



**STAMP Commission Expert Group**  
**3 December 2018**  
**10th meeting**

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Summary Record

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The Commission Expert Group on Safe and Timely Access to Medicines for Patients (STAMP) held its 10th meeting on 3 December 2018, in Brussels, chaired by Unit B5 - *Medicines: policy, authorisation and monitoring* of Directorate General Health and Food Safety. Representatives from 22 Member States and the European Medicines Agency (EMA) participated in the meeting. Invited representatives of organisations or associations were present for agenda items 3 - 5 (see attached list).

**1. ADOPTION OF THE AGENDA**

The draft agenda (STAMP 10/43) was adopted without changes<sup>1</sup>.

**2. APPROVAL OF PREVIOUS MINUTES**

The record of the 9th STAMP meeting (STAMP 9/42) was approved without changes.

[https://ec.europa.eu/health/sites/health/files/files/committee/stamp/stamp\\_9\\_final\\_record\\_en.pdf](https://ec.europa.eu/health/sites/health/files/files/committee/stamp/stamp_9_final_record_en.pdf)

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<sup>1</sup> The agenda and copies of the presentations are available on the STAMP webpage:  
[https://ec.europa.eu/health/documents/pharmaceutical-committee/stamp\\_en](https://ec.europa.eu/health/documents/pharmaceutical-committee/stamp_en)

### 3. REPURPOSING OF ESTABLISHED MEDICINES/ACTIVE SUBSTANCES

The Commission introduced the item referring to the document STAMP 10/44<sup>23</sup>, explaining that the issue of repurposing of established medicines had been discussed in previous meetings of the STAMP.

During the 9th meeting in June 2018 there had been a discussion on the proposal for a framework for repurposing existing medicines which had been developed through the collaboration of representative industry associations. Following discussion of the proposal the STAMP agreed that the proposal for the framework should be further developed through a working group.

The following Member States and stakeholder groups had volunteered to be part of the *ad hoc* working group: Belgium, the Netherlands, Norway, Spain, Sweden, the United Kingdom, EMA, Anticancer Fund, European Confederation of Pharmaceutical Entrepreneurs (EUCOPE), European Federation of Pharmaceutical Industries and Associations (EFPIA), European Organisation for Rare Diseases (EURORDIS), European Patients' Forum (EPF), European Society of Paediatric Oncology (SIOPE), International Association of Mutual Benefit Societies (AIM), Medicines for Europe (MfE). The working group was led by the UK and Spain and worked through exchange of emails and regular teleconferences.

The work had been split into two main areas: the proposal for a 'repurposing pathway' within the current regulatory framework (objective 1) led by SE, EMA and the UK and the topic of 'learnings and outstanding issues' to explore how the proposal for a framework would work in practice (objective 2) led by the Anticancer Fund. A third topic concerning possible supporting materials and communication had been discussed by the working group in a teleconference.

The UK introduced objective 1 by providing an overview of the interest in the issue of repurposing and explaining the scope of the proposed pathway/framework and what it would look like, namely the core components. It was also explained that the main purpose of the meeting was to define the possible pathway, discuss outstanding issues and to agree on the next steps.

It was emphasised that the pathway would use the existing regulatory framework and potential 'Champions' should be able to understand the regulatory process. A main goal would therefore be to provide support to academia and/or research organisations to help ensuring that the appropriate evidence meeting the regulatory requirements is collected. The overall aim would be to have new indications for existing medicinal products that are outside patent protection.

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<sup>2</sup> Numbering of documents corrected after meeting.

