Review system for NDA approval in the USA and Japan and their performance of review

The 6th Kitasato University-Harvard School of Public Health Symposium

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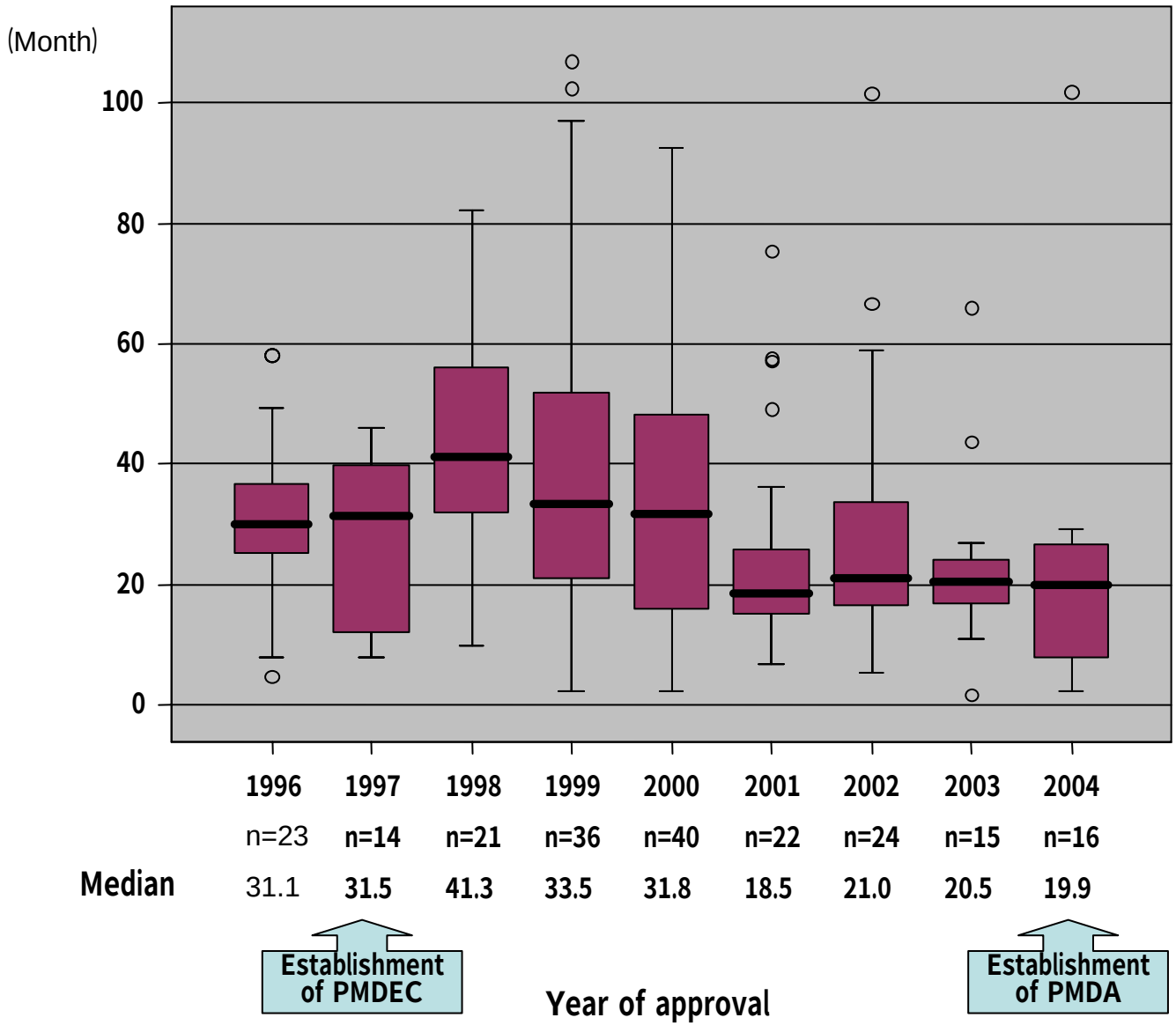
- Approval times of NMEs in Japan
- Staff scale of regulatory agencies
- Workloads on non-approvals

