EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Repurposing of established substances

Proposal for a repurposing framework for Not-for profit organisations

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Presented by Christelle Bouygues
Regulatory Affairs Officer

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Senators Hatch and Bennet Introduce Bipartisan Solution to Important Public Health Issue

Making Objective Drug Evidence Revisions for New Labeling Act Introduced to Senate

On Thursday, September 27, 2018, Senators Orrin Hatch (R-UT) and Michael Bennet (D-CO) introduced the Making Objective Drug Evidence Revisions for New Labeling Act or MODERN Labeling Act. The bill provides a solution to a recently identified public health issue impacting patients and their medical providers across the country.

The legislation specifically addresses the prevalence of outdated labels for drugs by giving the U.S. Food & Drug Administration (F… information relevant to the drug and its use. This Act also establishes a process through which the FDA can identify labels to be up… label holders to submit modifications to the notice.

> *"Medical providers need the most up-to-date information to make the right health care decisions for their patients," Sen. Be… update prescription drug information for older treatments using the latest clinical evidence. Passing this bipartisan legislati… in our health care system."*

Earlier this year, Friends of Cancer Research (Friends) published a study "Outdated Prescription Drug Labeling: How FDA-Approved… Practice," in the peer-reviewed journal Therapeutic Innovation and Regulatory Science. The article showed that most FDA-approve… effectiveness. To discuss this issue, Friends hosted a congressional briefing on the topic of outdated labels. This bill would provide… information about medicines over time.

> *"In an ideal world, a drug's label would contain all available information healthcare professionals need to prescribe it effect… and physicians are sometimes left to consult outside sources for up-to-date prescribing information," said Sen. Hatch. "I am… tools the FDA needs to better protect public health. I look forward to continuing to work with my colleagues, stakeholders, a…*

REVIEWS

Drug repurposing: progress, challenges and recommendations

*Sudeep Pushpakom[1], Francesco Iorio[2], Patrick A. Eyers[3], K. Jane Escott[4], Shirley Hopper[5], Andrew Wells[6], Andrew Doig[7], Tim Guilliams[8], Joanna Latimer[9], Christine McNamee[1], Alan Norris[1], Philippe Sanseau[10], David Cavalla[11] and Munir Pirmohamed[1]**

Abstract | Given the high attrition rates, substantial costs and slow pace of new drug discovery and development, repurposing of 'old' drugs to treat both common and rare diseases is increasingly becoming an attractive proposition because it involves the use of de-risked compounds, with potentially lower overall development costs and shorter development timelines. Various data-driven and experimental approaches have been suggested for the identification of repurposable drug candidates; however, there are also major technological and regulatory challenges that need to be addressed. In this Review, we present approaches used for drug repurposing (also known as drug repositioning), discuss the challenges faced by the repurposing community and recommend innovative ways by which these challenges could be addressed to help realize the full potential of drug repurposing.

findacure

Rare diseases Patient group training

The World Orphan Drug Conference, Europe

OrphanDrug

Discussion

Background of STAMP repurposing project

- Drug repurposing constitutes a dynamic field of drug development that can offer benefits to patients
- **STAMP** (Safe and Timely Access to Medicines for Patients): expert group of the European Commission with Member states & EMA, under the Pharmaceutical Committee, has focused its work on drug repurposing.
- For the repurposing topic, STAMP engaged extensively with **various stakeholders** (industry, healthcare professionals, patients - Eurordis, not-for-profit organisations - Anticancer Fund, HTA and pricing and reimbursement bodies)
- Focus was on drug repurposing for **new indications** for **well established** (off-patent) medicines in areas of **unmet medical need** that could offer additional therapeutic options to patients.

STAMP brainstorming on barriers / challenges

- Since 2016, STAMP carried out brainstorming sessions through:
  - Member State Questionnaire - Off-label use/ re-purposing,
  - repurposing case studies,
  - workshop
- 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;
  - off-label use
- Follow-up by a reflection on potential solutions.

