Institutional Capacity Building Plan

Authors:

Tomasz Jaworski, Marcin Tomasik, Leszek Borkowski (Poland)

Borys Danevych, Artem Grudinin, Yuliya Cherniavska, Serhiy Khoma (Ukraine)

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I. LIST OF ABBREVIATIONS

AMCU – Antimonopoly Committee of Ukraine

ARMA – Asset Recovery and Management Agency

CMU – Cabinet of Ministers of Ukraine

Consortium – consortium of independent consultants, retained by EBRD following a competitive selection procedure

EBRD – European Bank of Reconstruction and Development

EDMS – Electronic Document Management System

Food Safety Service – State Service for Food Safety and Consumer Protection

MoH – Ministry of Health of Ukraine

National Drug Policy – State Strategy of National Drugs Policy Implementation for 2017 – 2025

Plan – Institutional Capacity Building Plan

Project – consultancy project "Advice on Regulatory Improvements in Ukraine's Pharmaceutical Sector"

Report – Report on conformity of the process of state registration of medicinal products in Ukraine with the EU law and standards

DLS – State Administration of Ukraine on Medicinal Products and Narcotics

ScEC – Scientific Expert Council

SEC – State enterprise «State Expert Centre of the Ministry of Health of Ukraine »

STC – Scientific Technical Council

UMA or **new Agency**– Ukrainian Medical Agency

URPL – Polish Office for Registration of Medicinal Products, Medical Devices and Biocidal Products

II. LIST OF LEGAL ACTS

Constitution – Constitution of Ukraine of 28 June 1996

Criminal Code – Criminal Code of Ukraine of 5 April 2001

Law on Advertising – Law of Ukraine On Advertising of 3 July 1996

Law on Central Governmental Bodies – Law of Ukraine On Central Governmental Bodies of 17 May 2011

Law on Civil Service – Law of Ukraine On Civil Service of 10 December 2015

Law on Corruption Prevention – Law of Ukraine On Corruption Prevention of 14 October 2014

Law on Financing Sources – Law of Ukraine On Sources of Financing of Governmental Authorities of 30 June 1999

Law on Medicines – Law of Ukraine On Medicines of 4 April 1996

Decree 376 – Decree of the Cabinet of Ministers of Ukraine "On Procedure of State Registration (re-registration) of Medicines and State Registration (re-registration) Fee" of 26 May 2005 No. 376

Decree 647 –Decree of the Cabinet of Ministers of Ukraine "On Approval of the Regulation on the State Administration of Ukraine on Medicinal Products and Narcotics Control" of 12 August 2015 No. 647

Decree 753 – Decree of the Cabinet of Ministers "On Approval of the Technical Regulations on Medical Products" of 2 October 2013 No. 753

Decree 754 – Decree of the Cabinet of Ministers of Ukraine "On Approval of the Technical Regulations on Medical Products for In-vitro Diagnostics" of 2 October 2013 No. 754

Decree 755 – Decree of the Cabinet of Ministers of Ukraine "On Approval of the Technical Regulations on Implanted Medical Products" of 2 October 2013 No. 755

Order 426 – Order of the Ministry of Health of Ukraine on Procedure for Conducting Expert Evaluation of Registration Information for Medicines Submitted for State Registration (Re-registration) and Expert Evaluation of Information on Changes to Registration Information during Validity of Registration Certificate of 26 August 2005 No. 426

Order 690 – Order of the Ministry of Health of Ukraine "On Approval of the Procedure for Conducting Clinical Trials of Medicinal Products and Expertise of Materials for Clinical Trials and the Model Regulations on the Ethics Committee" of 23 September 2009 No. 690

Order 898 – Order of the Ministry of Health of Ukraine "On approval of the Pharmacovigilance Procedure" of 27 December 2006 No. 898

III. EXECUTIVE SUMMARY

1. This Plan is prepared by international consortium of experts engaged by EBRD as a part of Project.
2. While drafting this Plan, Consortium of experts relied on:
    - Initial goals of Project, including improvement of medicines registration system in terms of transparency, effectiveness, scientific level;
    - MoH vision, as well as MoH suggestion to extend the transformations to other areas of medicinal products regulation and control;
    - Vision of the industry associations, representing domestic and international pharmaceutical companies, R&D and generic;
    - Applicable EU practices.
3. The recommendations outlined in Plan concern two main areas: (a) building institutional capacity of the existing key participants of medicines registration system, and (b) gradual comprehensive development through transformation of the whole system.
4. In part of **institutional capacity building**, Consortium addresses important areas of the key regulator's operations, including:
    - improvement of organizational structure and key processes;
    - improvement of HR practices and implementation of KPI based approach to remuneration;
    - implementation of EDMS and eCTD format of dossiers;
    - development of external communications practices and increasing of transparency;
    - improvement at the level of financing.
5. In part of **gradual comprehensive transformation of the whole system**, the Consortium recommends reforming of governance, regulation, authorisation and control over medicines through:
    - Establishing a new independent governmental authority (with recommended name Ukrainian Medical Agency, proposed by Steering Committee) responsible for medicines marketing authorisation (registration), clinical trials and pharmacovigilance, medical devices conformity assessment coordination, as well as borderline products regulation.
    - Establishing UMA in form of central governmental authority with special status, allowing specific approach to financing of UMA, status of its employees (combination of leadership and administrative team with civil servants status and experts without civil servants status), remuneration of its staff, as well as implementation of industry specific requirements to conflicts of interest declaration by employees[1].

[1] Taking into account the existing strategy of public administration reform, we realize, that special status of UMA, recommended by us, may be re-considered in the future, when the reformed medicinal products regulation system is fully implemented and stabilized.

- Re-arranging, based on the best European practices, of functions and powers of the governmental authorities involved into medicines regulation, with MoH policy-making function, UMA market authorization function and DLS quality control/market supervision functions.

6. The following is expected as outcomes of the above transformations:

   - Establishing more transparent, efficient and professional system of regulation, authorization and control over medicines and medical devices in Ukraine, compliant with the best European practices;
   - Launching process of sustainable development of the system, allowing gradual approximation to EU model and standards, as well as improving exporting potential of domestic pharmaceutical industry players and overall investment attractiveness of the industry.

7. To implement the recommended transformations, the following key steps shall be made:

   - Taking a political decision to reform the system of governance, regulation, authorisation and control over medicines;
   - Amending legislation;
   - Amending/adopting subordinate legislation;
   - Establish new/re-arrange existing governmental/regulatory authorities.

8. Even before launching of the reform through amendments to legislation, the following steps shall be made already now by MoH/SEC:

   - improvement of organizational structure and key processes of SEC;
   - improvement of SEC's HR practices and implementation of KPI based approach to remuneration;
   - implementation of EDMS and eCTD format of dossiers;
   - creating and launching of comprehensive user-friendly portal concerning medicines, clinical trials and pharmacovigilance.

IV. ABOUT PROJECT AND ITS PHASE III

9. The Institutional Capacity Building Plan has been prepared as a part of a consultancy project "Advice on Regulatory Improvements in Ukraine's Pharmaceutical Sector", financed by the European Bank of Reconstruction and Development.

10. Project is part of a policy dialogue effort which EBRD undertook, at the request of Ministry of Health of Ukraine, in close cooperation with the pharmaceutical industry associations, World Health Organisation (WHO), the EU Delegation to Ukraine, and the relevant governmental bodies aiming to improve of pharmaceutical registration procedures in Ukraine to bring them in compliance with the EU standards.

11. The main objective of Project was to assist MoH in reviewing the pharmaceutical registration procedures in Ukraine to identify and implement potential improvements, to bring registration process in compliance with the EU standards. In the course of Project implementation, the objective was extended to cover assistance to MoH in reorganization of state regulatory administration in the area of medicines.

12. Project is performed by a consortium of independent consultants, retained by EBRD following a competitive selection procedure. Members of Consortium are:
    - Tomasik Jaworski Sp.p. (Leader of the Consortium, law firm based in Poland),
    - Danevych.Law (law firm based in Ukraine),
    - APC Instytut Sp. z o.o. (regulatory consultancy firm based in Poland),
    - Red Fox Consulting Ltd. (IT consultancy firm based in Latvia),
    - Odgers Berndtson (recruiting agency and business processes consultancy firm, former name: Talent Advisors).

13. Project is performed in close cooperation and dialogue with the regulatory authorities of Ukraine, international organizations and the representation of domestic and foreign industry. During each phase of Project regular meetings of the Steering Committee are convened, to report status of Consortium work, present findings and consult recommendations. Members of the Steering Committee include the representatives of the following institutions and organizations:
    - EBRD,
    - MoH,
    - SEC,
    - EU Delegation to Ukraine,
    - Association of Pharmaceutical Research and Development,
    - Union of organisations of employers in medical and microbiological industry of Ukraine,
    - Association of Pharmaceutical Producers of Ukraine,
    - Association of international Pharmaceutical Manufacturers,
    - American Chamber of Commerce,
    - European Business Association.

14. Representatives of Consortium had separate working meetings with Office of Reforms of CMU Secretariat and Ministry of Economic Development and Trade to discuss the changes proposed by Consortium.

15. Project is divided into 4 phases.

Phase 1 (May – November 2016)

16. During Phase 1 of Project experts of the Consortium reviewed the existing registration processes for pharmaceutical products in Ukraine, compared it with best EU practice and recommended measures to bring the registration processes in compliance with EU regulations. The experts held several meetings with the representatives of domestic and foreign industry, as well as with the representatives of state authorities (MoH, SEC, DLS). Experts' observations and recommendations were presented in the form of "Report on conformity of the process of state registration of medicinal products in Ukraine with the EU law and standards"[2].

17. Report comprised of two parts. First part was dedicated to detailed review of conformity of Ukrainian regulations with relevant EU laws. In the second part Consortium presented its observations and recommendations in several categories, including:
    - public health policy,
    - quality of legislation,
    - organization of registration process,
    - communication and transparency,
    - financing,
    - management of human resources,
    - use of IT systems.

18. Significant part of recommendations in Report were aimed at improving the capacity of institutions involved in state registration to fulfill their tasks, on the basis of existing structures and resources.

19. Report earned positive feedback from all stakeholders active in the Steering Committee. Findings of Report were accepted as accurate, and experts' views on recommended actions were shared by the interested parties. On several occasions, including the Steering Committee meetings, the representatives of private sector, as well as public institutions, expressed their expectations that Report should be followed by a detailed plan how to implement the recommendations.

Phase 2 (December 2016 – February 2017)

20. A number of high-level recommendations regarding the capacity of institutions involved in state registration of medicinal products in Ukraine were also formulated as a part of Consortium's input in elaboration of Ukraine's National Drug Policy.

[2] Available at http://www.moz.gov.ua/ua/portal/pre_20170123_b.html.

21. The purpose of Phase 2 of Project was to review and propose update to the draft National Drug Policy and Related Plan of Action in the area of medicines registration, and offer assistance to MoH in respect of key policy decisions.

22. Consortium proposed to update National Drug Policy by section devoted to state registration of medicinal products. The link between state registration and public health and economy was defined as follows:

    "*Effective and transparent medicinal products registration system is vital for ensuring the physical access to medicinal products with proven quality, efficacy and safety for patients in Ukraine. Ukrainian system of medicinal products registration has significant room for improvement, which could potentially spur further growth of Ukrainian pharmaceutical market and attract new investments to the Ukrainian pharmaceutical sector.*"

23. Consortium proposed, among others, the following solutions aimed to enhance the capacity of state registration system:
    - "*to address all key elements of state registration procedure at the level of Law on Medicines, including (…) institutions taking part in the procedure*";
    - "*to replace current model of state registration via collective order of MoH with the system of individual decisions on registration (individual marketing authorization for each medicinal product)*";
    - "*to concentrate competences and responsibilities in the hands of one specialized authority responsible for the whole procedure of evaluation and registration of medicinal products in the stipulated timeframe*";
    - *"to increase transparency of all elements of registration system in line with EU best practices, including developing the register of independent experts engaged for professional assessment of data obtained from studies of the medicinal product (opinions on this assessment are included in the registration dossier of the medicinal product submitted for state registration)*";
    - "*to significantly reform the drug registration authority in terms of efficiency of procedures, HR and IT infrastructure, particularly: to implement effective recruiting and remuneration policy and to adopt a policy of continuous strengthening the competences of employees, including international exchange programs, in order to ensure working conditions competitive with market standards*".

24. In the Plan of Actions, attached to National Drug Policy, Consortium proposed a number of specific actions to be taken in medium term or short term, among them:
    - introduction of an institution of individual decision on registration, to replace collective orders (medium term);
    - increase in transparency of registration system including the register of experts employed to evaluate applications (short term);
    - concentration of competences and responsibilities in the field of state registration of medicinal products in hands of one specialized authority (medium term);

- development and implementation of the effective HR policies concerning recruiting remuneration and continuous strengthening the competences of employees of the drug registration authority (medium term).

25. The National Drug Policy and the Plan of Actions[3] have been adopted by CMU.

Phase 3

26. Originally, the purpose of Phase 3 of Project was to prepare a plan of actions to enhance capabilities of existing institutions in the field of state registration of medicinal products.

27. However, during a meeting on 21 February 2017 with participation of the acting Minister of Health, Dr. Ulyana Suprun, Deputy Minister Mr. Roman Ilyk and Director of SEC, Ms. Tetyana Dumenko, representatives of MoH expressed their expectation that Plan is prepared for a newly created drug registration authority that could assume tasks in the field of medicines registration. In this respect MoH was also expecting to outline what changes in law were required to ensure functioning and taking over responsibilities in the area of state registration by newly created entity.

28. Due to the above, the scope of Phase 3 was adjusted to cover broader range of matters, namely:

    - preparation of the Institutional Capacity Building Plan (i.e. preparation of the organizational structure and general principles of functioning) for a new drug registration authority in the area of HR, transparency and decision-making, in line with the recommendations from Report pertaining to registration process organization;
    - preparation of the related legal step-plan, outlining what changes in existing laws are required to ensure a successful transfer from current institutional framework and organization of medicines registration process to the newly created entity.

