8 October 2018
EMA/MB/690649/2018 Adopted
Management Board

Minutes of the 101st meeting of the Management Board

Held in London on 4 October 2018

The chair opened the meeting welcoming Irena Storova, new member for the Czech Republic, Eija Pelkonen, new member for Finland, María Jesús Lamas Díaz, new member for Spain and Judita Hederova, new alternate member for Slovakia.

The chair confirmed the willingness by Catarina Andersson Forsman, Lorraine Nolan and Grzegorz Cessak to continue to act as topic coordinators for the programming document to be discussed in December, and by Nancy de Briyne to join them to provide specific focus on veterinary matters.

1. Draft agenda for 4 October 2018 meeting

[EMA/MB/297556/2018] The agenda was adopted with no amendments.

2. Declaration of competing interest related to current agenda

The Secretariat informed members of the Management Board that it had reviewed members' declared interests in accordance with the Board's policy on the handling of competing interests. Some potential competing interests relating to the day's agenda were identified concerning topics "*B.3 Revision of EMA breach of trust procedure for competing interests of and disclosure of confidential information by scientific committees' members and experts and B.5 Concept Paper for the Telematics strategy 2020-2025".* The Secretariat informed the board that all concerned members had been informed before the meeting. Should the need for a vote on the above topics arise, the chair would take up the matter again.

Members were asked to declare any specific interests that could not be drawn from their current declaration of interests that could be considered to be prejudicial to their independence with respect to the items on the agenda. No conflicts of interest were declared.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

3. Minutes from the 100th meeting, held on 6-7 June 2018 adopted via written procedure

[EMA/MB/395034/2018] The Management Board noted the final minutes, adopted by written procedure on 21 August 2018.

4. EMA Preparedness on Brexit

4.1 Update on EMA Brexit preparedness

4.1.1 Progress report on operational aspects

The implementation of the redistribution of the UK centralised products (CAPs) portfolio is proceeding as scheduled. The UK National Competent Authorities (NCAs) will remain accountable for the medicinal products for which they are (Co)-Rapporteurs until 29 March 2019. As of 30 March 2019 the new (Co)-Rapporteurs will take over full accountability and responsibility for the re-allocated medicinal products, but may be required to handle post-authorisation procedures from Q4 2018 onwards when it is envisaged that the procedures may be still under evaluation at the time when the UK withdraws from the EU and becomes a third country. An Executive Decision reflecting this approach was endorsed by the Management Board by written procedure on 19.9.2018. Cut-off dates for each procedure were extrapolated by averaging the length of each procedure from submission to outcome, and were agreed by the EMA Working Groups on Committees' operational preparedness and then presented to the Committees. An agreed knowledge transfer package to facilitate the new (Co)-Rapporteurs taking up accountability and responsibility is being finalised by EMA and will be made available in October.

At the meeting on 17 September of the EMA Working Groups on Committees' operational preparedness, next steps for the distribution of the workload for scientific advice for human medicines were discussed. The potential impact of Brexit on the supply of medicines and on inspections was examined, as well as the expertise needed from December 2018 onwards in the SAWP to fill expertise gaps due to UK delegates leaving. The election of the new SAWP chair is planned for December 2018.

EMA has defined a list of CAPs potentially 'at risk' of supply shortages, based on a survey of MAHs about timelines for submission of necessary regulatory changes. Based on a risk matrix, which includes different elements required to be changed before 30 March 2019, EMA is monitoring the submission of changes to the marketing authorisations. Marketing Authorisation Holders (MAHs) with products ranked in the highest risk level have been contacted to address any potential medicinal product supply disruption. Follow-up meetings were organised with MAHs for 'at risk' products, leading to a reduction of their number after companies stated that they will make the necessary changes in time. The number of remaining 'at risk' CAPs will still be subject to change as they are based on planned regulatory submissions . 'At risk' products will undergo a criticality assessment on their therapeutic use performed by CHMP/CVMP with the support of EMA. The Agency will subsequently liaise with each Member State with respect to the availability of therapeutic alternatives for each medicinal product, providing data available from the Article 57 database. The general overview will be maintained by EMA at EU level. It was also announced that the information provided today on the 'at risk' CAPs (updated where relevant), will also be sent to each Head of Agency.

4.1.2 Preparation for 2019 and 2020 WP, including impact and phasing-out of BCP

The Agency is addressing a situation where a 'business as usual' scenario is no longer possible by implementing a Brexit Preparedness Business Continuity Plan (BCP) based on temporarily scaling back

or suspending activities classified in 3 main categories (highest priority 1 down to priority 3). Phase 1 of the BCP was launched in 2017, followed by phase 2 in January 2018. An additional set of EMA activities have been temporarily affected as part of the BCP phase 3 launched on 1 October 2018 (the detailed plan was discussed under agenda item 4.1.3). The situation is now gradually shifting from Brexit preparedness to implementation. It is expected that the number of FTEs needed for Brexit preparedness/implementation will stabilise towards the end of Q4 2018 and start to gradually decrease as of Q1 2019. The board was presented with updated figures on staff's intention to relocate to Amsterdam, which take into account the survey conducted in June 2018 as well as the feedback from one-to-one discussions between staff and line managers. Between 1 January and 28 February 2019 the Agency will experience the loss of all its short-term contract personnel, as well as of a still to be defined number of long term contract staff due to resignations. From 1 March to 30 June 2019 EMA will be very reliant on teleworking and the Agency might also see an important increase in staff loss due to relocation. After 1 July 2019 and up to beyond 2020 further resignations might be expected although these will be matched with a further increase in recruitment of new staff. While the situation at the end of September appears now to be more positive with regards to longer term contract staff compared to February, it remains highly volatile. Staff retention support measures taken by EMA and the Dutch authorities seem to have had a positive effect, combined with the positive feedback from those staff who have already relocated.

