EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

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

STAMP 7/35
Summary record

STAMP Commission Expert Group
27 June 2017
7th meeting

Summary Record

The Commission Expert Group on Safe and Timely Access to Medicines for Patients (STAMP) held its 7th meeting on 27 June 2017, in Brussels, chaired by Unit B5 - *Medicines: policy, authorisation and monitoring* of Directorate General Health and Food Safety. Representatives from 18 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 7/32) was adopted without changes.

2. APPROVAL OF PREVIOUS MINUTES

The record of the 6th STAMP meeting (STAMP 6/31) was approved without changes:

http://ec.europa.eu/health/files/committee/stamp/stamp_stamp_record_draft_published_en.pdf

The group was informed that the "Report on activity of the Expert Group on Safe and Timely Access to Medicine for Patients (STAMP) 2015 – 2016" would be made available on the Health and Food Safety Directorate General web pages[1].

3. REPURPOSING OF ESTABLISHED MEDICINES/ACTIVE SUBSTANCES

The issue of repurposing of established medicines had been discussed in previous meetings. A background document (STAMP 7/ 33) had been circulated prior to the meeting. The list of questions included in the background paper provided the basis for the further consideration of the inclusion of new indications in the product information of existing medicines. Invited representatives of the Anticancer Fund, EFPIA[2] and Medicines for Europe joined the STAMP for the agenda item. There was a broad discussion of the issues and experiences were highlighted by some of the meeting participants.

Regarding the **research and evidence**, the question of the research that is needed to provide the evidence to support the inclusion of a new indication in the labelling information of a product was mentioned. Academic or not-for-profit organisation might have evidence on the use of a medicinal product in a therapeutic indication outside the labelled indications but often do not know application procedures for the authorisation of medicinal products. The collected evidence needs to be suitable to support the inclusion of a new indication in product information. Scientific advice provides a means for the researchers to have guidance on whether the planned research would potentially give suitable evidence. The cost associated with such advice might be outside the usual resources available to academic or not-for-profit organisations although fee reduction or waivers might be considered by some authorities. It was also noted that the procedures associated with EU funded projects means that the research design is included in the project proposal which, once agreed in an accepted proposal, can be difficult to change. This means that researchers need to identify at an early stage suitable study design/protocol. It was suggested that a regulatory pathway including scientific advice might be a mechanism to support the inclusion of new indications. One member mentioned their experience of the collection of evidence through government sponsored trials in cooperation with the pharmaceutical industry. The issue of the responsibility for the evidence was mentioned, noting that studies conducted by the marketing authorisation holder is under their own control, whilst evidence collected by third parties may be more difficult for them to use.

Potential sources of evidence mentioned by participants included registries and compassionate use programmes. It was noted that it can be difficult for an applicant to know whether the available evidence is sufficient or whether there is a need for clinical trials. Scientific advice could give guidance in certain cases. The question of knowledge sharing was also raised, in particular regarding non-clinical data which can help product development but is often held by the originator company and not made more widely available. It was mentioned that when an original product is withdrawn from the market it can be difficult to find the original data.

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1 https://ec.europa.eu/health/sites/health/files/files/committee/78meeting/pharm728_2ii_stamp_activity_report_final.pdf

2 European Federation of Pharmaceutical Industries and Associations

Regarding the **assessment of the evidence**, as in previous discussions, it was stressed that the standard/level of evidence to support the new indication should be the same as that usually applied in the assessment of the evidence for the authorisation of medicines or new indications.

The system of **authorisation**, is linked to a specific medicinal product and marketing authorisation holder. The academic and not-for-profit organisations do not usually go into the process of manufacturing a medicinal product which means the evidence they collect would generally need to be taken up by a marketing authorisation holder. If the new indication was imposed then there is the question of responsibility for the underlying evidence and the continued monitoring of the evidence concerning the indication. It was noted that the legislation requires that the pharmacovigilance related activities of the marketing authorisation holders includes the obligation to record adverse events that occur with off-label use of the medicinal product.

Ideas on alternative processes to support the introduction of new indications included the assessment of the indication linked to an active substance and not a marketing authorisation for a specific product. Reports by a regulatory authority or non-binding recommendations were also mentioned. It was highlighted that the European Public Assessment Report (EPAR) is product specific and reflects data assessed in the context of a specific regulatory procedure and is not related to an active substance.

The importance to engage marketing authorisation holders was stressed by representatives of the industry. If the introduction of a new indication is supported by a good business case then the extension of indication could be considered. However, the dynamics of the market can make it difficult to assess the balance of a business case. There are cases of withdrawal of the marketing authorisation for an active substance which later has a submission for a new authorisation in a different indication with a more limited patient group.

