Application of PBBM in regulatory submissions – Clinical, NDA/MAA & post approval

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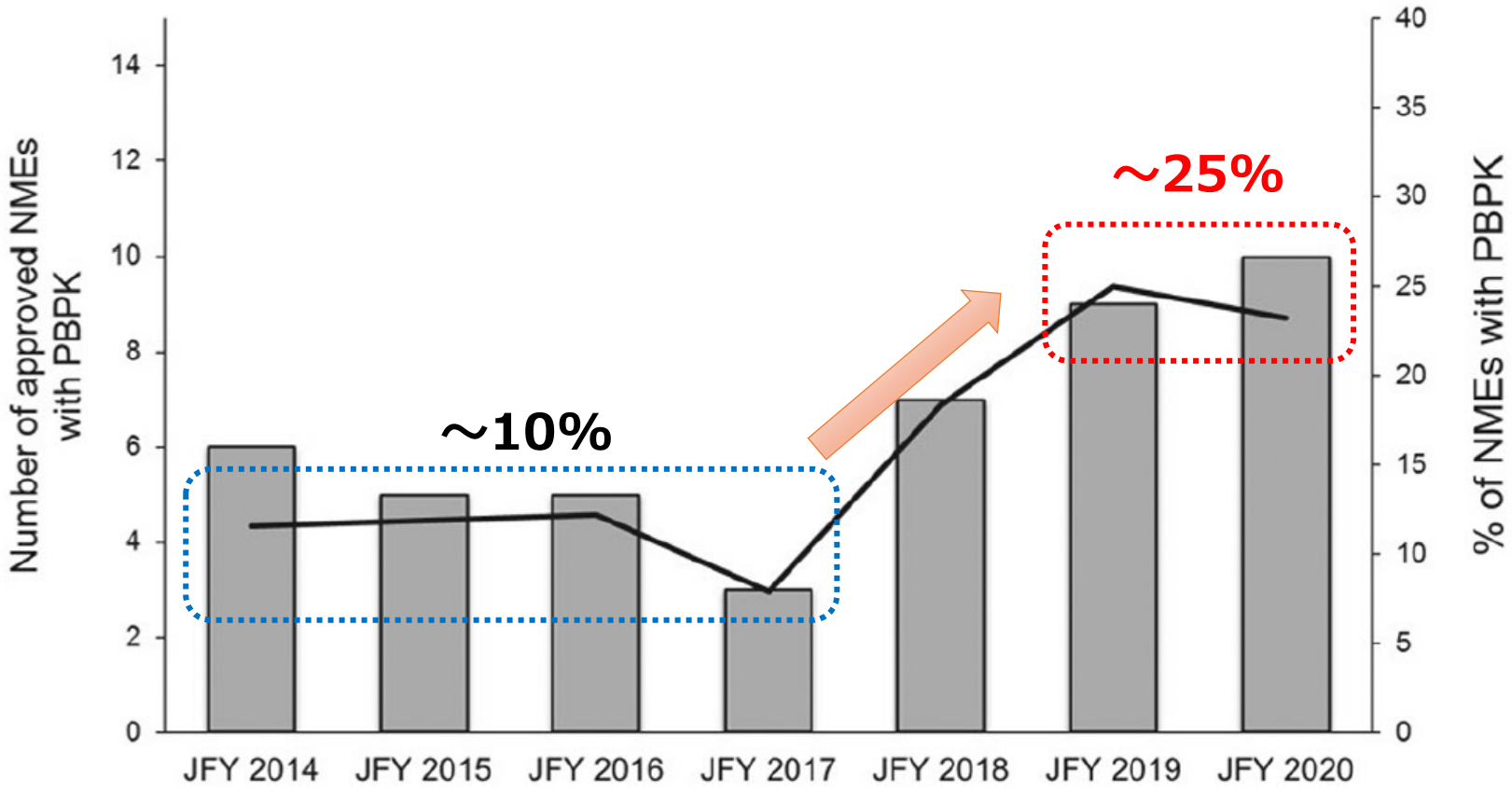
Trends in the number of PBPK model analysis used in application



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Review experience of quality assurance using PBBM at PMDA

- The number of applications using PBPK analysis are increasing.
- Until now, several applications was submitted in Japan.
- PMDA has several review experiences of quality assurance using PBBM.

