EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

Health systems, medical products and innovation
Medicines: policy, authorisation and monitoring

STAMP 9/42
Summary record

STAMP Commission Expert Group
8 June 2018
9th meeting

Summary Record

The Commission Expert Group on Safe and Timely Access to Medicines for Patients (STAMP) held its 9th meeting on 8 June 2018, in Brussels, chaired by Unit B5 - *Medicines: policy, authorisation and monitoring* of Directorate-General Health and Food Safety. Representatives from 21 Member States and the European Medicines Agency (EMA) participated in the meeting. Invited representatives of organisations or associations were present for selected agenda items (see attached list).

1. ADOPTION OF THE AGENDA

The draft agenda (STAMP 9/39 rev 1) was adopted without changes[1].

2. APPROVAL OF PREVIOUS MINUTES

The record of the 8th STAMP meeting (STAMP 8/38 corr) was approved with some editorial changes:

https://ec.europa.eu/health/sites/health/files/files/committee/stamp/stamp_8_final_record_en.pdf

[1] The agenda and copies of the presentations are available on the STAMP webpage: https://ec.europa.eu/health/documents/pharmaceutical-committee/stamp_en

3. REPURPOSING OF ESTABLISHED MEDICINES/ACTIVE SUBSTANCES

During the 8th meeting of STAMP it was agreed that the industry representatives would prepare a document on how industry can engage in repurposing activities and what a repurposing framework might look like. Representatives of European Federation of Pharmaceutical Industries and Associations (EFPIA) and Medicines for Europe collaborated and presented a repurposing framework proposal to the group.

The key elements of the outlined proposal for a framework for repurposing were that a 'champion' would put forward a repurposing proposal for regulatory assessment. There would be a regulatory assessment to evaluate whether the proposal is supported by the available evidence. In case of a positive assessment, this would be made public in a 'repurposing data pool'. There would be the possibility of a partnership between a 'champion' and marketing authorisation holders or other interested parties to pursue a repurposing opportunity and the introduction of a new indication for a medicinal product through the existing procedures.

The industry engagement with the process and the presentation of the proposal was welcomed by members of the group.

Regarding the overall scope and context of the proposed framework some participants considered that the focus should be on products where there is clinical experience of the use of the product for new indications through use outside the authorised indication. The information could potentially be included in the product information, in the indication itself or in the section of the summary of product characteristics concerning pharmacodynamics properties. One participant considered that information on lack of effectiveness should be included in the product information.

Some participants considered that "repackaged medicines", ones that had been withdrawn from the market and later reintroduced with a new indication, should be included in the scope. In reply it was explained that this scenario would be outside the framework. The framework would mainly cover active substances where there is more than one marketing authorisation holder (multi-source) with evidence generated by a third party and where the marketing authorisation holders have not taken action to update their product information. The proposed framework was intended for instances where there were no incentives.

The issue of the agreement between different parties regarding intellectual property rights in relation to the new data was mentioned as being a possible barrier to reaching agreement on the use of evidence generated by a third party. On the other hand, the publication of the data could restrict the possibility to seek intellectual property protection.

It was mentioned that the previous experience of a marketing authorisation holder in the therapeutic area of the new indication could affect their openness to include it in the product information.

With respect to the specific details of the scheme, it was clarified that the 'champion' would be a party other than a marketing authorisation holder and the framework was not intended for cases where the marketing authorisation holder should update the product

information. Many participants considered that the interaction between the champion and the marketing authorisation holder(s) should be at an early stage of the process. The industry representatives explained that early engagement was not excluded, but it would be important to have a means to identify the most promising data as there would otherwise be a risk of overload for requests to investigate potential new indications. To avoid potential overload of the system it was suggested that criteria for inclusion in the framework should be identified, such as fulfilling an unmet medical need and where the marketing authorisation holder is not already involved. One participant suggested that the health technology assessment bodies could also provide insight into therapies with treatment gaps.

It was stressed that the proposal for a repurposing framework would operate within the existing legal framework and regulatory tools. The evidence needed to demonstrate a positive benefit/risk balance assessment would be to the usual requirements.

The stage of evaluation by the regulators was commented on by several participants. It was considered that this should not be a detailed benefit/risk assessment. It was suggested that potentially a type of scientific advice, possibly focussed on the robustness of the data or advice on additional data collection strategies, could be the basis of the suggested regulatory evaluation. If the data is considered to provide a suitable basis for a variation to the authorised medicine(s) a benefit/risk assessment could be completed through a normal procedure following submission of a request for assessment to the regulatory authority by a marketing authorisation holder.

