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Stakeholders and Communication Division

# European Medicines Agency's interaction with industry stakeholders

## Annual report 2018-2019

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# Executive Summary

Over the last few years EMA has faced a number of challenges, in particular the United Kingdom's withdrawal from the European Union and the Agency's subsequent relocation to Amsterdam, which was completed in mid-January 2020. In order to manage the relocation, the Agency implemented a business continuity plan (BCP) to focus on core activities essential for public health. As part of BCP, annual stakeholder engagement reporting did not take place and a biennial report for 2018 and 2019 is presented here.

During this period, Industry stakeholder's engagement has primarily focussed on "Brexit" preparedness activities. EMA, the European Commission and Head of Medicines Agencies (HMA) continued to engage closely with industry stakeholders to prepare for the UK leaving the EU and becoming a third country. Dedicated webinars were set up to update stakeholders on Brexit-related activities. This has been done maintaining high levels of transparency in the interaction and putting public health at the forefront of all decision making.

Other industry stakeholder engagement highlights during the reporting period, include:

- Early input into and consultative dialogue to support the development and finalisation of EMA's Regulatory Science Strategy to 2025 for human and veterinary medicines. Industry stakeholders provided contributions through the public consultation and four stakeholder workshops enabled further consultation and input.
- Industry stakeholders also contributed to the work of the joint HMA-EMA taskforce on availability of authorised medicines, set up to provide strategic support and advice to tackle disruptions in supply of human and veterinary medicines and ensure their continued availability. A multi-stakeholder workshop was held in November 2018 which lead to the development and publication in 2019 of the HMA-EMA "Guidance on detection and notification of shortages of medicinal products for Marketing Authorisation Holders (MAHs) in the Union (EEA)". This guidance, specifically developed for industry aimed at providing guidance to marketing authorisation holders (MAHs) for reporting of shortages of medicinal products in the Union (EEA), based on a common EU definition of shortage.
- Following the detection of nitrosamine impurities in blood pressure medicines (angiotensin receptor blockers) known as 'sartans' mid 2018, MAHs were asked to review their manufacturing processes to mitigate the risk of presence of nitrosamine impurities. A multi-stakeholder meeting, including industry stakeholders, was organised in November 2019 (link) to discuss lessons learnt and a number of interactions took place with industry representatives to clarify the risk evaluation and testing process in 2019. Guidance for industry in the form of a Q&A was subsequently issued and kept regularly updated.
- In the field of veterinary medicines, the Agency continued to engage in constructive dialogue with its industry stakeholders on a variety of topics and held several important events, including a Veterinary Medicines Innovation Day in April 2018, and a stakeholder meeting in October 2018, which focused on the revision of the antimicrobial veterinary medicinal product risk assessment guideline, following a public consultation.
- EMA also continued dialogue with industry to prepare for implementation of new legislation on clinical trials, veterinary medicines and medical devices.
- Regular meetings between the EU telematics board and industry stakeholders were maintained. Stakeholder meetings also took place to progress work on IRIS, SPOR and electronic-Product Information (ePI).

- Agency's SME office continued regular engagement with SMEs in the human and veterinary medicines sectors, including advice and guidance, training and support to Brexit preparedness.

In 2020, EMA will continue to implement Brexit preparedness activities, while it gradually reinstates interactions with industry stakeholders once BCP measures have been lifted. EMA will continue to engage with industry as it commences implementation of its regulatory science strategy and develops together the next 5 years joint European Medicines Agencies Network Strategy together with HMA.

# Introduction

In accordance with the 'Framework for interaction between the European Medicines Agency and industry stakeholders' (hereafter referred to as "framework") adopted by the EMA Management Board in October 2015 (see Annex 1, and list of eligible organisations in Annex 2), this report provides an overview of EMA's interaction with its industry stakeholders in 2018-2019, covering both human and veterinary medicines. It also includes sections on industry stakeholders' interactions in the context of EU telematics project and in preparing for the implementation of legislation on clinical trials, veterinary medicines, and medical devices.

The Agency implemented its frameworks for interaction with stakeholders at reduced levels in 2018 and 2019 due to implementation of business continuity measures to prepare for Brexit and EMA's relocation. As a result, the number of stakeholder meetings were reduced, annual bilateral meetings with industry stakeholders were temporarily suspended and a planned industry stakeholder survey was put on hold. EMA participation in external stakeholder events was also reduced.

Resources were redirected to focus on Brexit-related activities. EMA, the European Commission and Members States through CMDh and CMDv engaged closely with industry stakeholders to prepare for the UK leaving the EU and becoming a third country. Dedicated webinars were set up to update stakeholders on Brexit-related activities (see further information under 'Brexit preparedness' below).

As part of BCP, annual stakeholder engagement reporting did not take place and a biennial report is presented here.

A high-level overview of the main areas where EMA maintained engagement and dialogue with industry stakeholder organisations in 2018-2019 is presented in the following section. Other meetings and events held with industry stakeholders throughout 2018-19 are listed in Annexes 3 and 4.

# Highlights from 2018-2019

## *Brexit preparedness*

EMA, the European Commission and EU Member States continued to work closely together to provide guidance to help companies marketing human and veterinary medicines in the EU prepare for the UK's withdrawal from the EU and minimise the impact on the supply of medicines. Based on the assumption that the UK would become a third country after Brexit, activities aimed at ensuring that companies would be ready and take the necessary steps to enable undisrupted supply of their medicines in the EU, for the benefit of patients.

As part of EMA preparedness activities, a targeted survey to Marketing Authorisation Holders of centrally authorised human and veterinary medicinal products was launched at the end of 2017 to gather information from industry on their Brexit preparedness plans, identify any concerns regarding medicines supply that may impact public or animal health, and plan for timely handling of regulatory submissions to support this process. A high-level summary of the overall results of the survey were published on the EMA website in July 2018 (link).

