Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

8th STAMP expert group meeting

Repurposing: Themes & discussion points from case studies

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Repurposing medicines

- Drug repurposing is the process of identifying a new use for an existing drug in an indication outside the scope of the original indication

- Drug repurposing constitutes a dynamic field of drug development that can offer real benefits to patients

- To build on what has already been achieved in previous STAMP meetings (4th, 5th and 6th), at the 7th STAMP meeting it was agreed that case studies would be developed by interested Member States and other bodies
  - Highlight by example from a variety of sources where barriers / challenges are and what solutions might be identified
  - Construct a paper that summaries the main themes presented with some discussion points and potential recommendations that might result into actions

- Case studies provided by Anticancer Fund, EMA, ES, NL & UK, & SE comments

- Views from the case studies should not be seen as official positions

Themes from the case studies submitted

Lack of interest from & difficulties in engaging with the pharmaceutical industry:

- Engagement with the pharmaceutical industry is desirable for the efficient and timely generation of the necessary data to conclude on the benefits and risks, and register a new indication

- Non-industry developers often raise the issue of how to proceed to registration if they are not the manufacturer and highlight the lack of regulatory experience and resource needed for filing an application

- If a MAH has no particular interest in the repurposing pathway, a new indication cannot be formally considered and approved by regulatory authorities

  - There may be difficulties in gaining access to an active substance / medicine, sourcing all relevant historical non-clinical and clinical data, and challenges in manufacturing a matched placebo if required for clinical studies

  - Overall the clinical development programme maybe more costly and longer than would otherwise be the case with industry collaboration

Themes from the case studies submitted

Lack of accessible information / data in the public domain:

- There are potential challenges for non-commercial drug developers in sourcing and obtaining all relevant existing historical data for a medicinal product

- In particular the non-clinical aspects of a dossier and the data that may support dose finding

- The lack of access to data means that there is the potential need to replicate expensive tests and even clinical studies, adding to the costs and extending the timelines for the investigation of the potential new therapeutic indication

Themes from the case studies submitted

Lack of a regulatory framework that recognises the challenges faced by non-industry researchers:

- Non-industry researchers may have limited regulatory awareness which can hamper developments or result in clinical trial or regulatory failures

- It is a challenge to know who to speak to and how to gather evidence for prescribers, channelling the data collection within a marketing authorisation

- Regulatory authorities do offer small and medium sized enterprises (SME) support and fee waivers, but these are not provided to the same level for the not-for-profit community
  - Innovation offices /innovation task forces appear to focus mainly on new innovative drugs and not necessarily innovative ways of using older active substance / medicines

- Greater advice and support is needed for organisations who may want to make use of an authorised, off-patent, medicine in an indication outside its authorisation where research has shown value to the patient

Themes from the case studies submitted

Lack of a regulatory framework that recognises the challenges faced by non-industry researchers:

- Advice should include explaining how medicines can be repurposed through the authorisation system or exploring under what circumstances / procedures medicines can be made available on an off-label basis

- The undefined legal and financial responsibilities associated with using repurposed medicines often lead to increased off-label use, which could entail safety and data collection issues, legal liability issues for the prescriber, reimbursement issues, and supply issues when medicines are withdrawn for their approved uses

- Clinical trials investigating new uses for off-patent drugs are often non-commercial, so there should be a way to apply for label extension by third parties or to ask for another type of official evaluation of the evidence by the competent authorities

- The flexibilities offered by the new clinical trial regulation regarding low interventional clinical trials could also be helpful for evidence generation

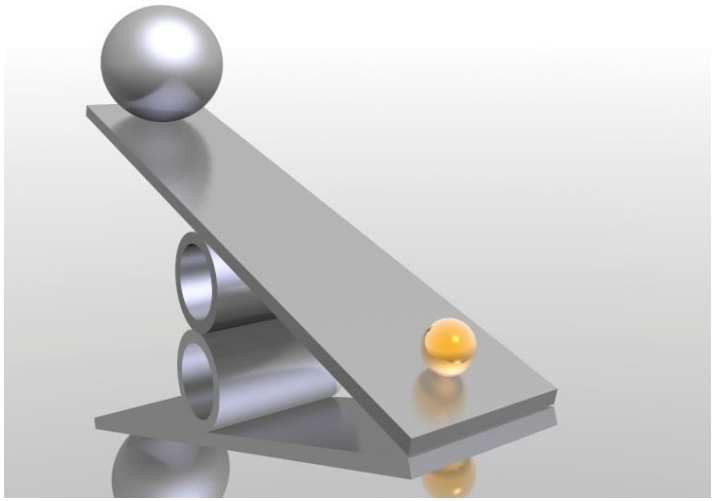
Themes from the case studies submitted

Potential advantages of access to real world data not realised

- Some not-for-profit organisations potentially have access to extensive data sets generated in registries in the ‘real world’

- It is not clear how regulatory authorities and others could use this data which is an untapped and valuable resource

- There needs to be a formal framework to bring this data into the drug development arena / regulatory setting with or without an identified marketing authorisation holder, to support appropriate use of the products



Discussion points

1. Discussion with industry on the specific incentives / motivation needed to support the development and uptake of new indications to innovator medicinal products and whether new rewards are required e.g. fee exemptions. However, incentives and pricing should be proportionate, particularly for well established indications

2. If an innovator company is not interested, how to identify, engage and incentivise a manufacturer of a generic or biosimilar who would apply for the new MAA

3. Determine the viability and desirability of a public health referral to ensure product information is up to date or consider another regulatory route to formally review existing data on the benefits and risks:

- French Temporary Recommendation for Use (RTUs) scheme aims to make off-label use safer, improve knowledge and encourages the company to submit an extension of indication request (6th STAMP)
- Recent USA FOCR proposal on outdated drug labelling; calls for US FDA to identify older products needing updates, contract out evidence reviews, correcting outdated labelling not reflecting current use in clinical practice

Discussion points

4. Guidance should be generated on how to access available data, freedom of information requests, where data could be located /requested

5. Develop a regulatory and product development ‘handbook’ that explains how and who to contact with relevant links for specific issues (EMA & NCA guidance, HMA EU-Innovation Network), available incentives including designation opportunities (e.g. orphan, PRIME)

6. Consider the introduction of a voucher reward system (similar to US FDA priority review voucher), to incentivise companies in taking forward key indications

7. Investigate mechanisms to encourage uptake of regulatory and scientific advice to ensure that the data generated can be submitted for an MA

- Alignment between different stakeholders should be facilitated, wherever possible

8. Consider if the EMA’s registry pilot and or HMA/ EMA Joint big data task force can offer some form of consensus regarding data collection in the real world setting

Summary

- The submitted repurposing case studies identified 4 main themes of issues:
  - Lack of interest from & difficulties in engaging with the pharmaceutical industry
  - Lack of accessible information / data in the public domain
  - Lack of a regulatory framework that recognises the challenges faced by non-industry researchers
  - Potential advantages of access to real world data not realised

- Discussion points
  - What specific incentives are needed to support the uptake of new indications and how to identify an interested manufacturer
  - What is the viability of a public health referral or other regulatory route to formally review existing data on the benefits and risks
  - How to generate guidance on accessing available data, who to contact, available incentives and support including designation opportunities
  - Value of a voucher reward system to incentivise companies in taking forward key indications in the repurposing pathway
  - How to encourage uptake of regulatory and scientific advice
  - Consensus on the utility of data collected in the real world setting

Thank You

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