To **analyse examples of previous experience** in detail it was agreed that a small group coordinated by the UK with volunteers from the Member States, EMA, industry and the not-for-profit organisations represented in the meeting should examine relevant case studies and report back to a future meeting of the STAMP.

There was discussion on certain other issues identified in the background document. Specifically regarding **scientific advice**, EMA explained that the structures were in place to provide scientific advice to academic or not-for-profit organisations but the fees can be an issue. If the fees for scientific advice are foreseen in the submissions for the Horizon 2020 projects then there would be the possibility for the cost to be covered in the project costs. One member mentioned that multiple requests for scientific advice should be avoided. The potential Coordination Support Action (CSA) funded by DG Research & Innovation (RTD) could give a comprehensive overview of the situation in the Member States on this issue.

The need to raise awareness through **education and training** of researchers of the regulatory procedures for the authorisation of new indications for medicines had been raised in the previous meeting. It was suggested that a handbook giving details of the steps that need to be considered could be developed, although another participant considered that the process of learning by doing is also important. There is an EMA user guide for small and medium sized enterprises (SMEs)[3] and there is a web page on research and development[4] which are

[3] http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/10/WC500004134.pdf

maintained updated with regard to available guidance and opportunities for interaction in the development phase of a medicinal product. One member mentioned that they are active in promotion of information about the regulatory framework for the authorisation of medicines to young researchers through their participation in the Horizon 2020 RTD funded PEARRL project[5].

It was **concluded** that the small group led by the UK would analyse examples of repurposing of existing medicines and report back to the next STAMP meeting.

4. UNITED STATES 21ST CENTURY CURES ACT

Mr Matthew Scherer of the United States Food and Drug Administration (FDA) gave a presentation on the U.S. 21st Century Cures Act which was adopted in 2016. He highlighted the titles of the Act which were most relevant to the FDA activities. The potential areas include: patient experience; clinical trials; advance drug therapies; trial design and evidence development (including real world evidence); patient access to therapies; expanded access policy. STAMP members appreciated the overview of the areas for future developments in the U.S. and there was particular interest in the developments on expanded access, trial design, real world evidence, repurposing of medicines and incentives.

The Chair thanked Mr Scherer for the interesting presentation noting that the future developments could be of interest to the group.

5. COMPASSIONATE USE

a. Eurordis position paper on compassionate use programmes

François Houÿez representing Eurordis presented the position paper and main recommendations of Eurordis on compassionate use programmes[6]. The presentation highlighted that there are differences between the Member States regarding access to medicines by patients prior to authorisation through compassionate use schemes and summarised the recommendation of Eurordis regarding how to make the system more equitable for patients across the EU.

During the discussion the question of balance was mentioned with regard to: whether there should be a charge or not for the medicines provided through compassionate use programmes (CUP); whether there needed to be an application for authorisation of the medicine submitted for assessment in the EU or whether products authorised in third countries could be considered; the need to avoid the use of CUP or other early access schemes as a means to by-pass normal authorisation procedures.

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4 http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_001768.jsp&mid=WC0b01ac0580b18a3a

5 Pharmaceutical Education And Research with Regulatory Links: Innovative drug development strategies and regulatory tools tailored to facilitate earlier access to medicines (www.pearrl.eu)

6 http://www.eurordis.org/publication/early-access-medicines-europe-compassionate-use-become-reality

The early access schemes in the Member States can include named patient and cohort schemes. In general CUP are based on presumption of efficacy of the new medicinal products and are usually considered following a request from the company developing the product. The position of Eurordis is that the scope of the schemes should be driven by the patients and regulators. The availability of information on new developments in the public domain can result in patients calling for CUP. One member asked if the possibility for compassionate use was being considered for products eligible for the PRIME (PRIority MEdicines) scheme. The Eurordis representative considered that it could be a good platform for such discussion. EMA indicated that this is not a specific part of the process.

One member outlined their procedures for CUP in which advice on the scheme is provided. When the advice is favourable regarding the product, the advice can be used as a basis for the company to provide the medicinal product to patient group(s) determined by the company itself.

Regarding the charging for medicines within CUP, this depends on the Member State, there are schemes that are free-of-charge, with a charge or a charge when the level of prescription of the product reaches a certain level or payback schemes.

b. Heads of Medicines Agencies activities on compassionate use programmes

The Belgium Federal Agency for Medicines and Health Products presented an overview of the activities of the Heads of Medicines Agencies (HMA) in the area of timely access to medicines, in particular action concerning compassionate use programmes. In 2016 an overview of the CUP and other early access schemes in Member States had been made available on the HMA website[7]. It is planned to update the overview document. It was suggested that the update should differente schemes into those related to cohorts of patients or those that operate on a named patient basis and the terminology used should be investigated.