Despite the proactive approach taken by EMA and the network there was still the risk of supply issues with some centrally authorised medicines if the UK were to leave the EU without a withdrawal agreement, in particular around the three Brexit deadlines of 31 March, 12 April, 31 October 2019, consequently, EMA closely monitored the evolving situation, continuously liaised with pharmaceutical companies and supported about their Brexit preparedness.

By the end of 2019 good progress had been made by companies to take the required steps to ensure that their centrally authorised medicines could remain and be supplied on and to the EU market. Just one marketing authorisation transfer for a human medicine was still pending. Good progress had also been made for products with qualified persons for pharmacovigilance (QPPVs) still based in the UK (58 still to be transferred) and pharmacovigilance master files (PMFs) based in the UK (64 still to be transferred) by the end of 2019.

EMA, the European Commission and Member States prepared a series of guidance documents to help companies taking the necessary regulatory steps to enable continued supply of their medicines in the EU for the benefit of patients. They were updated several times during the period covered by this report. The guidance is based on the assumption that in January 2021 the UK will become a third country where the EU laws will cease to apply. Specific industry stakeholders' meetings and webinars were organised jointly with the European Commission in March, April and September 2018 and January 2019 (See Annex 3).

## *Strategic reflections on Regulatory Science Strategy to 2025*

EMA worked closely with stakeholders to shape its plan for advancing regulatory science over the next five years, in both human and veterinary medicines.

In December 2018, EMA launched an extensive public consultation process to refine and prioritise key areas. The Agency reached out to a wide range of stakeholders, including industry, and hosted two workshops, one for human and one for veterinary medicines. Constructive feedback was received from in writing over 150 respondents from a broad range of stakeholder groups. The feedback was complemented with rich input and discussions at the workshops.

Following the public consultation, the Agency hosted two further multi-stakeholder workshops on human and veterinary medicines in November and December 2019 to finalise the strategy. The meetings served to get agreement on key areas where changes are required in the coming years. The importance of maintaining a similarly high level of engagement with all stakeholders in the implementation phase was acknowledged.

The finalised strategy is a key element of the European Medicines Agencies Strategy to 2025, which will be developed together with the Member States. It will enable EMA to engage further with industry stakeholders on the accelerated technological change and innovation in medicine development. It will also allow the Agency to identify the gaps between science and healthcare systems and bring together the various stakeholders needed to bridge those gaps.

## *HMA-EMA taskforce on availability of authorised medicines*

Unavailability of medicines in the EU, either because medicines are not marketed or due to supply disruptions, has been recognised by HMA and EMA as an area of great concern for public and animal health, which has a significant impact on end users. As causes of unavailability are multifactorial the solutions require actions at different levels involving all stakeholders, with industry being recognised as a key actor, an HMA-EMA task force is in place to develop and coordinate actions at EU level and to ensure continuity of supply for both nationally and centrally authored, human and veterinary medicines.

In November 2018, a workshop was organised by the HMA-EMA taskforce to provide information on the taskforce's ongoing activities and its expected deliverables, including how these would be affected by Brexit. It reinforced the importance of receiving stakeholders' perspectives and contributions to these deliverables and identified areas of agreement as well as areas for further discussion. As a consequence of this discussion, it was agreed to update deliverables of the taskforce taking into account feedback received at the workshop. In parallel to the multi-stakeholder discussion, a meeting involving EMA, HMA and industry associations was held to discuss specific issues for industry.

In July 2019, EMA and HMA published guidance for marketing authorisation holders on detecting and reporting medicine shortages. It aims to facilitate the early notification of shortages to regulatory authorities, allowing them sufficient time to make contingency arrangements where necessary. It contains an EU harmonised reporting template for use (if none is provided by the country in question). This important guidance was developed with relevant input from industry as a key stakeholder. A pilot project for implementing the guidance, was delayed because of BCP and will be launched in 2021.

Since April 2019, the task force has been running a pilot programme on establishing a single point of contact (SPOC) network to improve information sharing between Member States, EMA and the European Commission on important medicine shortages of human and veterinary medicines and to coordinate actions to help prevent and manage shortages. This also includes information sharing on alternative medicines that are available in other Member States.

The first phase of the pilot ran from April to August 2019 to test the functioning and usefulness of the information exchange via the SPOCs. During this phase, 24 Member States used the SPOC system and circulated 52 notifications of shortages. Industry was informed and involved as part of this initiative. The task force will run a second phase of the pilot in 2021.

## *Response to detection of nitrosamine impurities in medicines*

In June 2018, the European medicines regulatory network became aware of the presence of nitrosamine impurities (N-nitrosamines) in a class of medication used to control high blood pressure known as 'sartans'.

EMA's human medicines committee (CHMP) subsequently conducted a review of sartans, which finished in January 2019. A stakeholder consultation process, which included a multi-stakeholder meeting organised in November 2019, fed into a lessons learnt exercise and the formulation of a public report . The report included recommendations to help reduce the risk of impurities in medicines and ensure that regulators are better prepared to manage cases of unexpected impurities.

Over the period, EMA and national competent authorities have continued to monitor the presence of nitrosamine impurities in medicines, in co-operation with regulators from outside the European Union (EU), and work with MAHs to find rapid solutions to address any adverse findings. Following the detection of nitrosamines in a number of other medicines, a referral under Article 5(3) was launched in September 2019, to provide guidance to MAHs on how to review their medicines for the possible presence of nitrosamines and test all products at risk. The referral also looked at all available scientific knowledge on the presence of nitrosamines in medicines in order to advise regulatory authorities on actions to take if companies find nitrosamines in their medicines. A number of interactions took place with industry representatives to clarify the risk evaluation and testing process in the context of the referral. Guidance for industry in the form of a Q&A was issued and regularly updated.

Marketing authorisation holders should now review their manufacturing processes for all products containing chemically synthesised or biological active substances to identify and, if necessary, mitigate the risk of presence of nitrosamine impurities.