<sup>3</sup> Background papers and presentations are available on the STAMP webpage: [https://ec.europa.eu/health/documents/pharmaceutical-committee/stamp\\_en](https://ec.europa.eu/health/documents/pharmaceutical-committee/stamp_en)

The following seven ‘attributes’ mentioned in the background paper concerning objective 1 (STAMP 10/44 Annex page 3) were presented and discussed:

1. The proposed new indication should be in a condition distinct to the currently authorised indication(s) listed in section 4.1 of the relevant summary of product characteristics (SmPC) of a Member State (MS) or the European Union (EU)
2. There should be a valid marketing authorisation for the medicinal product containing the same active substance in the same formulation / dosage form, granted in a Member State or in the European Union
3. Repurposing should be encouraged in an area where significant public health benefits / Union interests are likely to be achieved
4. All authorised medicinal products containing the active substance should be out of basic patent / supplementary protection certificate (SPC) protection, and data and market exclusivity periods
5. The repurposing project represents a scenario that is not currently being fulfilled by a business organisation
6. There should be supporting evidence e.g. proof of concept from clinical data. It could include documentation from off label use, registry data, clinical trials or reported case studies
7. A Champion has been identified who is willing and able to take forward the roles and responsibilities required of the framework. A Champion can be a person/academic unit/learned society/research fund or payer with a particular interest in repurposing a compound/product for a new indication and who has data evidence/scientific rationale to do so.

For the first two attributes, the main discussion was about whether the proposed attributes would be too restrictive for a medicinal product to enter the proposed repurposing pathway/framework. The conclusion was that it should not be too strict, however, the right data would be required to support a possible repurposing. It was noted that when an active substance is presented in a different formulation (e.g. oral solution instead of tablet) there is a need for additional data, for example pharmacokinetics, which could add complexity to the process for the uptake by a business company. The wording of the document will be reviewed.

Concerning attribute 3 (a new indication for significant public health benefits), it was concluded that the pathway should be open to repurposing activities that would have important public health benefits.

As regards attribute 4 (the medicinal product should be out of patent / supplementary protection certificate protection), it was agreed that the word ‘all’ should be removed, it is sufficient that one product containing the active substance is out of basic data protection. It was mentioned that it could be difficult for Champions to know the intellectual protection situation for individual products.

As regards attribute 5, it was suggested that it should be deleted as it would not be fulfilled by a business organisation. On the other hand, it was considered that the attribute could be seen as competition. It was agreed to review the wording.

There was no discussion about attribute six (supportive evidence).

Attribute 7 defines the characteristics of the Champion. It was agreed that the text should be reviewed, suggested changes included: introductory text should be slightly altered ('a Champion is characterised by...') and to mention scientific as well as regulatory advice.

There were no comments regarding the sections "Proposed core components of a framework" and "Rate-limiting steps".

The proposal for a repurposing pathway outlined in the objective 1 document presented scientific advice as an entry point, this could happen at any stage of the development or clinical investigation. It was stressed that the Champion needs to understand the regulatory framework. The scientific advice is confidential to the applicant who requests the advice. However, after obtaining an advice, the Champion could consider to share the advice they had received under due diligence.

It was agreed that the document should refer to not only scientific advice but also to regulatory advice or guidance. The scientific or regulatory advice could be via the centralised (EMA) procedures or the mechanisms for such advice through national competent authorities (individual or multiple NCAs). In addition, in some cases there is the possibility for parallel scientific advice with health technology assessment bodies.

The participants discussed the incentives and disincentives for repurposing. The industry representatives explained their written comments regarding the outstanding issues. They mentioned that having the data reported and presented in a way which was ready to be included directly in an application for an assessment of a new indication would reduce this potential barrier or disincentive for marketing authorisation holders (MAH). In addition, they mentioned that consideration would be needed with respect to potential need of additional risk minimisation measures, or obligations for post marketing studies. The industry mentioned that possible obligations should be clear so that a MAH can understand what additional action might be required. Other participants questioned the ability of a Champion to present the data in accordance with the regulatory requirements.

Incentives which might apply in certain circumstances, such as one year data exclusivity, review of the price of the medicine and type of variation were mentioned. It was noted that pricing and reimbursement related issues are outside the proposal for a framework of repurposing.

It was noted that the concept of a regulatory data pool was no longer mentioned in the document. Some participants considered that if this concept could be developed it would be a means to simplify the update of product information for multi-source medicines.

