27 May 2021
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Stakeholders and Communication Division

Meeting summary - PCWP/HCPWP joint virtual meeting

2 March 2021, 12:45 to 16:15 and 3 March 2021, 09:45 to 13:15 CET

Co-Chairs: J. Garcia Burgos (EMA), K. Immonen (PCWP), U. Jäger (HCPWP) via WebEx

1. Welcome and introduction

1.1 Opening remarks

Juan Garcia-Burgos opened the meeting and welcomed all the participants.

Juan highlighted the focus of the meeting; update on COVID-19, the European reference network model, advanced therapy medicines, personalised medicine approaches, Big Data deliverables and ICH guidelines.

The co-chairs; Ulrich Jäger and Kaisa Immonen introduced themselves and welcomed the participants.

1.2 Welcome by EMA's new Executive Director

Emer Cooke (EMA Executive Director) addressed participants expressing her gratitude for their organisations' continuous support and commitment in jointly building what is a very successful model of engagement between regulators and patient, consumer and healthcare professional organisations. She highlighted the important role the PCWP and the HCPWP play in helping the Agency to fulfil its public health mission, naming same examples where their input within key areas, such as shortages, big data, product information and health crisis management, has been invaluable. Even though the first period of her mandate has been quite dominated by trying to ensure that the Agency responds adequately to the challenges posed by the pandemic, she emphasised that on top of COVID-19 the Agency and the regulatory medicines network continue with their core work of regulating all the other medicines. She underlined that EMA is also busy with the European Commission' legal proposal to expand EMA's mandate to act in preparation for and during public health emergencies. In this context, there is ongoing work to develop a plan for stakeholder engagement as part of the implementation of EMA's extended mandate and more details will be shared with the working parties once EMA Management Board has endorsed the direction of travel.

Emer reminded participants that last December, following adoption by their respective Management Boards, EMA and the Heads of Medicines Agencies published their joint strategy for the next five years. EMA is currently working on translating the strategic goals for each of these areas into concrete actions. Detailed work plans of both EMA and the national competent authorities are expected in the coming months, and these will include appropriate planning for stakeholder involvement throughout. She then concluded with a hopeful message of finally being able to see everyone face to face in EMA's building once it is safe to do so.

2. COVID-19 update

2.1 Update on vaccines and therapeutics

Marco Cavaleri (Head of EMA's Office of Biological Health Threats and Vaccine Strategy), gave a presentation on the latest information on COVID-19 vaccines and treatments (see presentation).

He started with an update on medicines intended to treat COVID-19 symptoms and reduce progression of the disease. There is some promising data on the use of monoclonal antibodies which has shown a reduction in disease in high risk patients, with fewer patients progressing to severe disease (a monoclonal antibody is a type of protein designed to recognise and attach to the spike protein of SARS-CoV-2, this stops the virus be able to enter the body's cells). These medicines are currently being reviewed by EMA through its rolling review program and we hope to be able to approve them as soon as possible.

During the comprehensive rolling review, ahead of a possible application for a marketing authorisation, EMA gives opinions (called 5.3 referrals) to provide a harmonised scientific opinion at EU level to support national decision making on the possible use of the antibodies prior to marketing authorisation, e.g. in compassionate use programmes or emergency use.

EMA is also currently conducting a review of Celltrion's monoclonal antibody regdanvimab (CT-P59), in addition to the ongoing rolling review of regdanvimab for the treatment of confirmed COVID-19 in patients who do not require supplemental oxygen therapy and are at high risk for progressing to severe COVID-19 and/or hospitalisation.

One key threat we need to keep in mind is that there is an increased resistance of SARS-COV2 variants to monoclonal antibodies. So we need to be cautious when using them as they may not be effective against the variants, for example we have seen that some monoclonal antibodies lost effectiveness against the south African variant. This is why a combination of therapies would be most effective against emerging variants. Ideally companies should work together to develop a cocktail of 2/3 monoclonal antibodies which would then work best against all strains.

Other types of therapies used to treat COVID-19 include immunoglobulins (antibodies produced naturally by the body's immune system to help fight infection and disease), so far only steroids have really shown any benefit in hospitalised patients. Tocilizumab seemed very promising to start but subsequent clinical trials did not show sufficiently good results. More recently data from the UK Recovery study which included a large dataset, found Tocilizumab was beneficial (small difference of 4% reduced mortality), so this will be studied further, together with other data, to determine its optimal use in patients, together with other treatments.