Furthermore, certainties around numbers of short-term contract personnel who will no longer be available after the end of February 2019 and on possible adequate replacement following the experience with the first round of external selection procedures are to be considered against uncertainties such as: the real numbers of longer term contract staff not relocating, staff on parental leave/unpaid leave, possible extent of a second wave of staff resigning at a later stage and the EU Budgetary Authorities' decision as regards the EMA request for additional resources, which has not yet been taken. Two scenarios on staff loss were modelled based on different assumptions concerning intentions to relocate, taking into account the most updated feedback provided by staff. In the best-case scenario the workforce would ensure carrying out category 1A, 1B and Brexit activities with a margin, while in the worst-case scenario around the time of the move the workforce would not be sufficient to continue to carry out all of those activities. It is anticipated that the final scenario will be in between these scenarios. Consequently, the 2019 and 2020 planning will be based on such intermediate scenario.

On the basis of current knowledge it can be anticipated that 2019 will be a year of transition, followed by a year of gradual recovery paving the way for the future. It is further expected that the normal working pattern of EMA staff could be disrupted during February and March 2019 and that additional measures will have to be taken during the timeframe around the physical relocation. Specific continuity arrangements will apply during the critical period between 11 February and 15 March, with a permanence to be established during the week of 4-8 March 2019. The board was invited to discuss the proposed approach, so that EMA can prepare the 2019 and 2020 Work Plan to be further examined by the Topic Coordinators in view of the adoption at the December 2018 board meeting.

The board commented on the overall high quality of the analysis performed and requested more detail about the possible consequences of a worst-case scenario. It was noted that the most likely scenario will be an intermediate one. In any event the BCP is in place to ensure that essential public health activities will be safe-guarded and in case of need further temporary measures could be introduced to achieve this objective. A new HR tool will allow access to up-to-date information on staff intention to relocate, therefore allowing effective monitoring and planning. About the question on what could be done to limit the impact of the worst-case scenario, the Executive Director reminded the board that extra capacity can only be available on short notice if NCAs are able to deploy their resources on a limited time bases to support EMA staff. The representative of the European Commission DG SANTE

welcomed the detailed presentation which will provide better arguments in the discussion on further resources with DG BUDG. He requested more information on the reasons for difficulties in hiring short time contract personnel in the Netherlands. The Executive Director explained that the local labour laws, as currently understood by the Agency, allow only timeframes that are too short and do not provide stability in an environment subject to high requirements of confidentiality. Furthermore, it would not be possible to apply tenders based on the relocation to the Netherlands during the last months of the Agency in the UK. The Agency is working to obtain a better knowledge of the labour laws in the Netherlands. Information was requested on geographical distribution and interest level in the selections run by the Agency. The Agency has experienced a high interest from all parts of Europe for its long term selections, and is launching now four selection procedures for short term 3 year contracts whilst in discussion with the Commission on an additional 40 contract agents.

4.1.3 EMA Brexit Preparedness Business Continuity Plan – Phase 3 implementation plan

[EMA/MB/680226/2018; EMA/DED/660449/2018] The Management Board noted the EMA Brexit Preparedness BCP Phase 3, for which the principles and methodology for the next phases of the EMA Brexit BCP had been presented at the June meeting. At that meeting the board was also informed that the launch of Phase 3 would take place on 1 October 2018 and that a detailed implementation plan would be provided at the October meeting. Phase 3 will have to be complemented by an additional set of temporary suspensions/reductions as of 1 January 2019, which will be launched as part of phase 4 of the BCP. Temporary suspension/scaling back of activities is currently scheduled to last until 30 June 2019. The category 2B activities that have been identified for phase 3 consume a high level of FTEs and should provide for interchangeability of staff following training/knowledge transfer. The areas concerned are international activities, guideline development, secretariat activities relating to a number of working groups and working parties, programmes and projects, stakeholder interaction and clinical data publication. EMA will publish information on the implementation plan after the meeting of the board.

Concerning a request for a possible exception to the BCP in publishing clinical data for specific products where there is high public interest, it was noted that the clinical data publication policy implementation plan does not foresee at this stage the publication for products that pre-date the coming into force of the policy, and for which the necessary data packages would not be available. Moreover, staff assigned to clinical data publication has currently been redeployed to different tasks due to the BCP. EMA clarified that work in the area of safety communications continues and due consideration will be given to any further action needed for particular products.

4.1.4 Facilitation of SNE relocation

In the context of enabling relocation to the Netherlands, and ensuring Business Continuity, some exceptional measures to facilitate the retention of Seconded National Experts (SNE) have been considered and will apply to SNEs who relocate from London to the Netherlands and whose place of origin was not in the Netherlands. Measures will concern application of an exception to extend renewals beyond the four-year term, up to a maximum of 6 years, continued payment of daily allowance when the seat of the Agency is still in London, and from London when the seat of the Agency is in Amsterdam during the transition period, as well as a lump sum payment equivalent to 30 days of daily allowance as relocation contribution. The monthly and daily subsistence allowance will be reviewed in line with the distances between the place of origin and the new place of secondment as of 30 March 2019. Administrative aspects of medical insurance have also been clarified.

4.2 Update on EMA-NL collaboration for relocation to Amsterdam

4.2.1 Progress report on the relocation to the Netherlands

The relocation of the EMA to the Netherlands proceeds as planned and can be monitored through the tracking tool published on the EMA website (https://www.ema.europa.eu/documents/other/ema-tracking-tool-relocation-amsterdam-main-milestones_en-0.pdf). Main milestones can be broken down in four work-streams, tracking progress with the construction of the permanent building and the preparation of the temporary building, staff relocation and financial, governance and legal matters. The tracking includes information on status of progress, milestones and party in charge of the action.