29. Consequently, on 26 April 2017, Consortium prepared its vision of the reform and presented it to the Steering Committee (Presentation constitutes Appendix No. 1 to this document) and to the representatives of MoH (on 8 June 2017, see Appendix No. 2 to this document). During the latter meeting Dr. Suprun and Mr. Ilyk expressed their expectations regarding several elements of Consortium's vision, including the legal form of the new registration agency and its scope of competence, as well as alignment of registration system development with development of post-authorization supervision system.

30. The Consortium modified its proposals accordingly, and presented them to the Steering Committee on 25 July 2017 (see Appendix No. 3) and in MoH on 26 July 2017 (see the summary of essential issues, listed in EBRD letter to MoH of 31 July 2017, Appendix No. 4).

31. The Consortium presented final version of the Plan on October 13, 2017.

Phase 4 (pending)

[3] https://www.kmu.gov.ua/ua/npas/pro-zatverdzhennarskimi-zasobami-na-period-do-2025-roku?fbclid=IwAR38rSjfTqg2jj8LmZZINA4-sOJ5h7KfaV2I4KM6GbstT3MXzbzYE4ENejU

32. Originally, the goal of Phase 4 of Project was to prepare draft Concept of the Reform, which could be a basis for a resolution to be adopted by the Cabinet of Ministers of Ukraine. After the approval of the Ukraine's National Drug Policy by CMU the Project was put on hold.

33. On January 31, 2019 the meeting of EBRD with MoH, SEC and DLS representatives took place. As a result of the meeting it was decided to update the Plan with recent amendments and developments, as well as provide additional clarifications to MoH, SEC and DLS on the following issues:

    - The status of experts of the central governmental body with special status;
    - Requirement to return the remaining funds of central governmental bodies to the State Budget at the end of the budget year;
    - Division of responsibilities between UMA and DLS (or new body).

34. The Consortium updated the Plan and submits it together with the Cover Letter which contains clarifications on the above issues.

V. ABOUT THE PLAN

35. The contents of this Plan are based on the modified proposal of Consortium, as presented to the Steering Committee on 25 July 2017 and accepted by MoH representatives on 26 July 2017.

36. Cornerstone of Plan is the idea of creation of a new state institution dedicated to state registration of medicinal products in line with the best practices of EU Member States.

37. Taking into account the existing strategy of public administration reform, we realize, that recommended by us special status of UMA, including special conditions of financing the authority, special status of employees, special level of salaries etc., may be re-considered in the future, when the reformed system is fully implemented and stabilized.

38. In part VI of this document we present our detailed recommendations regarding the features of UMA, including its tasks, legal form, organization of procedures, structure, human resources, transparency, financing and fees.

39. In part VII of the document we present a detailed plan of actions to implement the recommendations.

VI. KEY FEATURES OF UMA

VI.1. Tasks of UMA

40. The essence of the problem is the following:
    1) to define clear responsibility for state registration of medicinal products by establishing new entity, exclusively responsible for the whole process of state registration, from evaluation of applications to issuing individual decisions based on individual applications;
    2) to decide which other areas of responsibility relating to pharmaceutical market, apart from state registration (authorization), should be attributed to UMA;
    3) to decide whether UMA should be vested with responsibility also for other markets, apart from pharmaceutical market.

1.1. Allocation of responsibilities for state registration of medicinal products

1.1.1. Current status

41. Currently the functions relating to state registration of medicinal products in Ukraine are divided between two entities:
    - MoH, which is the policy-maker and the entity formally responsible for decisions concerning state registration of medicines, and
    - SEC, which is responsible for expert evaluation of dossiers, based on which MoH decides whether to approve or deny registration.

42. In practice, MoH does not have required recourses (in terms of personnel, expertise, infrastructure, procedural know-how etc.) to process and assess applications. The majority of resources and experience required to act as an effective state registration authority has been concentrated in SEC. The formal position of SEC in the system seems to be downgraded and disproportionate to the actual role this entity plays in the system of state registration.

43. In Report we have identified several shortcomings of the current model. The most important were the following:
    - Intertwining activities of MoH and SEC throughout the whole registration procedure[4]. As a result of combined responsibilities of MoH and SEC, these authorities seem to act by rotation in registration procedure and are forced to exchange documents or letters in the typical course of the procedure on at least 7 occasions. It is not efficient and causes delays.
    - Over-complicated procedure after SEC expert evaluation[5], which involves a number of purely formal activities undertaken by MoH.
    - Unclear division of responsibilities[6], with the legislation indicating MoH as the authority responsible for state registration of medicines, and regulations introducing the elements of institutional responsibility of SEC and, to certain extent, responsibility of individual experts.

[4] Paragraphs 460-461 of Report.

[5] Paragraphs 468-469 of Report.

- Blurring of responsibility for decisions in the course of medicinal products registration[7], due to complicated procedure, divided functions and massive involvement of advisory/scientific councils into SEC decision-making.
- Ineffective involvement of MoH in the procedure[8]. The role of MoH in the procedure, at its initial and final stage, is rather about formal approval than genuine examination of the case, not least because of limited resources (in comparison with SEC).

1.1.2. EU benchmark

44. Organization of state administration in the area of medicines registration and internal distribution of tasks is not subject to harmonization in the EU. Therefore, EU member states apply various models, depending on their legal traditions and assessment of current needs.

45. That said, a model, in which the expert evaluation and the formal issuing of decisions are vested in separate entities, is not frequently met.

Benchmark (Poland)

Historically, a model of divided responsibility was applied in Poland. In years 1991-2001 the formal decisions (resolutions) on registration of medicinal products were adopted by a collective body – the Commission for Registration of Pharmaceuticals and Medical Materials. The Commission consisted of 18 members, experts in medicine, pharmacy and veterinary medicine, appointed by Ministry of Health. The Commission acted with the administrative and scientific support from the state-owned, specialized scientific institute – Medicines Institute, especially from its special unit – Bureau for Registration of Pharmaceuticals and Medical Materials.

As the medicines registration system in Poland underwent a major reform in 2001, the responsibilities for registration of medicinal products remained divided for another decade. The power to issue individual decisions on registration was vested in the Ministry of Health, while the examination of applications became a task of a specialized administrative body – the URPL.

The system of divided responsibilities was assessed as ineffective, and was repealed in 2011. Since then, virtually all tasks relating to the medicines registration have been transferred to the President of URPL, who became a "central body of government", in many ways equal to a minister of the Cabinet. The Minister of Health became a second-instance (appellate) authority and retained general supervision over the operations of the President of URPL.

Main purpose of the 2011 reform was to separate functions relating to registration and reimbursement of medicinal products, the former being linked to safety, and the latter concentrated on public finance. In addition, the authors of the reform stated that the transfer of powers to one entity (the President of URPL) would allow to simplify and accelerate the registration

[6] Paragraphs 476-486 of Report.

[7] *Ibidem*.

[8] Paragraphs 490-493 of Report.

procedures, as well as would enhance safety of medicines.[9]

The reform fulfilled the intended objectives: it released the Minister of Health from the burden of getting involved in the registration procedure and offered to the President of URPL autonomy to take decisions based on independent scientific review.

1.1.3. Recommendations

46. In Report we made a tentative recommendation to either move all possible tasks in the field of state registration to SEC[10], or, optionally, to a newly created entity[11]. As an option, we also recommended to move the competence to issue individual decisions on state registration to SEC or the newly created entity, with MoH retaining only general supervision and hearing the appeals[12].

Following the discussions on the forum of the Steering Committee, as well as with MoH (described in more detail in section IV above), our ultimate recommendations are as follows:

a) All functions related to state registration of medicinal products should be transferred to one entity.

b) The entity dealing with the state registration of medicinal products should be a newly created entity, however, with the significant use of resources of SEC (UMA).

c) UMA should have power to issue individual decisions on registration.

d) It is necessary to ensure effective mechanism of subordination and instruments of MoH supervision over UMA, so that UMA remains a tool to implement the State's health and drug policies developed by MoH, and not a stand-alone player competing with MoH.

1.1.4. Required actions

47. The following actions are required to implement the recommendations:

a) Amendments to Law on Medicinal Products;

b) Amendments to Decree 376 or its replacement with a new legal act, or cancelling of the act if policy-making and regulation is fully assigned to MoH;

c) Amendments to Order 426 or its replacement with a new legal act;

d) preparation of the statute of UMA;

[9] See: Justification of the draft bill on the Office for Registration of Medicinal Products, Medical Devices and Biocidal Products, http://orka.sejm.gov.pl/Druki6ka.nsf/0/16BDD825AA458824C12577C200295A4C/$file/3490.pdf.

[10] Paragraphs 507-508 of Report.

[11] Paragraph 509 of Report.

[12] Paragraph 510-511 of Report.

e) appointment of Head and Deputies of UMA;

f) HR arrangements with heads of departments of SEC and other staff of SEC, and where applicable, also of MoH and DLS;

g) Administrative arrangements regarding the premises of UMA, equipment etc.;

h) Transfer of databases and IT tools from SEC, and where applicable, also of MoH and DLS, to UMA. Preparation of new IT tools dedicated to UMA;

i) Preparation of internal procedures of UMA and document forms;

j) Preparation of new portal of UMA;

k) Winding up of operations of SEC following relevant transition period.

1.2. Allocation of responsibilities for other tasks relating to medicinal products

1.2.1. Current status

48. Registration (authorization) of medicinal products is only one of areas of responsibility of the state pertaining to medicinal products.

49. In Ukraine, other tasks are distributed in the following manner:

Clinical trials:

50. Responsibilities in this field are divided between MoH (who formally accepts the applications and issues decisions / orders regarding clinical trials) and SEC (which evaluates the applications and provides recommendations for MoH).

Pharmacovigilance:

51. Responsibilities in this field are divided between MoH, SEC and DLS. SEC collects reports and is responsible for processing and evaluating of collected data regarding safety of medicinal products. MoH remains responsible for issuing administrative decisions in the area of pharmacovigilance based on the recommendations of SEC (e.g. order for a prohibition or temporary prohibition of medicinal products medical use). Based on MoH Order/instruction DLS may temporary or permanently suspend circulation of a medicinal product within 5 days.

52. MoH may also notify DLS on adverse reactions or poor quality of medicinal product. Based on MoH notification DLS may issue an administrative order on prohibition or temporary prohibition of circulation of medicinal product.

Manufacturing, Import and GMP compliance:

53. Manufacturing of medicinal products in Ukraine, as well as import of medicinal products to Ukraine, are licensed activities. Issuing licenses, as well as verification of capabilities of applicants to carry out licensed activities, are the responsibilities of DLS.

54. DLS is also responsible for post-licensing supervision over manufacturing and import of medicinal products.

55. All responsibilities pertaining to Good Manufacturing Practice, from pre-licensing check of GMP compliance, through regular and incidental controls, to issuing GMP certificates and recognizing foreign GMP certificates (issued by PIC/S inspectorates), rest with DLS as well.

Wholesale and retail sale:

56. Wholesale and retail sale of medicinal products in Ukraine is subject to licensing. DLS is the authority responsible for issuing licenses for these activities.

Control of quality:

57. Supervision over quality of medicinal products is, in principle, the responsibility of DLS. Competences of DLS in this respect include *i.e.*:
    - control over the quality of the imported medicinal products and medicinal products placed on the market (with the use of state laboratories, subordinated to or being a part of structures of DLS);
    - inspections of manufacturing sites, premises of wholesalers, pharmacies and other venues of storage and sale of medicinal products.

Promotion and advertising:

58. Apart from labelling requirements (which are evaluated in the course of state registration by SEC, and after placing on the market the compliance with the registered labelling is supervised by DLS), Ukrainian healthcare administration does not hold any specific powers in the field of supervision over promotion and advertising of medicinal products.

59. Legal requirements for advertising and promotion of medicinal products are set forth in Laws on Advertising and on Medicinal Products, and are enforced by AMCU and for Food Safety Service, or by way of private litigation in courts.

Pricing and Reimbursement:

60. There is only a limited reimbursement scheme in place, which allows patients to get for free/based on co-payment certain medicinal products for selected chronic diseases, which are reimbursed under “Affordable Medicines” program and insulins reimbursement program. At the same time, the number of trade names covered by the “Affordable Medicines” program has been steadily rising and as of March 2019 includes 257 trade names (compared to 157 in April 2017).

61. Expert Committee on Essential Medicines List under MoH remains the only separate specialized council dedicated to health technology assessment (HTA) for the purpose of pricing and reimbursement decisions of the state.

62. As of January 2, 2019, a new HTA department was created at SEC. So far, according to SEC, the HTA department assists the Expert Committee on Essential Medicines List with the HTA for the purpose of inclusion of medicines into the Essential Medicines List. Since the department commenced its operations very recently, considering the lack of regulatory framework on the HTA function, ongoing building of the department's capacity and expertise, it would be too early to discuss the HTA function in details. In 2019 MoH publicly expressed the intention for this department to become the core of the future separate institutionalized HTA authority.

1.2.2. EU benchmark

63. EU law does not interfere in the distribution of functions relating to medicinal products within national administration of Member States. In practice of various EU member countries two basic models may be distinguished:
    - a model of concentration of functions within one entity (typically a regulatory agency with sovereign powers) and
    - a model of separate entities: scientific agency and enforcement body.

