Expediting the availability of new medicines: What role do priority pathways and special designations play in ICH countries?



Magda Bujar • Neil McAuslane • Lawrence Liberti

Centre for Innovation in Regulatory Science – CIRS, London UK

Introduction

- Time to approval for new medicines is under constant scrutiny, by patients seeking quicker availability of new medicines, regulatory agencies looking to improve processes and pharmaceutical companies seeking a more timely and high-quality review.
- More flexible regulatory approaches have been formalised in ICH jurisdictions, providing options to accelerate the regulatory review process, particularly in response to unmet medical needs.
- CIRS carries out an annual study to monitor regulatory performance to identify the influence of factors such as the use of expedited pathways on new medicines' approval

Definitions

- *New active substance (NAS):* A chemical, biological, biotechnology or radiopharmaceutical substance that has not been previously available for therapeutic use in humans and is destined to be made available as a 'prescription only medicine', to be used for the cure, alleviation, treatment, prevention or in vivo diagnosis of diseases in humans
- *Approval time:* Time calculated from the date of submission to the date of approval by the agency. This time includes agency and company time.
- *Expedited review:* Includes EMA Accelerated Assessment; FDA and PMDA Priority

Objectives

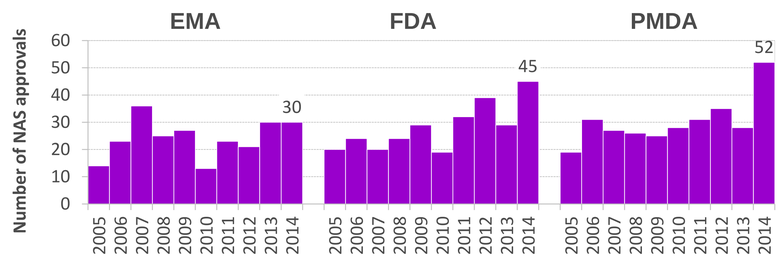
To review approvals of new active substances (NASs) by US FDA, EU EMA, and Japanese PMDA between 2005-2014 in order to evaluate the use by companies of the different review pathways and special designations available and the role they play in expediting the approval of new medicines

Methodology

Data for 825 NASs approved by ICH countries in 2005-2014 were collected from the public domain and for each NAS, the submission and approval dates, expedited pathways and orphan designations were identified to characterise the relation between approval time and review type.

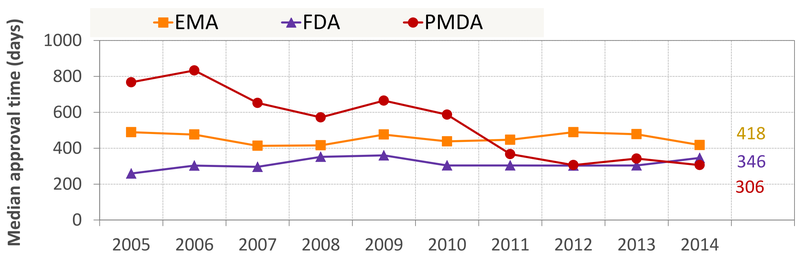
Results

Figure 1a: NAS approval numbers achieved a record high in 2014; PMDA approved the greatest number



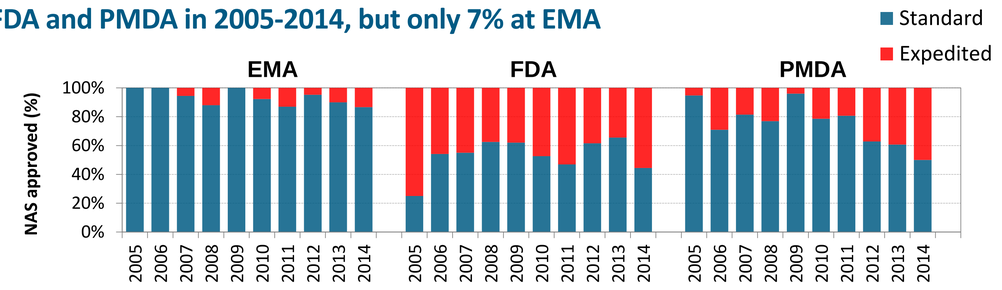
NAS approval numbers - Change from 05-09 to 10-14 — EMA ↓6% — FDA ↑40% — PMDA ↑35%