On 7 November the chair and vice-chair of the Management Board and the two topic coordinators for the building, Karl Broich and Audun Haga, will visit the sites of the SPARK and the permanent EMA building in Zuidas in Amsterdam with EMA. This will provide an opportunity to ask questions on all aspects of the buildings in order to report back to the board at the meeting in December. Concerning hospitality arrangements for delegates, these will be handled through an online travel and hotel booking platform of EMA, which will be presented later in the year.

A. Points for automatic adoption / endorsement

A.1 Management Board decision – Model rules on Temporary posting

[EMA/MB/391744/2018; EXT/742466/2017; EMA/MB/809113/2017] The Management Board adopted a decision laying down implementing rules on temporary occupation of management posts based on model rules for agencies. The rules clarify circumstances in which a staff member may be appointed to a temporary posting and further clarify the calculation of the differential allowance.

A.2 Management Board decision - Outside activities and occupational activities after leaving the Service

[EMA/MB/572454/2018; EXT/617512/2018; EMA/MB/568497/2018] The Management Board adopted a decision on outside activities and assignments and occupational activities after leaving the service by analogy to Commission Decision C(2018) 4048 final of June 2018. The decision introduces clarifications, simplifies processes and includes tighter procedures to implement provisions for occupational activities of staff after leaving the service.

A.3 Revision of budget structure from financial year 2019

[EMA/MB/225635/2018] The board endorsed the revision of the Agency's budget structure to create a budget item for the contributions to European Schools which will be needed when the Agency relocates to the Netherlands and staff members will enrol their children in the European Schools in The Hague or Bergen.

B. Points for discussion

B.1 Highlights of the Executive Director

EU activities

EMA was invited for the first time to participate in the Informal meeting of EU Health Ministers which was held in Vienna under the Austrian Presidency on 10-11 September. The opportunity was provided

to explain some of EMA's initiatives and to present the network and its activities. The Executive Director will have his annual exchange of views with the ENVI committee in Brussels on 19 November.

International activities

In phase 3 of the BCP EMA continues to participate, albeit in a reduced manner, to major events that address global health issues. The Agency attended the 2018 ICMRA Summit hosted by the FDA in Washington DC and the WHO-led ICDRA biannual meeting that took place in Dublin.

Network activities

EMA organised on 22 June the third regulatory awareness session in 2018 on medical devices to provide an update on its progress in the implementation of the new Regulation.

New corporate website

The new EMA website was launched on 27 September. Although the content and structure remain unchanged, a number of new features have been added to improve user experience and searchability, as well as use and display on mobile devices. The new website is hosted on the cloud based Next EUROPA Content Management System and is supported by DG-DIGIT.

Valsartan case

The first priority of this case is the protection of public health, while limiting unnecessary medicines shortages. The case has shown that the systems of Incident Management and coordinated evaluation and communication are functioning effectively and there is global engagement and alignment. Key features are the close interaction with national inspectorates in the EU, EDQM and OMCLs, as well as proactive collaboration with the US FDA, Health Canada, PMDA and others.

Population of data in databases

On 30 July data from the Article 57 database was made public on the EMA website, providing for the first time a complete listing of all medicines authorised in the European Economic Area (EEA) to stakeholders. Following a recommendation by the European Commission Internal Audit Service the Agency will present a plan for the continuation of the completeness checks on data in cooperation with the NCAs to the board in December.

There is a need to work together with the NCAs also to close remaining gaps in data on authorised actors and API manufacturers in the Eudra GDMP database and on Clinical Trials end dates in the EudraCT database.

Regulatory science strategy discussion

Two stakeholder workshops launching the consultation on Regulatory Science Strategy to 2025, one Human and one Veterinary, are planned for 24 October and 6 December. This bottom-up exercise was launched in 2017 through the scientific committees/working parties coordinated by the SciCoBo and has the objective to support strategic planning as well as help identify expertise gaps. Following a public consultation the document should be finalised by end of 2019 and form a key input into the preparation of the overarching European Medicines Regulatory Network 2025 strategy.

Court case on 30 Churchill Place

A hearing on the procedural decisions on how to run the on-going litigation between EMA and EMA's landlord was held on 26 September. The trial will start around mid-January and a first instance judgment could potentially be issued before 29 March 2019. The Agency is keeping the European Commission fully informed about any developments in this case.

Ombudsman public consultation on pre-submission

A public consultation on EMA pre-submission activities is about to be launched by the European Ombudsman.

Application of the new data protection regulation, implementation of GDPR

The General Data Protection Regulation (GDPR) came into force on 25 May 2018. EU institutions and agencies, including EMA, will be subject to a separate Regulation that will apply essentially the same requirements. The European Data Protection Board (EDPB) was established by the GDPR to issue general guidance to promote a common understanding of European data protection laws. There is a real concern and confusion about the GDPR within and outside the EU, also about the high level of potential fines for breaches of the new Regulation. It is now necessary to tackle the data protection issues with even more care, in collaboration with DG SANTE and DG JUST, as sound interpretation is necessary and EMA is suffering particular resource constraints in this area.

Workshops in Q4 2018

A multi-stakeholder workshop to discuss electronic product information (ePI) to agree common 'EU Key Principles for the use of electronic SmPC and PL formats' will be held on 28 November 2018. The HMA/EMA Task Force on the availability of authorised human and veterinary medicines will organise a multi-stakeholder workshop on 8-9 November 2018 to gather perspectives on how to address availability issues and include their input into the deliverables of the task force.