Another area of great interest is the use of anticoagulants; thromboembolism (blood clots in the blood stream) is one of the key causes of mortality in COVID-19 patients. The first data we have seen came from a National Health Institute (NHI) study testing different anti-coagulants in advanced patients in an intensive care unit (ICH) setting. Unfortunately, these studies did not show a significant benefit, however other studies have shown some potential benefits when used in the early phases of the disease. We need more confirmatory and definitive data on how, when and which ones are best.

Another product, an oral immunomodulator, Colchicine (an existing medicine), is currently being studied in trials with hospitalised patients. The Col-corona study conducted in Canada looked if there was a reduction in progression to severe disease, but unfortunately it only showed a marginal benefit - not enough to trigger a regulatory application. We look forward to seeing more data coming from larger ongoing studies (e.g. Recovery).

Different technologies have been studied in the development of COVID-19 vaccines; EMA has already approved two mRNA vaccines and two viral vectors. These have been the fastest to generate clinical

evidence, but there are also others under evaluation, including more traditional vaccine technologies, and some inactivated virus vaccine types e.g. from China.

The vaccines approved so far at EU level are Comirnaty (2 doses, 3-week interval) and Moderna (2 doses, 4-week interval); the dose intervals were those studies in the trials. Both vaccines provide a high level of protection from COVID-19; around 95% protection. There are also differences in storage temperatures between these two vaccines and Pfizer is currently trying to move to a formulation easier to handle which would help with the vaccination campaigns.

The recently approved vaccine is the COVID-19 AstraZeneca which includes data from UK and Brazil clinical trials merged together. It included a dose interval of around 4-12 weeks and looking at this subgroup showed an efficacy of around 60% (some other numbers were circulated but this is what was approved).

In terms of safety, we are closely monitoring all the data we receive now that the vaccines are rolling out in the member states to look for any emerging safety signals on top of what we already know. All these vaccines have a robust risk minimisation plan in place. The only important risk we have seen so far is anaphylaxis which has a slightly higher frequency than what we normally see in other vaccines. Studies are ongoing try to understand why, but this is well identified and described so well handled.

We are still waiting for additional safety information, e.g. overall long term safety, use during pregnancy, in immunocompromised patients, and in the elderly, as these groups were not included within the clinical trials, so we do not fully know their immune response and if the vaccines will be sufficiently safe and effective. There is no safety and efficacy data for those above 55 years from the trials, however when we look at the immune response of those over 65 who have had the vaccine, it seems similar to younger adults. In addition, there seems to be a better response with a longer interval period before the second dose.

Another important area is the emergence of variants and whether the current vaccines are able to maintain protection against COVID-19. The first step has been to start testing samples from vaccinated individuals to see if they have protection against emerging mutations.

In summary, EMA has discussed 181 therapeutics with developers, 50 vaccines have been identified for further discussion and 76 rapid scientific advices have been given for advanced vaccines and therapeutics.

The CHMP has provided advice to support emergency use of monoclonal antibodies at EU level and recently published a guidance on variant vaccines. There are continued discussions on upcoming conditional marketing authorisations for additional vaccines and of course importantly ongoing review of post-authorisation data on the effectiveness and safety of the vaccines and therapeutics.

After the presentation there was a 'Question and Answer' session with members; some aspects covered included:

Q: What information do we have on the use of vaccines in children? And on long-term safety?

A: Studies in adolescents have started, these will progress into lower age ranges. We need robust data, however this analysis is likely to go faster than we expect. The paediatric committee (PDCO) assessed the 'investigation plans' for children for all vaccines (called PIP).

A: It is still too early to have a full picture on long term safety of the vaccines, this will become clearer the more they are used and more data becomes available. So far, the overall prognosis is very good.

Q: What about vaccine use in elderly and frail adults – have trials done any frailty assessment?

A: Frailty has not specifically been looked at – although some such participants were included in the

trials and there were no signals of a change in protection or adverse reaction. It will be important to look at these aspects via real world evidence in a larger dataset to see if anything else emerges.

Q: What about the use of vaccines in children? – It seems paediatric investigations are only due in 2024? Many children with rare diseases are vulnerable and at risk so we cannot wait until 2024.

A: Indeed, it is impossible to have large paediatric efficacy studies, so we extrapolate via immunogenicity from adults. 2024 will be the last cohort, e.g. newborns. However, some of the data in older children will be available before the end of this year for some vaccines, with an interim report on immunogenicity, which could show sufficient benefit/risk data to approve use in these age groups.