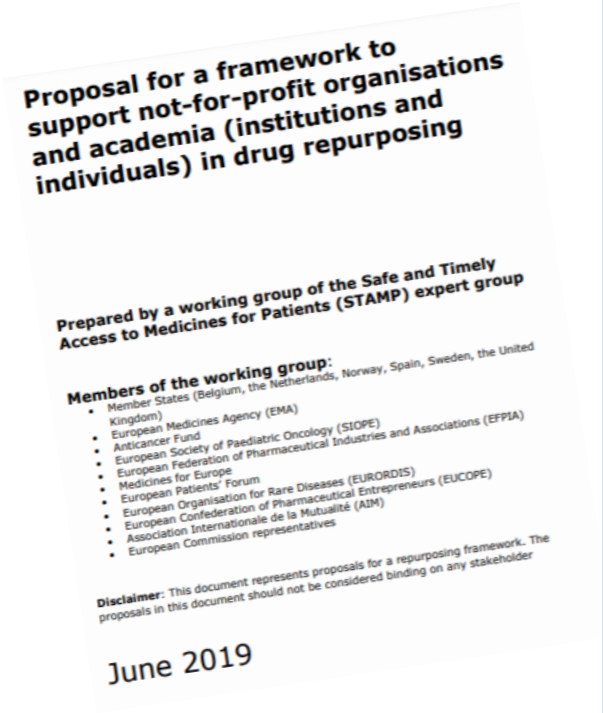
STAMP observations

- Clinical trials or data analysis from various sources investigating new uses for off-patent drugs are often conducted by non-commercial stakeholders
- Lack of interest from & difficulties in engaging with the pharmaceutical industry (e.g. due to lack of regulatory and/or financial incentives)
- Lack of accessible information / data in the public domain and lack of experience in generating data according to regulatory standards
- Lack of a regulatory framework that recognises the challenges faced by non-industry researchers
- Lack of knowledge and resources from not-for profit organisations and academia in terms of understanding the regulatory routes and requirements, no intent of being a MAH
- Challenges in finding a MAH to collaborate with to bring the indication on label.

Objectives of STAMP Repurposing framework

- To **target not-for-profit party** who has an interest in an indication of an already authorised medicinal product that is off-patent and out of regulatory protection in **an indication outside its authorisation** where research has shown **value to the patient**, with the aim of bringing a new indication on-label.
- to provide a **visible supportive framework to a not-for-profit organisations** and academia (described as Champions), who have **evidence and scientific rationale for a new indication**.
- To **provide advice and support to** facilitate **appropriate evidence generation** and filing of new uses, within the existing tools.

Scope of the framework



Proposal for a framework to support not-for-profit organisations and academia (institutions and individuals) in drug repurposing

Prepared by a working group of the Safe and Timely Access to Medicines for Patients (STAMP) expert group

Members of the working group:

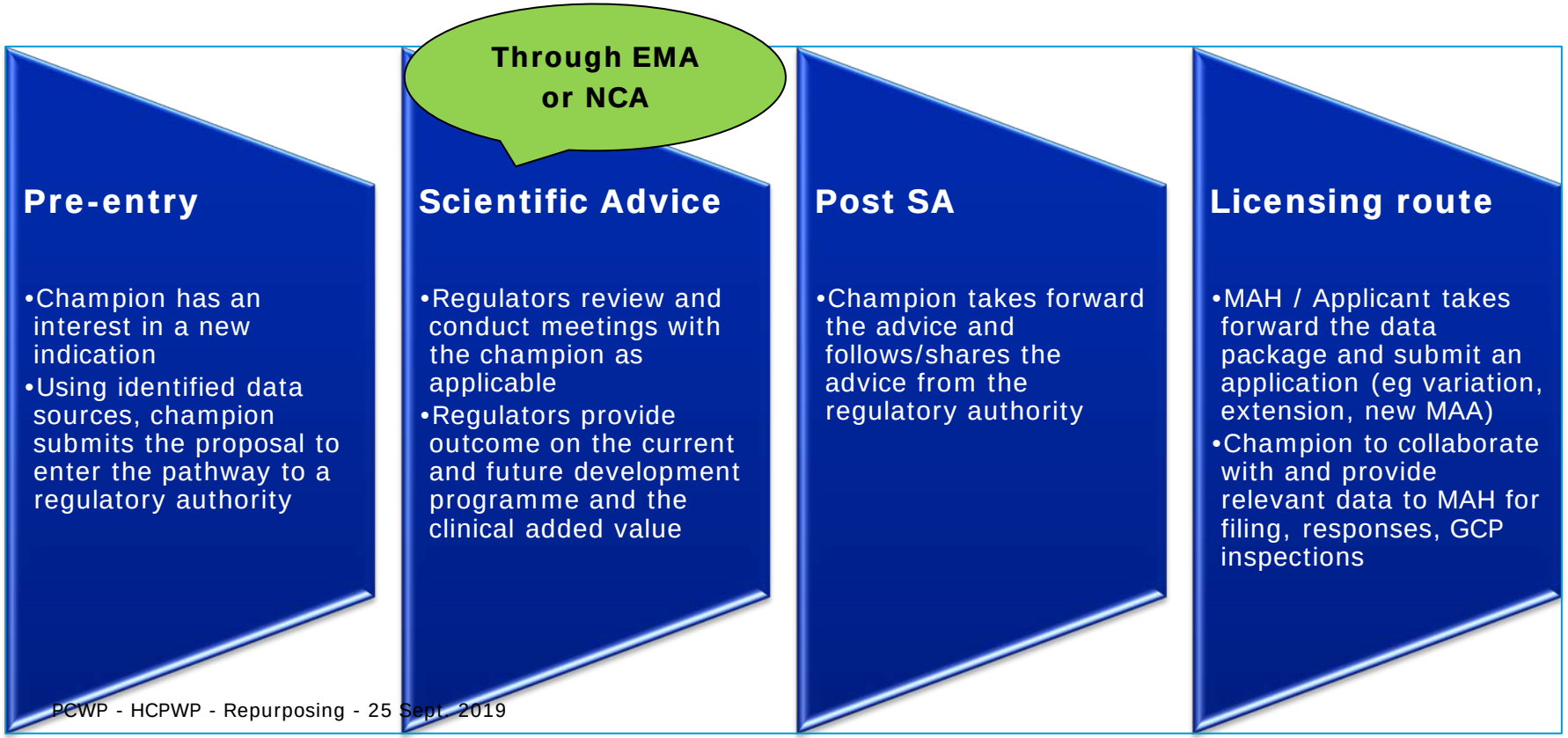
- Member States (Belgium, the Netherlands, Norway, Spain, Sweden, the United Kingdom)
- European Medicines Agency (EMA)
- Anticancer Fund
- European Society of Paediatric Oncology (SIOPE)
- European Federation of Pharmaceutical Industries and Associations (EFPIA)
- Medicines for Europe
- European Patients' Forum
- European Organisation for Rare Diseases (EURORDIS)
- European Confederation of Pharmaceutical Entrepreneurs (EUCOPE)
- Association Internationale de la Mutualité (AIM)
- European Commission representatives