Following the presentation by the Executive Director, several board members expressed satisfaction over the wide collaboration and good alignment in the valsartan case. A member regretted that Member States were not involved more deeply in matters of common interest with EMA such as the discussion on Regulatory Science. The Executive Director explained that the workshops are based on first steps lead by the Chairs of the Scientific Committees, and involving experts from the NCAs through the working parties. When starting to feed the outcomes of the workshops into the Work Programme, discussion at different levels and formats will be necessary. Currently first level information is required, which will also be supplemented by a public consultation in 2019. The representative of the European Commission agreed on the need to work closely with the Agency on the interpretation and implementation of the GDPR and to prepare specific information to stakeholders concerning clinical trials.

B.2 Report from the European Commission

Falsified Medicines Directive – Safety features

The new medicine verification system will be applicable as of 9 February 2019 and all national systems should be ready for it. 28 National Medicines Verification Organisations (NMVO) have been set up and 24 IT contracts out of 29 signed. However some Member States appear to be behind in the preparation, and hospital preparedness remains a concern. Member States are invited to monitor and support the signing of IT contracts, the on-boarding of users, and the pilot testing and preparedness of hospitals.

Finalisation of Regulation 726/2004

The amendments introduced as part of the new veterinary legislation are likely to be adopted and published in November 2018. The application of the amended provisions will undergo a phased implementation, with some changes applying immediately and others deferred to when the new veterinary rules start to apply three years later.

Brexit Preparedness Seminar 23 October 2018

The Seminar will have the objective of informing the Member States regarding the state of play from a Commission services' perspective, discussing the state of preparedness and measures taken at EU level by EMA and national regulators for the pharmaceutical sector, and getting feedback from Member States on preparedness measures taken at a national level.

HTA: state of play

The proposal for the Regulation on health technology assessment was adopted in January 2018. The European Parliament, on 3 October, adopted its report on the proposal with a large majority, and the Austrian presidency aims at obtaining agreement between the Member States on key elements by November 2018. The objective of the Regulation is to establish a framework and procedures for cooperation on HTA at Union level and to establish common rules for the clinical assessment of health technologies.

Evaluation of orphan and paediatric regulations

A study supporting the upcoming evaluation of the EU orphan legislation was launched in early 2018 and complements the studies on the economic impact of pharmaceuticals incentives on innovation, availability and accessibility (published last May) and the EC report on the Paediatric Regulation (the "Paediatric report"). As part of the evidence collection a public consultation is held between October and January 2019 as well as targeted stakeholder consultations, including of Member States, in October/ November 2018. A Commission Staff Working Document on the evaluation of the orphan and paediatric regulations will be prepared in 2019 and it will provide an evidence base which can be used by the next European Commission to consider the possible need for any future legislative changes.

Review of the EMA fees system

The Commission evaluation of the EMA fee system is ongoing and is expected to be finalised in December 2018. After the submission by the contractor of the final study reports a Commission Staff Working Document will be drafted and submitted for internal adoption. After agreement by the College, an impact assessment presenting possible policy options is expected to be initiated in 2019.

EU/US Mutual Recognition Agreement

The implementation of the EU-US MRA is proceeding according to programme. 15 Member States have been recognised by the FDA and a further 13 should be added by 15 July 2019. Two bilateral confidentiality commitments remain to be signed. On the veterinary side 13 audits in the EU are planned to start in November 2018 leading to a possible recognition on 15 July 2019.

International activities

A bilateral meeting took place with India to discuss among other topics international GCP standards and possible membership of PIC/s for GMP. The Commission together with the EMA met the US FDA for the annual bilateral, ATMPs and the MRA were discussed among other topics. A meeting of the ICH will take place in Charlotte, NC on 10 to 15 November 2018.

Multi-stakeholder meeting on Biosimilar medicinal Products

The yearly meeting took place on 14 September 2018 and gathered around 140 participants for an exchange of information on national policies and initiatives and on their uptake. EMA's contribution for the preparation of recently published information materials on biosimilar medicines for patients and healthcare professionals, was highlighted by the DG GROW representative.

Pricing and Reimbursement

A meeting of competent authorities for Pricing and Reimbursement with the support from the Commission took place under the Austrian Presidency with a focus on how to organise discussions on

an informal committee between Member States, in a more structured way, as the competencies on setting the actual prices and reimbursement levels are at a national level, whilst the EU Directive on transparency on procedural aspects is in force.

Following the presentation by the European Commission representatives a Board member expressed concern to DG GROW over the timelines for the implementation of the Medical Device and *In-Vitro* Medical Device Regulations, and highlighted that any delays could have serious consequences on supply of medicinal products that include or depend on devices for their use. The representative of DG GROW agreed that the timelines are demanding, but confirmed that implementation activities at the level of the European Commission are on track and that there are no intentions to change the implementation deadlines. The Commission will be available to provide a more detailed status update on the implementation preparation at the next meeting.

B.3 Revision of EMA breach of trust procedure for competing interests of and disclosure of confidential information by scientific committees' members and experts

[EMA/MB/641199/2018; EMA/MB/154320/2012, Rev. 2] The Management Board endorsed the revision of the EMA breach of trust procedure for competing interests of and disclosure of confidential information by scientific committees' members and experts which was updated to take into account experience gained with the first cases of breach of trust procedures. Overall the procedure has shown to be fit-for-purpose, and it was decided to extend its scope to the case of disclosure of confidential information by a scientific committee member or expert. A breach of trust procedure exists also for declarations of competing interests for Management Board members, and the Agency will propose to the board similar amendments through a written procedure to take place before the meeting in December.

