16 October 2017
EMA/580367/2017
European Medicines Agency

Executive Director's report to the Discharge Authority on measures taken in light of the European Parliament's recommendations (Discharge 2015)

Article 110(2) of the Framework Financial Regulation

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6. Notes that the result of the staff engagement survey carried out in 2015 represented a further improvement compared to 2013; observes however that identified remaining issues include collaboration across divisions, objectivity in decision-making processes and trust in senior management; acknowledges from the Agency that it created an action plan to address the remaining issues and adopted it in 2016; **calls on the Agency to report to the discharge authority on the implementation results of the action plan**;	The action plan to address key staff concerns was developed and implemented by a dedicated "Staff Engagement Action Group". A final report on the activities of this group was endorsed by EMA's senior management's Executive Board on 11 August 2017. The report states that out of the six endorsed proposals for actions, three are already in the implementation phase (internal mobility database; fact sheets for communication of decisions; regular team meetings), and three more are planned to follow (360 degree feedback process; personnel communication plan; better support for line managers). While it may take some time for all improvement actions to be fully embedded and take effect, particularly taking into account unforeseen workload generated by Brexit preparedness and relocation, the general principles and proposed actions are supported at all levels of the	**Partially implemented and ongoing**

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	Agency. Further evaluation through the next staff engagement survey will provide more insight on the effectiveness of their implementation.	
9. Acknowledges from the Agency that its revised policy on the handling of declarations of interests of scientific committees' members and experts entered into force in 2015; welcomes the fact that the declarations of interests of experts involved in the Agency's activities after the policy implementation date were evaluated against the revised policy; notes that the Agency performed systematic ex ante controls on the declarations of interests of new experts; notes moreover the conclusion of the annual ex post control on the handling of declarations of interests of committee members and experts participating in meetings; observes that the Agency updated the policy in October 2016 to further clarify the restrictions applied when an expert takes up a job in industry and to align the restriction applied in the case of close family members of committee, and working party members with interests in the industry, with those already applied to management board members; **calls on the Agency to provide the discharge authority with a summary of the impact assessment of the revised policy**;	The main change in the October 2016 revision of the Agency's policy on handling competing interests of scientific committees' members and experts consisted of increased restrictions applied in case of close family members of committees and working parties with interests in a pharmaceutical company. The implementation of this change resulted in 19 members and alternates of the human scientific committees (CHMP, PRAC, CAT, PDCO, COMP, HMPC – total number of members and alternates: 354) to become subject to more restrictions compared to the previous version of the policy. However, this had no major impact on the functioning of these committees. In 2016, 7 experts (2 committee members, 4 working party members, 1 expert) informed the Agency on their intention to become an employee in a pharmaceutical company. In line with the revised policy, those members were immediately fully restricted from further involvement in any Agency activity.	**Implemented**
15. Observes that the Agency adopted the Commission guidelines on internal whistleblowing in November 2014; notes also that the Agency is currently working on a policy to handle external sources' reports on matters within the scope of its responsibilities (i.e. external	The Agency's Management Board adopted the policy on the handling of external sources' reports on matters within the scope of its responsibilities in March 2017: • EMA's handling of information from external sources disclosing alleged improprieties concerning EMA activities related to the authorisation,	**Implemented**

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whistleblowing rules), and that approval of this new policy is planned to occur by the end of 2017; welcomes this policy which should strengthen even further the Agency's efforts to disseminate a culture of integrity and compliance in the preparation and submission of regulatory documents;	supervision and maintenance of human and veterinary medicinal products The policy, which was prepared in consultation with the European Commission and OLAF, came into effect on 17 March 2017. It aims to create an environment where individuals outside the Agency feel confident to raise their concerns on improprieties in their area of work, and submit information or evidence about improprieties they may have observed. The policy helps EMA assess these reports and coordinate any further investigation, while protecting the confidentiality of the reporting person. Further information on how the new policy is implemented is available on the Agency webpage below: http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_001825.jsp&mid=WC0b01ac0580b9fe95 An EMA SOP is available for EMA staff (SOP 129), setting out the internal procedures to handle external source reports (EMA/641948/2012). Confidentiality is stressed throughout the internal procedures. In 2016, EMA recorded no internal whistle blower cases and received 18 reports from an external source concerning alleged improprieties of a regulatory nature, potentially adversely affecting public health. EMA followed-up on each of these reports but did not identify any safety/efficacy concerns entailing the need to take specific regulatory action.	
18. Reminds the Agency that Directive 2003/63/EC states that medicines can only be considered for Union marketing authorisation if they have been tested in accordance with ethical guidelines, and reminds the Agency of its commitment to perform extra checks on clinical trials carried out outside the European Union	The EMA fully agrees that all clinical trials, wherever they are performed, must meet internationally agreed ethical and data quality standards or their equivalent, in order to protect the participating patients/volunteers. The primary responsibility for ensuring that a clinical trial is conducted in accordance with GCP, including ethical standards, lies with the sponsor of that trial and with the clinical investigators they select to carry out the trial. It is the	**Implemented and ongoing**

