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Quo Vadis? The Emerging Role of the Medicines and Healthcare Products Regulatory Agency (MHRA) in an Evolving Regulatory Landscape

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BACKGROUND

- The regulatory and reimbursement landscape is rapidly evolving, with an increasing focus on faster access to treatments. This includes a drive towards closer collaboration between health agencies (HA) and health technology assessment (HTA) bodies. Such as recent announcements by the MHRA and the National Institute for Health and Care Excellence (NICE) in the United Kingdom (UK) to further align assessment decisions and share operational information.
- Evidence standards are also continuously evolving. While well-conducted clinical trials remain the cornerstone of demonstrating a treatment's efficacy and safety, decision-makers increasingly allow the use of real-world data (RWD) to address evidence gaps, resolve uncertainties, and understand real-world patterns of use, effectiveness and safety.
- Following the UK's withdrawal from the European Union (EU), the MHRA initially remained closely aligned to the European Medicines Agency (EMA), allowing for reliance approval pathways through recognising market authorisations (MA) granted by other trusted regulators. However, recent announcements suggest a stronger strategic focus on establishing the MHRA as a fully independent regulator.

OBJECTIVE

- The objective of this research was two-fold; first, to understand the evolving landscape of regulatory filing routes, evidence requirements, and decision-making processes in the UK, EU and United States (US). And second, building on these findings, to describe the MHRA's potential future position as an independent regulator in the post-Brexit environment, including potential implications on reimbursement processes in the UK.

METHODS

- We conducted a pragmatic targeted review of publicly available information from three regulators (Food and Drug Administration [FDA], EMA, and MHRA). Sources included official websites, guidance documents, white papers, press releases, and relevant legal texts outlining regulatory frameworks.
- Prior to the information gathering, we defined key concepts of interest to guide the review, including filing routes and processes, evidentiary requirements, and decision-making frameworks.
- Searches were initially restricted to the past three years (2022-2025) but were extended where such a timeframe was not practical or feasible (e.g., for legal texts). A snowballing approach was used to identify supplementary information addressing the above concepts.
- The review focussed exclusively on new molecular entities and initial filing options. Areas out of scope included orphan designations, medical devices, highly specialised or purely paediatric indications, and drug manufacturing/quality assurance processes.
- A thematic analysis was conducted to compare the regulatory approaches across the Has and assess the potential impact of the MHRA's future direction on regulatory and reimbursement pathways in the UK.

RESULTS

Current regulatory landscape in the US, EU and UK

- The FDA and MHRA offer a unified filing process, with internal expert groups conducting the assessment and functioning as the decision-maker. This contrasts with the EMA's semi-devolved procedure reflective of the EU's Member States structure and power-sharing agreements.
- All three agencies rely on well-conducted (randomised) clinical trials that demonstrate a statistically significant difference in patient-relevant endpoints for initial drug approval. The FDA requires raw patient-level data access for independent verification, whereas the EMA and MHRA typically rely on company summary reports but can request raw data on an ad-hoc basis during MA assessment.
- All agencies acknowledge the value of high-quality RWD, although they differ in its primary use case.
- Foreign data are acceptable if applicable to local practice.

The MHRA's emerging role as an independent regulator

- The MHRA is shifting away from an initial post-Brexit reliance on international recognition pathways to focus on the national assessment procedure. In line with the UK Government's 10 Year Health Plan, this will allow the MHRA to shape operational processes, evidence needs and risk assessments.
- As part of this effort, the MHRA has signalled its willingness for a risk-proportional approach to allow greater flexibility in evidence requirements for innovative treatments addressing unmet needs.
- This includes the potential for stronger surrogate endpoint considerations to accelerate UK launches and upcoming guidance on the use of RWD to address evidence gaps.
- The Early Access to Medicines Scheme and Innovative Licensing and Access Pathway are tools to promote innovation, rapid medicines development and early access.

