Draft minutes of EMA – Payer Community meeting 2021

12 March 2021, 10:00 – 13:00

Role	Name
Co-chairs:	Timon Sibma (Payer Community) and Michael Berntgen (EMA)
Present:	Payer Community: Alex Correia (INFARMED), Anna Boehnlein (AOK), Anna Nachtnebel (Dachverband der Sozialversicherungstraeger), Annalisa Sammarco (AIFA), Anne-Claire Le Bodic (REIF), Benedetta Baldini (ESIP), Cara Usher (St James), Christine Dawson (ESIP), Claudia Scharl (Dachverband der Sozialversicherungstraeger), Cordelia Koppe (IKK), Dalhia Aissat (CNAM), Elin Bjornhaug (NOMA), Els Soete (INAMI-RIZIV), Evelyn Macken (MLOZ), Evert Jan van Lente (AOK), Filip Clinck (INAMI-RIZIV), Filipa Monteiro (INFARMED), Inês Costa (INFARMED), Jana Bogum (AOK), Jana Lukacisinova (SUKL), Jocelijn Stokx, Christian Mutualities, Johan Ponten (TLV), Juraj Slaby (SUKL), Jure Mikolic (ZZZS), Kärt Veliste (Estonian Health Insurance Fund), Lea (St James), Lisa Vervueren (INAMI-RIZIV), Lonneke Timmers (ZIN), Maelle Anciaux (INAMI-RIZIV), Magdalena Fabianova (SUKL), Marc van de Casteele (INAMI-RIZIV), Mareena Paldan (STM), Michael Ermisch (GKV-Spitzenverband), Milan Vocelka (SUKL), Nadia Amer (CNAM), Petra Fadgyas-Freyler (NEAK), Pierluigi Russo (AIFA), Robert Sauermann (Dachverband der Sozialversicherungstraeger), Roisin Adams (St James), Sibylle Reichert (AIM), Simon Roels (INAMI-RIZIV), Sofie Gustafsson (TLV), Tomas Boran (SUKL), Ulrich Mohr (DSV), Vaclav Smekal (SUKL) EMA: Emer Cooke, Ana Hidalgo Simon, Emil Cochino, Gianmario Candore, Hans-Georg Eichler, Harald Enzmann, Iordanis Gravanis, Martina Schüßler-Lenz, Sabine Strauss, Michael Berntgen, Peter Arlett, Peter Mol, Spiros Vamvakas, Xavier Kurz European Commission: Dimitrios Florinis, Flora Giorgio, Sylvain Giraud, Orsi Nagy, Ioana Siska, Julia Schmitz EUnetHTA: Marcus Guardian, Niklas Hedberg, Beate Wieseler, Claudia Wild NCAPR meeting participants (topic 7): Ana Correia, Anne Hendrickx, Athos Tsinontides, Ayla Lokhorst, Beatriz Macedo, Cecilia Tollin, Diana Lauritzen, Diogo Pereira, Emilie Sam, Gergely Nemeth, Leos Fuksa, Lucie Kravackova, Margarida Oliviera, O Pitsilidou, Panagotis Petrou, Patricia Vella-Bonanno, Ruth Lopert, Sarah Mortenhuber, Simona Bedrac, Sofia Cortesao, Stefan Meli, Sylvana Magrin Sammut, Trine Behnk Independent expert: Anna Bucsics

Timing	Preliminary draft agenda	Name
10:00	Welcome by the EMA, AIM and MEDEV	EMA: Emer Cooke Payers: Jocelijn Stokx (AIM), Chris Dawson (ESIP), Timon Sibma (MEDEV)