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before granting a drug market authorisation; **therefore, due to the special vulnerabilities of those tests, asks the Agency to report to the discharge authority every year on actions taken to ensure drugs for the Union market were tested ethically in lower and middle income countries, in accordance with the law**;	applicant's responsibility to ensure that any clinical trial included in their marketing authorization application (MAA) is carried out in accordance with the legal requirements and with international GCP and ethical standards. The European regulators have reinforced these standards in the Reflection paper on ethical and GCP aspects of clinical trials of medicinal products for human use conducted outside of the EU/EEA and submitted in marketing authorisation applications to the EU Regulatory Authorities. The EMA and the Member States authorities are carrying out a set of controls and inspections to verify information submitted by applicants related to the respect of such standards: the GCP Inspectors Working Group co-ordinates GCP related activities at Union level and publishes a report each year in which information is provided on inspections, where they are carried out, and action taken where applicable (GCP IWG 2016 Annual Report). Given the very large number of investigator sites distributed across many countries, and given the limited GCP inspection resource available (which must also inspect and supervise clinical trials in the EU, and control clinical trials in other third countries from which most data is obtained) the EMA approach has a number of dimensions: • Targeting inspection sampling through 'routine' inspection requests, to ensure coverage of clinical trials in a wide range of countries • Working with EU assessors to request 'triggered' inspections when needed (ie when specific concerns have been identified which need to be checked on-site) • Given that the above can only be applied to a sample of trials and concerns trials that have already been completed, EMA works with third country regulators to give training and build GCP inspection capacity across all countries, since this is the best way that EU can contribute to raising	

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	standards and increasing checks conducted by the local authorities in a prospective way. • Working with international partners (eg the US FDA) to share information and coordinate inspection coverage so that a higher number of inspection sites worldwide can be covered" EMA provides support to other regions through training and capacity building activities for international regulators to perform inspections in their jurisdictions, those include the GCP IWG Workshop and the On-line GCP Basic training, where many of the attendees were from outside the EU (Argentina, Bosnia and Herzegovina, Brazil, Canada, Chinese Taipei, Former Yugoslav Republic of Macedonia, Ghana, Japan, Malaysia, Mexico, Moldova, Montenegro, Nigeria, Rwanda, Saudi Arabia, South Africa, South Korea, Switzerland, Tanzania, Thailand, Uganda, Ukraine, USA, Zambia, Zimbabwe and representatives of the WHO). This training covers the full range of GCP including ethical aspects, the objective of which is to ensure the rights, safety and welfare of trial subjects are protected worldwide and that the data generated are reliable (which itself has an impact on the trial subjects and all future users of that medicine). In addition EMA informs the national authority when performing inspections outside the EU so that the local authority has an opportunity to observe and learn from the inspection carried out by an EU inspector. In 2016, at least 18 GCP inspections requested by the CHMP were observed by 3rd country regulatory authorities, including Belarus, China, Japan, the Russian Federation, South Africa and the USA. EMA tracks the geographical origins of subjects included in trials submitted in marketing authorisations applications to EMA. This tracking helps to identify trends and to target geographical regions for the EMA programme of routine GCP inspections. The number of GCP inspections in third countries carried out by the	

