Medicines & Healthcare products Regulatory Agency

Regulation of ATMPs in the UK – ‘With or Without EU’

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Disclaimer

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nor of the Medicines and Healthcare Products Regulatory Agency

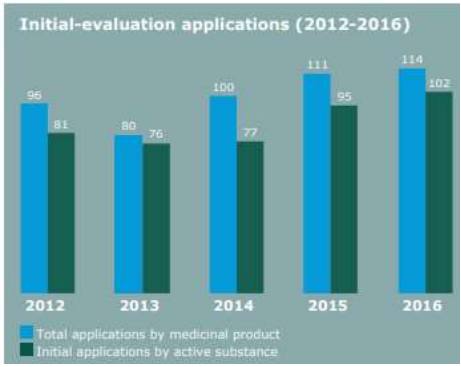
Medicines & Healthcare products Regulatory Agency

Mission and Overview

"We **protect and improve** the health of millions of people every day through the effective regulation of medicines and medical devices, underpinned by science and research"

- Government trading fund and an executive agency of the Department of Health and Social Care (DHSC)
- Around 1350 staff

UK Rapporteurships for centralised applications - 2016



From EMA Annual Report 2016

The future:

Brexit timeline: 23:00 GMT on 31 October 2019

If the UK and EU ratify the withdrawal agreement before then, the UK will leave on the first day of the following month

Scenarios:

1. **DEAL** - Ratification of withdrawal agreement UK and MHRA in Transition Period until 31 December 2020

2. **NO DEAL** – MHRA as freestanding regulator from 1 November 2019

No deal preparations:

- Statutory instruments passed by parliament
- Guidance on MHRA website

https://www.gov.uk/government/collections/mhra-guidance-and-publications-on-a-possible-no-deal-scenario

- Grandfathering of EMA licenses
- Transitional arrangements: Different options for 'in-flight' procedures
- CAPconversion@mhra.gov.uk for Brexit enquiries

CHMP Procedure on exit day	End of Procedure (usually Day 210)	Day 181-209	Day 180	Day 121 – 179	Day 120	Day 80 - 119	Before Day 80
Application status	Application is the subject of a CHMP positive scientific opinion	Assessment of Responses	In Clock Stop List of outstanding issues available	Assessment of Responses	In Clock Stop Review of scientific data available and List of Questions sent to applicant.	Application in the first assessment phase	
Applicant action	Submit application to MHRA for determination in line with CHMP Scientific Opinion[1]	(i) Submit EU application and responses to MHRA to complete assessment tailored to outstanding issues or (ii) await CHMP opinion then ask MHRA to complete its assessment	(i) When available, submit responses and the EU application to MHRA for In-Flight Assessment or (ii) Await Day 210 CHMP opinion and submit for Targeted Assessment if eligible.			(i) Submit EU application to MHRA for independent assessment whilst CHMP assessment continues or (ii) Await CHMP opinion then submit for targeted assessment if eligible	
Fee payable	No fee	No fee	No fee			In accordance with published fee schedule	
MHRA timeline	Determination as soon as practicable after submission and not later than Commission Decision	Assessment decision followed by determination as soon as practicable and not later than Commission Decision	(i) 60-day timetable with provisional assessment decision no later than 42 days after start (aligned to published CHM schedule) (ii) Targeted assessment with provisional assessment decision 42 days after start (See guidance on targeted assessment)			In accordance with published assessment guidance	

No deal - guiding principles at MHRA

- Alignment with European timelines: Renewals, orphan designations etc.
- Orphan products: there will be an Orphan scheme European decision taken into consideration
- Plasma Master Files: Recognised
- Biosimilars: Reference product from EU possible
- European Guidelines continue to apply as they stand on exit day

Underpinned by MHRA and EU mutual recognition agreements and continued participation in ICH, PIC/S, ICMRA

No deal - New Assessment Routes:

- Targeted assessment
- MHRA will evaluate the marketing authorisation application together with the Committee for Medicinal products for Human Use (CHMP) assessment reports submitted by the applicants, and will reach its opinion on approvability within 67 days of submission of a valid application to the MHRA
- Available for products containing new active substance and biosimilars

- Accelerated assessment Pathway
- MHRA will evaluate the marketing authorisation application and will reach its opinion on approvability within 150 days of submission of a valid application.
- available for all products containing new active substances, including biologicals for whom the applicants wish to obtain a marketing authorisation in the UK