B.4 EMA policy on access to documents

[EMA/MB/523307/2018; EMA/729522/2016, Rev. 1; EMA/127362/2006, Rev. 1; EMA/183710/2016] The Management Board adopted the revision of the European Medicines Agency policy on access to documents (Policy/0043) and endorsed the revisions of the Output of the European Medicines Agency policy on access to documents related to medicinal products for human and veterinary use and of the Output of the European Medicines Agency policy on access to documents non-related to medicinal products for human and veterinary use. The policy and output table on human and veterinary medicinal products have been in force since December 2010 and have been complemented with a new output table on documents not related to medicinal products. In December 2016 the board agreed to launch a three months public consultation on the documents. Numerous comments were received from stakeholders and were carefully considered in the new revisions. Among the main changes to the policy are a number of clarifications and the inclusion of a provision on requests that are abusive, repetitive and/or excessive in number. Furthermore, due to the high volume of requests resulting in excessive workload, and in order to avoid jeopardising EMA's core business tasks and performance, the Agency will, as foreseen by legislation, no longer process access to document requests from outside the EU.

B.5 EU Telematics Strategy 2020 – 2025 Concept Paper

[EMA/MB/593498/2018; EMA/586125/2018] The board endorsed the concept paper, which includes three top strategic business objectives that the network should achieve over the coming years with the support of Telematics. These are: better and more effective regulatory decision making; facilitate Research and Development in Europe; build trust in medicines by empowering patients, animal owners

and healthcare professionals. The Concept Paper was drafted by the IT Directors Executive Committee following a workshop in November 2017 with EU Telematics Management Board (TMB) members and the chair of the EMA Management Board, and in consultation with the EMA Scientific Committees. It was adopted by the EU TMB on 23 May 2018 and HMA on 13 July 2018. After endorsement by the Management Board work on the development of the Telematics strategy 2020-2025 will commence in autumn. The strategy will be developed in consultation with all major partner and stakeholder groups and is expected to be finalised and endorsed in 2019.

B.6 Clinical Trials Information System Required by the Clinical Trial Regulation

a) Update on the CTIS Project

[EMA/MB/552613/2018; EMA/552137/2018; EXT/INS/GCP/370512/2018; EMA/504594/2018] The board noted the Update on the Clinical Trials Information System (CTIS) Project for implementation of the Clinical Trial Regulation. The update shows an increase in the number of bugs identified, as EMA and the contractor have started to apply a broader range of tests that have resulted in discovery of new bugs, although the rate of fixing remains slow. As a result, the aggregate risk level has increased since end of May 2018. This risk level also takes into account the impact that the relocation of the EMA in March 2019 may have on activities that depend on physical co-location of teams and on retention of key EMA and contractor team members. Development of release 0.7 of the Portal and Database (auditable release) is complete and undergoing the final stage of bug fixing in order to meet Site Acceptance Test (SAT) criteria and enable the start of User Acceptance Test 7 (UAT7). Onsite UAT7 on EMA premises could take place in early 2019, once a successful SAT and Pre-UAT (in first half of November) by the MS and sponsor UAT Champions has taken place and the EU CTR Coordination Group has given the green light for UAT7. New planning shows UAT7 extended to 6 weeks and audit field work to take place after the EMA move to Amsterdam. Design of release 0.9 including the Safety reporting and assessment is nearing completion and its development began end of September. Preparations for the audit are ongoing, the CTIS Expert Group has nominated 3 members to join as technical advisors the tender assessment panel for the audit service. Once a specific contract for the audit has been established, EMA will arrange a meeting of the lead auditor with the Management Board's Topic Coordinator and the EU CTR Coordination Group representatives. All three phases of the external review of the CT Project Assurance Plan have been completed and recommendations have been prepared for consideration by the board.

b) Report on the Independent External Review of the Project

[EMA/MB/652420/2018; EXT/652463/2018; EXT/652445/2018; EXT/652475/2018] The Management Board noted the reports for phases 2 and 3 and an executive summary that highlights the most important findings and recommendations of the independent project assurance report. The findings and proposed recommendations for all 3 phases were presented on behalf of the independent consultant KPMG. Adding to the domains covered during phase 1 and reported on at the meeting of the board in June, phase 2 considered the domains of schedules, resource constraints and planning processes, skills and experience, communication and information management, demand management, while phase 3 looked at architecture and design governance, development approach, risk assessment and testing and UAT. On the basis of interviews and workshops with main project stakeholders, and of review of documentation provided by EMA, the contractor delivered a series of actionable recommendations.

c) Report from the EU CTR Coordination Group

The board heard the report by the Topic Coordinators (Xavier De Cuyper, Thomas Senderovitz, Karl Broich, Rui Santos Ivo and Ian Hudson) on behalf of the EU CTR Coordination Group and noted the document setting out objectives of the audit and criteria for confirming that the system meets the functional specifications and is fully functional, as well as the RACI matrix (see EMA/504594/2018 under B.6.a) which had been endorsed by the EU CTR Coordination Group at its meeting of 20 September 2018. If needed, a review of the RACI matrix will take place in January 2019. UAT7, which forms the basis of the audit, needs to be carefully prepared. Preparation is progressing well and it has been agreed to start Pre-UAT in early November. To provide more certainty of success UAT7 dates will be confirmed once the system has passed SAT and pre-UAT, and is likely to be scheduled after 7 January 2019. The EU CTR examined the outcome from the Independent External Review and recommended in particular four actions: the acquisition of additional external PMO support, re-structuring of IT delivery contracts, increase in business analysis capacity and mitigation of staff and knowledge loss, as well as enabling frequent co-location co-operation with off-shore development teams. In conclusion, the Coordination Group recognised the efforts and time spent in summer by all teams and noted the quality of the independent external review and their key findings. The high number of bugs and resource constraints and overall project risk still pose major obstacles. The Coordination Group therefore recommended to the board to further analyse the external review reports and work on the implementation of the main recommendations, to support the organisation of a pre-UAT7 and to mandate the Expert Group and the Coordination Group to supervise the UAT7 and prepare the action plan with a clear time frame for the December board meeting.