PMDA's Action to Address M&S

M&S Project Team（M&S PT） in PMDA

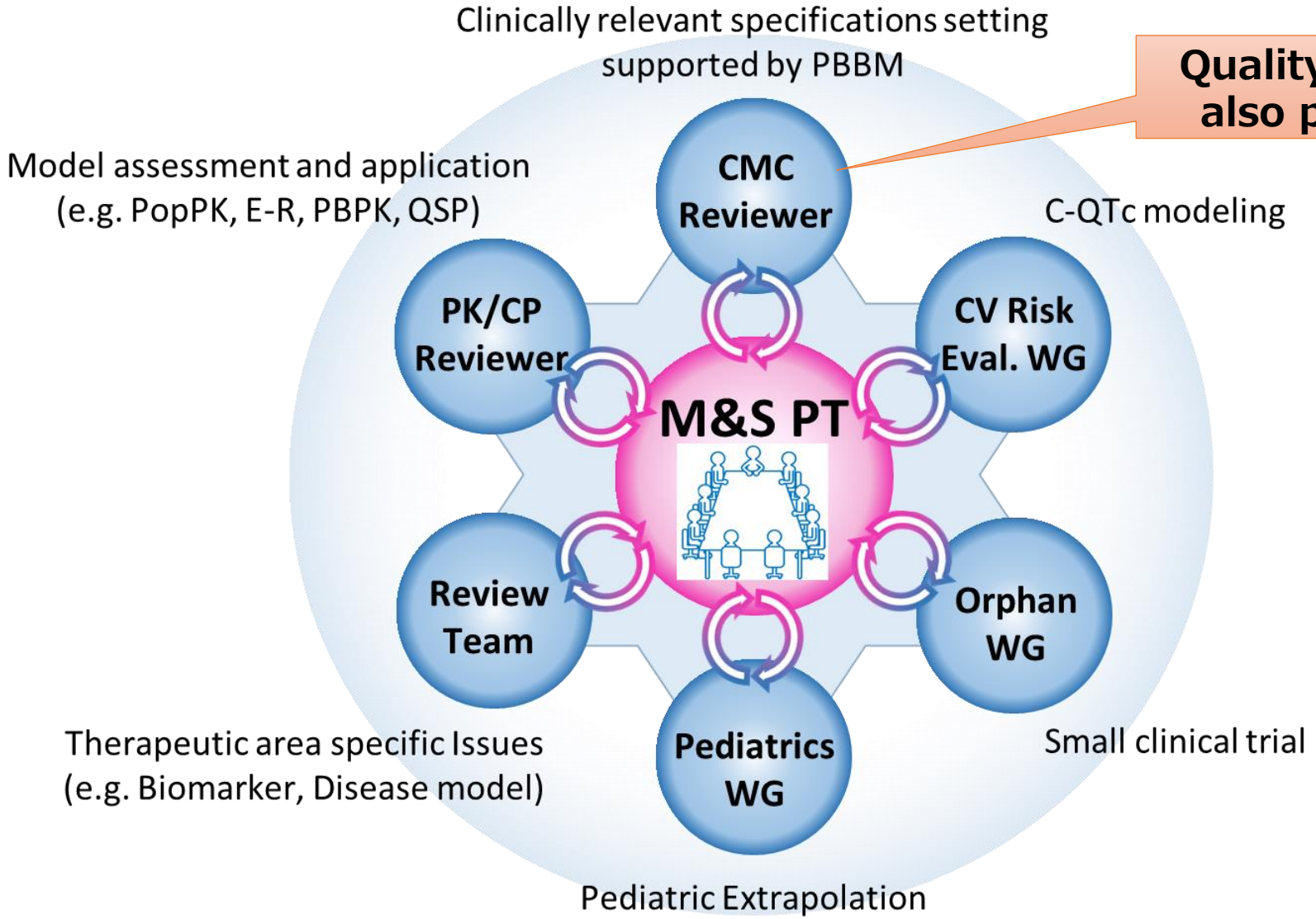
- Strengthening the review system for sharing and utilization of share and use of experiences/knowledge related to M&S