64. By way of example, a division of functions in 4 major EU jurisdictions is shown in the table below:

	Poland	Germany	France	UK
Clinical Trials	URPL	BfArM / PEI	ANSM	MHRA
Marketing Authorizations	URPL	BfArM / PEI	ANSM	MHRA
Pharmacovigilance	URPL	BfArM / PEI	ANSM	MHRA
Manufacturing and Import Licensing	GIF	regional governments	ANSM	MHRA
Wholesale and Retail Licensing	GIF	regional governments	ANSM	MHRA/ GPhC
Promotion and Advertising	GIF	regional governments	ANSM / CEPS	MHRA + self-regulatory bodies
Quality control	GIF	regional governments	ANSM	MHRA
Pricing, Reimbursement, HTA	MoH + HTA agency (AOTMiT)	MoH + health funds + HTA agency (IQWiG)	MoH + CEPS + health fund	health fund + HTA agency (NICE)

Key:
MoH *– Minister of Health*

URPL *– Urząd Rejestracji Produktów Leczniczych, Wyrobów Medycznych i Produktów Biobójczych [the Office for Registration of Medicinal Products, Medical Devices and Biocidal Products]*
GIF *– Główny Inspektor Farmaceutyczny [the Chief Pharmaceutical Inspectorate]*
AOTMiT *– Agencja Oceny Technologii Medycznych i Taryfikacji [the Agency for Health Technology Assessment and Tariff System]*
BfArM *– Das Bundesinstitut für Arzneimittel und Medizinprodukte [the Federal Institute for Drugs and Medical Devices]*
PEI *– Das Paul-Ehrlich-Institut*
IQWiG *– Das Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen [the Institute for Quality and Efficiency in Healthcare]*
ANSM *– L'Agence nationale de sécurité du médicament et des produits de santé [the French National Agency for Medicines and Health Products]*
CEPS *– Comité Economique des Produits de Santé [the Economic Committee on Health Care Products]*
MHRA *– the Medicines and Healthcare products Regulatory Agency*
GPhC *– the General Pharmaceutical Council*
NICE *– the National Institute for Health and Care Excellence*

65. In case of jurisdictions with tasks divided between two entities, the line of division is between matters which require strong scientific background, and those which are closer to classic regulatory and inspection powers.

1.2.3. Recommendations

We recommend that UMA is vested with regulatory powers in the field of state registration (marketing authorization), clinical trials and pharmacovigilance.

We recommend that GMP certification, inspection and licensing in the field of manufacturing and import, wholesale and retail sales, as well as state quality control of medicinal products, remain the competence of DLS.

66. Distribution of functions relating to pricing and reimbursement are not covered by our recommendations. We understand that these functions are currently concentrated in the structures of MoH and SEC.

67. We are of the view that the model of divided tasks in Ukraine between a scientific agency and an enforcement agency with inspection powers should be maintained, for several reasons.

68. **Firstly**, any reform concerning state health administration should be implemented in a manner which guarantees continuity of operations of state agencies. As it was stated in Report, the current system, despite its shortcomings, fulfils its basic functions by providing an operating and relatively stable institutional framework for authorizing medicines for placing on the market[13]. The same may be, in principle, said about the tasks of the state in the area of licensing and quality control.

69. In these circumstances implementation of a model of one big agency, combining functions of MoH, SEC and DLS, could potentially pose certain risks to the stability of the system. Given Ukraine's limited resources, UMA cannot realistically be built without relying, at least partially, on the staff and know-how of the current institutions. The tasks relating to scientific assessment

[13] Paragraph 503 of Report.

(registration, clinical trials, pharmacovigilance) require different type of expertise that licensing and inspections. The structures and resources of SEC and DLS have been developed for several years in their specific directions, resulting in different management cultures, approaches, know-how and staff profile. Forced unification of these structures could impair the effectiveness of the state in the field of registration and supervision over pharmaceutical market.

70. **Secondly**, the purpose of institutional reform of state administration in the area of medicinal products is to offer effective tools for the Minister of Health to shape and implement health and drug policies of the state. From this perspective two specialized institutions would likely be more operative and subject to effective supervision than one big conglomerate.

71. **Thirdly**, the key to the effectiveness of the system is ensuring the proper coordination of actions of DLS and UMA. This goal does not require unification of structures of SEC and DLS, but may be achieved through re-defining the positions of DLS and UMA in the system, by subordinating both agencies to MoH and equipping MoH with new supervisory powers over the operations of both entities.

1.2.4. Required actions

72. The following actions are required to implement the recommendations:

    a) *Amendments to Law on Medicinal Products;*

    b) *Amendments to Decree 376 or its replacement with a new legal act, or cancelling of the act if policy-making and regulation is fully assigned to MoH;*

    c) *Amendments to Order 426 or its replacement with a new legal act;*

    d) *Amendments to Decree 647;*

    e) *Amendments to Order 690, Order 898.*

1.3. Allocation of responsibilities for other health-related products

1.3.1. Current status

73. Tasks of state administration with respect to medicinal products are in some aspects similar to its tasks in other product markets, e.g. veterinary medicinal products, medical devices, biocidal products, functional food or cosmetics. These shared aspects include:
    - requirement of state approval, or at least notification to state bodies, before placing a product on the market;
    - trials of products in humans (medical devices, cosmetics);
    - post-marketing safety surveillance;
    - participation of the state in funding of products in therapies and/or their purchase by patients (medical devices, functional food).

74. In Ukraine the supervision over the aforementioned product markets is dispersed among various authorities:
    - competent authority for veterinary medicinal products is Food Safety Service;
    - competent authority for medical devices is DLS;
    - competent authority for biocidal products is Food Safety Service;
    - competent authority for functional food is Food Safety Service;
    - competent authorities for cosmetics are MoH and Food Safety Service.

75. Coordination over the operations of the above mentioned authorities is dispersed. Despite being legally responsible for ensuring public health, MoH has only limited powers to supervise some of these entities (*e.g.* DLS), and with respect to others MoH lacks any effective tools of impact (*e.g.* Food Safety Service).

76. There are also no regulations in place, which would offer guidance how to resolve conflicts between competing legal qualifications of borderline products, and which entity has authority to resolve them.

1.3.2. EU benchmark

77. EU law does not interfere in the distribution of responsibilities for supervision over respective product markets. EU member countries apply various models, from unification of supervision in the hands of one agency to dispersion of functions among numerous state entities.

78. For reference we present the approach to supervision of health-related products in 4 major EU jurisdictions in the table below. The table indicates whether a medicines registration authority in a given jurisdiction has powers also with respect to other types of products:

	Poland (URPL)	Germany (BfArM)	France (ANSM)	UK (MHRA)
Medicinal products – human	Yes	Yes	Yes	Yes
Medicinal products – veterinary	Yes	No	No	Yes, only where the company undertakes both human and veterinary activities
Medical devices	Yes	Yes, but competences divided with regional government	Yes	Yes
Biocidal products	Yes	No	No	No
Functional foods	No	No	No	No
Cosmetics	No	No	Yes	No

79. As follows from the above examples, it is a common approach to join regulatory powers with respect to medicinal products and medical devices. Supervision over other types of products may be included in the competence of medicines agency as well, however there seems to be no prevailing approach in the EU in this respect.

80. Over the recent years the nature of legal regulations concerning medical devices in the EU have evolved from rather technical, concentrated on conformity with technical standards, towards a model which in many ways resembles pharmaceutical regulations, especially in the following areas:
    - Clinical trials: duty to perform clinical assessment of medical devices (selected categories of devices and scientific review of results, certain categories of clinical trials subject to state approval, duty to report adverse events during clinical trials, international exchange of information on such adverse events)
    - Registration: growing requirements regarding the contents of pre-marketing notifications;
    - Post-authorization safety: companies to appoint persons responsible for regulatory compliance, requirement to adopt Risk Management Systems, requirement to record and analyse medical incidents (similar to adverse events), Quality Management System, traceability requirements, electronic reporting of medical incidents to state authorities;

- Supervision and sanctions: competent authorities equipped with powers similar to those with respect to medicinal products (*e.g.* inspections on site, suspension or recall from the market);
- Pricing and reimbursement, health technology assessment: in several countries medical devices are subject to similar pricing & reimbursement schemes as medicinal products (especially certain types of devices available in pharmacies, like insulin pumps, pen needles, test strips); medical devices are also becoming a subject to HTA analysis[14];
- Promotion and advertising: there are similar concerns regarding compliance with the rules of ethical public advertising, as well as relations with healthcare professionals.

81. An example of functions that may be exercised by a medicines agency with respect to medical devices is the scope of competence of Polish Office for Registration of Medicinal Products.

Benchmark (Poland)

Overview of selected activities of URPL in the area of medical devices:

1. *Clinical trials*
   a) *Granting permission to start and modify clinical trial*
   b) *Authority to request variation in clinical trial*
   c) *Authority to withdraw permission to conduct clinical trial and to stop clinical trial*
   d) *Supervision over clinical trials (including inspection of premises and documents)*
   e) *Conducting the Central Register of Clinical Trials*
   f) *Exchange of information and cooperation with European Commission and EU Member States*
   g) *Contribution to Eudamed (European Database on Medical Devices)*
2. *Conformity assessment*
   a) *Resolution of disputes involving classification rules and establishing:*
      - *the classification of medical devices,*
      - *the classification of medical device accessories,*
      - *the qualification of in-vitro diagnostic medical devices.*
   b) *Issuing decisions on qualification of particular devices into categories of medical devices*

[14] In Poland currently only medical devices which are reimbursed (available on prescription in a pharmacy i.e.: special dressings and blood glucose test strips) are a subject to HTA analysis (other medical devices are financed from public funds in a different way). However, Polish government is working on new medical devices' reimbursement system, which will cover more medical devices and thus will impose an obligation to perform HTA analysis on new medical devices. See. http://legislacja.rcl.gov.pl/projekt/12286460.

c) *Collecting and updating information on certification on Notified Bodies (certification is a task of MoH)*

3. *Placing the product on the market:*

   a) *Receiving all reports and notifications from manufacturers / distributors / representatives, regarding placing the device on the market (quasi-registration)*

   b) *Keeping a database of reports and notifications (including all modifications, updates)*

   c) *Issuing Certificates of Free Sale (confirming that a device has been authorized for marketing in Poland, for the purpose of export)*

4. *Post-marketing surveillance*

   a) *Collecting and analysing information on the safety of medical devices*

   b) *Supervision over manufacturers, authorised representatives, importers and distributors of medical devices (including inspection of premises and documents)*

   c) *Giving opinions to customs authorities on compliance of imported medical devices to prevent the marketing of non-compliant devices*

   d) *Issuing decisions on withdrawals of devices:*

      - *posing safety risks*
      - *wrongly qualified*
      - *with misleading names, labelling, instructions for use, promotional materials or presentations*

   e) *Investigating medical incidents with medical devices*

   f) *Exchange of information on safety with third countries, EU Member States and the institutions of the European Union*

   g) *Sending safety reports to the European Commission and other Member States*

5. *Inspection*

   In the field of clinical trials:

   a) *Condition of equipment and facilities used during the trial*

   b) *Methods of record-keeping and data storage*

   c) *Whether the clinical trial is conducted according to the protocol and approved protocol amendments*

   d) *Whether all study participants provided a signed and dated informed consent form*

   In the field of manufacturing, imports, distribution:

e) *Checking of production and storage facilities and their equipment*

f) *Requesting sharing of samples necessary for the testing and verification*

g) *Checking documentation of the medical device*

h) *Asking for information and explanations from employees of manufacturers etc*

82. To illustrate how conflicts regarding borderline products may be dealt with, Polish regulation may be given as an example.

Benchmark (Poland)

The competent authority for issuing opinions on borderline products is the President of URPL. His/her opinions are binding for other authorities competent with respect to non-medicinal products.

The President of URPL may issue an opinion either on its own initiative, at request of other state authorities, or at request of private applicants (in case of medical devices).

The President of URPL is assisted by the consultative and advisory committee – the Committee for Borderline Products. Its opinions on borderline products are based on the Committee's opinions.

The Committee is competent to:

- *issue opinions on the classification of a product as medicinal product, medical device or biocidal product;*
- *issue an opinion as to whether a substance that is an integral part of a medical device or an active medical device for implantation used separately would be a blood product or other medicinal product, and whether it could act on the human body in support of a medical device or an active medical device for implantation;*
- *perform other tasks assigned by the President of URPL in the field of borderline products.*

The meeting of the Committee is convened only at the request of the President of URPL.

The Committee issues opinions in the form of resolutions.

1.3.3. Recommendations

We recommend that the competences of UMA cover:

- ***medicinal products,***
- ***medical devices.***

We recommend that UMA is granted an exclusive right to decide about the legal status of ***borderline products****, if doubts arise as to their proper qualification.*

We recommend introduction of the interpretation rule in favour of qualification of a borderline product as medicinal product, unless it is proven that the product should be qualified otherwise.

UMA should have the right to decide, on the grounds of public health protection, whether to allow for a switch of a medicinal product to another regulatory category (e.g. cosmetic, food products).

83. At this stage we do not recommend extension of powers of UMA to other categories of health-related products, such as biocidal products, cosmetics, functional food, to allow UMA to concentrate on its core activities. Such extension, however, should not be ruled out for the future, when UMA becomes fully operative.

84. We do not recommend inclusion of veterinary medicinal products in the scope of competence of UMA. Despite the fact that the regulation of this sector in the EU is in many aspects similar to medicinal products for human use, the practical experience reveals possible overlaps with competences of administration responsible for agriculture, which may result in institutional conflicts. Extension of powers of UMA to veterinary medicinal products would imply dispersion of limited resources to matters which are not strictly linked to public health.

1.3.4. Required actions

85. The following actions are required to implement the recommendations:

a) *Amendments to Decree 647* (Regulation on DLS)*;*

b) *Amendments to Decrees 753 (Technical Regulation on Medical Devices), 754 (Technical Regulation on Medical Devices for in vitro Diagnostics), 755 (Technical Regulation on Active Implantable Medical Devices);*

c) *Take-over of DLS employees, which have sufficient expertise and experience in the sphere of medical devices.*

VI.2. Legal form of UMA

2.1. Essence of the problem

86. Currently SEC is operating as a state enterprise under control of MoH. Such form of the registration agency significantly limits its powers and role in the registration system. To strengthen role and independence of UMA in the registration system, while assigning efficient mechanisms of control over the system to MoH, UMA's legal form should be thoroughly considered.