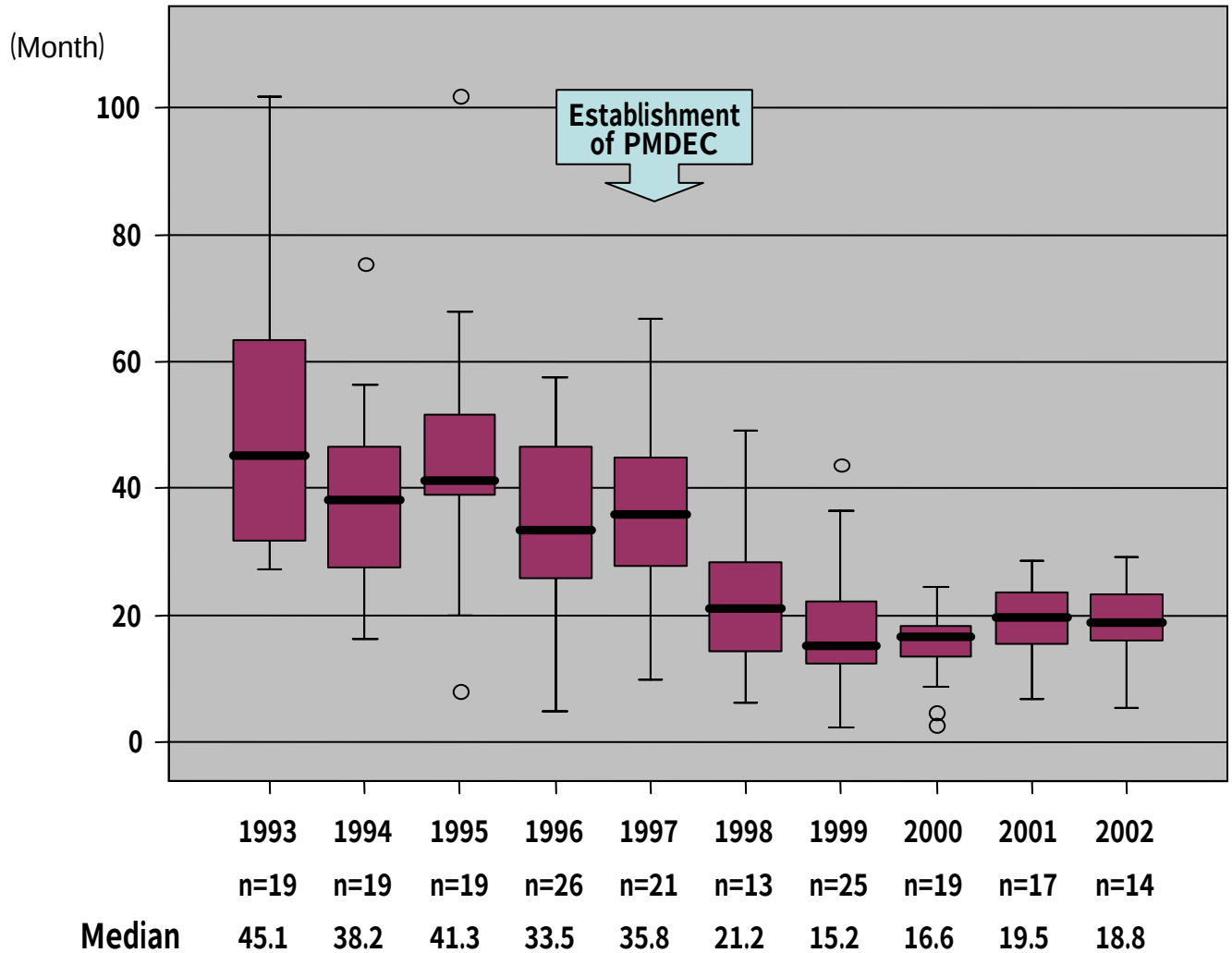
Approval times of NMEs in Japan by the year of approval