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	inspectors of the national competent authorities of the EU / EEA Member States on behalf of the EU has increased by more than four times between 2005 and 2016. Both routine and triggered inspections have increased over the time. In view of tens of thousands of sites conducting clinical trials worldwide, EMA and national authorities work with international partners to share inspection expertise, plans and outcomes, in order to widen the sample inspected, the impact of their inspection activities and coordinate responses to whistle blower reports. EMA along with the European Commission is building contacts with authorities in India, China, Russia, several African countries, and other countries where clinical trials are increasingly conducted, to share experience and training and build up expertise.	
19. Encourages the Agency to further raise awareness of its conflict-of-interest policy among its staff, alongside ongoing awareness-raising activities and the inclusion of integrity and transparency as obligatory items to be discussed during recruitment procedures and performance reviews;	Briefings and trainings on EMA's rules on competing interests are mandatory for all EMA staff and take place as follows: - Prior to taking up employment new EMA staff are sent the rules on competing interests and are assessed for any competing interest in accordance with article 11 of the staff regulations. - In addition, new staff are briefed by EMA's Staff Relations and Support Department (A-ST) on this subject on taking up duties and informed they must complete another declaration of interests on either the first or second day (this is followed up). They are also informed that, throughout their employment, a new declaration of interest must be filled in if their circumstances change. - Each year, staff members are required to self-train on the rules in advance of making their mandatory annual declaration. An email reminder is sent to each staff member each year with links to the Code of Conduct, which contains, amongst other documents the Rules concerning the handling of competing interests of staff. In making their annual declaration, staff are required to certify that they have read and understood the Code of Conduct. A-ST actively monitors	**Implemented**

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<tr><th>Observation of the Discharge Authority</th><th>Response and measures taken by the Agency</th><th>Status / Reference</th></tr>
<tr><td></td><td>response rates and follows up with staff, and if necessary their managers, if they fail to complete this within the deadline.

- Staff returning from Special Unpaid leave are also required to re-submit a new declaration of interest immediately upon return.

The Decision rules on competing interests of staff were reviewed in 2016 and both staff and managers were provided with training on the new rules. As of 2017, the annual review of competing interests of staff has been aligned with the appraisal exercise so that managers can review both processes in parallel.</td><td></td></tr>
<tr><td>25. Observes that in 2015, the Agency's IAC carried out audits in several areas, with no critical recommendations open at year-end; notes that, in the areas of security of product-related information, building blocks of assurance and video surveillance, the audits identified space for further improvements; acknowledges the fact that the Agency prepared action plans to address the identified issues; calls on the Agency to provide the discharge authority with the results of implemented actions;</td><td>For the 2015 audit programme, 42 of 64 recommendations have been successfully implemented.

<table><tr><th>Audit</th><th>Implemented</th></tr><tr><td>A15001 Video Surveillance</td><td>15</td></tr><tr><td>Critical</td><td>1</td></tr><tr><td>Very Important</td><td>8</td></tr><tr><td>Important</td><td>6</td></tr><tr><td>A15004 Security of Product Related Information</td><td>8</td></tr><tr><td>Very Important</td><td>4</td></tr><tr><td>Important</td><td>4</td></tr><tr><td>A15005 Building blocks of assurance</td><td>19</td></tr><tr><td>Very Important</td><td>3</td></tr><tr><td>Important</td><td>16</td></tr><tr><td>Minor</td><td></td></tr><tr><td>Grand Total</td><td>42</td></tr></table>
Key outputs from implemented recommendations are as follows:</td><td>Partially implemented and ongoing</td></tr>
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	A15004 Security of Product Related information • The Server and Storage Handbook was updated to improve the Agency's management of incidents and back-up arrangements • Access passwords are handled in accordance with updated Security Policy taking account of industry best practices. • The Service Desk revokes all system access rights for users leaving EMA upon receipt of official checklist. • Internal guidelines were developed for monitoring, logging and auditing the logs of the Agency's network and systems. • The Agency's system vulnerability scanning was reconfigured and updated. • Information Governance and access control for non-production environments were improved by the update of the Agency's security policy and the development of internal guidelines • The management of contractors has been enhanced by signing a new Framework Contract and a new Service Level Agreement. A15005 Blocking Blocks of Assurance • The Agency further developed its Multiannual work programme supporting the achievement of common strategic goals. The multiannual work programme is further detailed in the annual work programmes. Starting with the 2017 planning cycle, the multiannual and annual work programmes were combined in a programming document. Progress and achievement of the annual work programme are reflected in the midyear report and annual activity report. • The integrated planning and reporting framework was updated to address regular communication of the progress of the division activities to Executive Board. • The Agency established a planning, monitoring and reporting Group consisting of planning coordinators from all divisions in the Agency, with clear responsibility and assignment of responsibilities in all job descriptions.	