In 2020, further discussion is expected to continue within the EU network to establish a robust process to oversee, manage and monitor the implementation of Article 5(3) opinion, with adequate and relevant interactions with industry stakeholders.

EMA has given companies until the 31st March 2021to complete the risk evaluation. To complete the testing, companies have until 26 September 2022 for chemical products and until 1 July 2023 for biological medicines.

## *Identifying solutions for Big Data challenges*

In March 2017, the EMA-HMA Task Force on Big Data was established to identify the emerging challenges created by the increasing availability of data and related opportunities for supporting regulatory decision-making. It undertook detailed landscaping of the entire big data field (genomics through to m-health) and performed online surveys of both national regulatory agencies and the pharmaceutical industry on perspectives, expertise and challenges. This work helped develop an understanding of the challenges and the current state of expertise in the regulatory network.

In February 2019, the task force published an interim report (link) which provides a comprehensive summary of various data sources and sets out recommendations for understanding the acceptability of evidence derived from big data in support of the evaluation and supervision of medicines by regulators.

With the aim of moving on to considering solutions, the Task Force held a multi-stakeholder workshop including industry stakeholders in May 2019 to discuss regulatory solution for Big data challenges(link). This workshop was part of the wider stakeholders' consultation plan to enable practical recommendations to inform strategic decision-making and planning by the HMA and EMA and to contribute to the European medicines regulatory network's work on developing a five-year EU Network Strategy to 2025, on big data. This contributed to the drafting of the final report of the task force on Big Data, which included practical recommendations on how the network could make best use of big data by evolving its approach to data use and evidence generation in support of innovation and public health . This report is expected to be published early 2020.

## *Support for SMEs*

SMEs are recognised as a driver of innovation in the EU. The Agency promotes innovation and the development of human and veterinary medicines by SMEs through the provision of regulatory and administrative support to these companies.

As smaller companies are often not members of industry organisations, interaction with small and medium-sized enterprises is facilitated through the Agency's SME office, which was established in 2005 by Commission Regulation (EC) No 2049/2005, for company specific advices and support as defined previously. The Agency's SME office continued in 2018 and 2019 to provide advice and guidance, to organise training tailored to SMEs. It also issued a dedicated newsletter for SMEs registered with EMA. These companies also benefitted from various fee incentives to support their medicine-development programmes.

An overview of the support on offer to SMEs and an annual report is published on EMA's website (link). Key industry focussed activities for SMEs for the period 2018 and 2019 included the implementation of EMA's action plan for SMEs, the support to SMEs for Brexit preparedness and training on the newly developed IRIS platform for orphan medicinal products.

## *Human medicines*

To support core business activities in the area of human medicines, a limited number of industry stakeholder platform meetings took place in 2018, two on Research and development support and two on pharmacovigilance. Platform meetings in 2019, were cancelled due to BCP measures linked to EMA's relocation to the Netherlands.

Topics addressed in the R&D support meetings included aspects of orphan designation review, the implementation of the orphan notice, 'histology-independent indications' in the context of orphan designations; the upcoming rollout of a new tool for management of orphan designation applications, digital technology proposals in medicine development programmes, co-development with companion diagnostics and cross-decision maker collaboration in the space of horizon scanning activities. It also provided an opportunity to update on post-authorisation evidence generation activities, paediatric medicines and the PRIME scheme, parallel consultation with regulators and health technology assessment bodies and the paediatric action plan.

The pharmacovigilance platform in 2018 covered the following topics: the new Eudravigilance system and functionalities, including the pilot of Eudravigilance signal detection; new risk management plan guidance and template; emerging scientific and technological approaches to collecting and managing pharmacovigilance data, GVP modules update, PRAC workplan 2018 and specific pharmacovigilance aspects derived from the UK's withdrawal from the European Union.

During the period covered by this report, due to "Brexit BCP" implementation, Clinical data publication activities were put on hold and resources re-allocated within the Agency to "core business centralised" actives. However a webinar was held in January 2018 where updates on the Clinical Data Publication, EMA technical group on anonymisation (TAG) and industry proposals on Policy 0070 in relation to change management cycle, CCI redaction etc. were discussed link.

## *Veterinary medicines*

In 2018-19, the Agency continued to engage in constructive dialogue with its industry stakeholders in the veterinary field on a variety of topics, despite the reduction of activities related to the relocation of the Agency to Amsterdam. The Veterinary Medicines Innovation Day held in April 2018 to raise awareness and promote the support and measures that the Agency has to offer in the area of veterinary medicines innovation, saw high interest and participation from veterinary pharmaceutical companies and stakeholder associations.

A stakeholder focus group meeting on dose optimisation of established veterinary antibiotics in the context of summary of product characteristics harmonisation was held in October 2018. The purpose of the meeting was to allow a direct exchange of views on the considerations in the report on a pilot project that aimed to develop and test non-experimental approaches for dose optimisation and evaluating the consequences on withdrawal periods, target animal safety, and environmental risk assessment, with the objective of improving the SPC of veterinary antibiotics authorised in the European Union.

The Antimicrobials Working Party of the European Medicines Agency's Committee for Medicinal Products for Veterinary Use (CVMP) held a focus group meeting with stakeholders to discuss the revision of the antimicrobial veterinary medicinal product risk assessment guideline, following a public consultation on the draft revised guideline ending on 31 October 2018.

The annual European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) meeting for stakeholders held in April 2018 was organised by EMA to inform EU Member States, stakeholders and observers on latest activities related to the collection of data on the sales of veterinary antimicrobials,

on the draft guidance on provision of data on antimicrobial use by animal species and also to share information on activities for the containment of antimicrobial resistance.

An Interested Parties meeting was held with the CVMP Pharmacovigilance Working Party in September 2018, focussed on harmonisation, communication of pharmacovigilance data to the public, challenges for adverse event quality and how to encourage reporting of adverse events.

