



**STAMP Commission Expert Group  
28 June 2016**

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**Subject: Repurposing of established medicines/active substances**

- **General reflection**
- **Member State Questionnaire off-label use/repurposing-prepared and consolidated by the Medicines and Healthcare products Regulatory Agency (MHRA)-UK**

**Agenda item 3**

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At the STAMP meeting on 10 March 2016, the UK Medicines and Health products Regulatory Agency (MHRA) presented a background note on repurposing of established medicines/active substances (STAMP 4/20).

Four main types of repurposing activities were identified: new therapeutic indication for an already known drug; new administration route with the same indication; new combinations of medicines previously used as separate products for treatments; new drug/medical device combinations.

The STAMP discussion mainly focused on drug repurposing for new indications for well established (off-patent) medicines in areas of unmet medical need that could lead to faster development times, reduced costs of developments and offer additional therapeutic options to patients.

The discussion in the Group covered the following main points: the potential incentives and disincentives; the sources of evidence supporting repurposing; the involvement of academia; potential for imposition of changes to a marketing authorisation; and, off-label use.

On the basis of initial discussions the Group is invited to further reflect on the challenges and possibilities for repurposing with regard to the points identified above.

The Group considered that off-label use of medicines for patient access should be explored further and agreed that a questionnaire should be circulated to seek more information on

'important' authorised medicines widely used off-label. Five questions were posed to the Member States in a questionnaire prepared by MHRA:

**Question 1:** Do you consider that there are significant regulatory barriers for including new indications in the marketing authorisation for existing approved medicinal products?

**Question 2:** Do you have any specific national provision(s) for supporting off-label use of existing medicines?

**Question 3:** Please list the important drugs that your national provision currently or has recently supported. For each drug, please include the active substance, name, indication, framework of assessing benefit: risk and patient access, and reimbursement availability.

**Question 4:** Do you have any national incentives for supporting registration of 'off-label' indications for existing medicines in marketing authorisations?

**Question 5:** Do you have any other comments regarding off-label use and/ or re-purposing of medicines?

Comments were received the following Member States: Croatia, Czech Republic, Finland, France, Germany, Greece, Hungary, Ireland, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain and the United Kingdom.

The following gives an overview of the replies consolidated by MHRA:

*Question 1: Do you consider that there are significant regulatory barriers for including new indications in the marketing authorisation for existing approved medicinal products?*

The majority of Member States who responded did not consider that there are significant regulatory barriers to including new indications in existing marketing authorisations. Six Member States considered that there were significant regulatory barriers whilst 12 did not.

One common theme expressed by several Member States was that a new indication could only be sought by the marketing authorisation holder MAH, and that the clinical trial requirements for new indications could be considered to be burdensome. Comments from 'yes' respondents include that 'there is a need to discuss the option/feasibility of alternative designs for clinical trials, for alternative end points for clinical trials and for the increased use of real world data/information from patient registries' and 'From a regulatory point of view, requirements are sometimes far beyond of what would be reasonable, especially with medicines already being used off-label for a long time'.

*Question 2: Do you have any specific national provision(s) for supporting off-label use of existing medicines?*

Ten Member States have specific national provision(s) for supporting off-label use of existing medicines and 7 Member States do not. These provisions have a variety of structures and

frameworks, with some very well established mechanisms of supporting off-label use in some Member States. One Member State has introduced a new policy, the temporary recommendations for use (RTU), whilst others put the responsibility in a collegial internal committee at each hospital of the National Health Service. In at least one Member State, the Agency can establish therapeutic protocols and/or recommendations for the use (or not use) of medicines for conditions different to those authorised. One Member State was exploring how collaboration can be fostered between generics manufacturers and academics with a view to repurposing new indications for off-label uses of off-patent medicines.

*Question 3: Please list the important drugs that your national provision currently or has recently supported. For each drug, please include the active substance, name, indication, framework of assessing benefit: risk and patient access, and reimbursement availability.*

Member States presented a variety of drugs and frameworks where available. Frameworks included a searchable database for the National formulary reference to the use of medicines in some non-approved indications (off-label) and recommendations given by off-label expert commissions.

*Question 4: Do you have any national incentives for supporting registration of ‘off-label’ indications for existing medicines in marketing authorisations?*

Only 3 Member States have national incentives for supporting registration of ‘off-label’ indications for existing medicines with 11 MS answering no. One Member State has a specific drug rediscovery policy.

*Question 5: Do you have any other comments regarding off-label use and/ or re-purposing of medicines?*

Additional comments included concerns that any waiver of regulatory requirements might increase the risks. For smaller Member States, a central registry for doctors/health care professionals to log in and compile data regarding their off-label use of medicines might be useful, and suggestions that use of referral procedures might be a means of harmonisation of information (Efficacy and Safety) for off patent medicinal products.