Some identified outstanding aspects were: possibility of a repurposing checklist; role of different actors e.g. industry; basis of interaction with the Champion with the MAHs; understanding of what are the incentives for the Champions; how guidance can be provided; activities of other groups active in the field (e.g. EU Innovation Network, CSA STARS - Strengthening training of academia in regulatory sciences and supporting regulatory scientific advice).

The Anticancer Fund presented the outcome of the working group's consideration of the objective 2 topic of 'learnings and outstanding issues' (STAMP 10/44 Annex - Objective 2). The main goal of this objective was to consider the application of the

pathway to real life examples of products or indications that could follow the repurposing pathway.

Two cases were presented - one concerning a late entry into the pathway where phase III trials are already available. The other case has early data available already (phase I trials) and could follow an early entry into the pathway. Challenges for repurposing activities include - allowing for combination of repurposed medicines, gathering information on the existing marketing authorisation holders, preparing a dossier for scientific advice (need for guidance), reducing disincentives (e.g. cost of scientific advice) and uptake by a business company for the submission of the data package to apply for a new indication. Finally, possible candidate drugs for a pilot project were presented.

It was considered that early scientific advice could help with the development of research activities. Also running a pilot was seen as a good opportunity to test the concept of the repurposing pathway.

The main outcome of the discussion about objective 2 was that good ‘candidate’ compound(s) to test the proposed repurposing framework should be identified before the next STAMP meeting in March 2019. The development of additional guidance and a template could be considered in the light of experience of the pilot.

The Commission introduced objective 3 (STAMP 10/44 Annex - Objective 3). The Group noted that further development of guidance and raising awareness was expected to come through the experience of the pilot.

In conclusion, the working group was reconvened to continue developing the proposed pathway (objective 1), to identify the candidate compound(s) for the pilot to follow up objective 2, and consider further communication and supporting material. A representative of the project team from the CSA ‘STARS’ would be invited to join the working group.

#### **4. PRESENTATION BY INFECTIOUS DISEASES DATA OBSERVATORY, UK**

Ms. Laura Merson (University of Oxford) presented the work of the Infectious Diseases Data Observatory (IDDO – [iddo.org](http://iddo.org)). Professor Phillippe Guerin of IDDO also joined the meeting via a teleconference link.

IDDO aims at optimising treatment options for poverty related diseases by building data platforms. There are increasing demands to have the raw data made available but there are challenges to manage the shared data. The IDDO map the shared data from small trials into a standard format which allows further analysis. Building partnerships with regulators could help define priorities for data pooling and support the outcome of the further analysis of the evidence being included in relevant information sources.

During the discussion it was explained that the IDDO will share with other organisations, including the pharmaceutical industry, their planned analysis so that the methodology can be developed. After analysis the evidence collected is made available so that it can be considered by authorities and industry. It was noted that there are challenges on how to translate the evidence into recommendations for patients. The work that had been done encouraged data collection in a consistent or standardised way and helped to build networks at the level of the scientific communities.

The STAMP thanked the colleagues from IDDO for the interesting presentation and the further explanations about their work. It was considered to have potential relevance to repurposing of medicine if the evidence supported this.

## **5. EU COORDINATION AND SUPPORT ACTION – STARS: STRENGTHENING TRAINING OF ACADEMIA IN REGULATORY SCIENCES & SUPPORTING REGULATORY SCIENTIFIC ADVICE (CSA STARS)**

Ms. Stingl (German Federal Institute for Drugs and Medical Devices, coordinator for the CSA STARS) presented the ‘STARS’ project, a 3 year project under Horizon2020 with a budget of 2 million euros. Fifteen countries are partners in the project, but it is still open for others to join the project if they wished to.

The overall aims of the project are: to improve the direct regulatory impact of results obtained in medical research; to reach academic researchers very early in the planning of relevant grant applications; and to strengthen regulatory knowledge in general by reaching clinical scientists during professional training and qualification. It aims at improving regulatory decisions by filling the gaps in scientific needs for support of regulatory decisions. It also focuses on the improvement of the relations between academic groups, national funding bodies and regulators. There will be two European representative stakeholder workshops with a view to agree a consensus statement. At the end of the project there will be a stakeholder conference with global representatives.