Framework to enable the discussion beyond expertise and therapeutic areas

- Discussion between Clinical Pharmacology/PK, Biostatistics, Clinical medicine, etc.
- Sharing the experiences/knowledge between the review teams
- Collaboration with other project teams in PMDA

- Scientific evaluation and decision making of M&S related issues in product review
- Sharing the information within PMDA and with other stakeholders
- Collaboration with other regulatory agencies

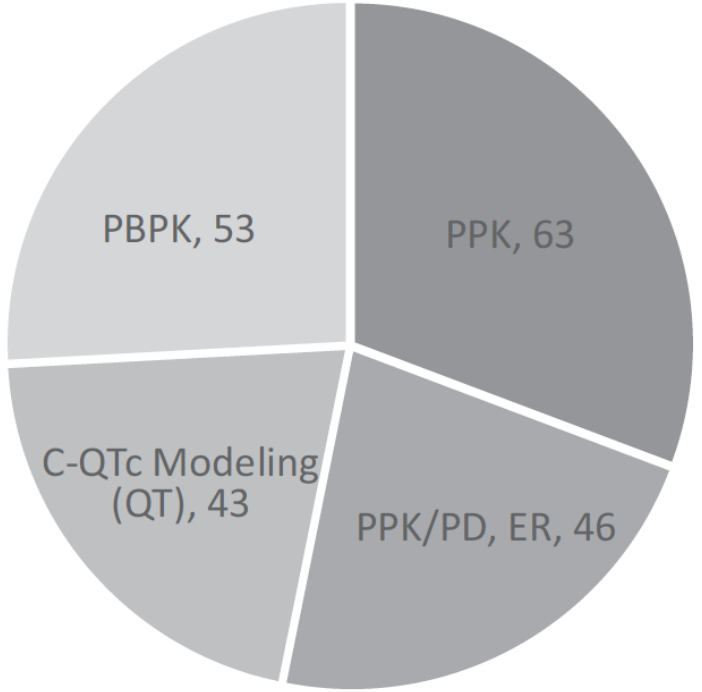
Collaboration between M&S PT and other project teams or reviewers



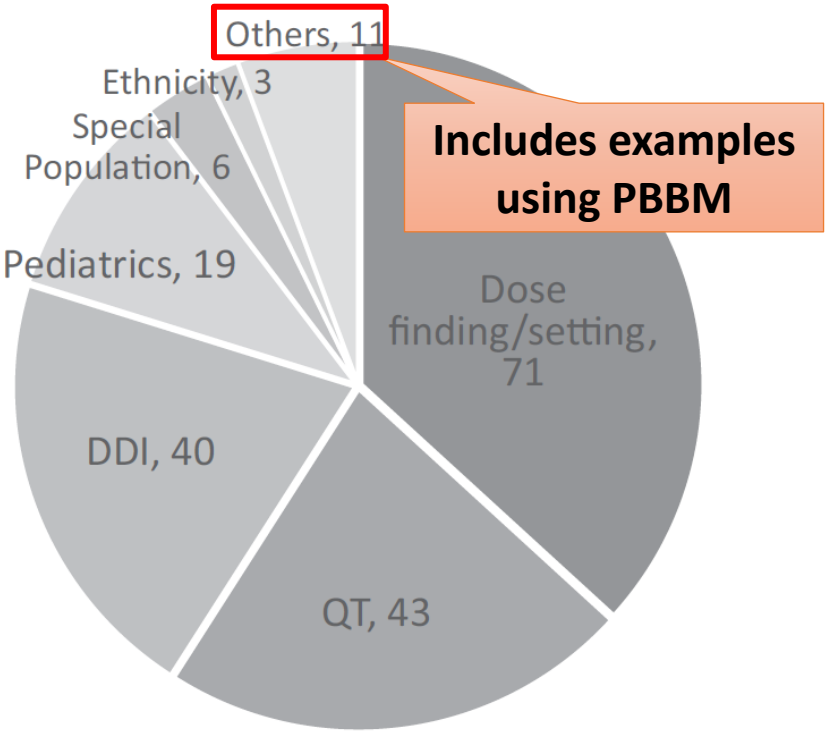
Number of cases in which M&S PT and the review team worked together