2.2 Safety surveillance

Georgy Genov (head of Pharmacovigilance office) presented an overview of safety surveillance for COVID-19 Vaccines (see presentation). He explained that EMA monitors all centrally approved medicines but when it comes to vaccine monitoring this is enhanced in several ways; for example an intensified frequency - EMA monitors adverse events and reviews relevant data every two days. There is heightened collaboration with international partners, both in terms of exchange of information but also building international research cohorts able to exchange immediate information on arising safety issues.

Marketing authorisation holders are required to produce monthly safety reports, which are reviewed by our safety committee (PRAC). EMA also funds studies for prospective monitoring – a small bridging study started in February, and a second larger one will start soon. EMA's COVID-19 taskforce also contributes to safety evaluations on emerging safety issues under consideration at the PRAC.

In terms of risk assessment and management EMA can commission and fund independent studies on any emerging safety issues. A new core risk management plan has been put in place which provides additional guidance to manufacturers in terms of risk management systems.

For public communication, the new vaccines safety summary updates are published on a monthly basis in addition to the usual PRAC highlights which includes all COVID related reviews which are starting.

Priya Bahri, (pharmacovigilance office), presented some more details on the monthly safety summary updates for all authorised vaccines, as part of EMA's transparency policy. The goal of these updates is to enhance transparency by providing timely safety updates. The information included within the updates is prepared in a manner to be as meaningful for the public as possible, based on the current evidence to date, whilst also being useful for those in communication roles e.g. journalists. The aim is to provide all the relevant safety information in one place (via links), i.e. EPAR, product information, paediatric investigation plan, risk minimisation measures, etc. This information is not always easy to find, therefore consolidating it in one document should make this easier.

The preparation of the updates is linked to the PRAC assessment processes and associated timelines, in addition to ad-hoc meetings, so sometimes documents are published outside of the regular monthly updates, if needed.

The format of the summary allows for it to be read on all devices, e.g. phone, laptop etc. The first page includes the key highlights with dates relating to the review period. The second page includes the actual updates (new information) sorted by safety topics to be easily navigable. The third page includes any other information on safety monitoring; general or medicine specific and the final page provides links to planned and ongoing studies. The document will further develop as more data emerges and may include graphics and tables. These safety updates have already been quite widely used, shared and posted by others, including media outlets, press and public health bodies. Feedback received to date has been good and EMA is very grateful to the patients and healthcare professionals

who review all of the summaries before they are published – all of their comments are considered and implemented when possible, or kept for later. EMA is keen to receive any feedback on how the document could be improved, and/or if any information is missing. This is a continuous learning exercise on 'real time reporting'.

2.3 EMA's vaccine outreach strategy

Melanie Carr (head of Stakeholders and Communication Division), presented an overview of EMA's vaccine outreach strategy (see presentation). The overall aim of the strategy is to raise awareness and trust in the quality, safety and effectiveness of vaccines, to empower the EU public and healthcare professionals to take well-informed vaccination decisions. More than ever, during a pandemic it is imperative for EMA to understand the public's needs and concerns and to ensure that information, from reliable sources, addresses these concerns. EMA endeavours to provide the public with easily accessible information in plain language, so they can have to hand the latest updates but also to understand the rationale behind important decisions on vaccines. EMA has put in place measures to enhance the level of transparency for COVID-19 medicines to make sure all new information and updates are communicated in real time. EMA also responds to queries from members of the public and media, holds press conferences, public meetings & uses social media to convey key developments. EMA is also collaborating with ECDC to provide content for the European Vaccination Information.

Continuous engagement and dialogue with patients and healthcare professionals is vital to understand what people want/need to know and the best ways to explain the science. This occurs through patient and healthcare professional representative participation in EMA's pandemic task force, other expert meetings as well as the regular review and user testing of information materials. EMA also works together with the European Commission, ECDC and other national medicines regulators exchanging the latest information.

EMA's public stakeholder meetings on COVID-19 are also a keyway to share the latest updates with the public; two such live meetings have already been held, one in December and one early January, the next one is scheduled later in March. We will continue to hold these meetings as often as needed. In the meantime all the relevant updated information can be found on EMA's COVID-19 webpages.

2.4 Next public meeting

Nathalie Bere (patients and consumers coordinator) provided an overview of EMA's next public stakeholder meeting on COVID-19 held on 26 March 2021 (see presentation). This is EMA's third public meeting and it builds on the positive feedback from the two previous meetings. The first part of the meeting comprises four presentations covering an overview of COVID-19 vaccines approved in the EU including those which are currently under review, an update of post-authorisation activities, including emerging safety data since EU authorisation of the first COVID-19 vaccines, and ongoing work to address new variants. An overview on the expected impact of COVID-19 vaccination on societies given by ECDC and finally an update on transparency and publication of clinical data for COVID-19 vaccines.