In the discussion that followed, some members addressed the implementation of the four recommendations by the EU CTR Coordination Group. The Executive Director confirmed that EMA has already started implementing some actions, such as improving co-location. As to others, the best and most immediate acquisition of additional external support would ideally come from the National Competent Authorities, as their experts have the most relevant knowledge. Budgets and resources will have to be carefully managed, also with the support of the board.

B.7 Update on the pilot of signal detection in EudraVigilance by marketing authorisation holders

[EMA/MB/493254/2018] The board noted the extension beyond February 2019 of the pilot agreed with the European Commission in 2017 as a transitional arrangement to prevent overload of the EU network when introducing the requirement for Marketing Authorisation Holders to continuously monitor EudraVigilance and inform EMA/NCAs of validated signals. The one year pilot for a phased implementation was started on 22 February 2018 focussing on a limited number of active substances. In view of the need for further experience and of the impact of Brexit on EMA and NCA operations and resources, the European Commission has agreed to extend the pilot. By September 2019 EMA will finalise a report to the Commission on the first year of experience, followed in December 2019 by a decision and communication on the next implementation phase including scope of products and date of coming into effect.

B.8 Annual report 2017 on Key Performance Indicators (KPIs) for evaluation, post-authorisation, inspection and scientific advice procedures for medicinal products for human and veterinary use (piloted procedures only)

[EMA/MB/543319/2018; EMA/479531/2018] The Management Board endorsed the Annual report on the performance of the Agency's scientific procedures: 'Key Performance Indicators (KPIs) for medicinal products for human and veterinary use' under the agreed pilot project started in 2011 with the aim to provide transparent reporting of the performance of NCAs under the Cooperation Agreement

(CA) between NCAs and EMA for services provided. Overall the report shows good performance across the portfolio and lifecycle of procedures. Slight loss of performance on timelines is made up for initial MA and Scientific Advice for human products by the growing volumes of work. Some drop in performance is found for the first time in veterinary scientific advice, while veterinary initial MA show an improvement in compliance. Performance for QRD is consistently high in the human area and slightly lower for veterinary. For post authorisation, performance is stable compared to previous years. For the first time, following request by the board, MNATs (multi-national assessment teams) are included in the statistics, although their numbers, even aggregated from 2015 to 2017, are too small to draw any significant conclusions for both human and veterinary procedures. GMP inspections show a lowered adherence to the reporting deadline, but remaining within acceptable delay, while GCP and PHV inspections remain at the same high performance standard as in previous years. All in all the report shows a very good and robust performance by the network, where it must be noted that any shift in timeliness does not reach the range beyond target and does not affect public health.

B.9 Ernst & Young (EY) study on MA procedures

The representative of DG SANTE introduced the study, commissioned to the contractor Ernst & Young, by the European Commission as part of the legal obligation to re-examine every 10 years the operation of the procedures laid down in 726/2004 on the basis of experience gained. Once finalised in 2020 the study will be submitted to the Council and European Parliament.

Two representatives of EY provided an overview of objectives and scope of the study, and introduced the methodology and consultation strategy. The evaluation aims to contribute to assessing the extent to which the current marketing authorisation systems for medicines meet the objectives laid down in the regulatory framework. The scope of the evaluation will include only medicines for human use, as a thorough evaluation for veterinary medicines was conducted in preparation of the proposal for the new veterinary regulation, and will focus on the centralised, decentralised and mutual recognition procedures in the 28 EU Member States and EEA countries from 2009 to 2017. The study will be based on effectiveness and efficiency criteria with regards to time and resources, but excluding assessment and evaluation of fees, which has been the subject of a separate study. Stakeholders and NCAs will be consulted by means of surveys, interviews and within case studies. An online survey of NCAs will be launched shortly, followed by up to 20 interviews with NCAs and field work in 8 Member States. It is expected that the final study will be submitted to the Commission in summer 2019.

As part of the methodology, it is foreseen that EY representatives will observe proceedings in the main EMA Committees and at the Management Board, and they attended the meeting for items B.10-12.

B.10 EMA Mid-year report 2018 from the Executive Director (January – June 2018)

[EMA/MB/600269/2018; EMA/449860/2018] The Management Board noted the mid-year report 2018 from the Executive Director. The report follows the structure of the work programme and presents information on the implementation of the objectives and activities from January to June. Preparation for Brexit is on target, with the building approval by the European Parliament Budget Committee on 22 March and the foundation stone laid on 28 May for the permanent building. The seat agreement was signed on 1 June. The Agency has further prepared by closely working with stakeholders and redistributing UK centrally authorised product portfolios for human and veterinary medicines. Highlights of key activities include the final opinion on valproate after the first public hearing at the Agency in 2017, and the second public hearing organised in June for quinolones and fluoroquinolones. The first two CAR-T cell medicines were recommended for approval in June and are also the first medicines supported through the Agency's PRIME scheme. Overall the performance at the Agency was stable, with some signs of change in the requests for PRIME eligibility and Innovation Task Force