2.2. Legal form

2.2.1. Current status

87. The Ukrainian system of central executive governmental bodies is comprised of several types of authorities, operating on different levels, with CMU playing the central role. Ministries, central governmental bodies (regular) and central governmental bodies with special status complement the system.

88. Pursuant to the Law on Central Governmental Bodies ***central governmental bodies*** are established by CMU decrees to implement certain functions of the state policy. The Ukrainian legislation in force contains detailed provisions regarding subordination of such bodies: each body is guided and coordinated by CMU through a minister, who is responsible for implementation of state policy in the relevant sphere.

89. ***Central governmental bodies with special status*** are established to regulate certain important spheres of the state policy (e.g. economic competition, management of state-owned property etc.)[15].

2.2.2. Recommendations

90. Comparing with regular central governmental bodies, central governmental bodies with special status have several distinctive features, making this form of governmental body more relevant for UMA, namely:

- **Rules of subordination and accountability**. Ukrainian legislation on central governmental system determines strict rules of subordination and accountability for regular central governmental bodies (subordinated to CMU) and for central governmental bodies with special status expressly referred to in the Constitution (various models of subordination). However, according to the Law on Central Governmental Bodies, laws of Ukraine may envisage different rules concerning subordination and

[15] The most notable governmental bodies with special status in Ukraine include: National Agency on Corruption Prevention, ARMA, AMCU, State Committee for Television and Radio Broadcasting of Ukraine, State Property Fund of Ukraine, National Agency of Civil Service of Ukraine.

accountability for central governmental bodies with special status, other than mentioned in the Constitution. For UMA more significant impact of MoH is desirable.

- **Status of employees.** One of the main challenges for transformation of the medicines registration authority from state enterprise to governmental body is status of employees of the newly created governmental body. Currently, SEC employees (including experts) do not have civil servants status and, therefore, (a) their salaries are not strictly limited by the general legislation on civil service, (b) hiring and dismissing procedures are relevantly flexible. If UMA is created in the form of regular central governmental body the remuneration of UMA's employees would be significantly lower comparing with the current wages paid in SEC, as well as with market level of wages of experts of similar level. In case UMA is established in form of governmental body with special status based on a law, its employees may be divided into 2 groups:
  - leadership and administrative staff having civil servants status, but with higher level of salaries comparing with civil servants employed by regular central governmental bodies, and
  - experts, without civil servants status, but being subject to additional specific restrictions, established by Law on Medicinal Products (including specific conflict of interests provisions, declaration of experts' income etc.).
- **Leadership.** The amended law on Medicinal Products may provide for specific procedure of appointment of UMA's leadership, different from the one applicable to regular central governmental bodies, as on numerous occasions the regular appointment procedure failed to meet its goal.

We recommend establishing UMA as a central governmental body with special status, which is the most suitable form and meets MoH vision and expectations for UMA.

Other comments:

To guarantee appropriate level of control, and to balance the position of agencies, we recommend changing the legal form of DLS similarly to UMA, into central governmental body with special status, and subordinating it to MoH in a similar manner. Such transformation of DLS will require amendments to the effective Ukrainian legislation in part of DLS's status, rules of subordination and accountability.

2.2.3. Required actions

a) Amendments to Law on Medicinal Products;

b) Amendments to Decree 376 or its replacement with a new legal act, or cancelling of the act if policy-making and regulation is fully assigned to MoH;

c) *Amendments to Order 426 or its replacement with a new legal act.*

2.3. Regulation

2.3.1. Current status

91. Article 24 of Law on Central Governmental Bodies expressly provides that the Constitution and laws of Ukraine may determine different rules applicable to central governmental bodies with special status (in contrast to regular central governmental bodies).

92. In Ukraine there is also no unified approach to regulating governmental bodies with special status. In practice, the governmental bodies with special status are either regulated at the level of Laws, or at the level of CMU Decrees.[16]

2.3.2. Recommendations

Taking into account the recommended specific rules concerning subordination (see section 2.4. below), status of employees and leadership appointment, as well as MoH strategic vision, UMA should be regulated at the level of Law.

To develop and adopt amendments to Law on Medicinal Products, in which to determine:

- *specific rules of subordination and accountability for UMA;*
- *status of employees (leadership, administrative staff and experts of UMA);*
- *higher level of salaries for employees having civil servants status compared to the regular level established by Law on Civil Service.*

Regulating UMA at the level of law would ensure stability of the whole registration system, as in such case much greater effort should be made to undo the changes to the medicines registration system.

Other comments:

Similar recommendation is applicable to DLS.

2.3.3. Required actions

Amendments to Law on Medicinal Products.

2.4. Subordination

[16] *E.g.* AMCU, ARMA are created by way of adoption of special laws, while National Agency of Civil Service of Ukraine is functioning on a basis of CMU Decree.

2.4.1. Current status

93. The Ukrainian legislation contains no restrictions regarding the rules of subordination of central governmental body with special status (save for bodies expressly referred to in the Constitution). Thus, there are no legal obstacles to make (through introducing necessary amendments at the level of Law) UMA more significantly subordinated to MoH (in contrast with regular central governmental bodies, subordinated predominantly to CMU).

94. Such specific subordination is needed to bring balance and stability into medicines registration system, where MoH will act as the policy-maker and appeal body, while UMA will retain full responsibility for medicines registration.

95. The following key rules of subordination may be applied:

CMU	MoH
Appoints of the Head of UMA, based on MoH nomination	Nominates candidate for the position of Head of UMA upon recommendations of the special selection committee
Forms special competitive selection committee, which recommends MoH the candidates for the Head of UMA position based on competitive procedure	Appoints deputies, nominated by the Head of UMA
----------	Determines the rules of exchange of information between all bodies functioning within medicines circulation system (including UMA and DLS)
----------	Audits the activity of UMA
----------	Cancels legal acts, adopted by UMA in cases, directly specified in the legislation.
----------	Drafts laws and CMU decrees related to the sphere of medicines

2.4.2. EU benchmark

96. The proposed approach to subordination between Ministries of Health and medicines registration bodies is applied in majority of EU Member States:

EU Member State	Subordination
Poland (URPL)	Ministry of Health
Germany (BfArM)	Ministry of Health
France (ANSM)	Ministry of Health
United Kingdom (MHRA)	Department of Health

2.4.3. Recommendations

To subordinate UMA predominantly to MoH. To design detailed rules of subordination at the level of Law.

Other comments:

Additionally, similarly to UMA, we recommend to introduce similar rules of subordination of DLS to MoH.

2.4.4. Required actions

Amendments to Law on Medicinal Products.

VI.3. Organization of the procedure

3.1. Current status

97. One of sections of our Report was dedicated to the organization of the registration process. Several observations and recommendations were made regarding the identified problems with duration of the procedure, its effectiveness and adopted model.

98. Our observations and recommendations regarding the adopted model of the procedure (combined responsibilities of MoH and SEC) are presented above. Other important observations include the following:
    a) Time limits for particular actions, as well as for the duration of the entire procedure, are often determined in an unclear and incohesive manner. There is no clear indication which entity is liable for delays, and no effective tools to enforce liability for delays.[17]
    b) Collective advisory/scientific bodies are heavily involved in the procedure on a regular basis, doubling the experts' work and potentially adding to delays and blurring responsibility for decision-making.[18]
    c) Responsibility for the process is unclear and dispersed among several institutions, internal units and even individual experts.[19] In addition, an extremely vague but severe Article 321(2) of the Criminal Code introduced in 2012 stipulates imprisonment for "violation of the procedure of state registration of medicinal products", which seems to be an additional factor discouraging persons and institutions involved from taking responsibility for the course and outcome of the procedure.
    d) No clear rules for involvement of external experts are in place, and in certain areas SEC performs its duties relying only on external experts.[20]
    e) State registration procedures are concluded with collective orders issued by MoH, which carry a number of decisions in many individual cases, usually not linked to each other. Means of appeal against such orders are limited and ineffective.[21]

99. In accordance with the established procedure, Applicants submit applications and cover letters to the "Single Window" of MoH. The transfer of these materials to SEC requires 1.39 business days, although the "Single Window" unit is actually situated at the premises of SEC.

100. As of March 5, 2019, SEC launched the so-called "Service Center" within its structure. Before its introduction, applications for medicine registration and clinical trial authorization were accepted at SEC by the experts themselves who then proceeded to assessment of the applications. This put an unnecessary burden of administrative work on experts and reduced the time they spent

[17] Paragraphs 441-455 of Report.

[18] Paragraphs 462-465 of Report.

[19] Paragraphs 476-486 of Report.

[20] Paragraphs 487-489 of Report.

[21] Paragraphs 494-496 of Report.

on the applications assessment *per se*. The newly introduced Service Center includes administrative personnel specifically trained and authorized to accept the applications for registration/clinical trials authorization, without involvement of experts in administrative tasks. Applications are then passed on to the experts on the day of receipt. This has allowed to increase SEC document admission hours from 10.5 to 27.5 hours per week, and free up to 45 hours of the time per an expert monthly. SEC expects that launch of the Service Center will improve SEC time management, quality and speed of its communication with the applicants. Since the Service Center has been launched very recently, its impact on improving the applicants' experience is difficult to assess.

101. SEC has the opportunity to accept registration forms in electronic form. However, applicants continue to submit them mostly in paper form. It takes about 1.5 business days to transfer data to the electronic form. Currently, applicants can submit electronically registration form for variations. SEC also works on developing an electronic form of applications for authorization of clinical trials and for introducing substantial amendments to the clinical protocols.

102. The template contract for expert evaluation provides for the 100% prepayment for SEC services, paid separately from the state duty for registration. Applicants often delay payment for services, which, in its turn, delays whole registration procedure.[22]

103. Substantive time in the registration is lost on:

- transfer of the dossier paper materials between the decision-makers (up to 15 working days);
- signing of accompanying documents (standard forms, confirmation of receipt of dossier materials (currently they are copied for all parties to sign the copy));
- postal communications with applicants even on minor issues (although SEC reports having transferred certain minor communications to non-paper format as of February 2019);
- delays on documents flow between SEC and expert groups/external experts.

104. Due to limited resources of the Department of Expertise, responsible unit moves registration dossier paper materials between SEC collective advisory/scientific bodies only on certain days of each week, which also leads to delays.

105. Specialized examination of dossier materials takes only up to 45 days for original, biological and biosimilar medicine out of total 210 days for the standard procedure. This time may, in certain cases, be insufficient given the complexity and volume of materials.

106. Currently IMS "Pharma Solution" does not allow to automatically generate proposals to ScEC and STC draft agenda for clinical trials, which delays consideration of respective conclusions by ScEC / STC.

[22] In particular, without confirmation of payment, case will not be included in the agenda of the ScEC / STC.

107. Detailed description of the current medicinal products registration procedure is attached as Appendix 5, and recommendations on improvements to be implemented are attached as Appendix 6[23].

108. Since January 2019, as per MoH instructions, a specialized HTA department has been created within SEC. So far, the department assists the Expert Committee on Essential Medicines List under MoH with the HTA of medicines-candidates for the National Essential Medicines List. Its other functions are currently unclear due to the lack of the developed HTA legislation. According to MoH, the expertise of the department will form the basis for the future independent HTA authority.

109. As of February 2019, SEC has also reported, *inter alia*:

- Increasing the number of internal experts;
- Introduction of additional module in IMS "Pharma Solution", which allows to monitor overall work load of every expert and identify which unit is responsible for delays. In terms of enforcing liability for delays, SEC Director stated that they do not provide bonus if an expert delays more than 20% of registration procedures.

110. In the meantime, collective advisory bodies are still heavily involved in the procedure on a regular basis; however, SEC management streamlined their work (SEC meets twice a month and STC meets four times a month) and now they do not have delays in consideration of particular cases.

111. Responsibility in terms of registration process remains unclear and dispersed among several institutions, internal units and even individual experts. In addition, an extremely vague but harsh Article 321(2) of the Criminal Code introduced in 2012 stipulates imprisonment for "violation of the procedure of state registration of medicinal products", which seems to be an additional factor discouraging persons and institutions involved from taking responsibility for the course and outcome of the procedure.

112. State registration procedures are still concluded with collective orders issued by MoH, which contain individual decisions in several (very often many) cases, not linked to each other. Means of appeal against such orders are limited and ineffective.

113. The contract for SEC expert services provides for the 100% prepayment for SEC services. However, applicants often delay payment, which, in its turn, delays whole registration procedure. In particular, without confirmation of the payment, expert opinions on respective medicines are not included in the agenda of the SEC/STC. However, as per SEC management, they have optimized processing and approvals of the contracts between financial and legal department.

[23] Since experts of Odgers Berndtson have reviewed all key functions of SEC from the point of view of business process effectiveness, detailed description of the current clinical trials approval procedure and recommendations on improvements to be implemented are attached as additional materials as Appendixes 11 and 12, and detailed description of the current pharmacovigilance procure and recommendations on improvements to be implemented are attached as Appendixes 13 and 14.

114. Optimization of the processes of document circulation and in particular the implementation of the system of electronic document management remains unsolved. We consider that this will reduce the total time of procedures for registration / re-registration of MPs.

3.2. EU benchmark

115. Apart from the issue of time limits, the organization of procedure is an internal matter of member states.

116. Regarding the time limits, Directive 2001/83 requires that the procedure for granting marketing authorizations for medicinal products is completed with maximum of 210 calendar days after the submission of a valid application.

117. Regarding other aspects of the course of procedure, various solutions are applied at national level.

Benchmark (Poland)

1) Role of advisory bodies

The following consultative and advisory committees assist the President of URPL:

- *the Committee for Medicinal Products,*
- *the Committee for Veterinary Medicinal Products,*
- *the Committee for Medical Devices,*
- *the Committee for Biocidal Products,*
- *the Committee for Borderline Products,*
- *the Pharmacopoeia Committee.*

The Committees consist of not more than 7 members each. Committees are convened on ad hoc basis, subject to needs of the President of URPL to consult on particular cases, usually a couple of times a year. The work of the Committees and expert groups is transparent (all information are available on the URPL website and in the Public Information Bulletin).