Approval times have decreased considerably

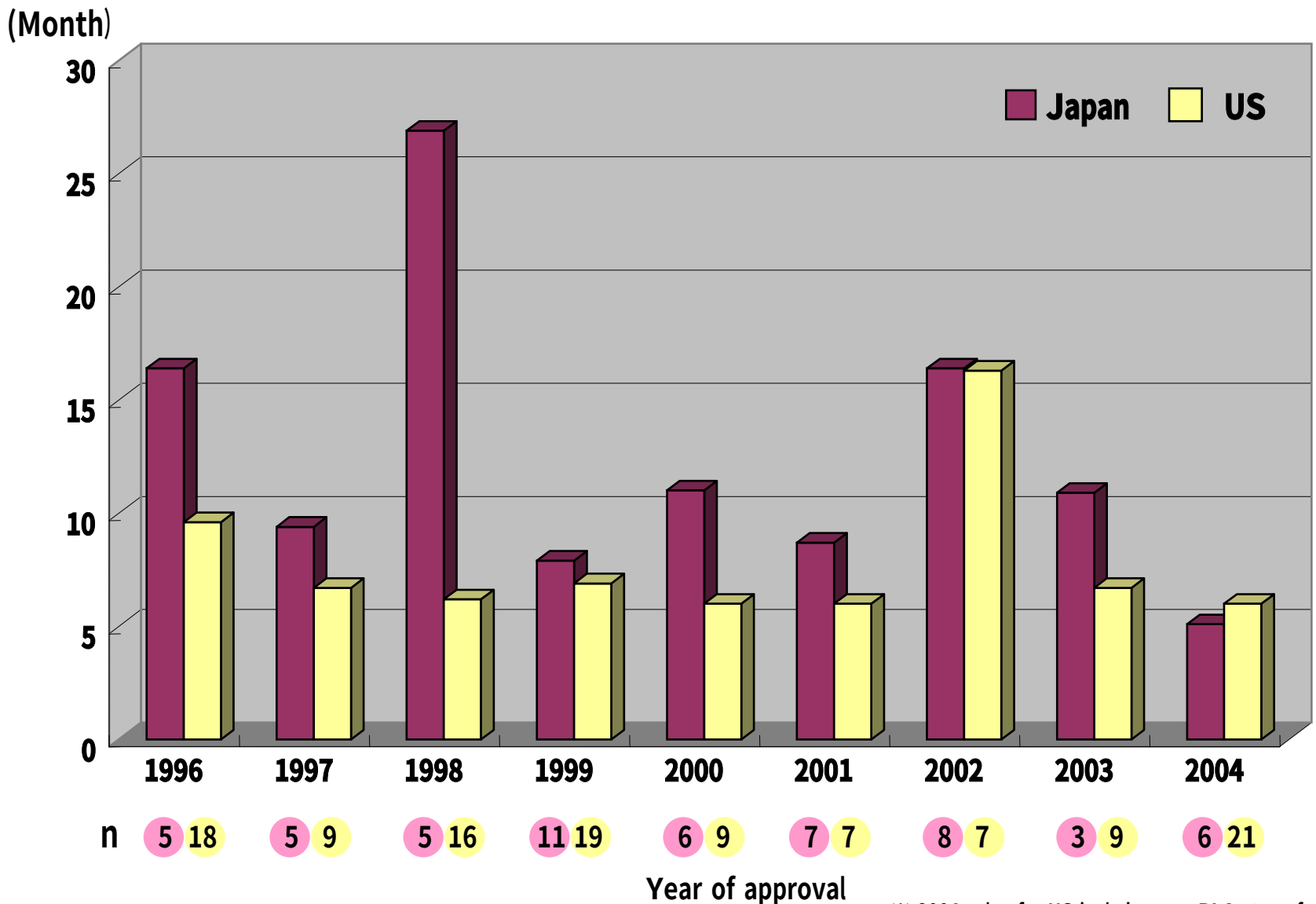


Approval times of NMEs in Japan by the year of NDA submission