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	• Fee forecasting Methodology has been reviewed. • The expenditure forecasting process has been streamlined with the creation of a single, central budget monitoring template. • Security of data entered into the SAP system has been further improved • Training programme has been further designed and implemented for all staff fulfilling financial roles, Including the Initiating Agents. All financial actors have received training in carrying out their tasks. • 'Code of professional standards' for staff verifying financial transactions' was signed-off. • Updated "Guidance document 0005 - SAP user creation, role assignment and maintenance" was approved by the Executive Director. <u>A15001 Video Surveillance</u> • The security policy was reviewed and updated. The public version of the security policy was also updated and published in the website. • Job description of key roles in the data protection area were reviewed and updated. This included the Job descriptions of Data Controllers, the Data Protection officer and the security officers. • A detailed security organogram was produced which details the organisation and management of the whole security area. • Data protection training was provided to all security staff contractors and records of their training are being maintained by the Security Office.	
33. Welcomes the information provided by the Agency to the discharge authority on its current contractual commitments and liabilities linked to its physical presence in the UK; notes with concern that the Agency's rental contract until 2039 does not include an early termination clause to release the Agency from the liabilities of rent and associated costs, and that the	The agreement for lease for the EMA office building was signed in 2011. It foresees a lease term of 25 years, commencing on 1 July 2014. This is a typical pre-let agreement for office developments in London, where the length of the lease was agreed as a package together with other terms, such as the provision of a long free-rent period and a significant contribution for the construction and fit-out of the building. Such terms were approved by the Management Board, the Council and the European Parliament in 2011.	**Implemented and ongoing**

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payable rent for the remaining period from 2017 to 2039 is estimated at EUR 347,6 million; **asks the Agency to report to the discharge authority on any developments on this matter;**	There is no break clause in the contract which was subject to the normal building approval process involving the Management Board, the Council and the European Parliament. The initial agreement for lease (2011) but also the start date of the lease (July 2014) were well ahead of the inclusion of an in-out referendum on the UK's EU membership in the 2015 Conservative Party manifesto in April 2015, the May 2015 general election, and the European Union Referendum Act of the December 2015, which committed the UK government to holding a referendum on its EU membership no later than 31 December 2017. Sub-letting (i.e. transfer a portion of EMA's rental rights to a third party for a temporary period) and Assignment (i.e. transfer EMA's contractual position to a third party) are foreseen in the contract under strict conditions, including the Landlord's prior consent. The "Task Force 50" has officially stated that all costs for the early departure from London and relocation of EMA and EBA to the new host Member State will have to be borne by the UK Government. In the meantime, as tenant, , EMA is analysing all possible options with the assistance of UK legal and real estate advisors, whilst keeping an eye on the negotiations between the European Union and the UK Government.	
34. Acknowledges the fact that the absence of a break clause was noted in the opinion of the Committee on Budgets of 24 May 2011 and that the rental agreement was signed in 2011 when a potential exit of the UK from the Union was not foreseeable; however, the costs associated with the relocation would reasonably be expected to be considered in the negotiations on the withdrawal agreement between the Union and the UK	The current EU27 position on the financial settlement with the United Kingdom, as presented by the "Task Force 50" is that the UK is expected to honour the specific costs related to the withdrawal process, including costs resulting from the termination of contracts for housing EU agencies that have to move as a consequence of the withdrawal, the costs related to the move itself and the costs related to installation in the new location. As regards the EMA, in a closed meeting in July 2017, the Agency provided to the European Parliament as budgetary authority an overall estimate of relocation costs	**Ongoing**