2) Responsibility for the process

Person authorized to issue individual administrative decisions is the President of URPL. The President may delegate his/her powers to Deputy Presidents, responsible for particular product sectors.

If the case cannot be resolved within the prescribed deadline, the President of URPL should notify the applicant, explain the reasons for delay and indicate the new date of hearing the case.

If an applicant's case has not been heard within the prescribed deadline, or the case is being handled in a lengthy manner (e.g. repetitive questions to documentation), the applicant may

submit a complaint to MoH.

MoH should examine the reasons for delay or lengthy proceedings, and if the complaint is justified, MoH shall:

- *set new deadline for hearing the case;*
- *order to identify the reasons for delay and persons responsible for delay;*
- *if needed, order to take measures to prevent similar delays in the future;*
- *state whether the delay was a flagrant violation of law (which opens the way to claim damages).*

An employee who failed to handle the case within the prescribed deadline shall be subject to disciplinary or other legal liability provided by the law or internal regulations.

3) Involvement of external experts

In case of complex issues, the President of URPL may, on a proposal from the Committee, ad hoc appoints external experts group, each time specifying its members, tasks and manner of operation.

4) Individual administrative decisions

In Poland there had been a system of collective resolutions, covering several cases at one time. Such system was repealed in 2001. Since then any and all decisions regarding registration of medicinal products have been taken in the form of individual administrative decisions.

The right to issue individual administrative decisions was originally vested in the Minister of Health (based on assessment and draft decision prepared by URPL), and since 2011 it is exclusive competence of the President of URPL. Appeals against his/her decisions are heard by the Minister of Health.

3.3. Recommendations

Initial recommendations:

All decisions in the field of registration of medicinal products should be taken in the form of individual administrative decisions of UMA, with the right to appeal (both on substantive and procedural grounds) to MoH.

Qualification Commission, ScEC, STC and Technical Expert Committee should be eliminated. Instead of them, specific newly formed advisory/scientific committees, one per product type (medicinal products, medical devices, borderline products) should be created. The role of such scientific/advisory committees should be strictly limited to specific cases and they may be involved solely at the request of the Head or Deputies, only on merits (not procedure) and only on issues which are precedential or otherwise doubtful from the point of view of scientific assessment. Each time a consultation is requested, the requesting person should explain the reasons for consultation

in writing, and to determine the exact scope of advice sought.

Experts should be liable only toward UMA and should be protected against liability vis-à-vis applicants (save for cases where an expert intentionally breaches the law).

The wording of Article 321(2) of the Criminal Code should be revised, so as to provide genuine safeguard for the proper course of medicines registration procedure, but at the same time to avoid unnecessary pressure and "freezing effect" on persons involved in state registration.

A set of rules should be introduced regarding the cooperation of UMA with external experts. In principle, seeking advice of external experts should be possible if performing expert evaluation is not possible based on UMA's own resources.

Optimization of the processes of document circulation and in particular implementation of EDMS will significantly reduce the total time of registration of medicinal products.

In addition, even before UMA is established, to increase efficiency of SEC business processes related to registration (and clinical trials) we recommend SEC management to:

1. *Allocate resources to implement EDMS (for details see Section 6.6. below) and improve dossier material internal logistics, as well as get prepared for dossiers eCTD format.*
2. *Consider increasing overall time requirements for the specialized examination of dossiers upon saving respective time on dossier materials logistics (obviously without increasing the overall timeframes for registration procedures).*
3. *Define clear criteria for scientific review of consolidated conclusions on medicinal products registration by ScEC/STC and only involve ScEC/STC to consider issues, which are precedential or otherwise doubtful from the point of view of scientific assessment.*

Following on our initial recommendations SEC management has improved the following areas:

- *SEC streamlined communication with the applicants and expert groups though creation of the "Service Center" and rearranging work of expert groups.*
- *According to SEC management, the IMS "Pharma Solution" already provides the possibility to automatically generate proposals to the SEC/STC draft agenda based on the consolidated conclusion after the specialized examination process.*
- *SEC management has allocated additional resources to move registration dossier materials between SEC departments on a constant basis (earlier it was done only on certain days).*
- *Allocated resources to implementation of the EDMS. Per our discussion electronic keys have been issued for all key personnel, but so far full-scale EDMS has not been launched as it requires electronic document storage.*
- *Improved the dossier material logistics between departments.*
- *Provided access for the members of Expert-Advisory Groups to existing IMS system "Pharma Solution" to enhance communication with them and speed up the specialized expertise procedure.*
- *Encouraged more applicants to submit their registration forms online. For example, today up to*

80% of applications for amendments in dossier materials are made online.

The following initial recommendations remain outstanding:

- *All decisions in the field of registration of medicinal products should be taken in the form of individual administrative decisions of new Agency, with the right to appeal (both on substantive and procedural grounds) to MoH.*
- *Qualification Commission, Scientific Expert Council, Scientific Technical Council and Technical Expert Committee should be replaced with advisory committees, one per product type (medicinal products, medical devices, borderline products). Advisory committees could be consulted only at the request of the Head or Deputies, only on merits (not procedure) and only on issues which are precedential or otherwise doubtful from the point of view of scientific assessment. Each time a consultation is requested, the requesting person should explains the reasons for consultation in writing, and determine the exact scope of advice sought.*
- *Experts should be liable only toward new Agency and should be protected against liability vis-à-vis the applicants (save for cases where an expert intentionally breaches the law).*
- *The wording of Article 321(2) of the Criminal Code should be reconsidered, so as to provide genuine safeguard for the proper course of medicines registration procedure but at the same time to avoid unnecessary pressure and "freezing effect" on persons involved in state registration.*
- *A set of rules should be introduced regarding the cooperation of new Agency with external experts. In principle, seeking advice of external experts should be possible if performing expert evaluation is not possible based on new Agency's own resources.*
- *Complete shift to the full scope EDMS shall be planned, designed, enacted and implemented.*

3.4. Required actions

a) *Amendments to Law on Medicinal Products;*

b) *Amendments to Decree 376 or its replacement with a new legal act, or cancelling of the act if policy-making and regulation is fully assigned to MoH;*

c) *Amendments to Order 426 or its replacement with a new legal act;*

d) *Amendments to Criminal Code;*

e) *Preparation of an internal regulation of UMA regarding the involvement of external experts.*

VI.4. Structure of UMA

4.1. Current status (SEC)

118. Organizational structure of SEC as of March, 2019 is attached as Appendix 7.

119. The current organizational structure of SEC has substantial room for improvement, as the distribution of functions between organizational units is rather ineffective and gives rise to potential delays in the procedure of medicinal products registration.

120. As of February 2019, SEC reports having no MoH supporting staff in SEC organizational structure (Administrative division) and on SEC payroll[24].

121. In general, the SEC management has realized our recommendation to create functional verticals and subordinate each of them to a separate deputy director:

    a. Clinical issues;

    b. Registration issues;

    c. Pharmacovigilance;

    d. Legal issues.

122. Yet, many minor units are subordinated directly to the Director.

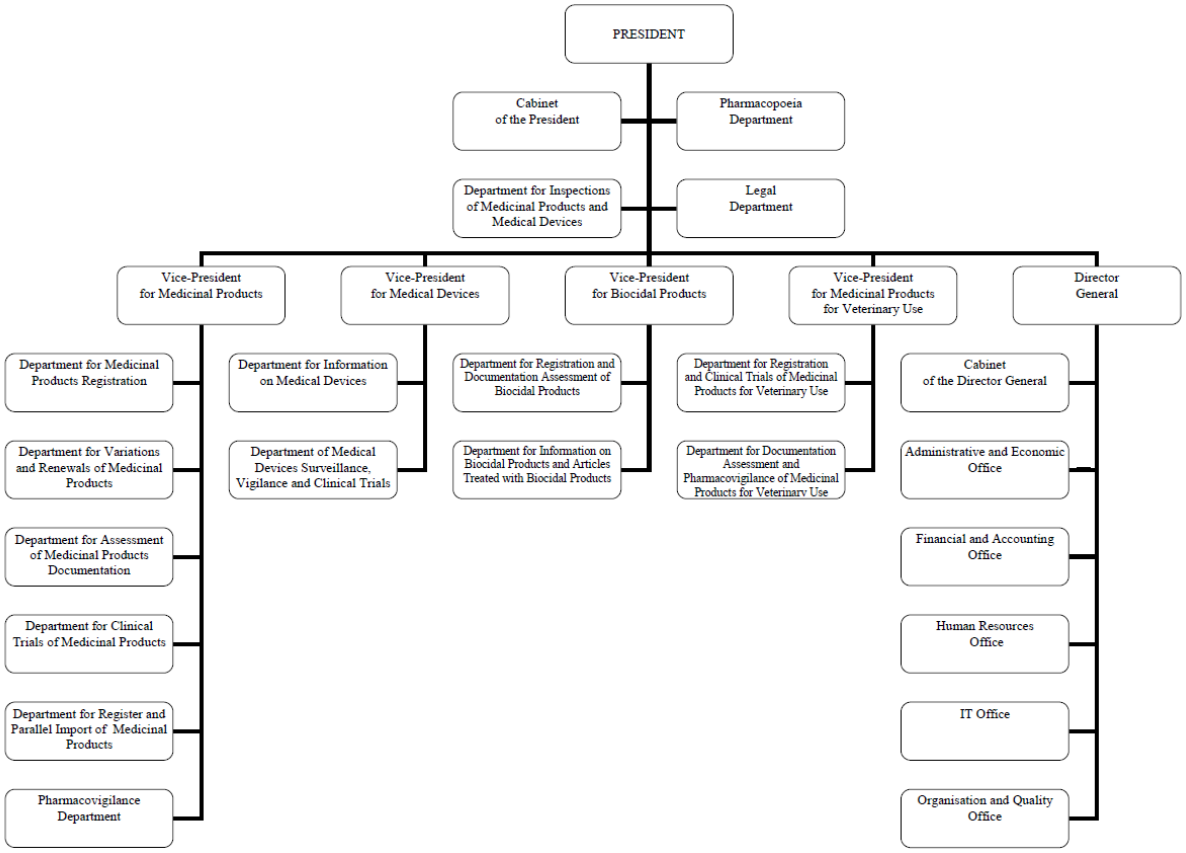
123. SEC management has strengthened control and communication with Expert Advisory Groups, in particular through their connection to the IMS “Pharma Solution”.

4.2. EU benchmark

124. EU law does not regulate the internal organization of health administration in member states. Each national agency has its own specific structure.

125. By way of example, the organizational structure of Polish Office for Registration of Medicinal Products is presented below.

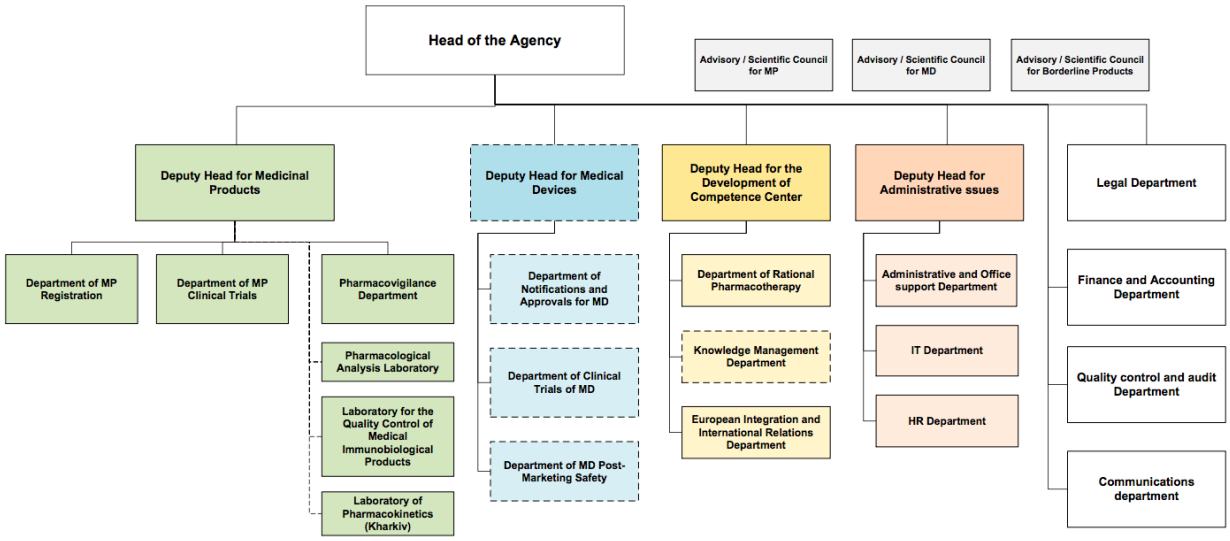
[24] Paragraph 638 of Report.



4.3. Recommendations

126. The proposed high-level organizational scheme of UMA is presented below. The scheme is fairly general and may be supplemented by additional elements and sub-units.

High-level to be organizational structure of the Agency



Initial recommendations:

We recommend that the structure of UMA is organized by:

- *two main sectors, with reference to types of products covered (medicinal products sector, medical devices sector), each headed by a Deputy Head,*
- *administrative sector which concentrates all auxiliary, non-scientific functions,*
- *separate sector acting as a "competence centre" for UMA.*

We recommend that only selected areas of UMA's operations are directly subordinated to the Head (legal, audit, and potentially also finance, communications), while in other areas the Head shall retain supervision over the respective deputies.

