. It also allows an 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;
- The risks affecting the operation of the internal audit.

In 2020, the Internal Audit Bureau was evaluated by the higher hierarchical body - the Ministry of Health and was not evaluated by the Romanian Court of Accounts.

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

- Internal public audit missions and recommendations made to the audited structures.
- Participation in the risk management process achieved by identifying and tracking risks in order to minimise / eliminate them;
- Informal counselling of the structures from the NAMMDR Organisation Chart.
- Improvement of internal control quality;
- Improvement of the activity of audited structures, materialised through recommendations of internal auditors systematised on the main audited fields;
- Assessment 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 applicable specific legislation in force;
  - Monitoring and achieving the performance indicators established at BAI level.
- Carrying out the activities included in the Work Program for 2020.
- Execution of the Activity Plan for 2021.
- Monitoring the implementation of the measures proposed through Public Internal Audit Reports.
- Auditing all NAMMDR activities and structures every three years.

19. Activity of the Prevention and Protection Service in the field of occupational safety and health (SPPSSM)

In 2020, the SPPSSM carried out the following types of activities:

- participation in the audit action of the sub-fund, in accordance with the internal public audit plan (January - March 2020);

− participation in the identification of hazards and assessment of the risks materialised by elaboration of: SSM's instructions for serious and imminent danger of injury and specific high risk areas; action plan to identify serious and imminent danger; occupational risk exposure sheets; the training theme in the field of occupational safety and health for 2020; regular occupational safety and health training for 2020; general introductory training topics - 2020; occupational safety and health policy - 2020.

In 2020, the Technical Support Group for emergencies generated by the COVID-19 pandemic was established; instructions and training related to the risk of infection with the new coronavirus (COVID-19) were developed, as well as a plan of measures for prevention of contamination with SARS-COV-2.

III. Priorities envisaged for 2021:

All NAMMDR structures have performed a self-assessment of their activity in 2020 and have formulated proposals and priorities for the upcoming 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, will remain the institution’s primary goal.

Thus, the proposals made for streamlining the activity, by various NAMMDR structures, are identified in several priorities for year 2021, among which:

- Supplementation of the staff with specialised staff in order to fulfil the proposed objectives;

- Participation of staff in online professional development courses specific to the activities they perform;

- 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 continuously developing medical-hospital technique;

− Allocating the necessary funds and taking the steps for setup of a functional computer system, similar to a database, with adequate capacity, able to store all monthly reported information related to 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, distributed through wholesale distribution, 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 of medical technologies through the contribution brought to the amendment and completion of legal evaluation criteria.

PRESIDENT,
The National Agency for Medicines and Medical Devices of Romania,
Roxana Ștefania STROE

