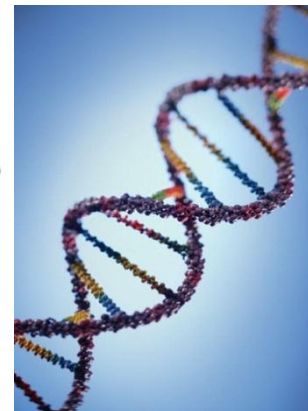




## Earlier Access to Medicines – Early Access to Medicines Scheme and Adaptive Licensing pilot

World Stem Cells & Regenerative Medicine 2014  
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CPRD



NIBSC



MHRA

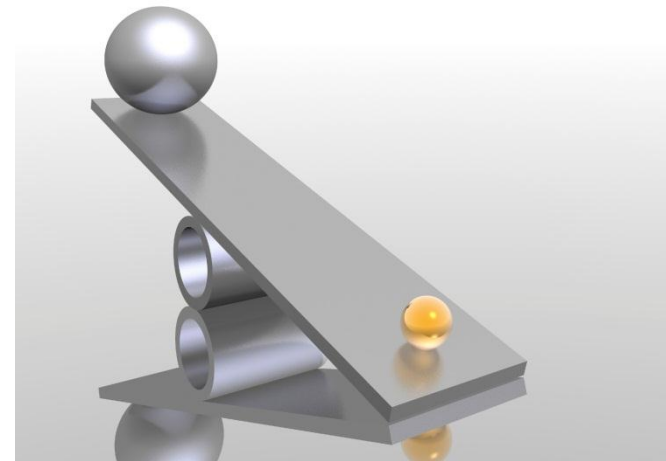
## Disclaimer

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- A key challenge confronting Regulators is earlier patient access to innovative medicines, particularly in areas of unmet medical need
- Ultimately there is often a fine balance between ‘denying’ patients potentially useful drugs and approving products for which the drug development is considered as immature
- However, it is recognised that with greater medical needs e.g. life threatening conditions with no adequate treatments, it is acceptable to make decisions based on a greater degree of uncertainty in the data

- ‘*Evidence versus access*’ balance



- Recently two initiatives were launched to try and address some of the pressing patient access issues:
  - A European initiative, adaptive licensing, an emerging concept of '*staggered marketing authorisation approval*', using existing regulatory tools
  - This more 'systems approach' involving more stakeholders, has also been called 'Medicines Adaptive Pathways to Patients'
  - A UK initiative, Early Access to Medicines Scheme, which aims to give access to medicines that do not yet have a marketing authorisation but meet an unmet medical need

# Early Access to Medicines Scheme



# EAMS Milestones

- Ministerial Industry Strategy Group
- The Prime Minister's Strategy for UK Life Sciences
  - Early Access to Medicines Scheme Consultation
  - Expert group on the innovation in the regulation of healthcare
- Early Access to Medicines Scheme consultation response
- Early Access to Medicines Scheme launch
  - Step I: the Promising Innovative Medicine (PIM) Designation
  - Step II: the EAMS Scientific Opinion



# Ministerial Industry Strategy Group (MISG)

- The MISG brings together government and the research-based pharmaceutical industry to promote a strong and profitable UK-based pharmaceutical industry
- In 2008, a proposal for an Early Access to Medicines Scheme was developed as part of a series of events established by the MISG
- The Regulatory Working Group forum considered there was support from all stakeholders that earlier access to medicines could bring benefits to patients
- The Working Group developed a framework for the EAMS
- Acknowledging that whilst access to such medicines will – at least in most cases – be at the end of the formal development stage, the scheme could still provide potentially life-saving treatments around one year earlier than at present



- In December 2011 the Prime Minister announced a new Strategy for UK Life Sciences
- One of the commitments was that the MHRA will bring forward for consultation proposals for a new 'Early Access Scheme'
- The MHRA and Department Health launched a joint public consultation from 13 July to 5 October 2012
  - 52 responses were received - overwhelming support
- The Government considered that the EAMS:
  - Addresses a public health need to improve access to important innovative medicines for patients with life threatening or seriously debilitating conditions without adequate treatment options
  - Demonstrates a commitment from the UK to pharmaceutical innovation, through the Promising Innovative Medicine designation and earlier patient uptake of new innovative medicines in the health service