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Government; **asks the Agency to report to the discharge authority on any developments on this matter**;	of 582.5 million euros, which includes liability for the current premises. We are not able to give a more reliable figure until we know the exact new location of the Agency (expected to be decided in the margins of the General Affairs Council (Art 50) on 20 November).	
35. Stresses the risk of budgetary volatility faced by the Agency as a consequence of the outcome of the UK referendum on Union membership; proposes, in the spirit of sound financial management, that the Agency be authorised to maintain a budgetary reserve to respond to unforeseen costs that may need to be incurred in 2017 and unfavourable exchange rate fluctuation, or beyond, as a consequence of that decision, to ensure that the Agency can continue to carry out its tasks effectively; **asks also in this respect the Agency to produce a comprehensive business continuity plan which deals with the double and connected risks of budgetary and business volatility;**	EMA has developed and initiated a business continuity plan to deal with the uncertainty and workload implications linked to the UK's withdrawal from the EU and the Agency's relocation. The plan was developed by a Task Force that was established immediately after the UK referendum to assess the consequences of the vote and prepare for both the necessary operational changes and the move to a new location. The business continuity plan is a tool that will help EMA take the difficult decision to reallocate the available resources as needed to maintain its priority activities over the next years. It categorises and prioritises tasks and activities according to their impact on public health and the Agency's ability to function. It also explains how some of these types of activities can be put on hold for some time to free up or channel resources into core activities that need to be maintained under any circumstances. The plan sets out three layers of priority. More details on the business continuity plan are included in the EMA press release of 1 August 2017 available below: http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2017/07/news_detail_002789.jsp&mid=WC0b01ac058004d5c1 For more details on how the business continuity plan will be activated in case of a situation with potential significant loss of staff, see EMA business continuity planning and impact of staff retention scenarios from the EMA staff survey (EMA/635491/2017). The EMA welcomes the European Parliament's proposal to authorise the Agency to maintain a budgetary reserve to respond to unforeseen costs and unfavourable exchange rate fluctuations that may be incurred in 2017 or beyond. In that	**Ongoing**

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	regard, it is relevant to note that the EMA is already now facing additional expenses and resource needs related to a number of preparatory activities which are required in order to plan for the relocation and to ensure business continuity. By way of example, in May 2017 EMA started to scale back activities in the outer layer of its business continuity plan, the so-called category 3 activities, to free up a significant number of staff by the end of 2017 who are focusing on the preparations for the UK's withdrawal from the EU and EMA's relocation. In addition, the Agency foresees that significant IT and infrastructure budget investments will need to be launched already in 2018 in preparation for a physical relocation in 2019, together with preparatory staff missions.	
36. Notes that the Agency launched a pilot project on "adaptive pathways" in March 2014 aiming to accelerate market authorisations for specific medicines using the so-called post-marketing authorisation; is concerned that the pilot project raises numerous public health concerns and undermines the core mission of the Agency, namely to ensure safety of medicines; **asks the Agency to report to the discharge authority on the project and the measures it has taken to ensure that this acceleration of the procedure does not undermine its core mission**.	The Agency would like to emphasise and reassure the discharge authority that the Adaptive Pathways (AP) concept does not change the standards for the evaluation of benefits and risks or the approach to 'uncertainty'. The AP concept does not change the standards of regulatory approval or compromises patient safety. A marketing authorisation will only be granted if the balance of benefits and risks for a defined patient population is found to be positive; the same principles and legal tools apply to AP as for any other new medicine. The aim of the AP concept is not to accelerate marketing authorisation, but rather to optimise the way medicines development will be planned to better meet the needs of patients with serious conditions for whom there may be no suitable treatments, and to ensure that patients can access approved medicines by generating an appropriate dataset. This prospective approach is particularly emphasised as a necessary way to optimise the post-authorisation planning. Accordingly, good planning of post-authorisation data collection is seen as reinforcing, not weakening, the essential role of EMA in protecting patient's health.	**Implemented**

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	All of the proposals received for an Adaptive pathways discussion are in line with the current framework of scientific advice or parallel scientific advice with HTA bodies. Currently it is estimated that none of the products involved in the AP pilot will receive a marketing authorisation before 2019. As for all other products evaluated by EMA, information on those products is accessible via the EPAR (public version of the assessment report), via publication of the clinical trial data submitted in the application, and via access to documents requests. Further information on the AP concept is available on the EMA webpage below: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000601.jsp	