No deal - New Assessment Routes ctd:

- Rolling Review pathway
- new route for marketing authorisation applications intended to enhance development of novel medicines. It does this by offering on-going regulatory input and feedback enabling the applicants to ‘get it right first time’ and reduce attrition due to avoidable regulatory pitfalls.
- available for all products containing new active substances, including biologicals for whom the applicants wish to obtain a marketing authorisation in the UK

https://www.gov.uk/guidance/guidance-note-on-new-assessment-routes-in-a-no-deal-scenario#accelerated-assessment-pathway

DEAL: Transition period

Details under negotiation

- No UK Rapporteurships
- UK recognises decisions taken at EMA level
- UK to participate in EMA committees if it is in the interest of patient safety for EU or UK

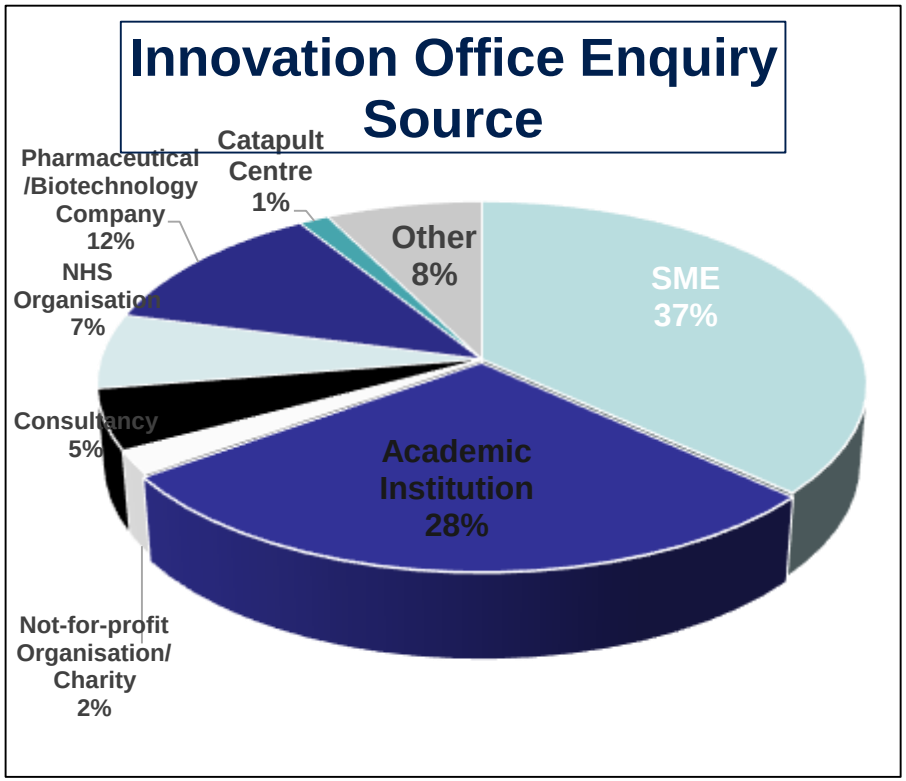
Brexit-independent offerings from MHRA

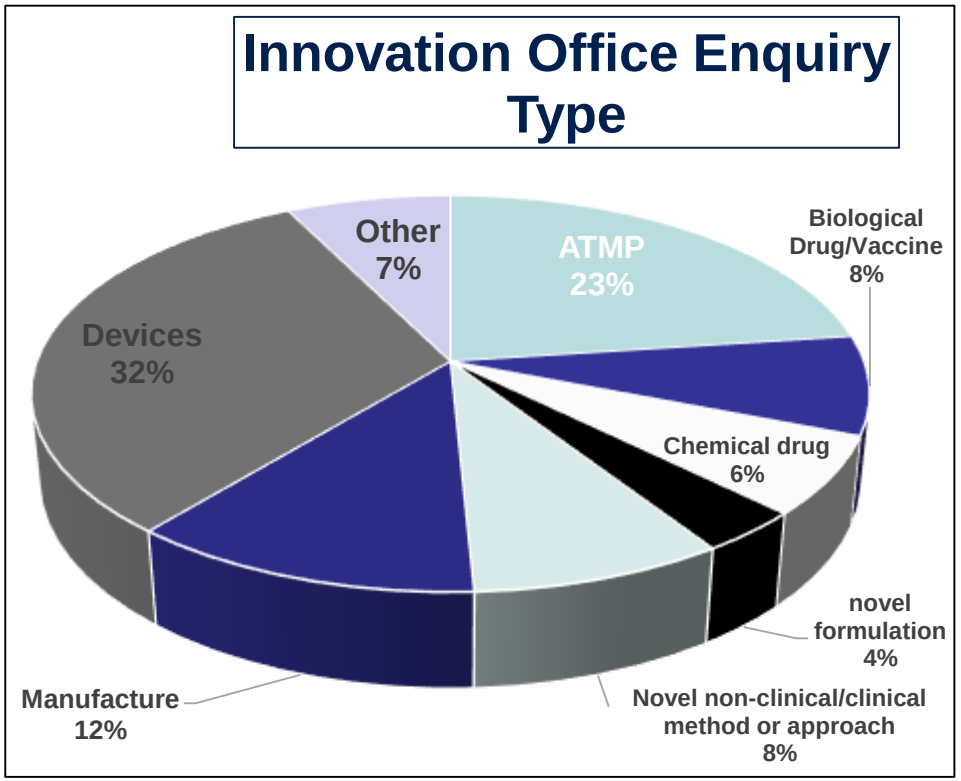
MHRA Innovation Office

- Launched March 2013
- Encourage early dialogue with researchers and companies
- Help clarify regulatory requirements
- Applicable to all of the MHRA product areas
- Provide regulatory / informal advice or scientific advice
- Request at any stage of product development
- Irrespective of existing guidelines
- Case studies published to encourage enquiries

- Since its introduction, the Innovation Office has responded to ~800 queries and held ~200 regulatory meetings.

Innovation Office - enquiry types and users





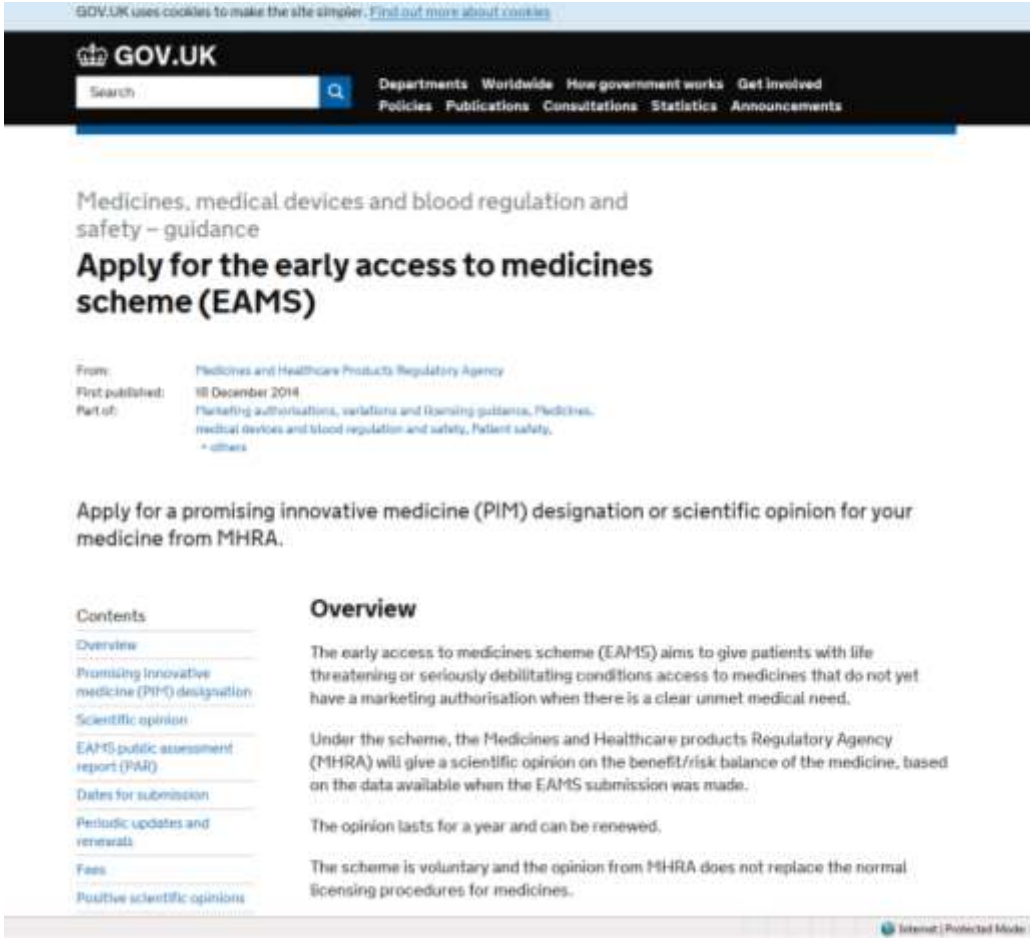
Regulatory Advice Service for Regenerative Medicine (RASRM)