The second part of the meeting is dedicated to listening to the public and stakeholders on their needs, expectations and any concerns; the participants inside the WebEx room can raise their hand to take the floor with a question or comment, or alternatively include it within the chat function. In addition, a live mailbox is monitored for those watching the broadcast to also submit a contribution.

A recording of the meeting, together with the presentations is published after the meeting.

EMA will continue to hold these public meetings as needed.

3. Medicines development and authorisation

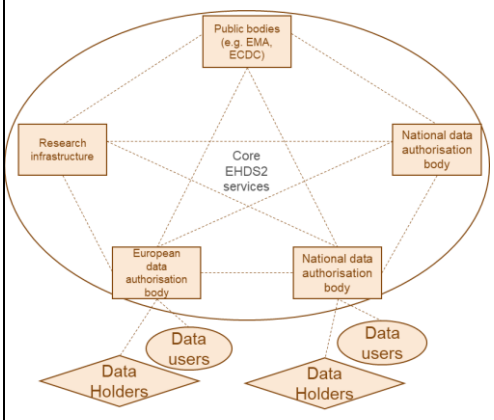
3.1 The European Reference Network model in the European Data Space

Jordi Llinares Garcia (EMA) introduced the topic by putting into perspective the potential for collaboration between the European research networks (ERNs) and EMA, for regulatory purposes (see presentation). As virtual networks that bring together healthcare providers across Europe, ERNs were created in the context of the implementation of Directive 2011/24/EU on the application of patients' rights in cross-border healthcare directive. ERNs aim to facilitate discussion on complex or rare diseases and conditions that require highly specialised treatment as well as concentrated knowledge and resources. By connecting experts and patient populations, ERNs also have the potential to facilitate clinical studies and test therapeutic interventions, putting them at the forefront of innovation in numerous rare disease fields.

Amongst the different approaches that could be taken by EMA for collaborating with ERNs, the framework of collaboration between EMA and academia, adopted in 2017 by EMA's Management Board, provides a set of tools that can support such objective. This includes the promotion and further development of regulatory support for translating academic research into novel methodologies and medicines, and the collaboration on areas of research on regulatory science, such as novel approaches, endpoints and methodologies. ERNs have also been clearly identified as a channel for accessing expertise across Europe in the Regulatory Science Strategy to 2025 (RSS 2025).

Martin Dorazil (European Commission) further explained how the ERNs model is consolidating and expanding. The 24 ERNs system will conclude the enlargement of its geographical scope and disease coverage by end of 2021. In parallel, steps are being taken to consolidate and ensure the financial and organisational sustainability of the ERNs system, including securing funding from the EU4Health Programme and Member States, and maintaining the clinical patient management system (CPMS[1]).

In addition, work is underway to develop a Joint Action for integration of ERNs into national healthcare systems, focusing on the implementation of the ERN Board of Member States 2019 Statement. Key areas of intervention include:



- Adapting or updating national rare disease plans/ strategies and establishing a legal framework for ERN integration
- Creating appropriate patient care pathways, developing clear systems for referral to ERNs to be used by the healthcare providers
- Providing information on ERNs at member state level, and
- Facilitating support by Member States (MSs) to ERN Coordinators, members and partners.

The European Commission is also supporting ERNs on their knowledge generation actions (e.g. clinical practice guidelines, ERN virtual academy, professional mobility programme, draft ERN training and education strategy) and research activities (e.g. support set up of ERN registries, link the registries with European Health Data Space, European Joint Programme for rare diseases).

[1] The CPMS is a web-based clinical software developed by sub-contractors of the European Commission and used by ERNs to support the running of virtual medical consultations. The Commission also provides secure electronic systems to authenticate the users and to authorise access for healthcare professionals of the ERN member hospitals to access the CPMS.

The creation of a common European Health Data Space (EHDS) is building on infrastructure at European level to potentially scale up existing initiatives such as the ERNs. The EHDS is intended to promote better exchange and access to different types of health data (electronic health records, genomics data, data from patient registries etc.), not only to support healthcare delivery (so-called primary use of data) but also for health research and health policy making purposes (so-called secondary use of data).