briefing meetings, which are being monitored. Post authorisation trends are at expected levels, with the exception of type II variations. GMP inspections continue to decrease as predicted following the Mutual Recognition Agreement with the FDA, while GCP inspections are rising as a consequence of the recent revision of classification. Performance of veterinary procedures is steady and supported by procedures linked to innovation, such as Scientific Advice and MUMS classification. From the budgetary perspective, revenue is lower than forecast, and will be carefully observed although it raises no immediate concern. The exchange rate fluctuation, reduced payments to Member States in line with changes in applications as well as slowing down in training and meeting costs due to Brexit, have contributed to balancing the budget but need to be monitored. Temporary agent occupancy rate is 99%, but with an increase in the number of resignations on the total number of staff leaving the Agency, which is likely to be linked with Brexit. It is estimated that 86 FTE will have been involved in 2018 in activities related to preparation for Brexit preparedness, as shown by the additional workload distributed over virtually all areas of the Agency. To help cope with the additional workload and help mitigate the risk of loss of expertise and knowledge during the relocation, the Agency had asked the board to endorse exceptional recruiting of additional Contract Agents with limited maximum 3 year contracts, starting with 20 FTEs in 2018 rising to 40FTEs in 2019. The European Commission has not yet granted this request. Recruitment at the Agency is proceeding according to a strict analysis and schedule placing significant demands on the Agency's resources. This resulted in a steep increase in the number of selection procedures carried out (more than doubled) and in the numbers of applicants.

B.11 Report from SAWP Chair

Rob Hemmings, Chair of the Scientific Advice Working Party, presented an update on the achievements and operational challenges of the Working Party to the board. Membership of the SAWP differs from other Working Parties and from the Committees as it is based on expertise rather than on national representation. Its 28 members have alternates and are all very active. An exercise in re-composition of the SAWP in the last few years has led to an increase in Member State and cross-committee representation. Workload has increased steadily over the last decade for requests of Scientific Advice, while request for qualification procedures have undergone a shift in focus, moving away from biomarkers and towards validation of clinical endpoints and scales, and towards qualification of methods and data sources/platforms. Parallel advice procedures with HTA bodies have experienced a significant increase from 2015, and their numbers appear now stable, with a variable number of NCAs participating. The ambition to advise on a single development programme has moved from trying to harmonise requirements of design features to working towards a single set that covers the different approaches applied by Regulators and HTA bodies. Patient involvement in the SAWP has increased dramatically in the last ten years, and has yet to reach a plateau. Coordinators recognise the added value of discussion with patients and the next step is to investigate whether input and preferences from the broader patient community can be elicited. Other developments for the SAWP concern the work done to inform decisions by CAT or CHMP on eligibility of PRIME products and the activities to support developers through discussion meetings and accelerated procedures. In the European regulatory ecosystem SAWP provides a platform for discussion for all committees for human medicines and for the working parties of CHMP and integrates the views in a single position. This is made possible by cross-committee membership, participation in the plenaries and through the support of an active secretariat. Looking at the wider European system, including the national competencies around Inspections and Clinical Trial authorisations, a reflection is needed on where there are opportunities to offer even broader advice to companies. Future challenges to the SAWP will come from the need to continue to ensure quality and consistency of advice with increasing numbers of procedures and breadth of consultation. The SAWP needs to continue to be up to date with the science feeding into novel products and novel strategies for development, and by new regulatory science topics such as companion diagnostics, robust evidence generation and the use of Real World Data.

There was interest among board members about the expertise in the SAWP and in the cross-membership with PDCO and PRAC. The Chair of the SAWP assured the board that good coordination by the EMA secretariat proactively ensures smooth consultations among Committees and avoids clashes among meetings that could be affected by cross-membership. Cross-membership *per se* does not mean overlap in activities, as different topics are discussed from different perspectives. Concerning the issue of whether the existing expertise is adequate to keep pace with technological advances, the Innovation Task Force helps with horizon scanning, but new unforeseen advances cannot be ruled out. Currently it can be expected that over the next 10 years digital, statistical and methodological expertise will be needed, as well as expertise in analysing real world observational data. The representative of patients' organisations informed the board that the benefits of the work done in the SAWP on registries and in the dialogue with HTA bodies are already visible, and stressed the importance of Scientific Advice in the developmental journey of a medicine through to patients. The representative of doctors' organisations reminded the board that Scientific Advice is requested by 60% of pharmaceutical companies. In order to achieve the harmonisation of HTA assessment, it is essential that all companies receive Scientific Advice involving HTA, and that there is increased transparency on the advice provided. The Chair of the SAWP added that the participation in the advice by HTA bodies is variable, depending on whether understanding of policy or of science prevails. The situation is evolving, hopefully moving constantly in the direction of a shared scientific understanding. He stressed that the scientific and logistic guidance to SMEs by the EMA secretariat in the pre-submission meetings is very valuable to allow them to prepare the documentation that meets requirements.

B.12 Impact of the new veterinary medicines legislation

The board heard a report on the current status of the preparation of the implementation of the new veterinary medicines legislation, which was discussed in three meetings during September. At the meeting in Brussels organised by the European Commission, representatives of HMA and EMA were informed that no formal action will be taken before the adoption of the legislation by the European Parliament and the Council foreseen in November 2018. EMA will be provided with the mandates to advise on 25 delegated and implementing acts, information on the IT databases supporting some essential business processes, as well as the revision of the Annexes. The Commission will set up a governance structure which will lead the implementation of the legislation. Priorities will be set based on the timelines contained in the legislation. On 19 September the HMA/EMA joint Task Force (TFCIVR) met in Paris and was attended by representatives of 18 NCAs, the Commission and EMA. Its objective is to support the implementation of the legislation. This first meeting of the Task Force was very constructive and focussed on the areas that will be mostly impacted, such as pharmacovigilance and AMR. A general agreement on a number of principles was achieved. At the meeting of EU TMB on 24 September the European Commission announced that it would take the lead for the oversight of the IT development and would then hand over the systems ownership function to EMA for running and maintenance. This was later confirmed in a letter. In conclusion, tripartite discussion to support implementation have started between the Commission, NCAs and EMA, and the TFCIVR was set up in a spirit of collaboration. There are however concerns on the short timeframe and on the fact that no additional resources have been made available to support the implementation of the legislation, which has significantly evolved from the analysis in the Impact Assessment carried out by the Commission in 2014. The Agency will request the Commission to carry out a new Impact Assessment to achieve more realistic information.