# Operation of the European Medicines Regulatory Network

## *EU Telematics*

EU Telematics maintain common information-technology (IT) services to implement European pharmaceutical policy and legislation. It supports and enables efficient working activities across the EU regulatory network through facilitation of the best use of available resources, improvement of the exchange of information between stakeholders, improvement in the quality and extent of harmonised information available in support of the work, to disseminate information to stakeholders and to enhance transparency, facilitate and promote partnership across the EU regulatory network.

Involving stakeholders in Telematics activities is crucial as information-technology (IT) systems underpin the work of the European Medicines Regulatory Network with wide-reaching impacts on the Agency's stakeholders, including pharmaceutical industry.

Meetings between industry associations and the EU Telematics Management Board (EU TMB) provide a forum to update and engage in dialogue on Telematics related activities. Two meetings with industry associations were held in 2018. The meeting that took place in February 2018 offered industry associations the possibility to receive the latest information about ongoing Telematics projects including the eSubmission roadmap while a plan for development of the Telematics strategy 2025 was also presented. An update from industry associations on their current IT initiatives of relevance to the Telematics domain was also given. The meeting in November 2018 was focused on EMA's relocation to the Netherlands and the impact on Telematics, feedback received from the industry associations on the Telematics Strategy Concept Paper and a presentation on the New Veterinary Regulation. The status of ongoing Telematics projects was presented, followed by a presentation on IRIS, EMA's Regulatory & Scientific Information Management Platform, and an update from industry associations on their current IT initiatives.

Due to EMA's relocation to the Netherlands only one meeting was held in 2019 which took place in November 2019. In the this meeting the EU TMB and industry associations had an opportunity to exchange views on the steps towards establishing a Target Operating Model, followed by discussions on the Telematics budget and portfolio planning in 2020, the EMA Future proofing exercise and its impact on EU Telematics and the next steps for the development of the Telematics strategy 2020-2025. An update on ongoing Telematics projects was delivered and industry associations presented their view on the future of Telematics in the Human and Veterinary areas.

## *New and enhanced EudraVigilance system*

During the reporting period (2018 and 2019), industry stakeholders continued to actively engage as part of the EudraVigilance Expert Working Group in numerous activities related to the operation of EudraVigilance (EV), which can be summarised as follows:

- Integrating EV with the Agency's Identity and Access Management (IAM) system;

- Resolving technical and procedural maintenance issues;
- The drafting of options for the mandatory use of the new ISO ICSR/ICH E2B(R3) standard. Based on a readiness survey directed to Member States and pharmaceutical industry associations and following consultation of the pharmacovigilance, clinical trials and IT governance of the EU Medicines Regulatory Network, the Pharmacovigilance Risk Assessment Committee (PRAC) considered the matter. Pursuant to Article 24(2) third subparagraph of Regulation (EC) No 726/2004, EMA's Management Board endorsed this approach on 19 December 2019, based on a recommendation by EMA's Pharmacovigilance Risk Assessment Committee (PRAC) PRAC recommended on 2 October 2019 that the use of the ISO ICSR standard based on the ICH E2B(R3) modalities and the related ISO standard terminology is to become mandatory as of 30 June 2022 as regards reporting obligations to EudraVigilance.
- The drafting of the EudraVigilance Operational Plan 2020 – 2022, adopted by PRAC in February 2020, which describes key activities and developments that will take place between 2020 and 2022 with impact on EV and its stakeholders.
- Furthermore, EMA continued to provide the following technical support to industry stakeholders:
- eLearning offerings and face to face training offerings to familiarise themselves with the EV system components, the ICH ICSR reporting standard as well as procedural aspects related to adverse reaction reporting and signal management.
- Testing with marketing authorisation holders (MAHs) and sponsors of clinical trials in the EEA for the electronic submission of ICSR to EV.

## *SPOR – ISO IDMP implementation*

EMA is continuing to implement the standards developed by the International Organization for Standardization (ISO) for the identification of medicinal products (IDMP). The ISO IDMP standards provide data elements, formats and terminologies to unambiguously identify medicines and exchange information about them. Following a phased implementation process, pharmaceutical companies will be required to submit data to EMA in accordance with the new formats and terminologies.

To facilitate the implementation of these ISO IDMP standards, EMA is delivering a set of master data management services for the four domains of master data in pharmaceutical regulatory processes: substance, product, organisation and referential (attributes such as pharmaceutical form and route) data. These four domains or areas are known collectively as SPOR.

EMA-Industry Change Liaisons have been appointed to facilitate close interaction with industry stakeholders on SPOR. The first two services, the Referential Management Service (RMS) and Organisations management service (OMS) were launched in back in June 2017. During 2018 and 2019 the work continued and an extensive consultation with stakeholders took place. Following launch of SPOR Application Programming Interface (API), four webinars were held (two in November 2018, one in December 2018 and one in January 2019). Consultation on EU Implementation Guide version 1 (EU IG V1) took place during webinars in January and April 2019. There were two webinars organised to discuss OMS Data Quality (September 2018 and February 2019), OMS Key User Group meet face to face in February 2019 and continued its work during multiple teleconferences. SPOR Task Force, Product management service and Substance management service Sub-Groups (PMS SG and SMS SG) meet face to face with stakeholders five times (March, June and December 2018, May and October 2019) to support further progress of development of the two SPOR services. In July 2019 a webinar was organised to discuss process changes for substance registration for clinical trials in the SMS.

## *Integrated regulatory and scientific Information Management (IRIS)*

EMA engaged with Industry Stakeholders to develop a new secure online platform for handling product-related scientific and regulatory procedures called IRIS (https://iris.ema.europa.eu/).

IRIS helps to streamline EMA processes and reduces the overall time needed for applicants to prepare and submit applications for scientific procedures. It also ensures better data quality through integration with other EMA systems. Users will be able to check the status of their applications across multiple devices and will receive automatic updates when their status changes.