# Early Access to Medicines Launch



- The MHRA launched the scheme on the 7<sup>th</sup> of April with a dedicated EAMS webpage, coordinator and guidance
- The scheme aims to give patients with life threatening or seriously debilitating conditions access to medicines that do not yet have a marketing authorisation when there is a clear unmet medical need
- The scheme is voluntary and the opinion from MHRA does not replace the normal licensing procedures for medicines
- Primarily aimed at medicines that have completed Phase III trials, but may be applied to completed Phase II trials in exceptional circumstances
- There is no set limit on the numbers of products entering the scheme provided they fulfil the criteria of the scheme

- MHRA is responsible for the scientific aspects of the scheme and the scientific opinion will be provided after a two-step evaluation process:
  - Step I, the Promising Innovative Medicine (PIM) designation
    - » The designation is an early indication that a medicinal product is a promising candidate for the EAMS
  - Step II, the Early Access to Medicines Scientific Opinion
    - » The scientific opinion will describe the benefits and risks of the medicine and will support the prescriber and patient to make a decision on using the medicine before its licence is approved

# Step I PIM Designation

- A Promising Innovative Medicine Designation is an early indication that a medicinal product is a promising candidate for the EAMS
- A designation is a prerequisite to enter the EAMS scientific opinion assessment (step II)
- The designation will be issued after an MHRA scientific meeting on the basis of non-clinical and clinical data available on the product, in a defined disease area
- Applicants may apply when data from early stages of clinical development indicates that the medicinal product fulfills the designation criteria
  - the product is likely to demonstrate significant benefit for patients in life-threatening or seriously debilitating conditions

**Step I**

**Step II**

'PIM' designation awarded on the basis of Phase I/II data

Early Access to Medicines pre-submission meeting

Enter Scientific review for EAMS opinion

'PIM' designation awarded on the basis of Phase II data

Early Access to Medicines pre-submission meeting

Enter Scientific review for EAMS opinion

Joint 'PIM' designation and Early Access to Medicines pre-submission meeting, on the basis of Phase III data (exceptionally Phase II)

Enter Scientific review for EAMS opinion



# 'Post PIM' Designation

- Following designation, the applicant is expected to complete a clinical development programme within a reasonable time period, in order to continue with an application for an EAMS scientific opinion
- Designation holders will also be encourage to utilise the MHRA's support services including:
  - The MHRA Innovation Office that helps organisations navigate the regulatory framework
  - Scientific advice, including:
    - Scientific advice for specific scientific issues
    - Broader scope meetings on less specific topics
    - Joint scientific advice meetings with NICE, regarding clinical study design that will be used to satisfy regulatory and NICE requirements



# Step II – Scientific Opinion

- The scientific opinion will describe the benefits and risks of the medicine and will support the prescriber and patient to make a decision on using the medicine before its licence is approved
- To enter step II, the Applicant must hold a PIM designation, complete the pre-submission template and attend (either in person or via teleconference) a pre-submission meeting
- The aim of the pre-submission meeting is to ensure that the suitability criteria for the scheme are likely to be met and to discuss the format of the data to be submitted to support the benefit/risk opinion
- After the pre-submission meeting, the MHRA will make a recommendation as to whether the product is considered a suitable candidate for step II of the EAMS
- However, it is ultimately the decision of the Applicant whether to proceed with an application