Establishment of PMDEC was very effective



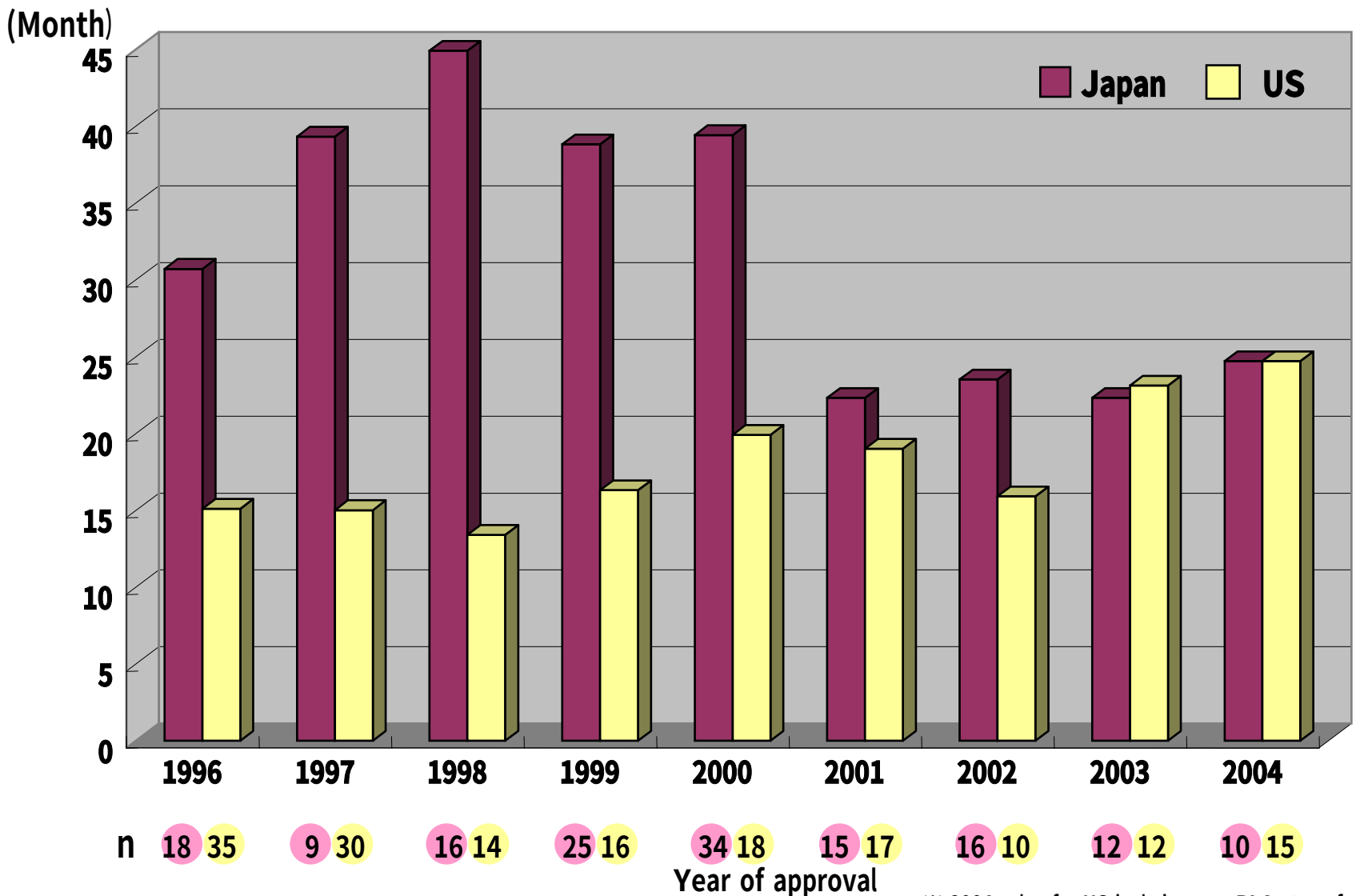
Approval times for priority NMEs by the year of approval (median)