The "competence centre" should be a unit dedicated to:

a) international cooperation, including
- *monitoring of developments of EU pharmaceutical legislation,*
- *international exchange of experts;*

b) knowledge management for internal purposes of UMA and of other state authorities in the area of public health;

c) sharing knowledge externally, including:
- *information centre for applicants and start-ups,*
- *conferences and trainings for applicants,*
- *certification of regulatory managers,*
- *paid scientific advice.*

There should be three advisory/scientific committees dedicated to respective types of products (for medicinal products, for medical devices, for borderline products). Advisory/scientific committees should be fully transparently formed, convened on ad hoc basis, depending on the needs and decisions of Deputies and the Head.

In addition, even before UMA is established, we recommend SEC management to:

- *(prior to the implementation of EDMS) increase the resources of coordination of expert materials function and establish performance indicators with a focus on increasing the speed of dossier materials transfer and increasing of communication efficiency between departments;*
- *consolidate all finance-related units under one centre of responsibility and separate the Administrative function from subordination of the Financial Department;*
- *allocate additional resources in the HR department to introduce and manage the new*

variable remuneration system based on key performance indicators;

- *increase financial and human resources of the IT function to implement and support integrated information systems, in particular to prepare for implementation EDMS;*
- *consolidate Office support function under single centre of responsibility (following implementation of EDMS).*

Additionally, we recommend to set up an independent strategic advisory body under the auspices of UMA (may be established by adopting an UMA's internal order), which would comprise of prominent experts (both local and international) in medical, pharmaceutical, medical devices spheres, experts from other related fields, including eHealth, HTA. The functions of such strategic advisory body would be to:

- *Enhance international cooperation of UMA with other scientific and regulatory bodies worldwide;*
- *Advise and issue recommendations for UMA on application of best international practices in management, process organization, medical issues;*
- *Help UMA leadership with development and implementation of its strategy.*

Following on our initial recommendations SEC management has improved the following areas:

Per SEC management information, all MoH supporting staff was excluded from the SEC organizational structure (Administrative division) and payroll. In addition, SEC have moved all external employees, previously working on civil contracts, to the Center's organizational structure.

Procurement and Transport functions were subordinated to the Administrative department.

SEC management has recently created a separate unit acting as a "competence center" for the SEC.

Additionally, the Administrative function was separated from the subordination of the Financial Department.

The following initial recommendations remain outstanding:

- *Create an administrative function which will concentrate all auxiliary, non-scientific functions under and Deputy director of operations or Administrative deputy director,*
- *There should be three advisory committees dedicated to respective types of products (for medicinal products, for medical devices, for borderline products). Advisory committees should be fully transparently formed, convened on an ad hoc basis, depending on the needs and decisions of Deputies and the Head.*

In addition, we recommend the SEC management to:

- *Prior to the implementation of the EDMS, increase the resources of Coordination of expert materials function and establish performance indicators with a focus on increasing the speed of dossier materials transfer and increasing of communication efficiency between departments.*
- *Consolidate all finance-related units under one center of responsibility. In current*

organizational structure this requires to subordinate the Accounting division to the Head of Financial Department and allocate additional resources in the HR department, it is necessary to introduce and manage the new variable remuneration system based on key performance indicators.

- *Increase financial and human resources of the IT function for promote implementation and support of integrated information systems, in particular EDMS system. Its development and implementation could significantly improve the efficiency of key business processes of the Agency.*
- *Pay additional focus to the cyber security resources as the SEC maintains and administers new highly valuable IT assets.*
- *Consolidate Office support function under single center of responsibility, ideally with direct subordination to the Director of Agency (after implementation of EDMS).*
- *Provide for the possibility of engaging the foreign experts (on a temporary basis) to expand competencies of the new Agency's Advisory Bodies and encourage the exchange of experience.*

4.4. Required actions

127. The following actions are required to implement the recommendations:

a) *Preparation of the statute of UMA;*

b) *Takeover of employees of SEC, and where appropriate, of MoH and DLS;*

c) *Supplementary recruitment of new staff, especially to the Competence Sector and Medical Devices Sector.*

VI.5. Human resources

5.1. Status of employees

5.1.1. Current status

128. As a general rule, employees of governmental bodies have the status of civil servants. Civil servants are defined in the Ukrainian legislation in force as citizens of Ukraine, who hold a civil service position in a governmental body, another state body, receive wages at the expense of the state budget.[25]

129. The legislation also establishes restrictions for civil servants to conduct paid activities (other than artistic, sport/coaching practice, medical practice and scientific activity), as well as limits the level of salary for them. Salaries of civil servants in Ukraine are regulated by legislation and are way below the market level in the private sector.

130. The legislation on civil service provides for too complex procedures and restrictions applicable to hiring and dismissing of civil servants.

131. Currently, SEC employees do not have status of civil servants. Consequently, transition to the new legal form will result in the need to revise the status of employees of UMA.

132. Since our previous review, the total staff of the SEC increased from 482 to 495 staffing units.

133. SEC management increased total the number of internal experts - from 105 to 135 (from 21% to 27% of total staff). It is worth noting that the new experts are less qualified and require additional training.

134. Per SEC management, salaries have been increased in several steps. The maximum income of a SEC expert has increased from UAH 11.5 thousand to UAH 14.4 pre-tax, which, given the current UAH exchange rate, is a change from about EUR 397 to EUR 466. This level of remuneration is still not satisfactory comparing to market level and should be gradually further increased.

5.1.2. EU benchmark

135. Each EU member country has its own solutions due to the state's administrative tradition. This also directly affects the status of medicines products agencies' employees.

Benchmark (Poland)

In Poland, civil service corps includes three categories:

- *civil service employees employed on the basis of employment contract,*
- *civil servants employed on the basis of nomination; the nominated civil servants as a prioritised group have some additional rights and obligation (e.g. the obligatory declaration of income) in compared to the civil service employees,*
- *persons occupying senior positions employed on the basis of appointment.*

[25] Article 1.2 of the Law on Civil Service.

It is not obligatory to be a member of the civil service corps to be an employee of the URPL.

The members of the Committees and the experts groups cannot be the URPL employees. Moreover, they are not the members of the civil service corpus. URPL can also employ officials under civil law contracts.

The principles of remuneration of civil service corps members are regulated in Civil Service Corps Act.

5.1.3. Recommendations

To make the medicines registration system more transparent, efficient and professional, remuneration of experts involved into the evaluation of safety, efficacy and quality of the medicines, shall not be limited by the legislation on civil service.

The above mentioned restriction to get engaged into other paid activities, applicable to civil servants, would also be a barrier for attracting top market specialists to UMA. This may be also said about complicated procedures and restrictions applicable to hiring and dismissing of civil servants, if applied to UMA experts.

We recommend dividing employees of UMA into 2 categories:

- ***Civil servants**. The leadership of UMA, as well as employees of administrative subdivisions, which are not involved in regulatory / scientific functions of the new body should have status of civil servants. To bring more transparency and avoid significantly different level of salaries between different UMA employees, higher wages for civil servants-employees of UMA should be established at the level of Law. Such approach is already implemented in another recently created governmental body with special status – ARMA.*
- ***Experts, contracted on the basis of labour/civil contracts**. The amended Law on Medicinal Products should contain provisions allowing UMA to employ individuals on the basis of labour/civil contracts to attract qualified personnel for expert positions. Additional strict rules on conflict of interest and prevention of corruption must be applicable to them.*

5.1.4. Required actions

To amend Law on Medicinal Products and establish a division of employees of UMA into 2 categories:

- *Civil servants (leadership and administrative staff);*
- *Employees on the basis of labour/civil contracts (experts).*

5.2. Leadership

5.2.1. Current status

136. Highly qualified leadership is a cornerstone of transparent and effective functioning of a governmental body. As of today the Director of SEC is appointed by MoH on the basis of competitive selection. The Deputy Directors are appointed by Director, as well as other staff of SEC.

5.2.2. EU benchmark

137. EU law does not interfere in the appointment of leadership of the governmental body responsible for registration of medicinal products. The EU member countries apply various models.

Benchmark (Poland)

The President of URPL is appointed by the Prime Minister, selected from an open and competitive selection, at the request of the Minister of Health. Prime Minister may also recall the President of URPL.

The Vice-Presidents of URPL are appointed and dismissed by the Minister of Health, at the request of the President of URPL, from persons selected by means of open and competitive selection. The Vice-President of URPL for Veterinary Medicinal Products is appointed and dismissed by the Minister of Health in consultation with the Minister of Agriculture.

Act on the Office for Registration of Medicinal Products, Medical Devices and Biocidal Products regulates the criteria and the procedure of the aforementioned selection.

Aforementioned criteria are inter alia:

- *higher education and professional title of medical doctor or master of pharmacy;*
- *knowledge of Polish and European Union law concerning medicinal products, biocidal products, and public finances;*
- *at least three years of managerial employment e.g. at universities or public administration competent for the health;*
- *full public rights.*

5.2.3. Recommendations

138. Respective provisions regarding selection of the Head of UMA (procedure, detailed requirements to the candidates) shall be stipulated in Law on Medicinal Products in the specific section regulating UMA.

We recommend to apply the approach to certain extent similar to ARMA leadership selection:

- *CMU appoints the Head of UMA based on Minister of Health nomination. Minister of Health shall nominate the Head of UMA based on the sort list of candidates selected in the course of competitive selection, conducted by special selection committee;*

- *Information on election of the Head of UMA shall be public. Meetings of the selection committee shall be open for interested audience;*
- *MoH shall appoint deputies nominated by the Head of UMA.*

5.2.4. Required actions

To amend Law on Medicinal Products.

5.3. Leadership KPIs

5.3.1. Current status

139. SEC does not have a system of key management performance monitoring or other relevant tools supporting the implementation of its strategy. Bonuses are merely used as a compensation for relatively low base salaries[26].

140. The variable part of key management and employee's remuneration is up to 100% of base remuneration and paid on monthly and quarterly basis. Out of total bonus – 60% is a monthly premium for execution of employees' duties and proper following of the established procedures. Another 40% of bonus is a premium for non-performance related factors, such as experience, use of English language etc.

141. As bonuses are not linked to any performance indicators and they are paid constantly, in most cases employees consider them as a common part of salary.

142. SEC key managers do not have clear incentives to increase the effectiveness and efficiency of their subordinates either through improvement of business processes or implementation of new practices and tools.

143. Currently HR and Financial divisions do not have necessary tools to implement and maintain complex performance monitoring system.

144. SEC management remains skeptical regarding the introduction of KPIs or other related tools supporting the implementation of their strategy.

145. Bonuses are not linked to employee's performance yet. However, if an expert delays more than 20% of registration procedure, such an expert does not receive a monthly bonus.

146. The variable part of key management and employee's remuneration decreased from 50% to 30% total remuneration and is paid on monthly and quarterly basis.

147. As bonuses are not linked to any performance indicators and they are paid constantly, in most cases employees consider it as a common part of salary. Therefore, we consider them as a part of base remuneration.

[26] Paragraph 680 of Report.

148. So far SEC management did not create clear incentives to increase the effectiveness and efficiency of their subordinates either through improvement of business processes or implementation of new practices and tools.

5.3.2. Recommendations

149. Implementation of the KPI system is aimed at supporting implementation of the strategy developed by MoH and to improve the efficiency of UMA by:

- raising the level of key officials' incentives to change *status quo* and improve efficiency of existing processes;
- ensuring transparency and full accountability of UMA's management;
- constant monitoring of management performance by MoH (for the Head of UMA) and by the Head of UMA (for other key officials);
- introduction of effective methods and tools for monitoring the implementation of UMA's goals.
- improving quality of information used in the process of monitoring the effectiveness of the Head of UMA.

150. **The methodological basis of our recommendations** are the international principles and recommendations on corporate governance:

- Recommendations of the Organization for Economic Cooperation and Development (OECD) on corporate governance in state enterprises;
- OECD Manual on Balancing Commercial and Non-Commercial Goals;
- World Bank Recommendations on corporate governance in state enterprises;
- Recommendations of the European Commission on the remuneration of directors of public companies.