- Also known as the ‘One Stop Shop’ – unique in providing access to all national regulators
- Launched in 2014 and received approx. 75 enquiries to-date
- Provides consolidated advice on Advanced Therapy medicines
- Other agencies such as such as the Health & Safety Executive (HSE) and Department for Rural Affairs (Defra) give advice when relevant
- RASRM enquiries are submitted via the usual Innovation Office online form: https://info.mhra.gov.uk/forms/innovation_form.aspx

MHRA Regulating Medicines and Medical Devices
HTA Human Tissue Authority
Human Fertilisation & Embryology Authority
NHS Health Research Authority
defra Department for Environment, Food and Rural Affairs
NICE National Institute for Health and Care Excellence
HSE Health & Safety Executive

Early Access to Medicines

- The MHRA launched the scheme April 2014
- Dedicated MHRA webpage with detailed guidance and application forms/ templates
- EAMS coordinator to ensure swift and efficient operation of the scheme: eams@mhra.gsi.gov.uk
- https://www.gov.uk/apply-for-the-early-access-to-medicines-scheme-eams



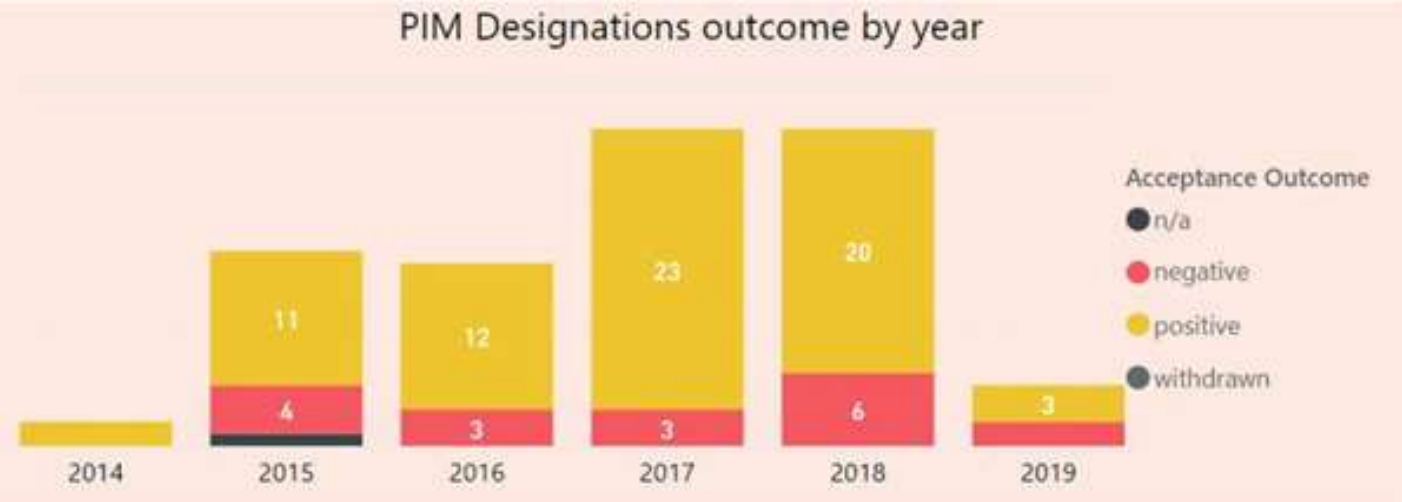
Early Access to Medicines

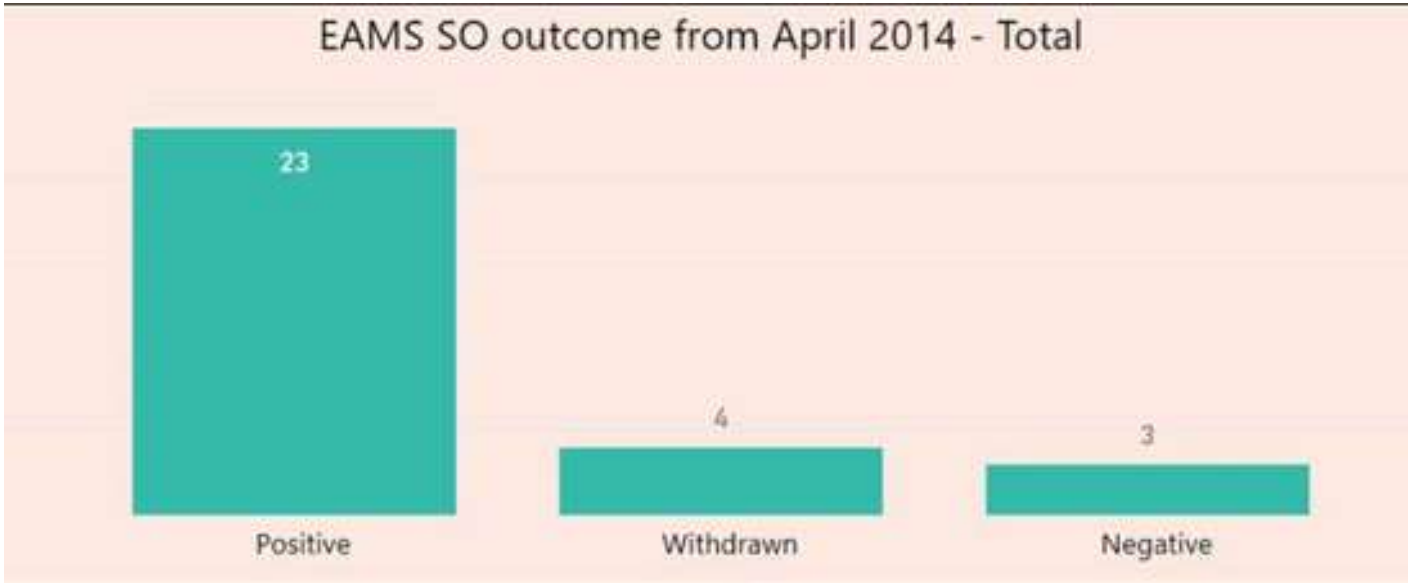
- medicines that are still being developed but cannot yet be made available as licensed treatments
- not a substitute for appropriate clinical development and inclusion of patients in well designed clinical studies remains the preferred option
- Primarily aimed at medicines that have completed Phase III trials, but may be applied to completed Phase II trials in exceptional circumstances

The criteria of suitability:

- ✓ High unmet need (life-threatening, seriously debilitating)
