Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

Reporting back from STAMP Working Group on repurposing

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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The legislation specifically addresses the prevalence of outdated labels for drugs by giving the U.S. Food & Drug Administration (F… information relevant to the drug and its use.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 u… 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Earlier this year, Friends of Cancer Research (Friends) published a study "Outdated Prescription Drug Labeling: How FDA-Approved… Practice," in the peer-reviewed journal Therapeutic Innovation and Regulatory Science.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 To discuss this issue, Friends hosted a congressional briefing on the topic of outdated labels.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…***

Drug repurposing: progress, challenges and recommendations

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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

By Rick Thompson | Rare disease world

In today's blog our CEO Rick tells us about his recent trip to the World Orphan Drug Congress last week.

A big part of our work at Findacure is raising awareness about the work of the rare disease community. This can involve speaking to a wide diversity of people, attending conferences, running races or writing this blog. Last week, we attended one of the larger rare disease conferences in the calendar, the World Orphan Drug Congress Europe 2018, with the aim of telling the European rare disease community about some of the rare disease work in the UK, as well as learning more about what is happening in the rare world today. The event was held in Barcelona, and featured some fantastic talks and discussion about all things rare.

The conference opened with a series of half day workshops that allowed delegates an in-depth look at some major topics in the rare disease field. Luckily for Findacure, we were front and centre, as I was chairing and delivering a large part of the workshop on drug repurposing.

The central question of the workshop was "is drug repurposing a sufficient business model to drive orphan drug development?". Between Pan Pattzlarka, Programme Director at the Ambrosini Fund, Dan O'Connor, Medical Assessor at the MHRA, myself we spent a four hour session delving into the world of drug repurposing. Pan and I highlighted the need for repurposing, and the strategic considerations when thinking of running a repurposing project. This inspired a lot of

OrpharDrug

STAMP & repurposing medicines

- Repurposing of medicines is an important topic at the STAMP

- STAMP has considered repurposing as an agenda item on the 4th – 9th meetings

  – Member State Questionnaire - Off-label use/ re-purposing - consider if there are significant regulatory barriers for including new indications, national provisions

  – Repurposing case studies developed by interested Member States and other bodies

  – Workshop at the STAMP with multiple stakeholders

    - Highlight by example from a variety of sources where barriers / challenges are and what solutions might be identified

  – Industry stakeholders considered the discussions and proposed what a supportive repurposing framework might look like

STAMP: EFPIA and Medicines for Europe proposal

- Provide a framework and pathway to any stakeholder who has evidence and scientific rationale to support a new indication for an off-patent substance/product already on the market

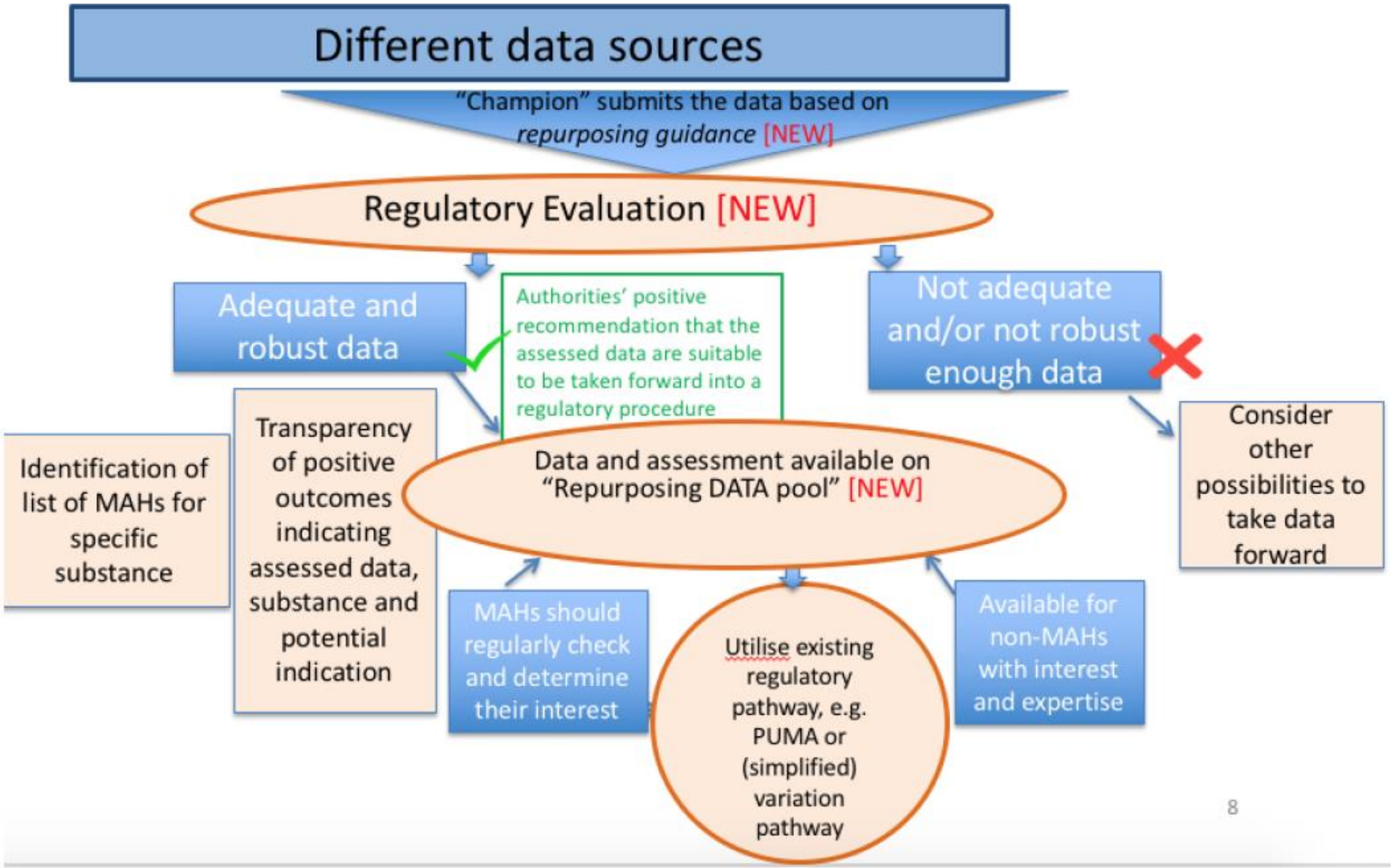
- A Champion can be a person/academic unit/learned society/research fund with a particular interest in repurposing a compound/product for a new indication – not a MAH