Initial recommendations:

- *include existing bonuses and premiums for key managers in their base remuneration;*
- *provide for non-monetary incentives, such as subsidized or fully paid trainings, post-graduate studies;*
- *set new performance-based bonuses with their levels varying from 20% to 60% depending on the level of position and type of function (higher for key functions for example Registration/ Renewal related and lower – for supporting functions, such as HR and IT);*
- *responsibility and KPIs system should cascade from higher to lower management levels so that actions and results of subordinates would support their manager's results;*
- *since the new KPI system will be a novelty for employees of UMA, leadership should provide detailed communication as to the goals and benefits of the new system;*
- *both Quality Control and HR functions should maintain the tools, developed based on Consortium experts recommendations (attached Matrix of responsibility as Appendix 8.2 and KPI Cards as Appendixes 9.1-9.17), as well as the link of KPIs with the existing*

organizational structure and business-processes to support the performance monitoring system in UMA;

- *the actual bonus for the period should be estimated as a sum of weighted KPI results. The composition of the KPI card (list of KPIs, weights and formulae) may be changed in the beginning of a reporting period.*

Following on our initial recommendations:

- *SEC management has increased salaries and included part of bonuses and premiums in employee's base remuneration. Overall variable part of remuneration decreased from 50% to 30%.*
- *According to SEC management, additional resources were allocated in the Methodology and quality support unit for development of performance management system.*

The following initial recommendations remain outstanding:

- *Link bonuses to employee's performance with bonus levels varying from 20% to 60% depending on the level of position and type of function (higher for key functions for example Registration/ Renewal related and lower – for supporting functions, such as HR and IT).*
- *The responsibility and KPI's system should cascade from higher to lower management levels so that actions and results of subordinates would support their manager's results.*
- *Since the new KPI system is a novelty for employees, the SEC management should provide detailed communication as to the goals and benefits of the new system.*
- *Both Quality Control and HR functions should maintain the tools we developed (Matrix of responsibility and KPI Cards) as well as the link of KPIs to existing organizational structure and business-processes to support the performance monitoring system in the Agency.*
- *The actual bonus for the period should be estimated as a sum of weighted KPI results (please see the picture below). The composition of the KPI card can be changed in the beginning of the reporting period.*

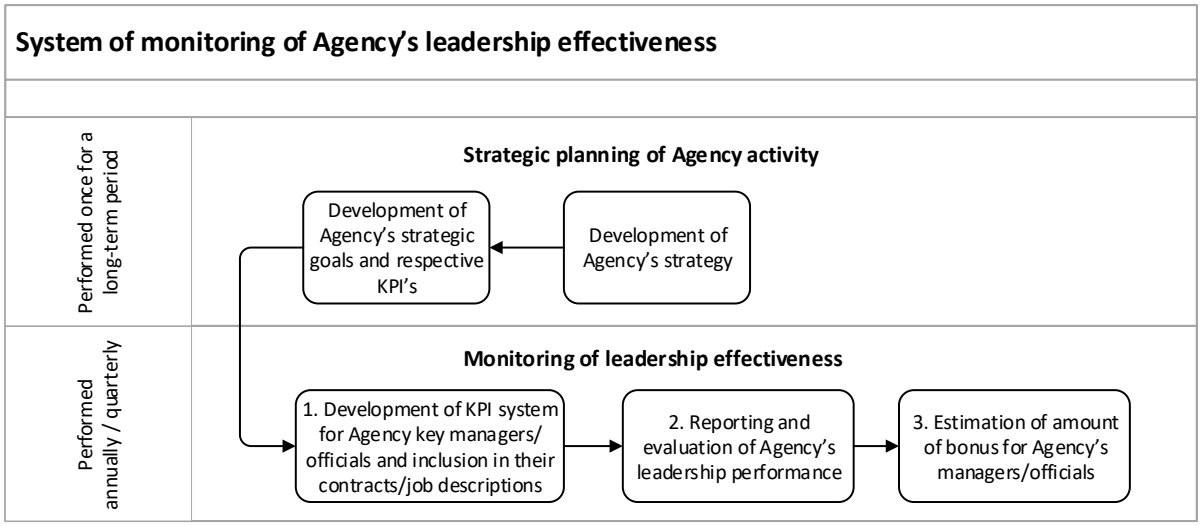
5.3.3. Required actions

To implement effective management performance monitoring system, even before UMA is established, it would be advisable for MoH/SEC management to:

- *implement the system of KPIs for the Director and key managers, that would support implementation of the strategy and enable MoH to correct SEC key managers actions by revising KPIs;*
- *set clear procedures for evaluation of managers' performance based on actual results for the period and estimation of respective bonuses;*
- *arrange a pilot project (for one quarter for N-1 and N-2 positions) to collect actual data*

and feedback from key managers, then adjust KPIs if necessary and cascade KPI system to the lower management levels;

- *include KPIs and details how variable part of remuneration is calculated and paid in the managers' contracts;*
- *provide respective units with tools and expertise to collect data for KPIs and implement performance monitoring for middle-managers and other employees of SEC;*
- *constantly review the list of KPIs for every position based on changes in the strategy implementation or organizational structure and feedback and results of periodical evaluation (please see the picture below, which applies to both SEC and UMA).*



VI.6. Transparency

6.1. Essence of the Problem

151. Ukrainian system of medicines registration is perceived by general public and industry as lacking sufficient transparency. It is often challenged by law enforcement authorities' inquiries due to lack of transparency (numerous cases of legal inquiries towards SEC for registration-related documents). The main issues are:

- no clear obligation to declare conflict of interest for experts at the level of Law, no mechanism of monitoring/renewing "no-conflict" status, no enforceable corrective actions/sanctions for violations in place;
- no clear obligation for experts to declare income (at the level of law);
- unclear decision-making process;
- limited access to information for general public and applicants;
- absence of unified electronic system of exchange of information within state administration and with applicants.

6.2. Conflict of interests

6.2.1. Current status

152. Currently, according to Law on Corruption Prevention experts of SEC are not clearly obliged to declare conflict of interests. However, SEC has initiated pilot project on declaration of conflicts for all employees. Positive experience of such pilot project shall be used by UMA.

153. Employees of UMA (civil servants and experts) will be bound by the provisions on declaration of income and conflict of interests pursuant to provisions of Law on Corruption Prevention.

154. The said Law, however, contains rather general provisions regarding conflict of interests due to the fact that it does not address industry specific aspects of conflict of interests. The current procedure of reporting on the conflict defines two types of conflict of interests in a very general manner, which creates uncertainty as to the scope of disclosure obligations:

- **Potential conflict of interests**: existence of private interest of a person in the sphere of his or her official responsibility that **may affect** impartiality of decision-making;
- **Real conflict of interests:** existence of private interest of a person in the sphere of his or her official responsibility that **affects** impartiality of decision-making.

6.2.2. EU benchmark

155. EMA model distinguishes three types of interest within pharmaceutical industry that may be applied to experts of UMA: direct, indirect and other interest.

***Direct interests** in pharmaceutical industry, according to the said approach, are:*

- ***Previous employment with a company**: any form of occupation, part-time or full-time, paid or unpaid, in a pharmaceutical company;*
- ***Consultancy to a company**: any activity where the concerned expert provides advice (including training on a one-to-one basis) to a pharmaceutical company regardless of contractual arrangements or any form of remuneration;*
- ***Strategic advisory role for a company**: any activity where the expert is participating (with a right to vote/influence the outputs) in a(n) (scientific) advisory board/steering committee with the role of providing advice/expressing opinions on the (future) strategy, direction and development activities of a pharmaceutical company, either in terms of general strategy or product related strategy, regardless of contractual arrangements or any form of remuneration;*
- ***Financial interests**: any economic stake in a pharmaceutical company (including possession of pharmaceutical companies' shares).*

***Indirect interests** in pharmaceutical industry are:*

- ***Previous participation in clinical trials as principal investigator**: an investigator with the responsibility for the coordination of investigators at different centers participating in a multicentre pharmaceutical industry instigated/sponsored trial or the leading investigator of a monocentre pharmaceutical industry instigated/sponsored trial, or the coordinating (principal) investigator signing the clinical study report.*
- ***Previous participation in clinical trials as investigator**: an investigator involved in a clinical pharmaceutical industry instigated/sponsored trial at a specific trial site which can be the responsible lead investigator of the trial at that specific site or a member of the clinical trial team who performs critical trial related procedures and makes important trial related decisions.*
- ***Reception of grant or other funding by an organization/institution**: any funding received from a pharmaceutical company by an organization/institution to which the expert belongs, or for which he/she performs any kind of activity, and which is used to support any activity of the expert whether or not it is related to research work.*[27]

***Other interests** in pharmaceutical industry are **close family member interests**: first-line members of the family of the expert (i.e. a spouse or a partner, children and parents).*

[27] EMA policy on the handling of competing interests of scientific committees' members.
and experts: http://www.ema.europa.eu/docs/en_GB/document_library/Other/2010/10/WC500097905.pdf.

All EMA experts are obliged to sign declarations of interests every year to ensure that they do not have any financial or other interests in the pharmaceutical industry that could affect their impartiality[28].

Experts may only be involved in EMA's activities upon assigning of their declarations with the interest level within the range of 1-3, depending on whether they have no (interest level 1), indirect (interest level 2) or direct (interest level 3) interest in the pharmaceutical industry and assessed the declared interests to determine their level of involvement.

6.2.3. Recommendations

Law on Medicinal Products should define additional specific rules regarding conflicts of interests to ensure high level of transparency.

We also recommend to apply positive experience of SEC in conflicts of interest area.

6.2.4. Required actions

To amend Law on Medicines.

6.3. Declaration of income

6.3.1. Current status

156. The wording of Law on Corruption Prevention does not give clear answer to question whether experts of SEC are subjects to income e-declaration, or not (unlike the top management of SEC).

157. UMA requires high level of public trust. Therefore, requirement to declare income should be applicable to UMA's experts.

6.3.2. Recommendations

Experts of UMA should be subjects to income e-declarations, irrespective of their status (both civil servants and experts). This shall be clearly provided by Law.

6.3.3. Required actions

To amend Law on Corruption Prevention.

6.4. Decision-Making Process

6.4.1. Current status

[28] EMA Public Declaration of Interests – template: http://www.ema.europa.eu/docs/en_GB/document_library/Template_or_form/2014/12/WC500178504.pdf.

158. Currently the main issue in the field of decision-making is lack of clear personalized responsibility for decision-making in the course of medicines registration.[29]

159. Blurring of responsibility is caused by dispersion of regulatory functions between MoH and SEC, SEC internal units, massive unregulated and often ungrounded involvement of advisory councils into decision-making.

6.4.2. EU Benchmark

Benchmark (Poland)

The President of URPL is responsible for issuing the marketing authorisation decision.

Prior to issuing the marketing authorisation decision, the President of URPL (through the URPL staff) e.g.:

- *verifies the application along with the accompanying documentation and*
- *develops an evaluation report containing a scientific opinion on the medicinal product with a justification and a summary of the assessment report, containing, in particular, information relating to the conditions of use of the product.*

The President of URPL may consult the decision with the Committee for Medicinal Products.

According to Polish Code of Administrative Proceedings, the case files of the administrative proceedings shall have a metrics (in writing or in electronic form), which indicates all persons who participated in undertaking actions in the administrative proceedings and all actions undertook by these.

6.4.3. Recommendations

Experts shall be responsible for their decisions within the medicines registration procedure vis-à-vis UMA. The Head of UMA shall have final responsibility for all decisions.

To avoid unnecessary blurring of responsibility by various advisory bodies. To involve advisory/scientific committees (for medicinal products, for medical devices, for borderline products) solely to consider presidential and highly complex cases. Role of advisory/scientific councils must be genuinely advisory.

To include to Law on Medicinal Products clear rules regarding criteria for the said councils' involvement in the procedure, its composition, etc.

To publish all decisions of such councils on portal of UMA.

6.4.4. Required actions

To adopt amendments to Law on Medicinal Products.

6.5. Communications

[29] Paragraph 480 of Report.

6.5.1. Current status

160. At the level of communications, there are two main areas to focus on: (a) access to information (data) and (b) interactions with applicants.[30]

161. Interface of the current SEC web-site is still not user-friendly and has poor system of navigation. English version of the website is not updated on a regular basis, and most parts of the website are not translated at all.[31]

162. The web-site of SEC contains very limited scope of information regarding particularities of submission of documents to SEC, as well as other important aspects of the procedures[32]:

- There are no detailed and comprehensive pages containing all relevant information about particular medicinal product, history of its registration and any subsequent re-registrations/variations;
- It lacks information on experts of SEC.

163. Interactions with applicants are often informal, not traceable. Formal communications are often conducted via regular post, which delays interactions. As of February 2019, SEC reports transferring some minor communications with applicants to the non-paper format (e.g. applicant is informed of signing of the contract by SEC by e-mail).

164. Since March 2019, SEC has launched the Service Center, aimed at improving SEC communication with applicants. The Service Center is composed of the administrative staff specifically trained and authorized to accept documents from and issuing them to applicants (tasks previously handled by experts). Launch of the Service Center has increased SEC document admission hours to 27.5 hrs per week, compared to 10.5 hrs previously. E-queuing has been implemented.

6.5.2. EU benchmark

165. Medicines products' agencies in EU have an extensive communication structure.

166. The main information channels are well-functioning websites. They provide variety of necessary and reliable information (e.g. lists of authorised medicinal products, information necessary to register medicinal products, fee rates, etc.).

167. Most of the websites are also available in English.

168. Other areas of communication are the access to public information and interactions with applicant.

Benchmark (Poland)

The website of URPL (http://www.urpl.gov.pl/pl) provides, among others, the following contents:

- *application forms for registration or re-registration,*

[30] Section VII.1 of Report.

[31] Section VII.1 of Report.

[32] Section VII.1 of Report.

- *application forms for initiation of clinical trial,*
- *fee information,*
- *guidelines for registration or re-registration issues (e.g. about SmPC),*
- *register of medicinal products,*
- *a list of medicinal products authorised by the President of URPL in the Public Information Bulletin in previous month;*
- *marketing authorisation holder's obligations,*
- *documents from Committees' work (e.g. positions, voting results),*
- *annual reports,*
- *Q&A's for applicants,*
- *description of the functioning and the structure of URPL.*

The website is also available in English.

Examples of other websites of medicines agencies with extensive contents:

- *UK* – https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency
- *Germany* – http://www.bfarm.de/DE/Home/home_node.html
- *France* – http://ansm.sante.fr/
- *Sweden* - *https://lakemedelsverket.se/*
- *Denmark* -- *https://laegemiddelstyrelsen.dk/*
- *Estonia* – *http://www.sam.ee/*
- *Lithuania* – *http://www.vvkt.lt/*
- *Latvia* - *https://www.zva.gov.lv/*

6.5.3. Recommendations

Official portal of UMA should be bilingual (Ukrainian and English version), contain all necessary and up-to-date information for applicants and general public. When EDMS is fully implemented, as an option, applicants may have access to their accounts within the system.

All templates, up-to-date information on progress of all conducted procedures (as required by Law on Medicines), statistics and results of annual and external audits shall also be presented on the portal.

UMA shall have publicly available information on all key officials and experts.

To increase the level of transparency of interactions with the applicants, including consultations prior to and in the course of registration procedure, by introducing a record of contacts during a procedure.

All the procedures concerning interactions with applicants shall be transparent, clear and publicly available. Moreover, the product information of UMA web portal should be constantly

updated for patients and HCPs.

The abovementioned peculiarities should be governed by the Law of Medicines.

Before UMA is established, SEC management may implement most of the above recommendations.

6.5.4. Required actions

To amend Law on Medicines.