Figure 1b: NAS median approval times converged within ICH between 2005-2014; PMDA was the fastest in 2014



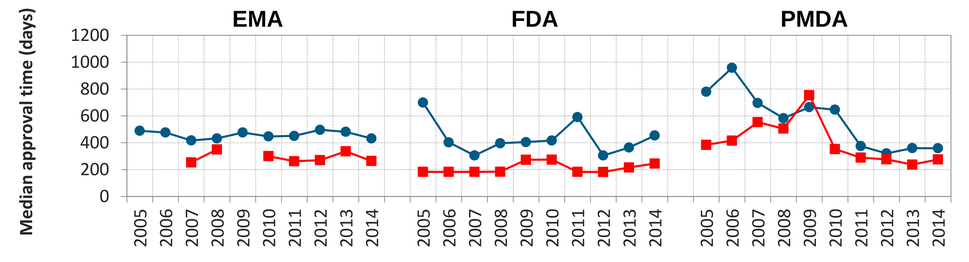
NAS approval times - Change from 05-09 to 10-14 — EMA ↑2% — FDA 0% — PMDA ↓50%

Figure 2a: Expedited reviews made up 44% and 28% of all NASs at FDA and PMDA in 2005-2014, but only 7% at EMA



% of expedited reviews Change from 05-09 to 10-14 — EMA ↑156% — FDA 0% — PMDA ↑107%

Figure 2b: Expedited review median approval times were similar across the ICH agencies in 2014 at 268, 245, and 278 days for EMA, FDA and PMDA



How much faster is expedited than standard review Change from 05-09 to 10-14 — EMA ↑30% — FDA ↓28% — PMDA ↓7%

Figure 3: FDA has the greatest number of mechanisms that can be used to facilitate the development and speed the review of medicines; 2010-2014 NAS numbers and approval times (days) are shown

FDA

		FT	BT	AA	FT/AA	FT/BT	BT/AA	FT/AA/BT	-
Orphan	Standard	509 (4)	0 (0)	622 (2)	304 (3)	0 (0)	0 (0)	315 (1)	335 (10)
	Expedited	257 (16)	193 (1)	319 (1)	177 (6)	986 (2)	126 (3)	142 (2)	275 (9)
Non-orphan	Standard	363 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	387 (63)
	Expedited	239 (15)	0 (0)	0 (0)	0 (0)	242 (3)	0 (0)	0 (0)	230 (17)

EMA

		CA	EC	CA/EC	-
Orphan	Standard	554 (7)	476 (1)	0 (0)	452 (14)
	Expedited	0 (0)	0 (0)	0 (0)	285 (4)
Non-orphan	Standard	547 (6)	517 (1)	0 (0	454 (76)
	Expedited	0 (0)	0 (0)	0 (0)	267 (8)

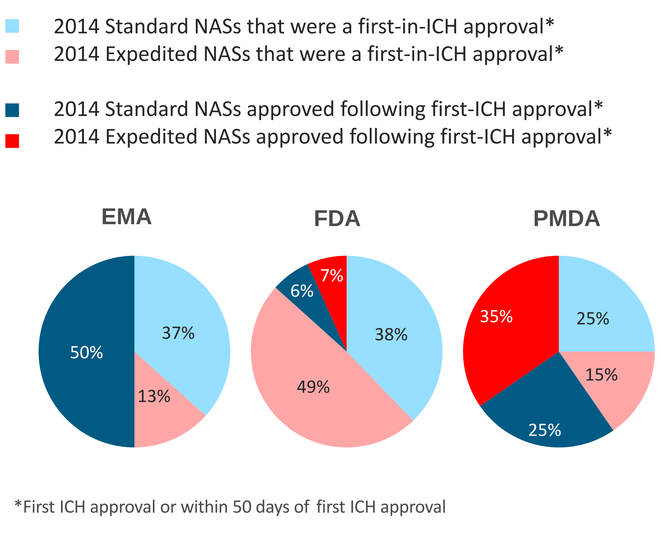
PMDA

		-
Orphan	Standard	0 (0)
	Expedited	273 (46)
Non-orphan	Standard	368 (112)
	Expedited	273 (16)