※ 2004 value for US includes new BLAs transferred from CBER

Approval times for standard NMEs by the year of approval (median)

Approval times have recently become close to the US



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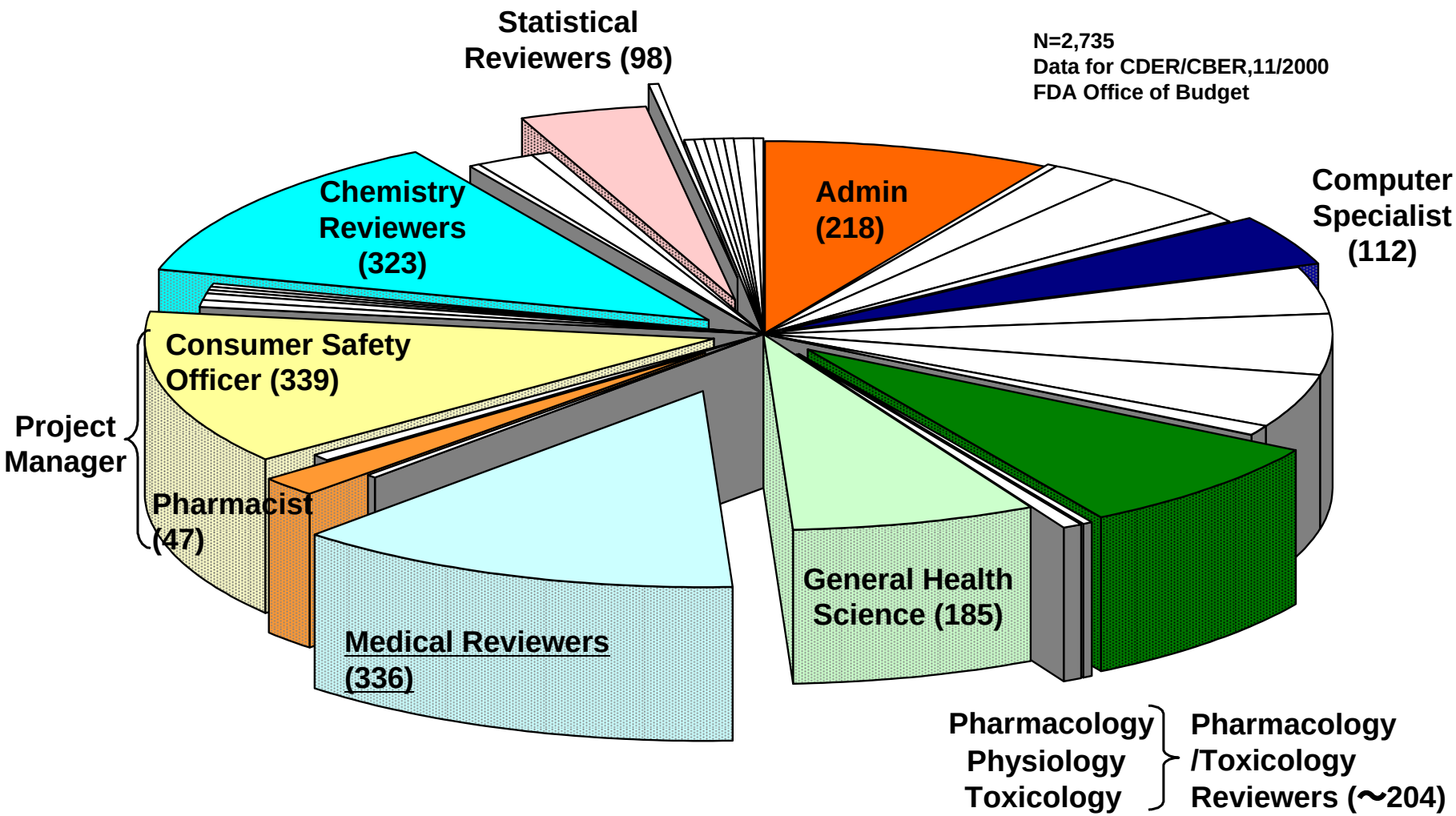
Comparison of the time goals and the staff between the PMDA and CDER