During the discussion it was clarified that the project would survey 5-7 academic groups in the countries involved in the survey. The aim is to have the consensus statement as a complement to the existing curriculum.

The STAMP welcomed the presentation of the project which seemed to be relevant to the repurposing initiatives.

## **6. EU ACTIVITIES RELEVANT TO TIMELY PATIENT ACCESS TO INNOVATIVE MEDICINES**

### **a. Presentation “Significant Benefit” across provisions**

A representative of EMA gave a presentation on the experience of the EMA Committees on the application of the concept of “significant benefit” across the different provisions in the legislation, namely the additional year of marketing protection, orphan designation, derogation from orphan market exclusivity, paediatric investigation plan waiver, new active substance status, conditional marketing authorisation and accelerated assessment.

The Chair explained that EMA had been invited to present their experience of above mentioned provisions referring to significant benefit given the previous discussions in the STAMP<sup>4</sup> about the definition of “unmet medical need” in relation to the application of the conditional marketing authorisation regulation<sup>5</sup>.

It was asked whether there is a harmonisation of understanding of the provisions. EMA explained that there can be differences as they serve different purposes, however they are

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<sup>4</sup> During 2<sup>nd</sup>, 3<sup>rd</sup> and 6<sup>th</sup> meetings

<sup>5</sup> Commission Regulation (EC) No 507/2006 on the conditional marketing authorisation (OJ L 92, 30.3.2006, p. 6)

reviewing the accumulated experience and that learnings could be a basis to support consistent application of each provision (albeit some differences may exist, based on the respective legal provisions and existing guidance). It was mentioned that the health technology assessment also assesses the relative effect of medicines and there is an exchange of information between EMA and HTA bodies within the EUnetHTA<sup>6</sup> project.

#### **b. Update on the revision of Regulation (EC) No. 726/2004**

The Commission updated the STAMP on the outcome of the discussions in the European Parliament in the Council and the amendment of Regulation (EC) No. 726/2004<sup>7</sup>. During the discussions on the revision of the legislation to take account of the changes to the veterinary legislation the co-legislators had proposed amendments which would impact on the Commission Regulation (EC) No 507/2006 on the conditional marketing authorisation. The new amendments include the introduction of the definition of “unmet medical need” into Regulation (EC) No. 726/2004. In addition, a new provision has been introduced that provides the possibility for action to be taken on a conditional marketing authorisation when the specific obligations have not been fulfilled. The legislation was expected to be published in the Official Journal of the European Union around the end of the year<sup>8</sup>.

#### **c. Update on activities relevant to timely access to medicines**

The Chair noted that there continued to be political interest in the issue of access to medicines and gave update on recent activities:

- The Commission had launched studies to support the evaluation of the Orphan and Paediatric Regulations<sup>9</sup>. The studies cover the topics of the regulatory system, incentives and access to medicines and are expected to be completed in 2019<sup>10</sup>.
- The Austrian Presidency organised an informal meeting of Health Ministers during which the issue of availability of medicines, particularly for small markets, the benefit for patients, availability and prices was discussed<sup>11</sup>.
- The Presidency also held a conference on the regulatory activities and research activities, exploring the relationship between public funding of research and the interest of the healthcare systems<sup>12</sup>.

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<sup>6</sup> European network for health technology assessment - <https://www.eunethta.eu/>

<sup>7</sup> Regulation (EC) No 726/2004 of the European Parliament and of the Council laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use (OJ L 136, 30.4.2004, p.1)

<sup>8</sup> Published 07/01/2019 - Regulation (EU) 2019/5 of the European Parliament and of the Council of 11 December 2018 amending Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, Regulation (EC) No 1901/2006 on medicinal products for paediatric use and Directive 2001/83/EC on the Community code relating to medicinal products for human use (Text with EEA relevance) (OJ L 4, 7.1.2019, p. 24)