Some participants raised concerns about whether the information available in a ‘data pool’ could encourage the use of medicines outside the authorised indication (off-label use) and could be a disincentive to the updating of the product information. Regarding off-label use, some participants mentioned that when determining the appropriate treatment the treating physician would take the medical needs of the individual patient and the available options into account. With respect to lack of incentives, there was a suggestion that prescription by indication could limit the sale of the medicine to those which include the indication. Although this suggestion was not supported by some other participants.

The documents circulated on the proposal for a repurposing framework mentioned some possible incentives. The industry representative explained that the incentives mentioned were focused on ones that could be applicable to the champions rather than the marketing authorisation holder. They had not covered economic incentives in the background documents. Their vision of the framework would be to prioritise the regulatory evaluation to the most relevant therapeutic indications, reducing the burden and reducing the impact of disincentives.

Some points regarding liability were made during the discussion. Firstly, the question of liability of a physician who prescribes a medicine when there is not sufficient evidence to support its use in the indication was raised. In reply another participant noted that this might already be the case where products assessed by another jurisdiction are used on a case-by-case basis. In addition, it was noted that scientific advice is non-binding and the regulatory authority is not considered liable for the advice it provides.

The need for academia to be aware of the regulatory framework for the authorisation of medicines and for them to be informed of the opportunities to link with the marketing authorisation holder was mentioned. The group was informed that the submissions for

the Horizon 2020 coordination and support action (CSA) funding were being assessed. It was suggested that the successful consortium should be invited to present the project to the STAMP.

It was suggested that the Heads of Medicines Agencies (HMA) should be informed about the development of the repurposing framework. It was also highlighted to the group that the EU-Innovation Network could be a useful point of contact. It was noted that the HMA was regularly updated on the discussion in STAMP. It was agreed that information on the detail of the proposed framework could be shared with these groups at a later stage.

The group agreed that the proposal for the framework was an interesting start and that it should be further developed to include more details. To facilitate the process of elaborating the proposal for a framework, it was agreed that the drafting group should be extended to representatives from Member States and other organisations. The following points were mentioned for the consideration of the drafting group:

- Inclusion of additional steps and provide additional information about the envisaged processes;
- Identify possible criteria to prioritise the medicines that could be potentially considered within the proposed framework;
- Explain the 'data pool' concept and how it would operate.

The Chair thanked the industry representatives for their presentation and engagement. The meeting participants were asked to send comments on the proposal by 30 June 2018. Representatives of the Member States, EMA and other organisation were invited to contribute to the drafting group that would update the proposed framework and report back to the next STAMP meeting.

4. ACTIVITIES RELATED TO REAL WORLD DATA

A Commission representative introduced the topic of real world data, highlighting that the Commission *Communication on enabling the digital transformation of health and care in the Digital Single Market; empowering citizens and building a healthier society* of April 2018 on digital health and care[2] identifies three pillars for action: health data (e.g. electronic health records); connect and share data for research; and, empowerment of patients and patient centred care. The scope of the second pillar 'connect and share data for research' covers use of real world data in clinical research, for regulatory purposes and to support decision makers on effective market access. The intention would be to build pilots on the ongoing initiatives.

A EMA representative initially presented the activities of the HMA and EMA activities on big data. In addition, the EMA activity on real world data, in particular regarding regulatory access and common data models, were presented. The second part of the

[2] See: https://ec.europa.eu/digital-single-market/en/european-policy-ehealth For the Commission Communication see: https://ec.europa.eu/digital-single-market/en/news/communication-enabling-digital-transformation-health-and-care-digital-single-market-empowering and the accompanying staff working document: https://ec.europa.eu/digital-single-market/en/news/staff-working-document-enabling-digital-transformation-health-and-care-digital-single-market

presentation concerned the HMA-EMA Joint big data taskforce activities and their interim results. The taskforce is expected to report by the end of 2018.

The projects in the Innovative Medicines Initiative (IMI) and other Commission funded research activities related to real world data were presented by representatives of the IMI and the Research and Technology Directorate General. There has been an increasing focus on use of real world data in research. Some specific projects, their objectives and outputs were presented.

Patient registries provide real world data on specific patient groups. The EMA gave a presentation on the lesson learned from patient registries imposed as part of the post-authorisation obligations related to a marketing authorisation. Also presented were: the EMA patient registries initiative; initiatives on parallel regulatory and health technology assessment engagement; and, EUnetHTA activities. Ideas on how regulators can support disease registries were outlined to the group.

The Commission sought feedback from the group on the outstanding data gaps and how to progress in the area of real world data and the inclusion of different actors.

The potential overlap in the collection of data in the post-authorisation setting and the definition of a clinical trial was mentioned by one participant. It was noted that real world data has been used throughout the lifecycle of a medicinal product and that data can also be used by different organisation - regulators, health technology assessment bodies, pricing and reimbursement bodies. It was suggested that the possibilities for sharing experience should be investigated.