- ✓ product offers benefit or significant advantage over and above existing treatment options
- ✓ Potential adverse effects likely to be outweighed by benefit
- ✓ The Applicant is able and willing to supply the product and to manufacture it to a consistent quality standard (GMP)

PIMS and EAMs statistics since 2014





Scientific Advice

- The MHRA can provide both regulatory and scientific advice to companies on any type of medicinal product;
- It can provide advice on all aspects of development (regulatory, non-clinical, quality and clinical)
- Approx. 300 scientific advice meetings are held per year;
- Companies can request to have a scientific advice meeting at any stage of development; they are most useful before submission of a Marketing Authorisation Application (MAA) but can also be after an MAA is granted e.g. concerning a variation to an existing product licence;

- See MHRA website for the on-line request form at:
- http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Informationforlicenceapplicants/Otherusefulservicesandinformation/Scientificadviceforlicenceapplicants/Requestforscientificadviceform/index.htm

MHRA broader scope advice

- Useful for innovative approaches that are not tied to just one development programme
  - *e.g.* novel trial design, new manufacturing process
- As approaches are new formal written answers are not given
- Informal feedback given at a face-to-face meeting

Parallel scientific advice from the MHRA and NICE

- Since April 2010.
- After a joint scientific advice meeting the MHRA and NICE will produce separate documents to answer the respective questions raised by the Company.

Thank you!

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