N1 (N2) = Approval time (Approval number)
FT = FDA Fast Track Development Program
BT = FDA Breakthrough Designation Development and Review Program
AA = FDA Accelerated Approval Program

CA = EMA Conditional marketing authorisation
EC = Exceptional circumstances
- = No products were assessed using a formal expedited pathway

Figure 4: For NASs approved by each agency in 2014, FDA has the highest percentage of first-in-ICH* approvals compared with EMA and FDA, resulting in shortest drug lag to patients



*First ICH approval or within 50 days of first ICH approval

Conclusions

- Expedited pathways and special designations played an important role in FDA and PMDA in accelerating the approval of innovative medicines over the last decade, thereby enabling treatments for diseases with little or no effective medicines, including orphan diseases, to be made available to patients in a timely manner.
- The proportion of expedited reviews was consistent for both parts of the decade for FDA, but PMDA doubled its number of expedited NASs during this time. This relates mainly to a change in process at PMDA, enabling the use of a expedited process for new medicines to meet the needs of Japanese patients.
- However, although Japan historically had the longest review times, the median regulatory approval times in Europe were the slowest amongst the three countries. This is partly due to a lack of wide use of European expedited pathways.
- Although the number of EMA expedited NASs increased only slightly in 2010-2014 compared with 2005-2009, 2010-2014 expedited approval times were considerably faster compared with standard and in 2014 were very similar to expedited speed at both FDA and PMDA.
- The scarce use of expedited pathways in the EU suggests that either the criteria for an accelerated approval are much stricter for EMA than FDA and PMDA or that certain aspects of the process limit its use by companies or its designation by the agency.
- Indeed a perception survey carried out by Liberti and colleagues showed that 87% of respondents believe that the EMA pathway either does not meet the goal or needs improvements to expedite reviews of important new medicines.
- Based on the role expedited reviews play in both USA and Japan, wider use of the EMA accelerated pathway or the creation of new facilitated routes may be needed to ensure the timely availability of important new medicines, including orphan NASs, to patients in Europe.

Data Source

CIRS Regulatory Review Times database

Bibliography

Bujar M., McAuslane N. 2014. *R&D Briefing 54: New Drug Approvals in ICH Countries 2004-2013: Focus on 2013. Centre for Innovation in Regulatory Science*. Available at: http://circsi. org/sites/default/files/CIRS_R&D_Brief ing_54_%20ICH_ approval_times_2004-2013_22 apr2014.pdf

Bujar M., McAuslane N. 2014. *R&D Briefing 55*: *The impact of the changing regulatory environment on the approval of new medicines across six major authorities 2004-2013. Centre for Innovation in Regulatory Science*. Available at: http://circsi.org/sites/default /files/R&D%20Briefing%2055%2016122014. pdf

Liberti L et al: Adaptive Licensing and Facilitated Regulatory Pathways: A stakeholder perception survey. Presented at the annual Winter Meeting of the WHO Collaborating Centre for Pharmaceutical Policy and Regulation, Utrecht University, Utrecht, The Netherlands. January 13, 2015.

U.S. Department of Health and Human Services. 2014. *Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics.* Available at http://www.fda.gov/downloads/drugs/guidanc ecomplianceregulatoryinformation/guidances/ucm358301.pdf

Center For Innovation in Regulatory Science

Mission
To maintain a leadership role in identifying and applying scientific principles for the purpose of advancing regulatory and HTA policies and processes in developing and facilitating access to medicinal products

Contact
mbujar@cirsci.org
mcauslane@cirsci.org
lliberti@cirsci.org

Presented on 13-15 April 2015 at the 2015 EuroDIA, Paris, France