Timing	Preliminary draft agenda	Name
10:10	Introduction and adoption of draft agenda	Co-Chairs
10:15	Synergies in evidence generation: Identifying commonalities in EMA and MEDEV strategies	EMA: Michael Berntgen MEDEV: Evert Jan van Lente
10:35	Commission initiative for enhanced cooperation between P&R authorities: Evidence generation to improve P&R decisions.	SANTE B4: Orsi Nagy
10:50	Cooperation on registries: a) Learnings from the EMA registry initiative b) Learnings of cases from regulators and from HTA/payers	Payers: Lonneke Timmers (ZIN) EMA: Emil Cochino, Xavier Kurz, Ana Hidalgo-Simon
11:30	Short break	
11:40	Defining evidence gaps to drive discussions on early evidence generation: learnings from EMA/MEDEV debriefings	Payers: Anna Bucsics EMA: Spiros Vamvakas
12:05	Better use of Real-World Data: a) Payer perspective on transparency on appropriate use and expectations regarding effectiveness vs data from clinical practice b) EMA analysis of the use of real-world data and the development of a Data Analytics and Real World. Interrogation Network (DARWIN)	Payers: Johan Pontén, Sofie Gustafsson EMA: Peter Arlett
12:35	RWE4Decisions project: how to take more informed reimbursement decisions with RWE?	Payers: Marc Van de Casteele (RZIV, INAMI)
12:50	Outlook and concluding remarks	EMA: Hans-Georg Eichler Payers: Evert Jan van Lente

This was the third meeting between the European Medicines Agency (EMA) and European healthcare payer umbrella organisations, namely representatives from the Medicine Evaluation Committee (MEDEV), the Association Internationale de la Mutualité (AIM) and the European Social Insurance Platform (ESIP). The objective was to continue the exchange on topics of mutual interest with a view to explore synergies and foster mutual understanding and cooperation to help improve timely and affordable access of patients to new medicinal products. The thematic focus at this meeting was on evidence generation along the product life-cycle.

In her welcome address, EMA's Executive Director Emer Cooke noted that optimising the path from development, evaluation through to access to medicines is what drives EMA and healthcare payers to collaborate. It is widely recognised that prospective planning of evidence, engagement in methodologies as well as mutual understanding of decision making are paramount. The more it is ensured that clinical evidence is designed to substantiate the clinical benefit, or its clinical value, the better decision makers deliver in the interest of the patient. Regulators and healthcare payers should identify concrete areas for engagement and demonstrate the value of cooperation. EMA's Regulatory Science Strategy to 2025, the European Medicines Agencies Network Strategy to 2025 as well as European Commission's Pharma Strategy all highlight the aim to bridge from evaluation to access through collaboration. These considerations were echoed by the leads of the three healthcare payer

umbrella organisations, Jocelijn Stokx (chair of AIM's Pharmaceutical Working Group), Chris Dawson (director of ESIP) and Timon Sibma (co-chair of MEDEV), in their introductory remarks.

Synergies in evidence generation: Identifying commonalities in EMA and MEDEV strategies

EMA's Regulatory Science Strategy to 2025 highlights the aim to bridge from evaluation to access through collaboration with payers. Recognising that the introduction of innovative medicines into healthcare systems requires multiple decision making and that sometimes, difficulties in obtaining reimbursement for newly authorised medicines can lead to delayed, restricted or no access for patients, there is a need for engagement between regulators and payers. To facilitate the transition from evaluation to access, several actions to enhance collaboration with payers are proposed, such as enabling involvement of payers' requirements in the prospective discussion of evidence generation plans, including post-licensing evidence generation, and establishing more structured interaction between EMA and payers to support information flow, whilst respecting remits. The goal to "Optimise the path from development, evaluation through to access for beneficial medicines (innovative and follow-on) through collaboration between medicines regulators and other decision makers" features equally in the European Medicines Agencies Network Strategy to 2025.

The MEDEV Reflection paper on national strategies for new medicines coming to the market was stimulated by the fact that new technologies pose new challenges for payers, expanding their current role. The two challenges for payers regarding new technologies are uncertainty on the effectiveness and safety at the time of marketing authorisation, as well as pricing. Recognising the different remits of payers and regulators, discussing these challenges should include the topic of high unmet medical needs (lack of adequate treatment options, disease severity, rarity) in order to justify exceptional measures, horizon scanning of technologies with potential major therapeutic impact, discussing pre- and post-marketing evidence generation, taking into account evidence needs of payers and HTA, and cooperation on registries and post evidence generation.

The complementary perspectives in these different strategy documents were the principal guide for the discussion at this meeting.