Review or Consultation

Model type



Objectives*



* Includes multiple cases

[April 2016 to March 2021]

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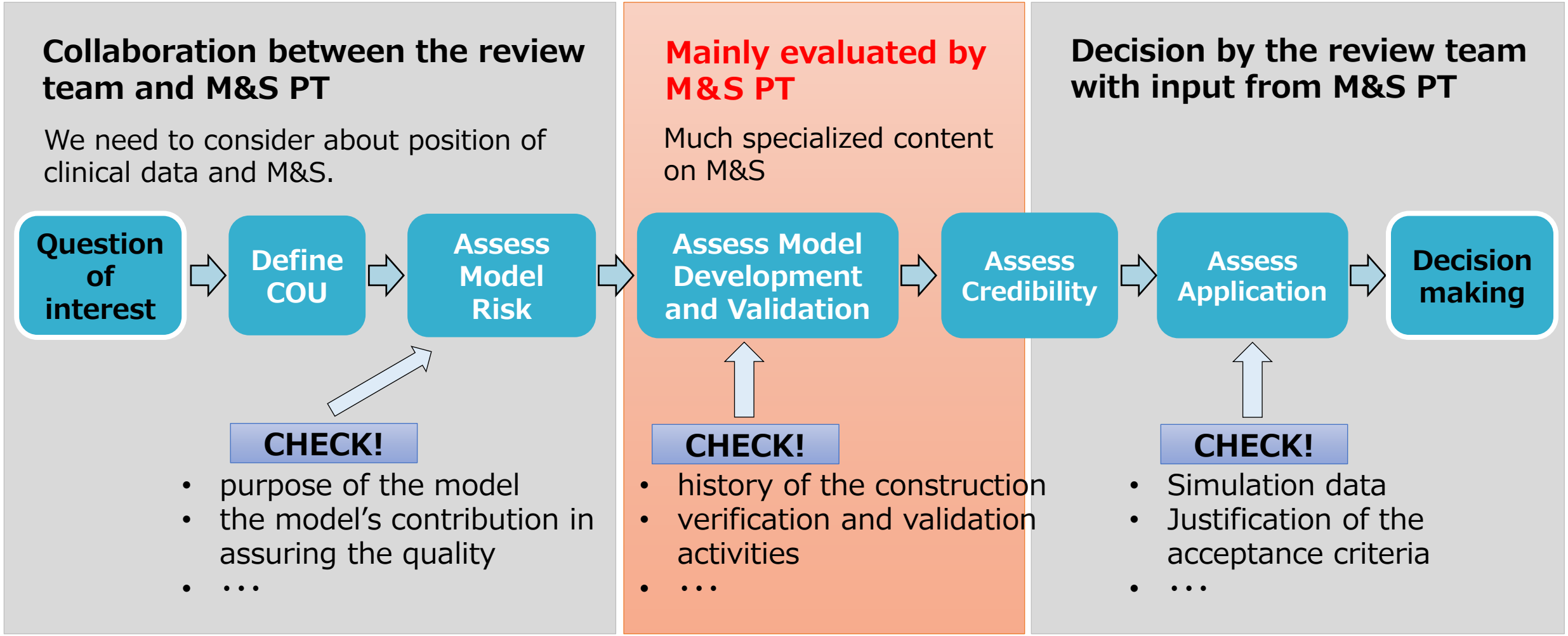
Flow of consideration in M&S PT



Considerations for setting acceptance criteria using PBBM

for example…

- Approach to Model risk in assuring the quality of the product
  - Low-Impact: used to support product and/or process development
  - High-Impact: used for acceptance criteria setting
- Credibility of the model for its intended purpose
- Validity of simulation scenarios using the model
  - Are conservative scenarios considered?
- Validity of proposed acceptance criteria
  - Are more robust acceptance criteria considered?

Summary

- PMDA has several review experiences of quality assurance using PBBM.
- Quality reviewers also participate in the M&S PT.
- We recognize that not only the validity of the model, but also the appropriateness of the acceptance criteria using the model, is important.