Aiming at almost the same performance with only 1/10 staff

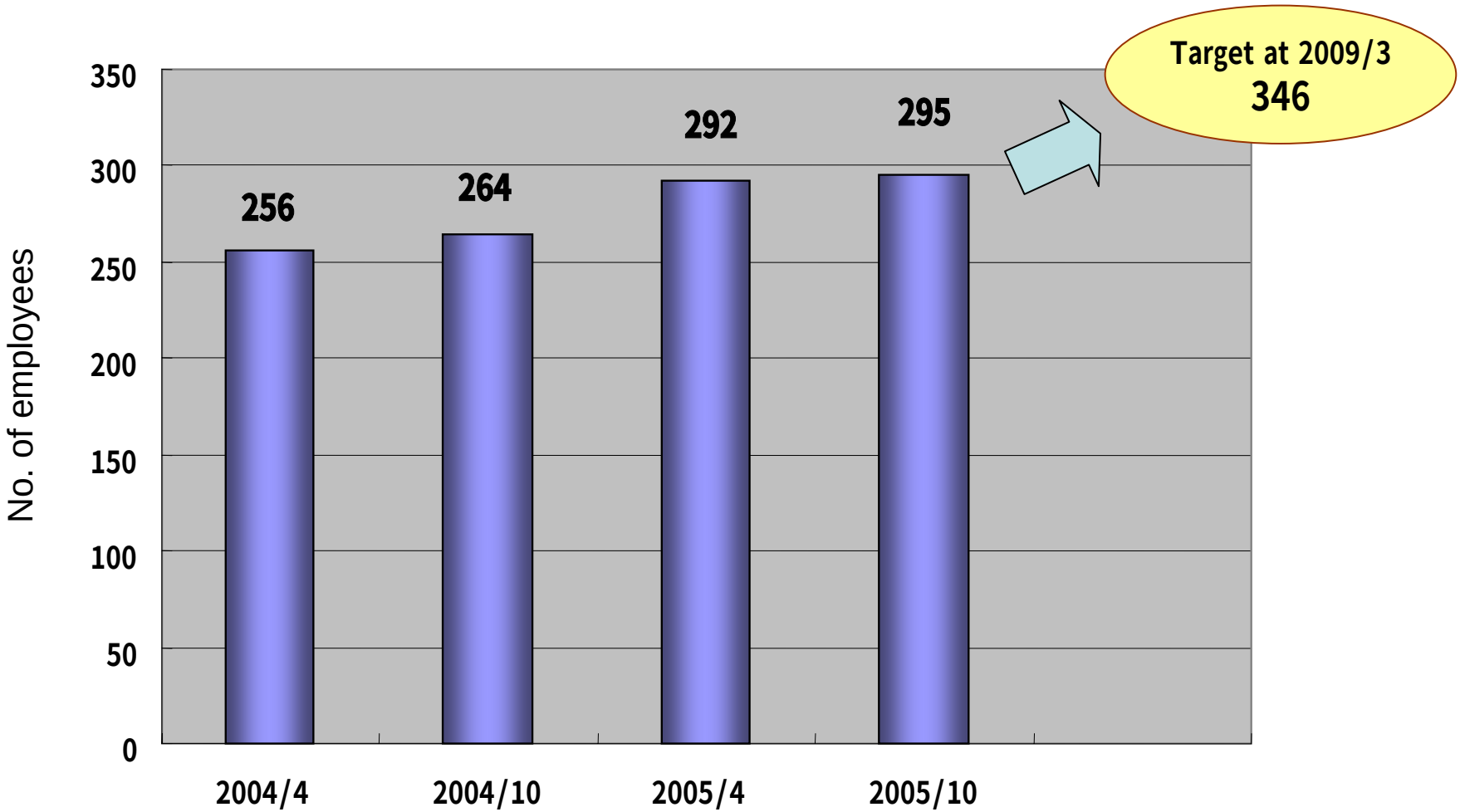
	PMDA	CDER
Time goals for review	Priority: 50% in 6M Standard: 70-80% in 12M	Priority: 90% in 6M Standard: 90% in 10M
No. of employees	295 (As of October, 2005)	2,395 (FY 2005)