In the discussion that followed, some members made reference to the experience with the CTIS project and the possible lessons learned, such as the need to set up from the beginning a structure similar to the Coordination Group. The agreement taken in Paris to build the databases and IT systems on minimum designs with incremental improvements to take place later was welcomed. The

representative of DG SANTE informed the board that also the impact on the Commission was likely to have increased with the legislation now likely to be adopted, as it foresees a high volume of secondary legislation. The Co-chair of the TFCIVR recommended the board to consider carefully the resources needed for the implementation of the veterinary legislation within 3 years, such as the IT applications and the SPOR, when discussing the Programming document at the December meeting.

List of written procedures finalised during the period from 22 May 2018 to 10 September 2018

- Consultation no 5/2018 on the appointment of Loizos Panayi as CHMP alternate, proposed by Cyprus ended on 18 June 2018. The mandate of the nominee commenced on 19 June 2018.
- Consultation no 6/2018 on the appointment of Mario Melazzini as CHMP alternate, proposed by Italy ended on 19 June 2018. The mandate of the nominee commenced on 20 June 2018.
- Consultation on the adoption of the Agency's final accounts 2017 ended on 25 June 2018. The procedure was adopted.
- Written procedure for adoption of the 100th Management Board meeting minutes, ended on 15 August 2018. The minutes were adopted.

Documents for information

- [EMA/MB/634092/2018; EMA/573646/2018] Report on EU Telematics
- [EXT/671688/2018] Feedback from the Heads of Medicines Agencies
- [EMA/MB/540105/2018] Outcome of written procedures finalised during the period from 22 May 2018 to 10 September 2018
- [EMA/MB/584626/2018] Summary of the transfers of appropriation 2018

List of participants at the 101st meeting of the Management Board, held in London, 4 October 2018

Chair: Christa Wirthumer-Hoche

	Participants
Belgium	Xavier De Cuyper *(member)*
Bulgaria	Bogdan Kirilov *(alternate)*[1]
Czech Republic	Irena Storová *(member)*
Croatia	Siniša Tomić *(alternate)*
Denmark	Thomas Senderovitz *(member)*[1] Mette Aaboe Hansen *(alternate)* Tina Soon Engraff *(observer)*
Germany	Karl Broich *(member)* Wiebke Loebker *(observer)*
Estonia	Kristin Raudsepp *(member)*
Ireland	Lorraine Nolan *(member)* Rita Purcell *(alternate)*
Greece	*Apology received from Aikaterina Antoniou*
Spain	María Jesús Lamas Diaz *(member)* César Hernández Garcia *(alternate*) María Jesús Alcaraz Tomas *(observer)*
France	Dominique Martin *(member)* Jean-Pierre Orand *(alternate)* Miguel Bley *(observer)*
Italy	*Apology received from Mario Melazzini (member)* Gabriella Conti *(observer)*
Cyprus	Loizos Panayi *(member)*
Latvia	Svens Henkuzens *(member)*
Lithuania	Gintautas Barcys *(member)*
Luxembourg	Laurent Mertz *(member)*
Hungary	Beatrix Horvath *(alternate)*
Malta	John-Joseph Borg *(member)*
Netherlands	Hugo Hurts *(member)* Birte van Elk *(observer)*
Austria	*Apology received from Thomas Reichhart (alternate)*
Poland	Grzegorz Cessak *(member)* Magdalena Pajewska-Lewandowska *(observer)*
Portugal	Rui Santos Ivo *(member)*
Romania	Alexandru Velicu *(member)* Ada Georgescu *(observer)*
Slovakia	Judita Hederová *(alternate)*
Slovenia	Stanislav Primožič *(alternate)*
Finland	Eija Pelkonen *(member)*

[1] Competing interest declared resulting in no participation in decision with respect to agenda points B.3 and B.5

	Participants
Sweden	Catarina Andersson Forsman *(member)* Åsa Kumlin Howell *(observer)*
United Kingdom	Ian Hudson *(member)* Robert Hemmings *(SAWP Chair)*
European Parliament	Björn Lemmer Tonio Borg
European Commission	Andrzej Rys (DG SANTE) *(alternate)* Carlo Pettinelli (DG GROW) *(member)* Jerome Boehm DG Sante *(observer)* Chloe Spathari (DG GROW) *(observer)*
Representatives of patients' organisations	Yann le Cam
Representative of doctors' organisations	Wolf Dieter Ludwig
Representative of veterinarians' organisations	Nancy de Briyne
Observers	Runa Hauksdottir Hvannberg (Iceland) Brigitte Batliner (Liechtenstein) Audun Hågå (Norway
Representatives from Ernst & Young	Emilie Balbirnie *(partial attendance)* Virginie Lefebrve Dutilleul *(partial attendance)*

European Medicines Agency	Guido Rasi Noël Wathion Nerimantas Steikūnas Stefano Marino Fergus Sweeney Agnes Saint-Raymond Alexis Nolte Ivo Claassen Melanie Carr Anthony Humphreys Enrica Alteri Zaide Frias Marie-Agnes Heine Christine Bugge Anabela Marcal Petri Paakkonen Wim Nuyts Hilde Boone Silvia Fabiani Sophia Albuquerque