For the purpose of secondary use of health data, and in order to support ERNs' research activities, it is important to understand the concept of the so-called EHDS2 NODEs. These nodes are the entry point for stakeholders into the EHDS. They can be established by national or trans-national stakeholders and follow common policies and interoperability specifications. *Data holders* make health data available for research, health policy making or regulatory activities whilst. *Data consumers* use data for research, health policy making or regulatory activities.

Finally, the EC is focussing on demonstrating the ERNs system's added value and is planning a public consultation in the coming months to evaluate and monitor ERNs' added value.

Rima Nabbout (EJP RD) completed the session explaining how ERNs are part of the European joint programme on rare diseases (EJP RD). This is a large programme that integrates existing infrastructures, networks, trainings, funding programmes and tools, expands them and develops new essential ones to offer a harmonized (and centralized) rare disease research ecosystem that is easy to use for scientists and produces benefits for patients in the most efficient way (see presentation).

A discussion followed which concluded that through their direct activity on research an innovation and continuous exploration of innovative approaches to treatment and development, ERNs offer several opportunities to regulators, including access to very rich data, expertise, and direct contact with clinical issues and patients. There is therefore great potential for dissemination and collaboration on regulatory science and translational initiatives. Some participants called however for more concrete actions that go beyond occasional outreach and can foster further engagement between ERNs and regulators. Other participants pointed to their organisation's commitment to help their relevant ERN's work getting embedded in the medical community.

Participants were invited to share their views with the Secretariat on how to continue exploring further engagement with ERNs, with the agreement to return to this topic in an upcoming PCWP/HCPWP meeting. The focus should then be on integration with EMA RSS2025 and HMA/EMA Big Data recommendations.

3.2 Timely patient access to Advanced Therapy Medicinal Products (ATMPs)

Martina Schüssler-Lenz (Chair, Committee for Advanced Therapies) presented on the EU framework for gene and cell therapy medicinal products, including tissue-engineered products, established by Regulation 1394/2007 (see presentation). For all three product classes, called advanced therapy medicinal products, a centralised marketing authorisation is mandatory. EMA's Committees for Advanced Therapies (CAT) and for Human Medicinal Products (CHMP) and the network of national agencies are responsible for the scientific evaluation of the marketing authorisation applications. Since the regulatory framework for ATMPs was established, 17 ATMPs have been authorised in the EU. However, the pipeline of new ATMPs is much bigger, as seen from the significant numbers of different products discussed by the CAT in scientific advice and classification procedures.

Martina explained that ATMPs' enormous potential is well recognised but cannot be dissociated from the fact that safety and efficacy follow-up of patients treated with authorized ATMPs is mandatory and alignment of post-authorisation evidence generation between regulators, HTA bodies, pricing and reimbursement bodies is key to ensure timely patient access. CAT/EMA has identified gaps in the implementation of registry-based studies and is taking actions in PRIME, scientific advice, interaction

with downstream decision makers. She concluded by highlighting the areas where patient and healthcare professional input is needed:

- CAT – patient and HCP´s expertise, input, weight highly appreciated
- PASS/PAES protocols – input regarding patient relevant outcomes (Zolgensma)
- Disease registries – exchange knowledge and information
- Registry-based ATMP studies – advocate for acceptance by patients and physicians, national decision makers
- Scientific advisory groups (SAGs) – contribute with knowledge and expertise
- EMA/CAT based outputs – communicate and close information gaps

A discussion followed leading to the conclusion that further engagement with CAT is highly welcomed and can be strengthened. In addition, there are several ATMP-related topics that could be considered for upcoming PCWP/HCPWP meetings, including early access programmes, cross-border access to advanced therapies, data capture at point of care level (including registries), and patient relevant outcomes.

3.3 Personalised medicine approaches for the next generation of medicines

Opening the discussion on the topic, Anthony Humphreys (Head of EMA Regulatory Science and Innovation Taskforce) pointed to the fact that there is an abundance of strategies emerging from different fronts.

For example, the EMA Regulatory Science Strategy to 2025, adopted in March 2020, addresses many initiatives in the field of advanced therapies, novel clinical trial design, availability and access discussions, data science and real world data sources, and efforts in special populations, that lend themselves to the personalised medicine agenda.

In the meantime, as we were confronted with the COVID-19 pandemic and the reality it brought forward in terms of overall response capacity of EU scarce resources, flagship strategies with a much broader scope have been published, i.e. the Pharmaceutical Strategy for Europe (published in November 2020) which launched an ambitious revision of the pharmaceutical legislation and highlighted the dilemma between innovation – with personalised medicine at its forefront – and securing supply of the top 200 high-volume stock medicines in the EU.