The IRIS platform was first launched in 2018 for orphan designation procedures, expended to Parallel Distribution and the Innovation Task Force's consultation product related procedure submissions in respectively 11 February 2019 and 24 May 2019. For the development phase of IRIS, EMA interacted with industry stakeholders via the IRIS industry stakeholder volunteers' group. The purpose of this group was to support the IRIS procedural expansion delivery by receiving demonstrations and providing feedback.

IRIS users satisfaction measurement survey was circulated to orphan designation and parallel distribution users in Q4 2019. This feedback has been used for the design of the next development of IRIS for scientific Advices for human and veterinary procedures evaluation process management expected to take place in 2020.

## *Towards electronic product information (e-PI) for EU medicines*

A report from the European Commission (EC) in March 2017, and a subsequent EMA action plan, identified areas where the Summary of Product Characteristics (SmPC) and Package Leaflet (PL) could be improved to meet the needs of patients and HCPs and proposed actions to address these shortcomings. These wide-ranging actions relate to enhancing readability, improving patient input in development and testing, promoting best practices and developing an electronic format.

The use of electronic means for better dissemination of product information is one of the key priorities listed in an EMA action plan

Throughout 2018 and 2019, a joint EMA-Heads of Medicines Agencies (HMA)-EC collaboration worked on the latter: identifying stakeholder needs from a future electronic PI for medicines (ePI) and mapping ongoing initiatives in the field to create an overview of the current landscape.

A multi-stakeholders workshop held at EMA on 28 November 2018 brought together patients, consumers, healthcare professionals, pharmaceutical industry, academia, not-for-profit organisations and regulators to discuss stakeholder needs and concerns, give an overview of the main ePI initiatives ongoing in the EU and decide how to move forward with a common approach. The workshop was the culmination of a year of mapping and consultation on the topic, and it offered a platform for stakeholders to discuss together.

The outcome of the workshop was a draft proposal for 'key principles' for ePI in the EU. These key principles were the subject of a 6-month public consultation (from January to July 2019). Following the consideration of submissions received during the public consultation, the key principles were updated. They now represent EMA-HMA-EC guidance on ePI and form the basis of follow-up implementation plans for ePI in Europe.

# Consultation prior to the implementation of new legislation, policies and initiatives

## *Implementation of Clinical Trials Legislation*

During the course of 2018-2019, the Agency continued to collaborate closely with its partners and stakeholders to implement the new Clinical Trial Regulation, adopted in April 2014. EMA continued to work on the first two projects under its responsibility: the EU Portal and Database and Clinical Trial Safety Reporting (SUSAR and Annual Safety Reports) which form the Clinical Trials Information System (CTIS). The EudraCT legacy is a third project and will start once CTIS is close to delivery.

Within the governance structure for the Clinical Trials programme, industry stakeholders take part in regular CTIS stakeholder meetings (8 meetings took place in 2018-2019). During the meetings a regular update on the progress of the CTIS project was provided as well as discussions on specific topics such as user acceptance testing, submission of multiple substantial modifications, prioritisation of development requirements for CTIS, project delivery methodology and the CTIS product vision. In 2018 a series of workshops/ demo sessions were organised with a core group of sponsors to provide an overview of the functionalities developed by the time and to discuss specific requirements for further work. Ad hoc discussions took place on topics of particular interest including various submissions, user management in the system, publication of trial information and workload management in CTIS. More recently, stakeholders were invited as part of an extended project team to provide specialised input mainly through a small group of nominated sponsor product owners.

In this period the development of Clinical Trial Safety Reporting was successfully finalised and the building of the EU Portal and Database continued steadily. Industry stakeholders are involved through the nominated product owners in the design and validation of system functionalities to ensure that the system meets user needs. The product owners also took part in assessments of the readiness of CTIS for audit. System functionalities were shown in stakeholder meetings. A wider participation of representatives is engaged in User Testing, where representative end users from industry contribute together with those from national competent authorities and ethics committees of Member States, the European Commission and associations representing users of public information – in particular patient and consumer and healthcare professional associations.

## *Veterinary medicines Regulation*

The new Veterinary Medicines Regulation (Regulation (EU) 2019/6), which will become applicable on 28 January 2022, will modernise the existing rules on the authorisation and use of veterinary medicines to take account of the innovation taking place in sector by, for example, reducing the administrative burden for applicants. It aims at increasing the availability and safety of veterinary medicines and enhances EU action against antimicrobial resistance.

To help stakeholders keep track of the upcoming changes, EMA launched a new webpage with information on EMA's scientific and technical recommendations, as well as updates on other activities such as the preparation for implementation progresses. Aspects related to implementation of the NVR were also discussed with stakeholders as part of the workshops run to elaborate EMA's Regulatory Science Strategy. There will be further interaction with industry stakeholders in 2020 to prepare for implementation.

### *Preparation for the implementation of Medical Device and In-Vitro Diagnostic Legislation*

In 2018 and 2019, the Agency continued preparations for implementation of the two new EU regulations on medical devices -Regulation (EU) 2017/745 on medical devices and Regulation (EU) 2017/746 on in vitro diagnostic medical devices which introduce new responsibilities for EMA and for NCAs for medicinal products.

In June 2018, EMA hosted a targeted multi-stakeholder workshop on predictive biomarker-based assay development in the context of drug development and lifecycle, to discuss the concept paper published in 2017 and taking into account the new requirements for consultations on companion diagnostics. Participants to this meeting were invited from pharmaceutical industry, medical device industry, regulatory authorities and notified bodies. The workshop breakout sessions facilitated stakeholder input and discussion on identified critical issues such as technical, analytical and clinical considerations for co-development, as well as regulatory and procedural aspects.

EMA engaged with industry stakeholders in the context of implementation of MDR/IVDR on a number of other occasions in 2018, including the EMA Research and Development platform meetings organised in May and November, the Interested Parties meeting organised by the Biologics Working Party in June and the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) Interested Parties meeting in November.