It was **agreed** that the HMA timely access subgroup should follow up on the issue of CUP and report back to a future STAMP meeting.

c. Compassionate use programmes – discussion

A background document (STAMP 7/34) had been circulated. Some members noted that the CUP were the responsibility of the regulatory authorities but considered that there is a need to work with the bodies responsible for pricing and reimbursement. One member explained that their named patient schemes were usually applicable when there was no therapeutic alternative and no possibility to enter a clinical trial whilst their compassionate use cohort schemes were often used when the clinical trial recruitment had been completed. Another member stressed that clinical trials were be best way to investigate new products. Patients are aware of the new developments so the regulators often need to be able to respond to requests from patients to have access to medicines before authorisation.

[7] http://www.hma.eu/fileadmin/dateien/HMA_joint/02-_HMA_Strategy_Annual_Reports/08_HMA_Publications/2016_05_HMA_H_website_Compassionate_use_program_statement_Rev07_2017.pdf

EMA highlighted that it would be useful to understand the experience of Member States regarding the Committee for Medicinal Products for Human Use (CHMP) opinion foreseen under Article 83 of Regulation (EC) No 726/2004 so that it could be assessed whether there is a need to review the existing mechanisms.

The Chair summarised that it was not the intention to change the purpose of CUP and that the lead was with the national competent authorities. CUP should not be in competition with clinical trials. It was agreed that the HMA subgroup on timely access would collect information on the experience in the Member States and keep STAMP informed.

6. PRIME (PRIORITY MEDICINES) SCHEME – FIRST YEAR OF EXPERIENCE

The EMA gave a presentation on the first year experience of the PRIME scheme[8] and reported on the meeting marking the first year anniversary of the scheme which had been held on 19 May 2017[9].

Some members noted that there had not been any potential new antibiotics included in the scheme. EMA explained that, although this had been specifically mentioned at the launch of the scheme, the need to have compelling evidence and the very limited number of requests received for antibiotics meant that so far there had not been any products identified for the scheme. Furthermore, the feedback received during the first anniversary meeting of PRIME was that while the scheme can encourage applicants, it will not on its own incentivise development in a specific area.

Joint scientific advice with health technology assessment (HTA) bodies was seen as potentially important aspect of the scheme. Opportunities for further collaboration with HTA for PRIME products would be discussed in the EUnetHTA Joint Action[10] .

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

a. *Ad hoc* Synergy Group

The STAMP was informed that following the call for volunteers for the *ad hoc* Synergy Group of representatives of regulatory and HTA bodies, the representatives in the *ad hoc* group had been endorsed by the Pharmaceutical Committee and the HTA Network. On the regulators side the follow Member States had volunteered: the Czech Republic, Denmark, Greece, Spain and the EMA. The HTA bodies are represented by France, Germany, Italy, Portugal, the United Kingdom and EUnetHTA. There had been a face-to-face meeting on the 26 June 2017. The work of the group would be mainly coordinated by teleconferences. The first activity of the group is the mapping of the ongoing EU level activities identified in the HTA Network reflection paper.

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8 http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000660.jsp

9 http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/events/2017/03/event_detail_001407.jsp&mid=WC0b01ac058004d5c3

10 European Network on HTA (http://www.eunethta.eu/).

ACTION POINTS AND POINTS TO CONSIDER FOR THE NEXT MEETINGS:

- Group of Member States and external stakeholders led by the UK to analyse examples of repurposing of existing medicines and report back to a future STAMP meeting;

- HMA timely access subgroup to follow up on the issue of compassionate use programmes and report back to a future STAMP meeting.

The next meeting of the STAMP Expert Group is planned for **8 December 2017 (tbc).**

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27 JUNE 2017 STAMP EXPERT GROUP - EXTERNAL PARTICIPANTS

Name	Affiliation	Agenda items
Gauthier Bouche	Anticancer Fund	1-4
Elise Melon	EFPIA - European Federation of Pharmaceutical Industries and Associations	1-4
Beata Stepniewska	Medicines for Europe	1-4
Catarina Pereira	Medicines for Europe	1-4
Matthew Scherer	U.S. Food and Drug Administration	4
François Houÿez	EURORDIS – Rare Diseases Europe	5a (via teleconference)