The Europe's Beating Cancer Plan (published in February 2021) also brought forward a very holistic approach to personalised medicine and there is a need for the EU regulatory medicines network to reflect on what are the real points of engagement with this plan in the years to come.

Considering also the European Medicines Agencies Network Strategy to 2025 (EMANS 2025), he called for a specific reflection on what is the ambition on personalised medicine and emphasised that the PCWP and HCPWP can be very influential in shaping an EMA agenda for the next 10 years up to 2030.

Ejner Moltzen (ICPerMed) provided an overview of the scope, visions and actions of ICPerMed (see State of the Art Report and Vision Paper) and updated participants on key discussions held during the second conference of ICPerMed "Personalised Medicine – From Vision to Practice" in February 2021 (see presentation).

He pointed out to two important sources of information:

- The Action Plan, which provides a general overview over the field of personalised medicine;
- The ICPerMed database, which gives an overview on the actions in the field of personalised medicine performed in the ICPerMed member states and may assist in finding suitable funding opportunities and information about potential funders per country and/or region.

Ejner highlighted that the focus is now to move from early research towards implementation in healthcare, with genomic medicine holding the capacity to profoundly change patient care. Routine

genome sequencing combined with general health care data will enable a high number of patients to benefit from personalised diagnostics and personalised therapeutic care. Currently the main focus is on cancer and rare diseases, but personalised approaches within more common diseases such as metabolic, cardiovascular, neurological as well as infectious diseases are starting to appear. Increased attention to personalised prevention is also starting to appear.

ICPerMed is committed to demonstrate the importance and the need to address personalised medicine challenges regarding patient preferences, data harmonisation, personalised medicine implementation into healthcare systems, collaboration between academia and industry and on health economics aspects. To this end, its Governance was revised in October 2020 to incorporate five new working groups for the next three years. These include clinical studies, healthcare, patient empowerment, education and curricula, and health economic value.

Importantly, he noted that a new ICPerMed Stakeholder Forum was also being created to foster new partnerships and networks to share ideas and best practice examples, identify key issues and fields to be addressed and to establish new communication and dissemination channels. PCWP and HCPWP members were invited to join this forum.

Participants raised several comments which can be summarised as follows:

- What is understood by personalised medicine varies from a very narrow to a broad and holistic concept
- Possible ramifications of personalised medicine in restricting access to therapies need to be further discussed
- Need to consider possible trends to move from rare to personalised diseases and how to assess efficacy and safety in very small populations; concerns around standard clinical trial/research studies not working with very low numbers and with using predictive algorithms alone
- Suggestion to establish bridges with work developed by ERNs and their registries
- Suggestion to find resources to support the personalised medicine approach for other diseases beyond cancer
- For areas with no disease-modifying treatments available (e.g. Alzheimer's disease), what conversations can take place with patient stakeholders to create a level of interest and understanding in anticipation of therapies being available
- How to measure cost-effectiveness on personalised medicine in daily practice
- The need to bring a strong primary care perspective view and stimulate adoption of electronic medical records and development of predictive algorithms which incorporate the prevention dimension and not only treatment options
- Develop strategies and guidelines for pharmacogenomic testing that integrate primary care
- Need for a transversal approach to personalised medicine which includes among others the areas of information and communication, research, authorisation and regulation, and data collection

Participants were invited to share their views with the Secretariat with the agreement to return to this topic in an upcoming PCWP/HCPWP meeting. The focus should then be on identifying concrete points of engagement in the context of the different strategies and the ICPerMed vision to 2030 with a view to build an EMA Vision for personalised medicine which embraces a holistic view of personalised medicine, including both prevention and treatment.

4. Big Data

4.1 Implementation of HMA/EMA Big Data Steering Group deliverables

Nikolai Brun, co-chair of the HMA-EMA Big Data Steering Group (BDSG), gave an update on the work of the steering group during 2020 (see presentation). Nikolai highlighted that the published workplan is very much aligned with the top 10 recommendations of the Big Data Task Force (11 including veterinary medicines). As shown in the slides, progress has been made on all recommendations during 2020.

The BDSG has been working with international partners, such as FDA and Health Canada to collaboration on real world evidence. The Aim to have an International meeting in Q4. There was a multi stakeholder workshop in December 2020 and a follow up stakeholder forum will be held at the end of 2021. These workshops and forums are a good interactive way of working and will continue in 2021.