In February 2019 EMA published a webpage on Medical Devices and published the first of a series of guidance documents to help applicants prepare for obligations stemming from the new Regulations, which will come into full effect in May 2020 and May 2022, respectively.

A Questions and Answers (Q&A) document published in February and updated in October 2019, was developed jointly by EMA and the CMDh, in close collaboration with the European Commission, and focuses on implementation of Article 117 of the medical devices Regulation which stipulates that marketing authorisation applications for medicines with an integral medical device must include the results of the device's assessment of conformity by a notified body. Approximately one in four centrally authorised medicines includes a medical device component, and the majority of these involve an integral device. Industry stakeholders highlighted a number of issues and challenges in implementing the requirements of MDR Article 117, during the CMDh interested parties meeting held in May 2019. Further updates to the Questions and Answers document are planed ahead of implementation of the MDR and IVDR.

In June 2019, EMA released for public consultation a draft guideline on the quality requirements for medical devices in combination products. This guideline is being developed jointly by the EMA Quality and Biologics working parties and aims to clarify the information necessary for assessment of medicinal products that have an integral device, co-packaged device or a reference to a specific device in the SmPC. Multi-stakeholder comments were received during the public consultation, including those received from pharmaceutical industry, medical device industry, notified bodies and patient groups. The guideline is due for finalisation in 2020 and further exchanges with stakeholders are expected including plans to host an EMA multi-stakeholder workshop with a focus on the new requirements of Article 117 of the MDR.

## Plans for 2020

Looking at 2020, after EMA's successful relocation from London to Amsterdam in March 2019, EMA is expected to gradually resume core business activities and other industry stakeholders interactions

which have been withheld due to incremental phases of BCP implementation in 2018 and 2019, such as its regular industry stakeholders' meetings and platforms.

Brexit preparedness activities will continue during the transition period until 2021 and the Agency will continue its dialogue with industry to avoid any potential disruption in EU medicines supply. Learnings from "Brexit" preparedness will be reviewed to improve and make industry stakeholders' interactions more efficient and agile.

Following publication of EMA's Regulatory Science strategy 2025, a reflection will be initiated towards its implementation and how its goals and objectives will be taken forward as part of the joint European medicines agencies network (EMAN) strategy to 2025. This strategy will pave the way for the next 5 years. Through its high-level goals and recommendations, it will shape and feed into the more detailed workplans of the Network's members in future years. The implementation of both strategic initiatives will require important dialogue and interactions with industry stakeholders.

Shortages of medicines will remain a priority in the EU and the HMA/EMA task force will continue its work in the coming years, including the launch of a pilot project for the implementation of guidance to industry to improve the reporting of shortages. Also, the newly created SPOC system will continue to be tested. A concept paper providing recommendations and best practice to stakeholders for shortage prevention and management is being prepared. Finally, a multi-stakeholder workshop is planned to follow-up on developments brought forward by the EC Pharmaceutical Strategy and the EMAN strategy to 2025.

Regarding the potential for nitrosamine contamination, further discussion will continue within the EU network to establish a robust process to oversee, manage and monitor the implementation of Article 5(3) opinion. Marketing authorisation holders will continue the review of their manufacturing processes for all medicines containing chemically synthesised or biological active substances to identify and, if necessary, mitigate the risk of presence of nitrosamine impurities with relevant additional industry guidance and interactions.

The Agency will pursue constructive dialogue with its industry stakeholders to continue to prepare for the implementation of new legislation such as the veterinary legislation and the medical device legislation.

As advances on research and innovation bring new treatment opportunities and important changes throughout the lifecycle of medicines, regulators will need to adapt in order to deal with such wave of innovation; active and continuous dialogue with stakeholders, including industry, will be necessary to foster adequate progress in this respect.

Engagement with industry stakeholders will also be critical in other areas such as big data, mainly through activities of the joint HMA/EMA Big Data Steering Group. An EU Big Data 'stakeholder implementation forum' will be created to enable active dialogue with key EU stakeholders, including pharmaceutical, medical devices and technology industry representatives.

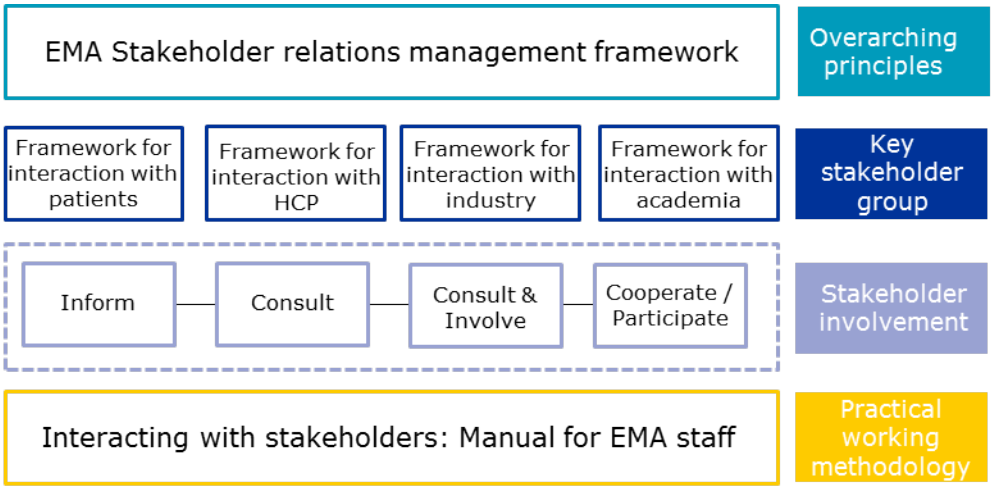
This Stakeholder report on interactions with industry stakeholders was presented to the Management Board during its December meeting, 2020.

**Annex 1**

## Stakeholder relations Management Framework

EMA has defined guiding principles its key stakeholder interactions in its Stakeholder Relations Management Framework. Although the involvement of stakeholders in EMA activities is not a 'one size fits all' methodology, the aim is to streamline engagement across the various stakeholder groups, which include patients and consumers, healthcare professionals, and academia and align working methodologies where possible. EMA reports annually on its interaction with all its key stakeholder groups.