Figure 1. Simplified overview of drug approval timelines

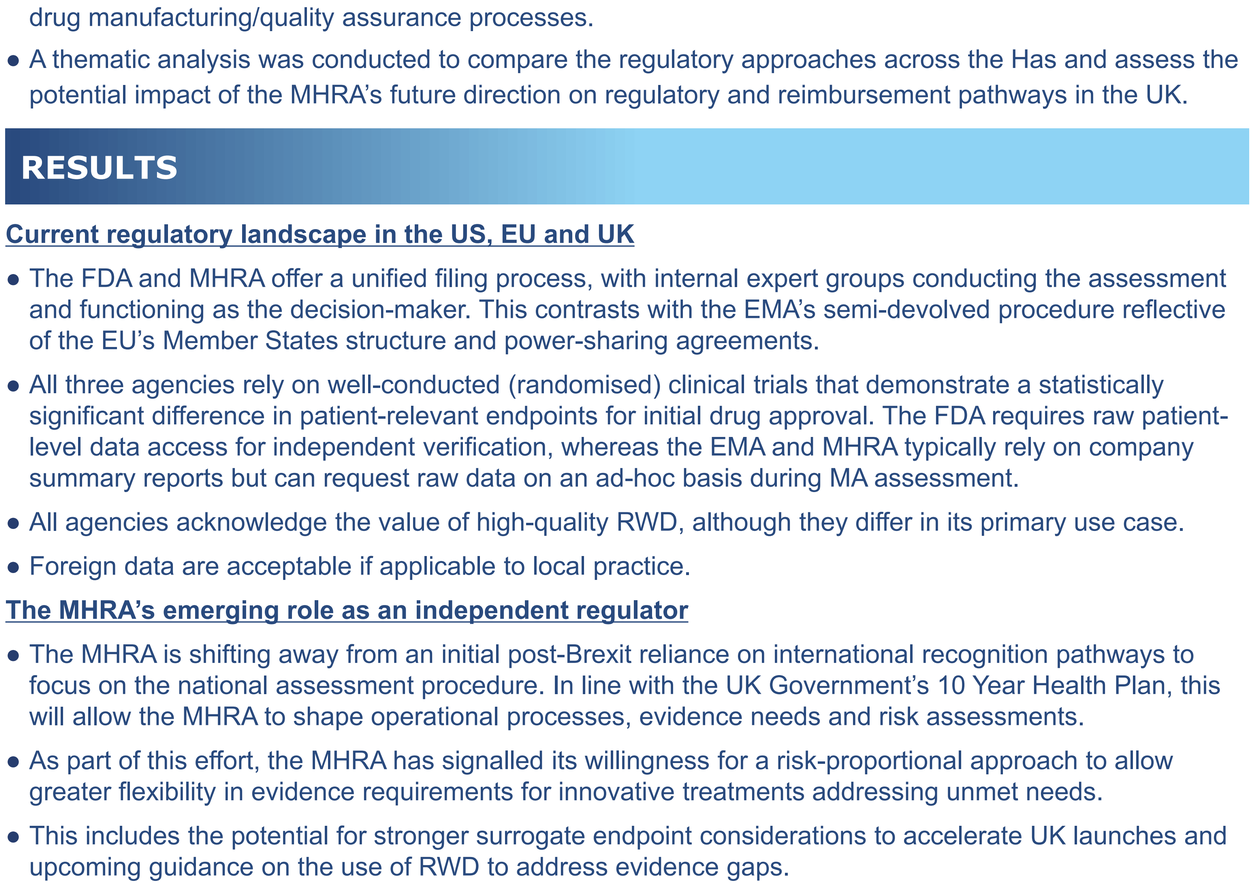

Table 1. Overview of drug approval pathways and requirements

	FDA	EMA	MHRA
Filing routes and processes			
Main filing route	• New Drug Approval	• Centralised Procedure	• National Route
Other available routes	• Expedited pathways (Fast Track, Breakthrough Therapy, Priority Review, Accelerated Approval)	• Alternative routes (decentralised/ mutual recognition), Accelerated Assessment	• International Recognition Procedure, Concurrent Review (Project ORBIS and ACCESS Consortium), Rolling Review
Review body	• Centralised process led by internal FDA scientists (CDER) • Optional external Advisory Committee	• Assessment by two "Rapporteur" teams from different EU Member States • Peer review and final recommendation by CHMP	• National scientific review or international recognition • Expert advice by the CHM
Final decision-maker	• FDA internal review team and senior management	• European Commission	• MHRA internal team
Assessment methodology	• Company summary data and report • Raw patient-level data access required for independent verification and additional subgroup and safety analyses by the FDA	• Relies on the company's statistical analyses and study reports • EMA can request raw data on ad-hoc basis (pilot project to assess routine raw data access)	• Relies on company's statistical analyses and study reports • MHRA can request raw data to perform additional analyses.
Evidence requirements			
Clinical trial data requirements	• Well-controlled, randomised trials • Single-arm trials and/or external controls allowed under specific circumstances • Strong emphasis on statistically significant effects on a "hard" clinical endpoint (e.g., survival, disease progression, or QoL)	• Well-controlled, randomised trials • Single-arm trials and additional available data (e.g., existing studies in literature) also considered • Refers to ICH guidelines for efficacy and safety endpoints, as well as disease area specific guidance	• Well-controlled, randomised trials • Single-arm trials allowed under specific circumstances • Endpoints must be scientifically sound, ethically justified, and adequately reflect the study's aim, (e.g., efficacy and long-term safety)
RWD use and requirements	• Primarily used to support a new indication for an already approved drug or address post-approval study requirements • Data quality and scientifically rigorous study design essential	• Used to support pre-authorisation and post-approval assessments • Data quality, rigorous study design, and fit-for-purpose data essential	• Encouraged for rare diseases and informing decisions on new medicines and devices • Data sources, quality and validation essential
Required subgroup analyses	• Gender, age, race, and disease specific subgroups if applicable	• Guidance on the conduct of subgroup analyses only	• Guidance on the conduct of subgroup analyses only
Data locality	• Foreign data must be applicable to US populations and clinical practice, and have been generated in line with GCP	• Foreign data must have been generated in line with GCP and ethical principles equivalent to EU legislation	• Foreign data must be applicable to UK populations and clinical practice
Diversity	• Diversity Action Plan required to ensure trial enrolment is reflective of US demographics	• Inclusion and diversity plan required to ensure trial populations reflect the diverse groups likely to use the medicinal product	• No specific plan required yet, but trial data must reflect the full diversity of the UK population