In terms of the next steps, these have also been planned along the 11 recommendations – with the aim of delivery on all topics during 2021. There will be several workshops held during 2021 including on data quality, on real world data meta-data, on artificial intelligence and on data standards. A European health data space pilot has been initiated by the European Commission and medicines regulation will likely be a key use case.

Peter Arlett (Head of EMA Data Analytics and Methods Taskforce) then gave more details on the DARWIN EU project (see presentation) – the vision is to establish a network of data, expertise, and services, called Data Analysis and Real-World Interrogation Network (DARWIN EU), to support better decision-making by EMA and NCA scientific committees on the benefits and risks of products via rapid access and analysis and increased reliability, validity and representativeness of EU health data (Published business case for DARWIN). The network concept of DARWIN EU is distributed network for fast access and analysis; via a federated network so the data stays local and exchanged data is aggregated and anonymised. DARWIN EU will include a common data model but will also have the ability to accept data sets not yet transformed into a common model. The aim is to deliver a full version of DARWIN EU 2023, but earlier pilots could deliver as soon as 12 months from now. DARWIN EU will need to rapidly evolve to embrace new tools coming out of the EU health data space (EHDS).

In relation to COVID-19 the European Commission adopted the Health Union Proposal end of 2020 with specific legal provisions to use real world data in responding to health crisis etc; DARWIN EU will be a principle vehicle to deliver this.

Overall the benefits of DARWIN EU will be to increase quality of decision-making, provide faster access to safer, more effective and innovative medicines with their optimised safe and effective use on the market.

So far, the project has been initiated and funding has been identified, including long term maintenance funding via EMA's fees regulation. During 2021 work continues with EMA committees to define use cases, a coordinating centre will be established through a public tender. The DARWIN EU advisory board will also be established, including patient and healthcare professional representatives from PCWP/HCPWP (call to be made).

In conclusion, good progress on all the recommendations has been made so far in 2020 and this is set to continue during 2021. There will be option to join the various workshops and the working parties will be kept updated.

After the presentation there was a 'Question and Answer' session with members; including:

Q: within the EU and different countries there is different coding for primary and secondary care. Can

we harmonise coding, perhaps through training initiated in medical schools?

A: data standardisation will be an important component of using a federated system – indeed the difficulty at the moment is that there are many different ways to code medicines, and this is also a challenge for registries. We do not have an immediate solution, but dialogue is ongoing, and there are other initiatives e.g. EHDEN also working on this. Implementation of AI will also facilitate. Regarding training we can discuss with PCWP/HCPWP how to share within educational authorities and to make the material freely available.

Q: Could ENCEPP play a role?

A: ENCEPP, as an effective network of academics and service providers focuses on good practice governance principles & methodological practice. DARWIN EU will operate at an operational level, writing protocols and running analysis of data in different MS. The two will be complementary.

Q: What about the United Kingdom – how does it impact DARWIN?

A: Benefits from analysing Healthcare data should not be limited by boundaries. A lot of good data originates from UK so we hope to be able to continue to leverage it going forward.

5. ICH guidance

5.1 Good Clinical Practice (E6/E8)

Fergus Sweeney (Head of EMA Clinical Studies and Manufacturing Taskforce) provided a progress update on the ongoing ICH Good Clinical Practice (GCP) renovation process (see presentation). This review includes both the ICH E6(R3) Guideline for Good Clinical Practice, addressing global standards for clinical trial conduct, and the ICH E8(R1) which stablishes clinical trial design principles. A dedicated PCWP/HCPWP workshop on this topic was organised in June 2020 (meeting report).

The review of ICH E8(R1) is coming closer to finalisation, following the public consultation phase in October 2019 for which members of PCWP and HCPWP also contributed. Protection of clinical trial participants, scientific approach to trial design and patient engagement in trial design are key principles outlined in the new introduction section of this guideline, stating that 'consulting with patients and/or patient organisations in the design, planning and conduct of clinical studies helps to ensure that all perspectives are captured'. The review is expected to enter step 4 – adoption of the harmonised guideline – by mid-2020.