<sup>9</sup> [https://ec.europa.eu/info/law/better-regulation/initiatives/ares-2017-6059807\\_en](https://ec.europa.eu/info/law/better-regulation/initiatives/ares-2017-6059807_en)

<sup>10</sup> Information on studies:

[https://ec.europa.eu/health/sites/health/files/human-use/docs/pharmaceuticals\\_incentives\\_study\\_en.pdf](https://ec.europa.eu/health/sites/health/files/human-use/docs/pharmaceuticals_incentives_study_en.pdf);

[https://ec.europa.eu/health/sites/health/files/files/paediatrics/docs/2017\\_childrensmedicines\\_report\\_en.pdf](https://ec.europa.eu/health/sites/health/files/files/paediatrics/docs/2017_childrensmedicines_report_en.pdf);

[https://ec.europa.eu/health/sites/health/files/files/paediatrics/docs/paediatrics\\_10\\_years\\_ema\\_technical\\_report.pdf](https://ec.europa.eu/health/sites/health/files/files/paediatrics/docs/paediatrics_10_years_ema_technical_report.pdf);

[https://ec.europa.eu/health/sites/health/files/files/paediatrics/docs/paediatrics\\_10\\_years\\_economic\\_study.pdf](https://ec.europa.eu/health/sites/health/files/files/paediatrics/docs/paediatrics_10_years_economic_study.pdf)

<sup>11</sup> <https://www.eu2018.at/calendar-events/political-events/BMASGK-2018-09-10-informal-health.html>

- The new research programme Horizon Europe is being planned, it is proposed to have a health cluster in which health, including pharmaceutical related topics, would be covered.

Finally, the Chair encouraged the participants to consider the role that STAMP could play in the further development of the activities related to access to medicines for discussion in the next meeting.

**ACTION POINTS AND POINTS TO CONSIDER FOR THE NEXT MEETINGS:**

- Working group to update the proposed repurposing framework and report back to the next STAMP meeting.
- STAMP participants to reflect on role and future activities of the Group in relation to timely access to medicines.

The next meeting of the STAMP Expert Group is planned for **15 March 2019**.

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<sup>12</sup> Matching Health Needs and Pharmaceutical Research – How to set the research agenda for public health - <https://www.eu2018.at/calendar-events/political-events/BMASGK-2018-09-25-Matching-Health-R-D.html>

### 3 DECEMBER 2018 STAMP EXPERT GROUP - EXTERNAL PARTICIPANTS

<b>Name</b>	<b>Affiliation</b>	<b>Agenda items</b>
Lydie Meheus	Anticancer Fund	3 - 5
Ciska Verbaanderd	Anticancer Fund	3 - 5
Jillian Harrison	Belgian Healthcare Knowledge Centre (KCE)	3 - 5
Francesca Cattarin	The European Consumer Organisation BEUC	3 - 5
Kaisa Immonen-Charalambous	European Patients' Forum (EPF)	3 - 5
Sini Eskola	European Federation of Pharmaceutical Industries and Associations (EFPIA)	3 - 5
Mareike Ostertag	European Federation of Pharmaceutical Industries and Associations (EFPIA)	3 - 5
Christine Dawson	European Social Insurance Platform (ESIP)	3 - 5
Olga Kozhaeva	European Society for Paediatric Oncology (SIOPE)	3 - 5
Diego Ardigo	European Confederation of Pharmaceutical Entrepreneurs (EUCOPE)	3 - 5
François Houžez	EURORDIS - Plateforme Maladies Rares	3 - 5
Pascal Garel	European Hospital Healthcare Federation (HOPE)	3 - 5
Menno Aarnout	International Association of Mutual Benefit Societies (AIM)	3 - 5
Beata Stepniewska	Medicines for Europe (MfE)	3 - 5
Carolina Martinez Berganza	Pharmaceutical Group of the European Union (PGEU)	3 - 5

Laura Merson	Infectious Diseases Data Observatory / Oxford University	4 - 5
Phillippe Guerin	Infectious Diseases Data Observatory / Oxford University	4 (via teleconference)