Decision-making			

Outcome options	• Approval
	• Refusal to Approve (resubmission required to address shortcomings)
	• Refusal to File (insufficient information provided for a full review)
		2-step approach:
		• EMA decision:
		  • CHMP positive scientific opinion
		  • CHMP Negative opinion
		  • Re-examination of opinion on company request
		• EC decision
		  • Implementing decision
		  • Not implementing decision
			• Grant of MA for 5 years (renewal possible afterwards)
			• Conditional Grant
			• Refusal

Conditional approval	• Accelerated Approval based on surrogate endpoints, requires confirmatory evidence	• CMA for medicines addressing unmet medical needs based on less comprehensive data	• CMA for medicines addressing unmet need or emergency use, where comprehensive data are expected soon

The impact of the MHRA's future direction on UK reimbursement timelines remains uncertain

- Closer alignment between MHRA and NICE decision-making processes and Scientific Advice aim to accelerate UK launches. However, this also presents logistical challenges.
  - NICE committee meetings and guidance documents may need to be public ahead of market approval.
  - The criteria for accelerated NICE assessment are stringent and difficult for most appraisals to meet (e.g., unconditional acceptance of NICE topic selection, no additional data provided after evidence submission, cost-effectiveness approved in first committee meeting, no appeal). This pathway excludes complex submission, for which a definition is currently lacking.
  - It is also unclear how regulatory approval based on lower evidence standards (e.g., short-term or surrogate endpoints) will align with the traditionally conservative nature of NICE committees, which are cautious about accepting uncertainty.

CONCLUSIONS

- The MHRA's shift to a more independent regulator seems to prioritise a risk-proportional approach and greater use of RWD to accelerate patient access. This includes increasing alignment between NICE and the MHRA to cut reimbursement times by 3–6 months.
- While this promises faster access, success depends on resolving the unclear criteria for accelerated NICE review and defining how both agencies will manage the inherent uncertainty from approvals based on less mature evidence.
- Global harmonisation of regulatory requirements has the potential to support equitable access to medicines, yet the impact of divergence by health authorities and HTA bodies remains uncertain.

DISCLOSURES

This project was sponsored by Roche Products Ltd.

ABBREVIATIONS

CDER, Center for Drug Evaluation and Research; CHM, Commission on Human Medicine; CHMP, Committee for Medicinal Products for Human Use; CMA, conditional market authorisation; EC, European Commission; EMA, European Medicines Agency; EU, European Union; FDA, Food and Drug Administration; GCP, Good Clinical Practice; HTA, health technology assessment; ICH, International Council for Harmonisation; MA, market authorisation; MHRA, Medicines and Healthcare products Regulatory Agency; NICE, National Institute for Health and Care Excellence; PDUFA, Prescription Drug User Fee Act; QoL, quality of life; RFI, request for information; RWD, real-world data; UK, United Kingdom; US, United States

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