Disclaimer: This document represents proposals for a repurposing framework. The proposals in this document should not be considered binding on any stakeholder

June 2019

1. **New indication to be in a condition distinct** to the currently authorised indication(s) by a MS or the EU (section 4.1 of SmPC)
2. To target an **area where significant public health benefits / Union interests** are likely to be achieved
3. There should be **a valid marketing authorisation** for the medicinal product out of basic patent/ SPC protection, and data & market exclusivity periods
4. There should be **supporting evidence** e.g. proof of concept from clinical data (registry data, clinical trials or reported case studies, etc)
5. A **Champion is willing and able** to take on the roles and responsibilities

Overview of the framework



Who can be a champion?

Not-for profit organisations and Academia

A Champion is typically charact

a. Is not a pharmaceutical company or is not financed or managed by private profit organisations in the pharmaceutical sector ("PPO"), nor has concluded any operating agreements with any PPO concerning their sponsorship or participation to the specific research project at the time of entry into the framework
b. Is able to coordinate and / or foster the research programme up until the point of full industry engagement
c. Is initially responsible for liaising and leading the interactions with regulatory authorities and industry / other stakeholders such as patient groups
d. Is transparent regarding interactions with relevant pharmaceutical company(s)
e. Files the initial request for scientific/regulatory advice on the basis of the available data
f. Where feasible and appropriate, provides information to the MAH during the MAA submission / process (e.g. regarding GCP compliance of the clinical trial(s), responses to questions from regulatory authorities)

Next step: Piloting the framework

A **learning exercise** providing insight into the characteristics of repurposing development programmes to support champions

Assessment of the **clarity and comprehensibility of the core components and milestones of the framework**

Assessment of the **steps followed by the champion to enter the repurposing framework**

Project progress after SA i.e. continuation of programme development and compliance with SA outcome

Identification of gaps in the existing guidance available on the EMA/HMA/NCA websites

Where are we?

- July 2019: Agreement of the Pharmaceutical Committee on the proposal for the framework on repurposing to be tested through a pilot which will be overseen by Repurposing Observatory Group.
- The “ Repurposing Observatory Group” (RepOG) to report to STAMP / Pharmaceutical Committee, composed of “Champion interest groups” (e.g. Eurordis, AntiCancer Fund), industry and regulatory representatives
- The RepOG is working on supporting documents for the launch of the pilot.

References

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- European Patients' Forum
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- European Confederation of Pharmaceutical Entrepreneurs (EUCOPE)
- Association Internationale de la Mutualité (AIM)
- European Commission representatives

EC website - STAMP

https://ec.europa.eu/health/documents/pharmaceutical-committee/stamp_en

EC website – Pharmaceutical Committee

https://ec.europa.eu/health/documents/pharmaceutical-committee/human-meeting_en

Any questions?

Further information

christelle.bouygues@ema.europa.eu

Temporary visiting address Spark building • Orlyplein 24 • 1043 DP Amsterdam • The Netherlands
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