Reviewers in the FDA



Source: K. Todaka. Clin Eval *31* 567-71(2004)

Number of employees of the PMDA



Voices of CDER's reviewers -1

Office of Inspector General's survey
401 responses from CDER (estimated response rate; 47%)

Reviewer concerns about time pressures

40% of respondents who had been at FDA at least 5 years indicated that the review process had worsened in terms of allowing for in-depth, science-based reviews.

6M for a priority review: *inadequate* 58%
10M for a standard review: *inadequate* 25%

Less use of advisory committees

FDA managers pointed out that they have little time to hold these meetings

No. of AC meetings CDER held for NDAs

Year	1998	2001
No. of AC meetings	40	23

Source: "FDA's Review Process for New Drug Applications: A Management Review" OFFICE OF INSPECTOR GENERAL. March 2003. (http://oig.hhs.gov/oei/reports/oei-01-01-00590.pdf)

Voices of CDER's reviewers -2

Even FDA has many problems

Workloads are contributing to staff turnover

On an internal CDER survey, 50% of reviewers indicated that their workloads are influential reasons to consider leaving FDA.

Attrition rates within CDER for FY 2001

Medical officers	Pharmacologists	Overall
8.4%	6.9%	5.5%

Less time for reviewers to participate in professional development and to conduct research to improve drug development

- 59% indicated that they have little time to participate in professional development activities.
- Reviewers have little time to conduct research on drug development using the clinical trial databases FDA has obtained from sponsors.

Source: "FDA's Review Process for New Drug Applications: A Management Review" OFFICE OF INSPECTOR GENERAL. March 2003. (http://oig.hhs.gov/oei/reports/oei-01-01-00590.pdf)

Number of employees of regulatory agencies in EU

Much more employees are secured in EU

UK	France	Germany
747	About 900	About 1,100
MHRA 2003/04 Annual report Average number of staff employed during the year	AFSSAPA HP Number of professionals	BfArM HP Number of employees including administrative staff