- The Champion puts forward a repurposing proposal for regulatory evaluation
  - Standard format data package according to guidance, including description of the existing supporting data for indication

- Regulator facilitates early identification of the MAHs and increases their readiness to make an eventual regulatory submission

- Regulator decides whether proposal is supported and the evidence is robust enough
  - If assessment is positive, it is made available in a ‘repurposing Data pool’ – possibility of partnership of ‘champion’ with MAHs or other interested parties

Repurposing Framework



STAMP: EFPIA and Medicines for Europe proposal

- The proposal generated much discussion at the STAMP meeting and a repurposing working group was set up with multiple stakeholders to consider the proposals and further develop the framework

- Members of the working group, supported by the EC are:

  - Member States; Belgium, The Netherlands, Norway, Spain, Sweden, 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)

STAMP: Repurposing Working Group

- The group worked by email and teleconference and identified three main objectives:

- Objective 1: Complete the steps of the pathway with non-regulatory and regulatory aspects and other stakeholder interactions, including practical aspects for each step

  – Leads EMA, SE & UK

- Objective 2: Test run the pathway and provide ‘real life’ examples of product(s) / indications that could have been put through the pathway - consider how a pilot for testing the repurposing pathway might be introduced

  – Lead Anticancer Fund

- Objective 3: Supporting materials and communication, agree methods to disseminate the existence of the pathway and develop the guidance / infrastructure for pathway to work in practice

  – All

• Concept of the Champion further developed

- A Champion 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

- Criteria to qualify as a champion include:
  - Is not a pharmaceutical company / business organisation
  - Is able to coordinate and or foster the development programme up until the point of full industry engagement
  - Is initially responsible for liaising and leading the interactions with regulatory authorities and industry / other stakeholders such as patient groups
  - Is transparent regarding interactions with relevant pharmaceutical company(s)
  - Files the request for regulatory advice on the basis of the available data

Defining the scope of the pathway

1. The new indication should be in a condition distinct to the currently authorised indication(s) listed in section 4.1 of the relevant SmPC) of a MS or the EU

2. There should be a valid marketing authorisation for the medicinal product containing the same active substance in the same formulation / dosage form

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/ SPC protection, and data & market exclusivity periods

5. Project represents a scenario not currently being fulfilled by a business organisation

6. There should be supporting evidence e.g. proof of concept from clinical data (off label use, registry data, clinical trials or reported case studies)

7. A Champion is willing and able to take on the roles and responsibilities

Proposed core components of the framework

- The process of repurposing may be described as voluntary steps within the existing regulatory framework
  - Some key milestones to the repurposing project are not regulatory activities

- **KEY AIM**: The aim of the proposal is to provide a visible supportive framework to a stakeholder who has evidence and scientific rationale for a new indication that fits the scope criteria, with an interest to bringing the indication on-label

- Scientific Advice (SA) is the main regulatory tool that is considered important to support repurposing projects

- Guidance can be provided to the Champion on the regulatory and scientific aspects of the project

- Both legal and non-legal incentives may be important to different stake-holders

- For industry the nature of the business case will be important as well as minimising the perceived barriers

Proposed core components of the framework

1. Pre-entry	Champion has an interest in a new indication
2. Pre-entry	Using identified data sources, the Champion submits the proposal to enter the pathway to a regulatory authority
3. Repurposing SA	Regulatory authority conducts meeting with the Champion and as applicable other relevant stakeholders
4. Feedback	Regulators provide feedback on the current and future development programme and the clinical added value
5. Post SA	Champion takes forward the recommendations and follows / shares the advice from the regulatory authority
6. Licensing route	MAH holder(s) take(s) forward the data package, constructs a regulatory dossier and submits a marking authorisation

Summary

- The working group has further developed some of the elements of a repurposing pathway including the role of the Champion and the scope criteria

- Elements discussed cover only one possible scenario of the repurposing of medicinal products – offering of regulatory scientific advice

- The project has moved forward but there are outstanding:

  - Need to develop a repurposing checklist and topics to cover the repurposing scientific advice meeting
  - Consider ways to support the Champion, including if and how a fee waiver for a scientific advice meeting could be made, provide contact points from industry to aid communication with MAH, other support
  - Determine the feasibility and practicalities of the pathway by piloting with a live asset and Champion (Objective 2)
  - Develop further guidance that clarifies in more detail the individual identified roles and pathway milestones (Objective 3)

Objectives for today

- To further define and discuss the proposed pathway, consider outstanding issues and missing elements

- Agree the next steps for the repurposing project, actions and responsibilities

And

- **To thank the European Commission for their support and input into the project and all the members of the group for their hard work and contributions**