Figure 1: Illustration of stakeholder relations management framework




In addition to the stakeholder specific framework documents highlighted in figure 1 above (Patients and consumers, EMA/637573/2014; Healthcare Professionals, EMA/688885/2010; Industry stakeholders, EMA/591272/2014; Academia, EMA/125511/2017), EMA has put in place a working methodology[1] in terms of the level of stakeholder involvement. Four levels of involvement in EMA activities have been identified:

1. Inform (to enable feedback e.g. news items, Q&As, Information Days);
2. Consult (via written consultation e.g. guidelines development, public consultations);
3. Consult & Involve (based on direct interactions e.g. focus groups, platform meetings) and,
4. Co-operate (jointly engaging towards a common technical goal e.g. technical expert groups).

The first 2 levels of stakeholder involvement referred to above are open to all external parties and do not require specific stakeholder eligibility criteria to be applied. Any organisation can register with the EMA as an interested party to receive information and notice of written consultations in selective areas of interest (via StakeholdersDB@ema.europa.eu).

For more direct involvement (i.e. at the latter 2 levels) eligibility criteria are applied to ensure that the organisations, which EMA consults and involves directly or co-operates with, represent the broadest array of relevant stakeholders. Multi-stakeholder dialogue is encouraged wherever possible, with all

[1] The working methodology is aligned with the European Commission's Better Regulation package

eligible organisations meeting the relevant criteria for participation. The list of eligible industry organisations is published on the EMA website (link), see also Annex 2.

Finally, a manual aims to support the systematic integration and translation of these overarching principles and relevant frameworks for interaction into the Agency's day-to-day operations. Together, these building blocks ensure a consistent approach to stakeholder relations management across a variety of stakeholder groups and interaction types.

**Annex 2**

## List of eligible industry stakeholder organisations (as of 23 July 2020)

With reference to the Criteria to be fulfilled by industry stakeholder organisations involved in EMA activities, (EMA/323235/2016), the following organisations have been deemed eligible to be consulted and involved directly or to co-operate with the Agency in specific areas. All of the organisations in this list are also included in the EC Transparency Register, which provides further detailed information (link)

| Name of organisation | Acronym | Website |
|---|---|---|
| Active Pharmaceutical Ingredients Committee | APIC | http://apic.cefic.org/ |
| Alliance for Regenerative Medicine | ARM | www.alliancerm.org |
| AnimalhealthEurope (previously known as IFAH-Europe) | N/A | www.animalhealtheurope.eu |
| Association of Clinical Research Organizations | ACRO | www.acrohealth.org |
| Association of the European Self-Medication Industry | AESGP | www.aesgp.eu/ |
| Association of Veterinary Consultants | AVC | www.avc.at/ |
| Avicenna Alliance | N/A | https://avicenna-alliance.com/ |
| ECA Foundation | ECA | https://www.eca-foundation.org/ |
| European Association for Bioindustries | EuropaBio | www.europabio.org/ |
| European Association for Logistics and Transportation in Healthcare | EALTH | www.ealth.org/ |
| European Association of Euro-Pharmaceutical Companies | EAEPC | www.eaepc.org |
| European Coalition on Homeopathic & Anthroposophic Medicinal Products | ECHAMP | www.echamp.eu/ |
| European Confederation of Pharmaceutical Entrepreneurs | EUCOPE | www.eucope.org/ |
| European Contract Research Organization Federation | EUCROF | www.eucrof.eu/ |
| European Federation of Pharmaceutical Industries and Associations | EFPIA | www.efpia.eu/ |
| European Federation of Statisticians in the Pharmaceutical Industry | EFSPI | www.efspi.org |
| European Group for Generic Veterinary Products | EGGVP | www.eggvp.org/ |

| Name of organisation | Acronym | Website |
|---|---|---|
| European Healthcare Distribution Association | GIRP | www.girp.eu/ |
| European Industrial Gases Association | EIGA | www.eiga.eu |
| European Industrial Pharmacists Group | EIPG | www.eipg.eu |
| European Manufacturers of Autogenous Vaccines & Sera | EMAV | www.emav.be |
| Europharm SMC | Europharm SMC | www.europharmsmc.org/ |
| Eye-Care Industries European Economic Interest Grouping | ECI-EEIG | www.eci-eeig.org |
| Health Sciences Records & Archives Association | HSRAA | https://the-hsraa.org |
| International Plasma and Fractionation Association | IPFA | https://ipfa.nl/ |
| International Society for Pharmaceutical Engineering | ISPE | www.ispe.org/ |
| Medicines for Europe | N/A | www.medicinesforeurope.com/ |
| Medtech & Pharma Platform | MPP | https://www.medtech-pharma.com/home/ |
| MedTech Europe | MTE | www.medtecheurope.org/ |
| Plasma Protein Therapeutics Association | PPTA | www.pptaglobal.org/ |
| Vaccines Europe | VE | www.vaccineseurope.eu/ |