Annex: List of acronyms used in this Report

Acronym	Meaning
ANMDMR	Agenția Națională a Medicamentului și a Dispozitivelor Medicale din România - National Agency for Medicines and Medical Devices of Romania
ATI	Anestezie Terapie Intensivă - Intensive Care Unit
APP	Autorizație de Punere pe Piață - Marketing Authorisation
ANS	Autorizație pentru Nevoi Speciale - Authorisation for Special Needs
API	Autorizație pentru Import - Import Authorisation
AIP	Autorizație pentru Import Paralel - Parallel Import Authorisation
AR/ NUI	Sistemul de Alertă Rapidă / Informații non-urgente - Rapid Alert System / Non-urgent Information
BPF	Bună Practică de Fabricație - Good Manufacturing Practice
BPD	Bună Practică de Distribuție - Good Distribution Practice
CA	Consiliul de Administrație - Administration Council
CAPP	Comisia de Autorizare pe Punere pe Piață - Commission for Marketing Authorisation
CNAS	Casa Națională de Asigurări de Sănătate - National Health Insurance House
CaNaMed	Catalogul Național al Prețurilor Medicamentelor de uz uman - National Catalogue of the Prices of Medicinal Products Authorised for Marketing in Romania
CNSCBT	Centrul Național de Supraveghere și Control al Bolilor Transmisibile - The National Centre for Surveillance and Control of Communicable Diseases
CMR	Colegiul Medicilor din România - Romanian College of Physicians
CFR	Colegiul Farmaciștilor din România - Romanian College of Pharmacists
CNCAV	Comitetului Național de Coordonare a Activităților privind Vaccinarea împotriva COVID-19 - National Committee for COVID-19 vaccination activities
CAT	Comitetul pentru terapii avansate - Committee for Advanced Therapies
DGIF	Direcția Generală Inspecție Farmaceutică - General Directorate for Pharmaceutical Inspection
DFVMR	Direcția Farmacovigilență și Managementul Riscului - Pharmacovigilance and Risk Management Directorate
DPE	Direcția Proceduri Europene - European Procedures Directorate
DCCM	Direcția Control Calitatea Medicamentelor - Medicinal Product Quality Control Directorate
DPN	Direcția Proceduri Naționale - National Procedure Directorate
DCP	Autorizare prin Procedura Descentralizată - Authorisation through Decentralised Procedure
DAPP	Deținătorul Autorizației de Punere pe Piață - Marketing Authorisation Holder (MAH)
DCI	Denumire Comună Internațională - International Non-Proprietary Name (INN)
DSU	Dosarul Standard al Unității - Unit Master File
DGEA	Direcția Generală Evaluare Autorizare - General directorate for evaluation and authorisation
EMF /EFC	Educație Medicală / Farmaceutică continuă
IGPR	Inspectoratul General al Poliției Române - General Inspectorate of Romanian Police

INSP	Institutul Național de Sănătate Publică - National Institute of Public Health
MRP	Autorizare prin Procedura de Recunoaștere Mutuală - Authorisation through mutual recognition procedure
MRP-RU	Autorizare prin Procedura de Recunoaștere Mutuală cu Utilizare Repetată - Authorisation through Mutual Recognition Procedure-Repeat Use
OMS	Ordinul Ministrului Sănătății - Order of the Minister of Health
OUG	Ordonanță de Urgență - Emergency Ordinance
OSMR	Organizația de Serializare a Medicamentelor din România - The Romanian Organisation for Serialisation of Medicinal Products
RPAS	Raport Periodic actualizat privind Siguranța - Periodic Safety Update Report (PSUR)
PS	Proceduri de sistem - System Procedures
PO	Proceduri operaționale - Operational Procedures
RAPI	Reacții Adverse Post-vaccinale Indezirabile - Undesirable Post-vaccination Adverse Reactions
RA	Reacții Adverse - Adverse Reactions
RMS	Stat Membru de Referință - Reference Member State
SPPSSM	Serviciul de Prevenire și Protecție în Domeniul Securității și Sănătății în Muncă - the service for prevention and protection of occupational safety and health
SNVM	Sistemul Național de Verificare a Medicamentelor - National Medicinal Product Verification System
SMI	Stat Membru Interesat - Concerned Member State
SMC	Sistemul de management al Calității - Quality Management System
EMA	Agenția Europeană a Medicamentului - European Medicines Agency
Eudra GMDP	Eudra GMDP - European Inspections Database operated by EMA
EDQM	Directoratul European pentru Calitatea Medicamentului şi Îngrijirea Sănătății - European Directorate for the Quality of Medicines
HMA	Șefii Agențiilor Medicamentului - Heads of Medicines Agencies
MSS	Studiu supraveghere piață - Market Surveillance Study
PSURSA	Evaluări unice ale rapoartelor periodice actualizate privind siguranța - Periodic Safety Update Report Single Assessments
PRAC	Comitetul pentru evaluarea riscurilor în materie de farmacovigilență - Pharmacovigilance Risk Assessment Committee
PTS	Proficiency Testing Study - studii de testare a competenței laboratoarelor
SRLM	Strategic Review and Learning Meeting - întâlnire strategică pentru evaluare şi studiu
OCABR	eliberarea oficială a seriilor de medicamente biologice - Official Control Authority Batch Release
VHP	procedura VHP pentru evaluarea armonizată a cererilor de studii clinice - Voluntary Harmonisation Procedure
WGEO	Grupul de lucru pentru aplicarea legislației/combaterea falsificării medicamentelor - Working Group of Enforcement Officers