In relation to ICH E6(R3), the Expert Working Group (EWG) review goals aim to focus on:

- Comprehensive principles that remain relevant as technology evolves and clinical trial design advances
- Risk-based approach and proportionality
- Thoughtful process throughout clinical trial conception, design, conduct and analyses

Fergus reminded participants that the ICH E6(R3) EWG includes also academic experts nominated by the different ICH regulatory regions and for Europe this is Prof Martin Landray following the HCPWP nomination last year. He then explained that the EWG's work is continuing and the group is still progressing towards step 2 of the ICH guidance development process (https://ich.org/page/formal-ich-procedure). In particular it has worked on the principles and introduction of ICH-E6(R3), and major principles are now outlined and explained. Unlike ICH-E6(R2), the draft principles for ICH-E6(R3) contain further explanations and important considerations and are designed to be interdependent. The principles address multiple key concepts including:

- Focusing on critical to quality factors, such as the risks to participants and risks to trial results
- Highlighting the importance of risk-based, proportional approach to determining trial processes and design elements
- Encouraging the incorporation of innovations that are customized to fit the design and purpose of the trial
- Engagement with stakeholders

Once the updated ICH E6 Guideline achieves Step 2 of the ICH guidance development process, public input will be invited and considered. Step 2 will involve simultaneous publication of both the draft principles and Annex 1, along with an introduction and a glossary. Public comment will be invited at that point since the principles need to be seen and commented on alongside the details in Annex 1. In May 2021 ICH E6(R3) EWG will organise a web conference to present the current draft of the GCP principles as a work in progress.

Members will be kept informed of upcoming public consultations and other stakeholder engagement activities and were invited to continue raising awareness of the importance of these guidelines and their impact in clinical research.

5.2 Patient data reflection paper

Milton Bonelli (EMA) gave a presentation on the ICH reflection paper (see presentation). He started by giving high level background on the structure and membership of ICH, followed by an overview of how the ICH assembly and management committee lead the operations of the different drafting groups comprised of experts who draft the various guidances.

ICH develops different types of documents; with *guidelines* usually being the final outcome. This usually starts with new topic proposed by an ICH member organisation, including EMA/European Commission. For some complex areas ICH will decide to first draft a reflection paper to articulate the strategy intended to address various aspects of a broader problem that would benefit from harmonisation; a reflection paper includes high level principles, usually in much less detail than in the final guideline.

One of four current ICH reflection papers is on patient focused drug development (PFDD) which identifies key areas for incorporation of patient data in medicines development with the aim to improve the quality and relevance of patient data informing regulatory decision-making. The reflection paper focuses on two key aspects: meaningful clinical outcomes for patients and patient preference information for benefit risk assessment. The paper proposes two guidelines, structured as a set of relevant questions that the guidelines should address to help all stakeholders in medicine development and use.

The focus of first guideline is to gain understanding on what disease effects and treatment burdens matter most to patients that might be addressed by a medical therapy and what would be the best way to measure these in a clinical trial, with appropriate endpoints able to capture clinically meaningful changes from a patient perspective.

The second proposed guideline focuses on patient preferences, which can inform medicine development, benefit/risk assessment and ultimately marketing authorisation application decisions. The guideline would include methods and approaches to identify and explore what patients might consider to be acceptable trade-offs of expected risk(s) in return for an expected benefit with a new medicine. It also aims to cover what methodological considerations for the conduct of patient preference studies are needed to provide credible and reliable findings to support regulatory decision making.

The public consultation ends early March, the working parties were encouraged to submit comments if not already done.

It was also highlighted that the PCWP had started working on a draft guidance in this area, but it has been postponed due to business continuity planning (due to Brexit and COVID) so this ICH reflection paper is very timely and it would be a pragmatic way forward for EMA, its working parties and relevant committees, to now collaborate with ICH and work together to produce global guidance. Non-ICH stakeholders, such as healthcare professionals and patients would be involved to the extent possible, following the initial footprint given from the recent renovations of ICH E6 and E8 guidance.

There followed a short question and answer session:

Q: How can the working parties be involved?

A: The intention at ICH level is to have a level engagement similar to E6 and E8 consultations – having a range of information from the different points of view allows a discussion and outcome informed by these perspectives. PCWP/HCPWP are uniquely placed at EU level to contribute, but there needs to be a structured way to the capture views, also taking into account capacity of organisations, so we will reflect on the best way, probably we will convene a dedicated subgroup.

6. Satisfaction survey

6.1 What do the 2020 results tell us?

Maria Mavris (EMA) presented the results to the Satisfaction Survey on participation in EMA activities in 2020 (see presentation). This survey aimed to collect views from stakeholders on different aspects of their involvement, such as the ease of use of EMA systems, their experiences of participating in EMA meetings and the benefit of their involvement. The results enabled a compilation of quantitative and qualitative data which will contribute to identify good practices and points for potential improvement.