Commission initiative for enhanced cooperation between P&R authorities: Evidence generation to improve P&R decisions

The European Commission presented on the topic of affordability in the Pharmaceutical Strategy for Europe. In this context the cooperation in a group of national competent authorities for pricing and reimbursement (NCAPR) is fostered, to facilitate mutual learning and best-practice exchange on pricing, payment and procurement policies. Since December 2020 SANTE B4 had organised three meetings also involving public healthcare payers (NCAPR+) with a focus on implementing actions on affordability under the Pharmaceutical Strategy. Topic areas are evidence for action, exchange on pricing, payment and procurement policies, and market entry and competition. It was recognised by the group that EMA has valuable information to feed into pricing and reimbursement decisions. However, in its current format this information is available but not always easily accessible, such as specific information on extensions of licences (indications) or conditional marketing authorisation (MA), as well as Real World Data (RWD) and Real World Evidence (RWE). The group therefore aims to collaborate on relevant topics of mutual interest.

Cooperation on registries

EMA reported on preliminary results of a study on use of RWE in marketing authorisation applications. The objective was to characterise RWD/RWE submitted in marketing authorisation applications and line extensions for new indications in 2018-2019 and its contribution to benefit-risk decision-making. It was found that 41.1% of all marketing authorisation applications in the observation period had RWE data as part of the evidence discussions, of which around two thirds were collected only post-authorisation. Looking specifically at registries as data sources, the majority were disease registries which is a positive development. They are mostly cohort studies to generate post-authorisation safety and sometimes also efficacy data.

Turning to the learnings from the EMA registry initiative, a feasibility analysis on the guideline on registry-based studies was initiated. The aim was to answer the questions regarding the feasibility of the use the infrastructure of the registry for a specific registry-based study, and whether a traditional non-intervention study would be a better choice, e.g. a prospective cohort study. Comments received during the consultation provided generally strong support but also noted that registry holders may not collaborate before a contract with the marketing authorisation applicant or holder (MAA/MAH) is in place. It was also pointed out that it may be burdensome for small registries to engage early with regulators and that patient registries are not designed for recording and reporting of adverse events and serious adverse reactions recording in real time, except for new registries with appropriate processes in place. It was considered important to note that the feedback also highlighted the need to involve HTA bodies and payers in early discussions.

An HTA/payer perspective on registries to evaluate drugs reviewed experience from initial and follow-up HTA, quality of care review as well as appropriate use studies. It was felt crucial to have registries embedded into a learning cycle. From the Dutch experience, bottlenecks in the use of registries were due to the need to address different aspects (purpose; completeness; data sharing; funding). Four case studies in colorectal cancer, haemophilia, an ultra-rare orphan drug and multiple myeloma were reviewed. The need for independence of the registry and leadership by academia / clinicians was stressed. On this basis, it was noted that in the context of disease registries, cooperation between EMA and payers / NCAPR concerning post-licensing evidence generation (PLEG) should be initiated (early dialogue; support independent registries; sharing data). These reflections were emphasized through a review of the implementation of EMA requirements in post authorisation studies for (advanced therapy medicinal products (ATMPs) using the EBMT-registry (European Society for Blood and Marrow Transplantation).

The discussion centred around the quality of registry data, the timing of when RWE can be generated, the mechanisms to identify relevant registries early, experience with coverage for maintenance of registries, as well as ownership of the data. It was generally recognised that this will be a key area for future engagement.

Actions:

- Collaborative efforts involving both regulators and payers with a particular focus on ATMPs
- EMA and healthcare payers in the context of the NCAPR workshops to identify mechanisms for engagement on registries

Defining evidence gaps to drive discussions on early evidence generation: learnings from EMA/MEDEV debriefings

MEDEV performs a horizon scanning of upcoming approvals, with an outlook of a few months for new products that come onto the market based on, among other sources, the EMA and FDA websites and

scientific literature. Topics that are covered in these briefings include CHMP highlights (EMA's Committee for Medicinal Products for Human Use), re-assessment of orphans after positive CHMP opinion and new medicines under evaluation (both non-orphans and orphans). Topics that are usually not covered are highlights of other committees (e.g., Pharmacovigilance Risk Assessment Committee (PRAC), Committee for Advanced Therapies (CAT), Paediatric Committee (PDCO, products for which eligibility to PRIME (PRIority MEdicine) was denied, orphan designation and new generics and biosimilars under evaluation. The purpose is to give MEDEV participants a heads up and an opportunity to discuss important new products and developments.