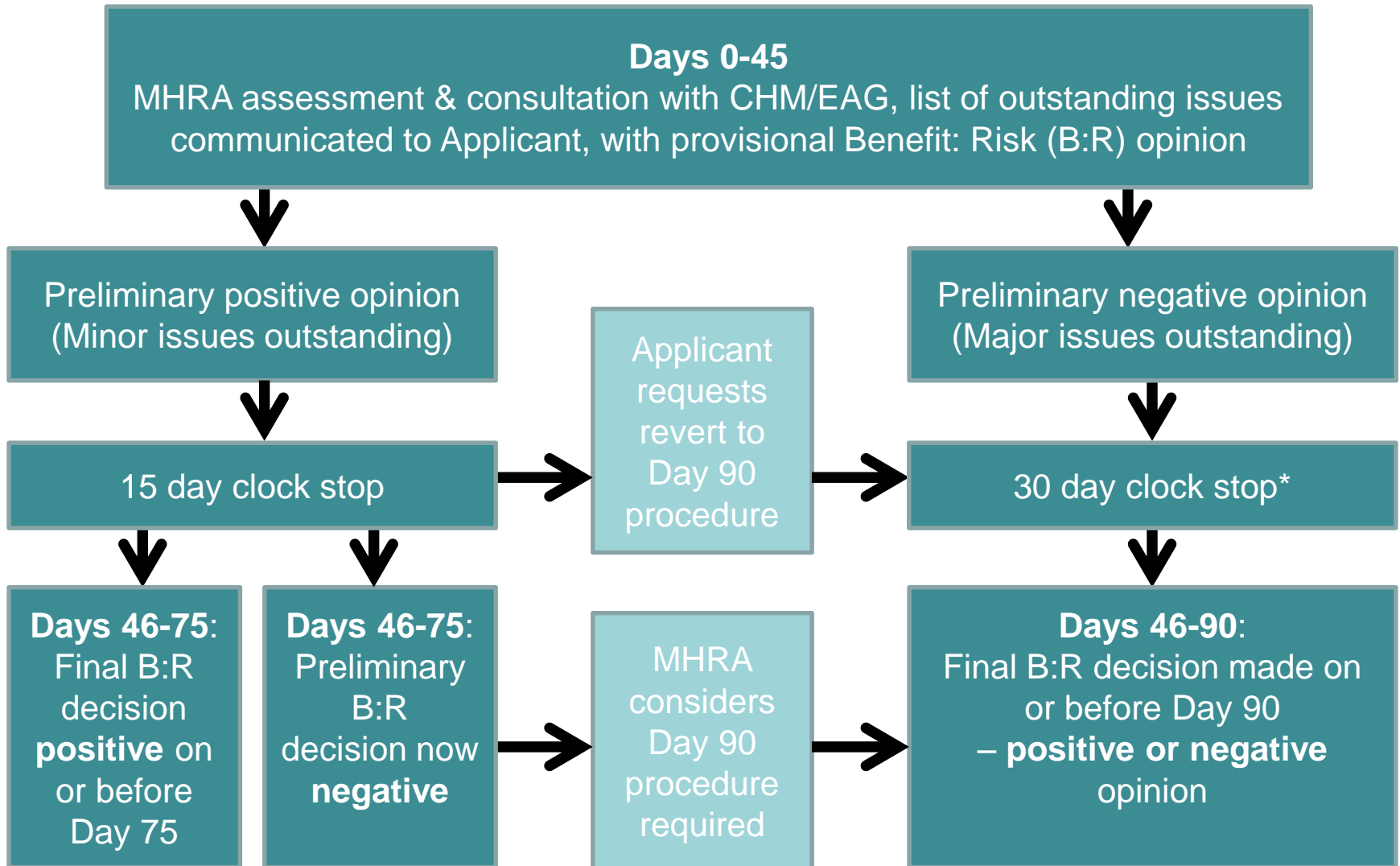
# Entry into Step II

- Data format requirements are in line with established regulatory guidance (CTD) and/ or option to submit non-CTD data
- The EAMS dossier should be submitted in electronic format by the date specified and agreed after the pre-submission meeting
- Late or invalid dossiers will not be able to enter the scheme on the preferred date as the timetables are set to coincide with our expert committee meetings
- The assessment timetable is fast and flexible, 75 (90) days vs. 150 or 210 days in the EMA centralised procedure (minus clock stops), with options:
  - Lengthen clock stops if required
  - Close before Day 75 if all issues are resolved



## Day 75 Timetable

## Day 90 Timetable



\*in exceptional circumstances, the Applicant can request additional 30 days (30+30)

# The Scientific Opinion

- The scientific opinion will describe the benefits and risks of the medicine, based on information submitted to the MHRA by the Applicant in a public assessment report (PAR)
- The PAR will be made available on the MHRA's website to assist clinicians and patients in making treatment decisions
- More detailed product information will be provided in the EAMS Treatment Protocol, which will detail the conditions for use, ensuring safe and efficacious use of the product
- The scientific opinion will be valid for one year, renewable if necessary and appropriate
- Negative opinions will not be published