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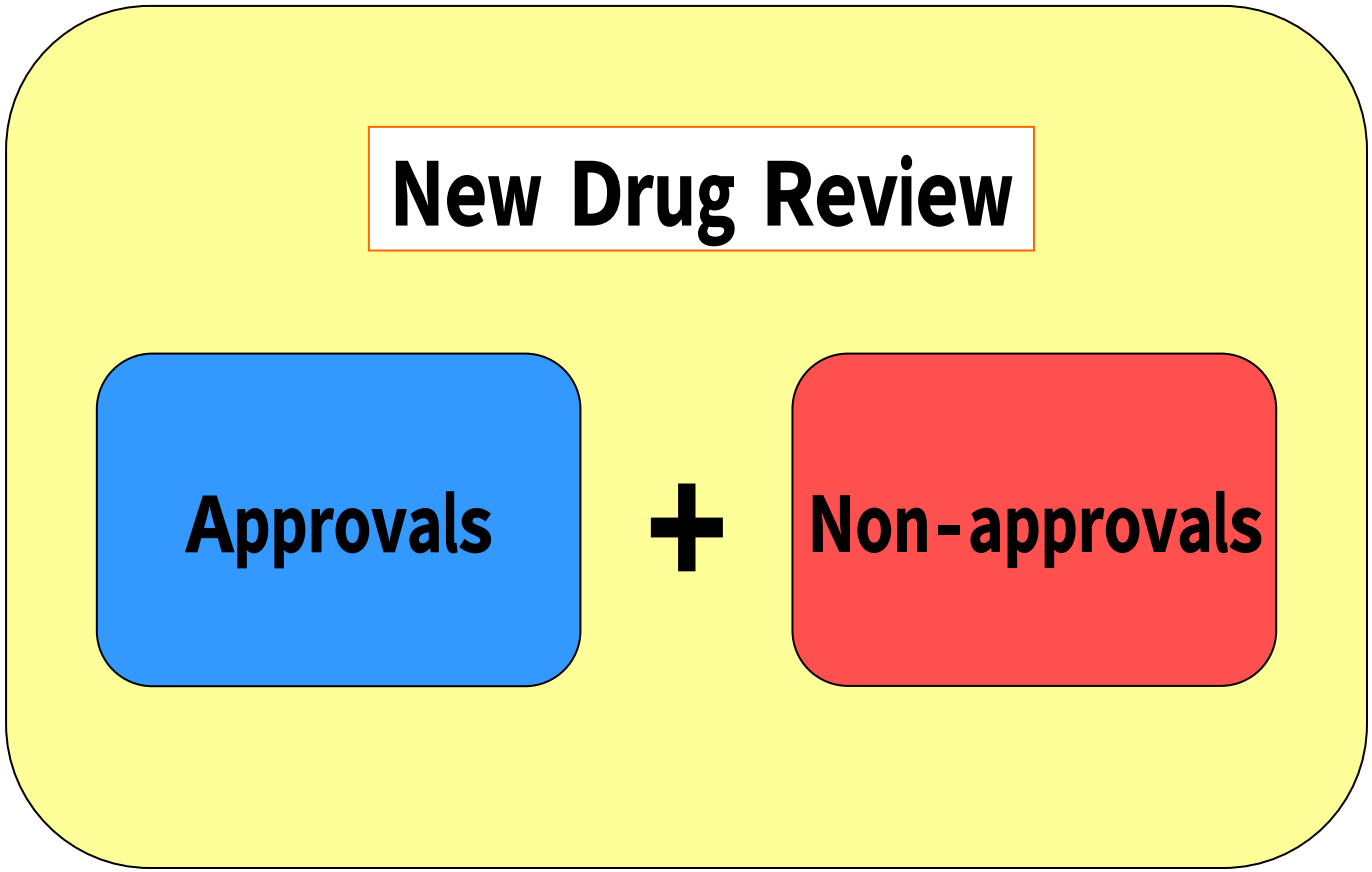

How about the workloads for non-approvals?

Review progress of not-approved NDAs submitted after 1997 (median)

Non-approvals seem to take longer times

	Non-approvals*		Approvals	
	Month	n	Month	n
First interview	2.4	14	2.0	128
Last interview	8.7	14	3.3	128
Review report (1)	15.4	2	12.0	132
Expert discussion (1)	16.3	6	12.7	110
Notification of non-approvability	12.4	6	-	
Sponsor's acceptance of withdrawal	20.1	16	-	
Approval	-		16.3	145

* :Data of only 16 non-approvals

Source; OPIR Research Paper No.24

PMDA's review results of new drugs in FY2004

	NDAs	Withdrawn	Approved	Under review
Submitted before FY2004	140	12	41	87
Submitted in FY2004	89	4	17	68
Total	229	16	58	155

74

Source: PMDA annual report

1/5 were non-approvals in FY2004

Non-approvable NDAs could be labor intensive

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Influence the review progress of approvable NDAs*? ? ?*

Measure

Further use of pre-NDA consultation

Thank you for your attention