EMA contributes to the briefings with information on new medicines recommended for approval (applicant, type of MA, orphan status, presentation, and indication as per CHMP opinion). The information provided by EMA is deemed very useful by MEDEV members. The CHMP highlights are rapidly published, and the publication of negative opinions, withdrawals and medicines under evaluation provides a quick and useful overview. EMA also harmonizes the product information for generics and continues to improve European public assessment reports (EPARs) and EMA's website. These all provide valuable input for the debriefings during the MEDEV meeting.

There are however also limitations and constraints on these briefings. There's sometimes a lack of information when the EPAR has not been published yet, like the rationale for accepting comparators in clinical trials, for extrapolation of indications and acceptance of single-arm trials. Furthermore, when the EPAR is published, information gaps may still exist or further clarification is needed (e.g. about trial data reported in the summary of products characteristics (SmPC), EPAR or published trials rationale for 'significant benefit' in the orphan designation review).

Proposals to further improve this area include: to coordinate dates and times to ensure EMA's participation, to include EUDRA CT (European Union Drug Regulating Authorities Clinical Trials Database) and/or the (NCT identifier in the EPARs ensuring that citations of scientific literature referred to in the EPAR are always complete (this is already increasingly the case), to provide more insight into development support as well as driving payer input into scientific advice via PRIME (e.g. through MoCA, Mechanism of Coordinated Access to orphan medicinal products) and via the MEDEV liaison at EMA.

Actions:

- The MEDEV briefings with EMA participation will continue.
- A framework for payer input to evidence generation prior to marketing authorisation to be developed.
- Relevant leanings should be cascaded through the lead contacts, in order to allow optimisation of regulatory documents for down-stream decision making.

Better use of Real-World Data

Payers and EMA presented and discussed their experiences and perspectives on evidence generation and the challenges of using registries and routine data as sources of real-world data for evidence-based decision-making post-market authorisation at EU and national level.

In Sweden, TLV is working on a national project to develop the use of RWD. There is a great variety of national health data and connecting these is the focus of this project. The main focus is not disease specific registries, but instead the national health registries held at the National Board of Health and Welfare. Sweden is using one unique social security number for this, making connecting this data easier.

Looking to the future and in line with plans for a European Health Data Space (EHDS), EMA presented its new EU-level initiative for a Data Analytics and Real World Interrogation Network (DARWIN) that should play an important role in the future in the use of real-world data both for regulatory and payer decisions by setting up an European RWE network. Once the initiative starts an advisory board will be installed, in which a seat for the payer community will be available.

During the discussion, it became clear that having one unique number for EU citizens is a great advantage for connecting data, creating great opportunities. Privacy in general and the General Data Protection Regulation (GDPR) in particular, however, must be rigorously observed.

Participants from the NCAPR meeting under the Portuguese presidency, which was held in parallel, joined this particular topic at the EMA - Payer community meeting. The focus of the NCAPR meeting was affordability of health care under the pharmaceutical strategy, in which one of the aspects was the impact of RWE on price negotiations, making the review on "Better use of Real-world data" relevant for their discussions.

Action:

- EMA to formally invite a representative of healthcare payers to take a seat in the DARWIN Advisory Board

RWE4 Decisions project: how to take more informed reimbursement decisions with RWE?

The RWE4 Decisions project was introduced. The project focuses on how more informed reimbursement decisions can be made with the use of RWE. The project started in 2016 under the name TRUST4RD. In subsequent papers, real-world evidence was described as supportive to payers' decision on highly innovative medicines. Interviews with stakeholder expressing their expectations led to the concept of a learning network in order to promote collaboration before and after reimbursement decisions. This learning network is therefore multi-stakeholder. The RWE workshop of September 10th 2020 was discussed and lessons learnt. The plea for a creation of a multistakeholder EU learning network should be designed for Member States to implement evidence-based decision-making and be supported by EU funding. Robust methodologies in alignment with other initiatives are needed.

Action:

- A number of workshops will be held in the next months to which different stakeholders are invited.

Outlook and concluding remarks

Evert Jan van Lente thanked both MEDEV members and EMA for their active participation in increasing the collaboration between payers and EMA and encouraged stakeholders to take that collaboration to the next level. Hans-Georg Eichler's take away message was that both payers and regulators should embrace the wealth of evidence in order to deal with new technologies and uncertainties, focusing on insights and the organisation of data.