It was suggested that the development of a sustainable platform for different players to access data would be important. It was explained that a future IMI project is moving away from registries as a way to collect data and part of the project was intended to identify the needs of the regulators.

It was noted that there were various activities which could be used as a basis for EU level pilots. It was suggested that a stakeholder meeting could facilitate the creation of a platform for the different bodies to access different data sources (electronic health records, registries). The evaluation of the evidence gaps and identification of core elements could be an important aspect and also to avoid duplication of efforts. The current situation is that there is not a standard set of core elements collected in different registries and there can be additional information on certain information relevant to benefit/risk evaluation of the medicine.

The Commission summarised that there are well identified needs for regulatory purposes and the outcome of the HMA-EMA taskforce is awaited. There is a need to explore the synergies between regulators and other bodes along the medicinal product lifecycle. With respect to sustainability of research, output is important and it should be possible for these to be used by others such, as regulators, HTA bodies. There is a need to avoid duplication of efforts and pilots could help to identify the gaps in evidence, they can be used to gain insight for other registries or means of data collection.

5. STUDY REPORT ON THE IMPACT OF PHARMACEUTICAL INCENTIVES ON INNOVATION, AVAILABILITY AND ACCESSIBILITY OF MEDICINAL PRODUCTS

The study on "*the impact of pharmaceutical incentives on innovation, availability and accessibility of medicinal products*" had been completed by an external contractor. The study report was published on 28 May 2018, the conclusions and recommendations are those of the author.

The main findings of the study were presented by Commission representatives. The background of the study was the EU single market strategy, in particular with respect to the intellectual property and protection rights. In addition, in the 2016 Council conclusions invited the Commission to prepare an overview of the pharmaceutical incentives. The results of the study will be considered in the analysis requested by the Member States in 2016 and the ongoing evaluation of the Orphan and Paediatrics Regulations.

Some Members noted that the longer the protection period was there were more innovations but considered there is still a need to see how such innovation can be accessible to patients across the EU, including consideration of the impact of incentives on pricing and access to the medicines.

6. UPDATE ON OTHER EU INITIATIVES RELEVANT FOR TIMELY PATIENT ACCESS TO INNOVATIVE MEDICINES

a. *Ad hoc* Synergy Group

An update on the work in the *ad hoc* Synergy Group was given by a representative of the Italian Medicines Agency (AIFA) on behalf of the Chair of the Synergy Group. A preliminary analysis of the mapping exercise was presented. The mapping mainly concerned the activities of the regulators and health technology assessment (HTA) bodies in the pre-authorisation/pre-marketing phase (e.g. early dialogue/scientific advice, definitions, horizon scanning, research), at the time of authorisation/market entry (e.g. information exchange, regulatory assessment reports), and the post-authorisation/post-marketing phase (e.g. studies, late dialogues, real world data). The next step is to prepare a report on the exercise. It was suggested by one participant that the report should also include ideas on how to continue and develop collaboration between the regulatory and HTA bodies.

ACTION POINTS AND POINTS TO CONSIDER FOR THE NEXT MEETINGS:

- Comments on the proposal for a repurposing framework to be sent by 30 June 2018.
- Creation of a drafting group to update the proposed repurposing framework and report back to the next STAMP meeting. Representatives of the Member States, EMA and other organisation were invited to join the group.

The next meeting of the STAMP Expert Group is planned for **3 December 2018.**

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8 JUNE 2018 STAMP EXPERT GROUP - EXTERNAL PARTICIPANTS

Name	Affiliation	Agenda items
Lydie Meheus	Anticancer Fund	3
Ciska Verbaanderd	Anticancer Fund	3
Jillian Harrison	Belgian Healthcare Knowledge Centre (KCE)	3
Jelena Malinina	The European Consumer Organisation BEUC	3
Kaisa Immonen-Charalambous	European Patients' Forum (EFP)	3
Victoria Kitcatt	European Federation of Pharmaceutical Industries and Associations (EFPIA)	3
Sheuli Porkess	European Federation of Pharmaceutical Industries and Associations (EFPIA)	3
Christine Dawson	European Social Insurance Platform (ESIP)	3
Olga Kozhaeva	European Society for Paediatric Oncology (SIOPE)	3
Delphine Roulland	European Confederation of Pharmaceutical Entrepreneurs (EUCOPE)	3
François Houÿez	EURODIS - Plateforme Maladies Rares	3
Menno Aarnout	International Association of Mutual Benefit Societies (AIM)	3
Caroline Kleinjan	Medicines for Europe (MfE)	3
Catarina Lopes Pereira	Medicines for Europe (MfE)	3
Passarani Ilaria	Pharmaceutical Group of the European Union (PGEU)	3

Carole Rouaud	Standing Committee of European Doctors (CPME)	3
Nathalie Seigneuret	Innovative Medicines Initiative	4