**Annex 3**

## Regular stakeholder meetings with industry representation held in 2018-2019

| Event name | Topic | Participants | Frequency |
|---|---|---|---|
| Industry Platform meeting on research and development support | Research and Development | Industry Stakeholder Associations, EMA, Committee and Member States Regulators as appropriate | 1-2 times/year<br>- 18 May 2018 link<br>- 23 Nov 2018 link |
| Industry Platform meeting on the operation of EU Pharmacovigilance legislation | Pharmacovigilance | Industry Stakeholder Associations, EMA, Committee and Member States Regulators as appropriate | 4 times/year but reduced due to EMA Brexit BCP implementation.<br>- 20 Mar 2018 link<br>- 28 Sep 2018 link |
| Stakeholders forum on the implementation of the Pharmacovigilance legislation | Pharmacovigilance | Multistakeholders, including Industry Stakeholder Associations, patients, consumers, healthcare professionals. EMA, Committee and Member States Regulators as appropriate | Annually<br>- 24 Sep 2018 link |
| Webinars on the implementation of EMA policy on publication of clinical data (Policy 0070) and guidance to industry | Clinical data publication | Industry Stakeholder Associations, EMA | 2-4 times/year but reduced due to EMA Brexit BCP implementation.<br>- 29 Jan 2018 link |
| EudraVigilance training | Pharmacovigilance | Users of EudraVigilance, including Industry Stakeholder Associations, EMA and Member States Regulators | 25 trainings held in 2018<br>22 trainings held in 2019 |
| EU clinical trials information system Stakeholders Meeting | Clinical Trials/IT | Multi-stakeholders, including Industry Stakeholder Associations, patients, consumers, healthcare professionals, EMA and | 2-3 times/year<br>- 11-12 Jan 2018<br>- 25 Apr 2018<br>- 26 Sep 2018 |

| Event name | Topic | Participants | Frequency |
|---|---|---|---|
| | | European Commission | |
| EU Telematics Management Board | Information Technology | Industry Stakeholder Associations, EU-TMB, EMA | 1-2 times/year<br>- 15 Feb 2018 link<br>- 08 Nov 2018 link |
| European Union International Organization for Standardization (ISO) for the identification of medicinal products (IDMP) / Substance, Product, Organisation and Referential data (SPOR) task force meeting | IT/Data Management Standards | Industry Stakeholder Associations, Software Vendors, EMA, Member States Regulators as appropriate | 2-4 times/year + additional virtual meetings on ad hoc basis<br>- 23 Mar 2018 link<br>- 22 Jun 2018 link<br>- 4 December 2018 Link<br>- 24 May 2019 Link<br>- 16 October 2019 Link |
| European network of paediatric research at the European Medicines Agency (Enpr-EMA) Coordinating Group and networks meetings | Paediatrics | Multi-stakeholders, including Industry Stakeholder Associations, patients, consumers, healthcare professionals, EMA | 2 times/year<br>- 08 Jun 2018 link<br>- 22 Oct 2018 link<br>- 19 Feb 2019 link<br>- 04 Jul 2019 link |
| Workshop of the European network of paediatric research at the European Medicines Agency (Enpr-EMA) | Paediatrics | Multi-stakeholders, including Industry Stakeholder Associations, patients, consumers, healthcare professionals, EMA | Annually<br>- 07 Jun 2018 link<br>- 14 Oct 2019 link |
| Industry stakeholder meetings on Brexit | Brexit | Industry Stakeholder Associations, EMA | - 23 Mar 2018 (human) link<br>- 20 Apr 2018 (veterinary) link<br>- 24 Sep 2018 (human and veterinary) link<br>- 28 Jan 2019 (human and veterinary) link |

**Annex 4**

## Overview of stakeholder events involving industry stakeholders in 2018-2019

| Meeting date | Meeting title | Stakeholder type | EMA website |
|---|---|---|---|
| 20 February 2018 | Substance, product, organisation and referential data (SPOR) impact on veterinary stakeholders | Multi-stakeholder | link |
| 20 March 2018 | Multi-stakeholder workshop to further improve the implementation of the Paediatric Regulation | Multi-stakeholder | link |
| 16 March 2018 | EudraVigilance and signal management information day | Multi-stakeholder | link |
| 19 April 2018 | European Medicines Agency veterinary medicines innovation day | Industry | link |
| 03-04 May 2018 | Workshop on the reflection paper on statistical methodology for the comparative assessment of quality attributes in drug development | Multi-stakeholder | link |
| 04 May 2018 | Heads of Medicines Agencies (HMA) / European Medicines Agency (EMA) Joint Big Data Task Force meeting: identifying solutions for big data challenges | Multi-stakeholder | link |
| 08 June 2018 | Haemophilia registries workshop | Multi-stakeholder | link |
| 13 June 2018 | EMA public hearing on quinolone and fluoroquinolone medicines | Multi-stakeholder | link |
| 12 October 2018 | Focus group meeting on dose optimisation of established veterinary antibiotics in the context of summary of product characteristics harmonisation | Multi-stakeholder | link |
| 24 October 2018 | Multi-stakeholder workshop to launch consultation on European Medicines Agency (EMA) human regulatory science to 2025 | Multi-stakeholder | link |
| 26 October 2018 | Info day for micro, small and medium-sized enterprises (SMEs): regulatory toolbox for medicines and combined devices developers | Industry | link |
| 9 November 2018 | Multi-stakeholder workshop with the HMA/EMA task force on availability of authorised medicines | Multi-stakeholder | link |
| 26 November 2018 | Stakeholder workshop on support to quality development in early access approaches, such as PRIME and Breakthrough Therapies | Multi-stakeholder | link |
| 03 December 2018 | European Medicines Agency stakeholder interaction on the development of medicinal products for chronic non-infectious liver diseases (PBC, PSC, NASH) | Multi-stakeholder | link |

| Meeting date | Meeting title | Stakeholder type | EMA website |
|---|---|---|---|
| 06 December 2018 | Multi-stakeholder workshop to launch consultation on European Medicines Agency (EMA) veterinary regulatory science to 2025 | Multi-stakeholder | link |
| 07 December 2018 | European Medicines Agency EudraVigilance and signal management information day | Multi-stakeholder | link |
| 16 January 2019 | Follow-up stakeholder meeting on Allergen Immunotherapy for Children | Multi-stakeholder | n/a |
| 18-19 November 2019 | Multi-stakeholder workshop on draft 'Regulatory Science to 2025' strategy (stakeholders for human medicines) | Multi-stakeholder | link |
| 05-06 December 2019 | Multi-stakeholder workshop on draft 'Regulatory Science to 2025' strategy (stakeholders for veterinary medicines) | Multi-stakeholder | link |