# EAMS Summary

- Open for applications since 7<sup>th</sup> April 2014
- Aim to give patients with life threatening or seriously debilitating conditions access to medicines that do not yet have a marketing authorisation when there is a clear unmet medical need
- The MHRA is responsible for the scientific aspects of the scheme and the scientific opinion will be provided after a two-step evaluation process
- Detailed guidance and templates can be found on the EAMS webpage
- Support through the EAMS coordinator, to provide help and assistance regarding any aspect of the scheme
- New scheme – New processes - MHRA plan to collection information from applicants on their experiences of the scheme (using an electronic survey)



# Adaptive Licensing



# Adaptive Licensing (AL)

- Adaptive licensing is proposed to be stepwise learning under conditions of acknowledged uncertainty, with iterative phases of data gathering and regulatory evaluation - a life-cycle approach
- This is in contrast to traditional drug licensing approaches that are based on binary decisions, where an experimental therapy is transformed into a ‘fully’ vetted therapy at the moment of licensing
- The aim is to maximise the positive impact of new drugs on public health by:
  - Balancing timely access for patients to treatments that promise to address serious conditions where there is an unmet need
  - With the need to provide adequate evolving information on the benefits and harms

# Adaptive Licensing (AL)

- AL is defined by the EMA as a prospectively planned, adaptive approach to bringing drugs to market;
  - Starting from an authorised indication, most likely a “niche” indication
  - Followed by iterative phases of evidence gathering and progressive licensing adaptations, concerning both the authorised indication and further therapeutic uses of the drug
- AL uses the regulatory processes that exist with the EU framework
- Stakeholders other than regulators and industry need to be involved in planning and agreeing the manner in which clinical trial and post-authorisation data will be generated for decision making:
  - e.g. Reimbursement authorities, patient organisations, societies involved in treatment guidelines

# The EMA pilot

- An AL discussion group was set up by the EMA in 2012, with members from across the various scientific committees e.g. CHMP, COMP
- Following work performed by the group, the EMA recently launched an adaptive licensing pilot (March 2014) to discuss prospective case studies
- The purpose of the pilot is to provide a framework for informal interactions by discussing ‘live assets’, i.e. medicines currently under development
- It is hoped that all stakeholders will be able to address a range of technical and scientific questions
  - Help refine how future AL pathways might be designed
  - What might be achieved by AL
  - How best to address the potential blocking factors
  - To identify additional hurdles or issues that may not have become apparent yet

# The EMA pilot

- Guidance and a framework to guide discussions of individual pilot studies has been published, alongside some retrospective case studies
- Discussions on possible AL pathways of a live asset are of an exploratory nature
- Thus the pilot offers a safe-harbour environment for informal, non-binding discussions between regulators and companies with an ‘asset’ that may be suitable for this approach
- Strengths and weaknesses of all options for development, licensing and assessment may be explored openly and discussed without fear or favour in advance of more formal interactions e.g. scientific advice
- Companies who are interested in participating are invited to submit medicines for consideration as prospective pilot cases
  - Live assets shall be experimental drugs or biologicals in the early stage of clinical development to enable actionable input from stakeholders (prior to initiation of confirmatory studies)



# The EMA pilot

- Companies should complete a high-level framework on which to base the pilot study
- Product name/identifier
- Summary of relevant product data and development to date (Licensing history and interactions with health authorities/payers/HTA bodies)
- Proposal for development under adaptive licensing
  - ‘adaptive’ strategies for development, licensing, patient access, appropriate utilization, and monitoring that could be considered, using existing regulatory tools
- Outline a vision and timeline for how regulatory, payer and other stakeholders’ interactions might look, including indicative timelines for regulatory evaluation and decision making through the product lifecycle

# AL Summary

- AL would not result in a new type of Marketing Authorisation as the process would use existing regulatory tools e.g. 'Conditional' MA
- The novel aspects of an adaptive licensing from the perspective of the regulator relate to increased dialogue with other stakeholders and increased collection and utilisation of post-authorisation data
- Possible benefits of AL could include:
  - Maximize the positive impact of new drugs on public health by balancing timely access for patients with the need to provide adequate evolving information on benefits and harm
    - More rapid access to patients in greatest need
  - Streamlined drug development with efficient generation of evidence to satisfy the needs of multiple stakeholders using parallel 'Scientific Advice'
  - Potential for more rapid return on investment
  - Earlier dialogue promoting more certainty for the drug developer

**Thank You**

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