6.6. E-GOV

6.6.1. Current status

169. Currently MoH has already initiated the implementation of the eHealth system. For this purpose, State enterprise "Electronic Health" was created. The main goal of this enterprise is to administer eHealth central database and control the further development of the system. A process of transferring all medical documents and processes of interaction from paper format to electronic and creating unified registers of institutions, doctors, patients, medicines, etc is already initiated. The full implementation of eHealth system should bring Ukrainian public health system to a new level. While developing and implementing EDMS UMA should also follow this trend and become part of the eHealth system.

6.6.2. Recommendations

UMA shall work based on EDMS and have unified electronic system that will be connected with all stakeholders, such as MoH, DLS, State Customs Service of Ukraine, etc.

This transformation requires very significant and constant alignment with other eHealth initiatives.

Shift from paper based process approach to EDMS will enhance process performance, improve efficiency and transparency of processes.

EDMS should contain at least the following functionalities:

- *secure file-transfer system used for exchanging information for regulatory purposes (electronic document flow);*
- *special electronic network linking "public health authorities";*
- *database of authorised medicinal products;*
- *system monitoring which facilitates the post-authorization safety of medicines through safety reports.*

The requirement to implement and use EDMS shall be defined at the level of Law.

It is important to ensure that implemented EDMS will be transferable to UMA and subject to some form of update and will remain operative after the start of operation of UMA.

6.6.3. Required actions

To amend Law on Medicines.

VI.7. Financing and fees

7.1. Current status

170. Currently fees for medicines registration in Ukraine comprise of registration fee, payable to the State budget and fees for various types of expert evaluation procedures, payable directly to SEC based on the contract with the applicant[33].

171. In the Report Consortium outlined several issues in the sphere of financing:

- Relatively low overall fees for state registration[34] (despite the regular increase of fees for expert services on at least an annual basis[35]);
- Fees for expert review are not regulated by the legislative acts[36];
- No significant investments are made into development of the system[37].

172. The legislation on central executive governmental bodies prohibits financing of such bodies from any other sources than the state budget. This approach is also supported by MoH in respect of financing UMA. Currently, there is only one exception at the level of legislation (direct payment by customers for security services rendered by a National Police of Ukraine division), which means that exceptions are possible in certain cases.

7.2. EU benchmark

173. Most EU member states' agencies are financed from the central budgets or special funds.

Benchmark (Poland)

"Being a state budget-funded entity, the Office for Registration of Medicinal Products, Medical Devices and Biocidal Products receives allocations for its statutory activity from the Ministry of Health (under heading 46 – Health) as a third level budget holder, and it transfers its revenue to the bank account of the state budget.

The primary source of revenue for URPL are the fees charged in the framework of its statutory activity, in particular in connection with the authorisation of medicinal products for human use and veterinary medicinal products, granting of parallel import licenses for medicinal products for human use and veterinary medicinal products, authorisation of clinical trials, veterinary clinical trials, clinical trials of medical devices, reports and notifications of medical devices, authorisation of

[33] Paragraph 593 of Report.

[34] Section VIII.1. of Report.

[35] Latest increase was in February 2019, according to SEC.

[36] Section VIII.2. of Report.

[37] Section VIII.3. of Report.

biocidal products and sales of „Polish Pharmacopoeia" publications."[38]

Benchmark (UK)

The Framework Agreement between the Department of Health and the Medicines and Healthcare products Regulatory Agency stipulates that:

"The Agency operates as a trading fund in accordance with the requirements of the Government Trading Funds Act 1973 and the Medicines and Healthcare products Regulatory Agency Trading Fund Order 2003. The trading fund was established on 1 April 2003.

In accordance with Section 3 of the Government Trading Funds Act 1973 (as amended by the Government Trading Act 1990), all sums received by the Agency as payment for services provided in connection with funded operations (within the meaning of the Government trading Funds Act 1973) will be paid into the trading fund and all expenditure incurred will be paid out of the fund.

The Agency is funded from:

- *national fees charged by the Agency directly to organisations for the fulfilment of statutory or other regulatory obligations; fees must be calculated in line with the principles as set out in Managing Public Money;*
- *EU fees charged by the EMA to organisations and then shared among those agencies, such as the Agency, undertaking particular activities on behalf of the EU network;*
- *other charges for non-statutory services, including sales into wider markets;*
- *research*

In agreement with the Department, the Agency will ensure that income/expenditure related to national statutory fees is aligned; this will include the process for setting/reviewing regulatory fees."[39]

7.3. Recommendations

To secure financing of UMA at the level adequate to its new functions and profile, as well as required development of UMA its infrastructure, we recommend setting at the level of the law, that an appropriate portion of the registration fees payable by the applicants is directed to UMA, while the remaining amount – to the state budget.

As an alternative (although less recommended), the legislation may provide for a portion of registration fees (payable by applicants to the state budget in full) guaranteed re-direction from

[38] *The URPL annual report for 2016,* urpl.gov.pl/sites/default/files/zalaczniki/Raport%20roczny%20%202016.pdf.

[39] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/507765/DH_and_MHRA_Framework_Agreement_A.pdf.

the special fund of the state budget to UMA.

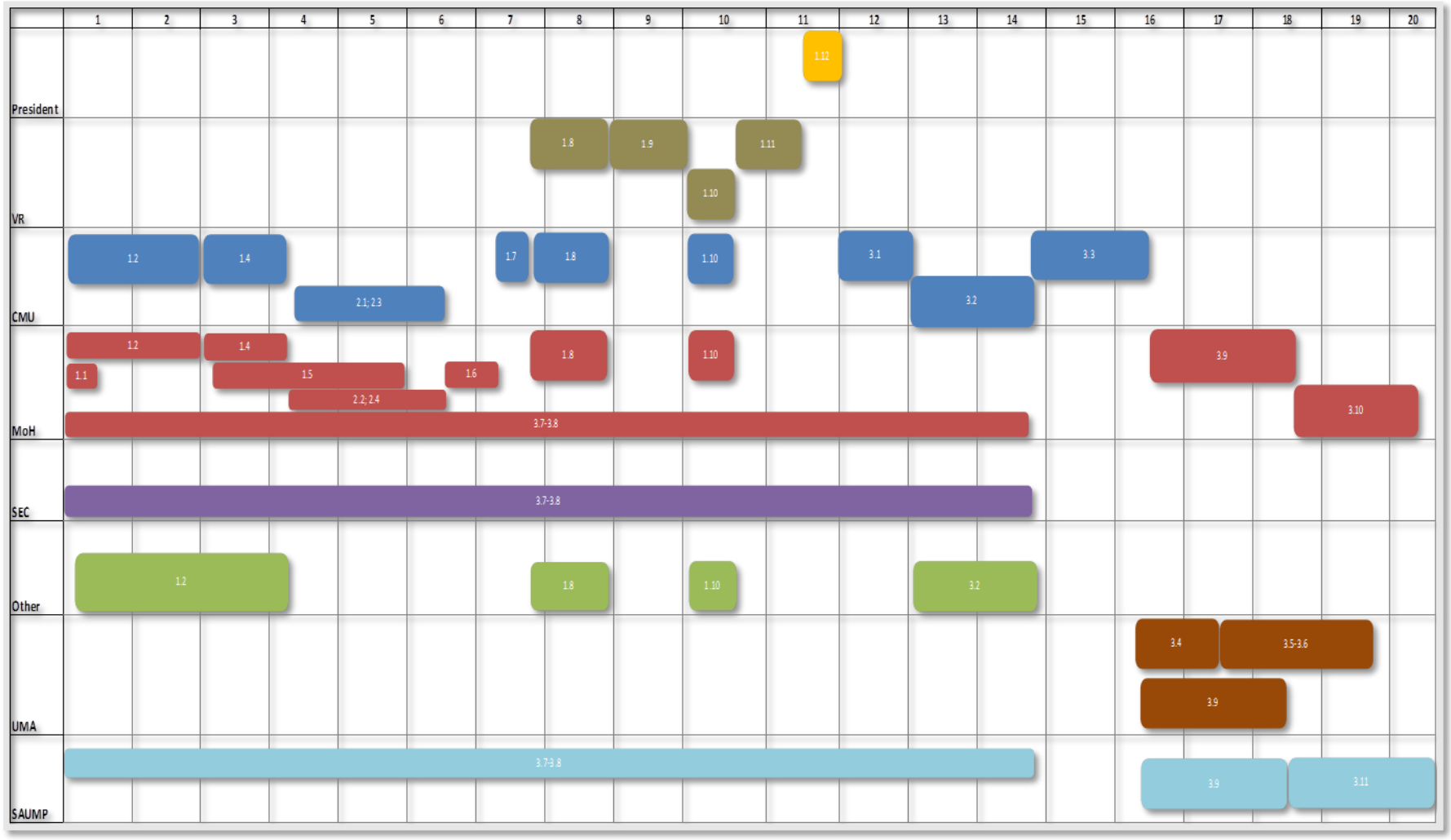
Another recommendation is to implement the model of paid by applicants scientific advice by UMA[40]*.*

7.4. Required actions

To amend Law on Medicinal Products, as well as Law on Financing Sources and Budget Code.

[40] Paragraph 571 of Report

VII. ACTION PLAN



EXPLANATORY NOTES TO ACTION PLAN

Actions	Involved stakeholders	Estimated timeframes
1. Adoption and implementation of legislative changes		
A. Policy decision		
1.1 Adoption of decision to pursue the reform of medicinal products registration system	MoH	15 days
1.2 Drafting the concept of reforming system of medicinal products registration	MoH	2 months
1.3 Submission of the concept to CMU	MoH	10 days
1.4 Adoption of concept of reforming system of registration of medicinal products, which is based on the proposed changes to laws	CMU	1 month
B. Adopting legislation		
1.5 Drafting of needed changes to the Ukrainian laws	MoH	3 months
1.6 Public Consultations regarding proposed changes to laws	MoH, General public	20 days
1.7 Submission of the draft changes to laws to Parliament	CMU	10 days
1.8 Preliminary review of the proposed changes to laws	Parliament Committees, MoH, CMU	1 months
1.9 Adoption of the needed amendments to the legislative acts in the first hearing	Parliament	1 months
1.10 Consultations within Parliament Committees regarding possible amendments to the draft laws to be proposed for the second hearing	Parliament Committees, MoH, CMU	15 days
1.11 Adoption of the needed amendments to the legislative acts in the second hearing	Parliament	1 month
1.12 Signature of adopted amendments and their entry into force	President	15 days

2. Implementing the adopted changes at the level of by-laws		
2.1 Amendments to Decree 376 or its replacement with a new legal act, or cancelling of the act if policy-making and regulation is fully assigned to MoH	CMU	2 months
2.2 Amendments to Order 426 or its replacement with a new legal act	MoH	2 months
2.3 Amendments to Decree 647	CMU	2 months
2.4 Amendments to 690 , Order 898	MoH	2 months
3. Setting up operations of UMA		
3.1 Decision to establish UMA and approval of UMA's statute (regulation)	CMU	1 month
3.2 Administrative arrangements regarding the premises of UMA, equipment etc.	CMU, UMA, MoH	2,8 months
3.3 Appointment of Head and Deputies of UMA	MoH, CMU	1,5 months
3.4 Preparation of internal procedures of UMA and document templates	UMA	1 month
3.5 Takeover of employees of SEC, and where appropriate, of MoH and DLS	UMA	2 months
3.6 Supplementary recruitment of new staff, especially to the Competence Sector and Medical Devices Sector	UMA	2 months
3.7 Preparation of new website of UMA[41]	UMA, SEC, MoH	14 months
3.8 Creation of integrated information system that will contain[42]: • secure file-transfer system used for exchanging information for regulatory purposes (electronic document flow);	MoH, UMA, SEC	14 months

[41] The new portal may be created and launched by SEC simultaneously with actions, described in Sections 1-2.

[42] The integrated information system shall be created and launched simultaneously with actions, described in Sections 1-2.

• special electronic network linking public health authorities; • database of authorised medicinal products; • system which facilitates monitoring the post-authorization safety of medicines through safety reports		
3.9 Transfer of databases and IT tools from SEC, and where applicable, also of MoH and DLS, to UMA. Implementation of new IT tools dedicated to UMA (including EDMS)	MoH, UMA	2 months
3.10 Winding up of operations of SEC following relevant transition period	MoH	2 months
3.11 Winding up of operation of DLS following relevant transition period	DLS, CMU, MoH	2,5 months

VIII. LIST OF APPENDICES

Appendix 1. Presentation for the EBRD Steering Committee, 26 April 2017.

Appendix 2. Presentation for the meeting in the Ministry of Healthcare of Ukraine, 8 June 2017.

Appendix 3. Presentation for the EBRD Steering Committee, 25 July 2017.

Appendix 4. EBRD Letter to MoH of 31 July 2017.

Appendix 5. Detailed description of the current medicinal products registration procedure.

Appendix 6. Recommendations on improvements to be implemented in medicinal products registration procedure.

Appendix 7. Detailed organizational scheme of SEC.

Appendix 8. Matrix of responsibility:

8.1 Matrix of responsibility as is.

8.2 Matrix of responsibility to be.

Appendixes 9.1 – 9.17. KPI Cards for SEC Key Personnel.

Appendix 10. List of laws and bylaws to be amended, replaced, cancelled.

IX. ADDITIONAL MATERIALS[43]:

Appendix 11. Detailed description of the current clinical trials procedure.

Appendix 12. Recommendations on clinical trials procedure.

Appendix 13. Detailed description of pharmacovigilance procedure:

13.1 Description (analysis of info cards).

13.2 Description (specialized expertise).

Appendix 14. Recommendations on pharmacovigilance procedure:

14.1 Recommendations (analysis of info cards).

14.2 Recommendations (specialized expertise).

[43] All the additional materials are prepared by Odgers Berndtson team in the course of SEC key functions analysis. The materials are provided as a courtesy and may be used by SEC and UMA in the future as a basis for revision and improvement of clinical trials procedures and pharmacovigilance procedures. In that case we recommend that applicable EU legislation is additionally taking into account in the course of analysis and improvement.