Key aspects and milestones for a successful scientific and clinical validation - Regulatory

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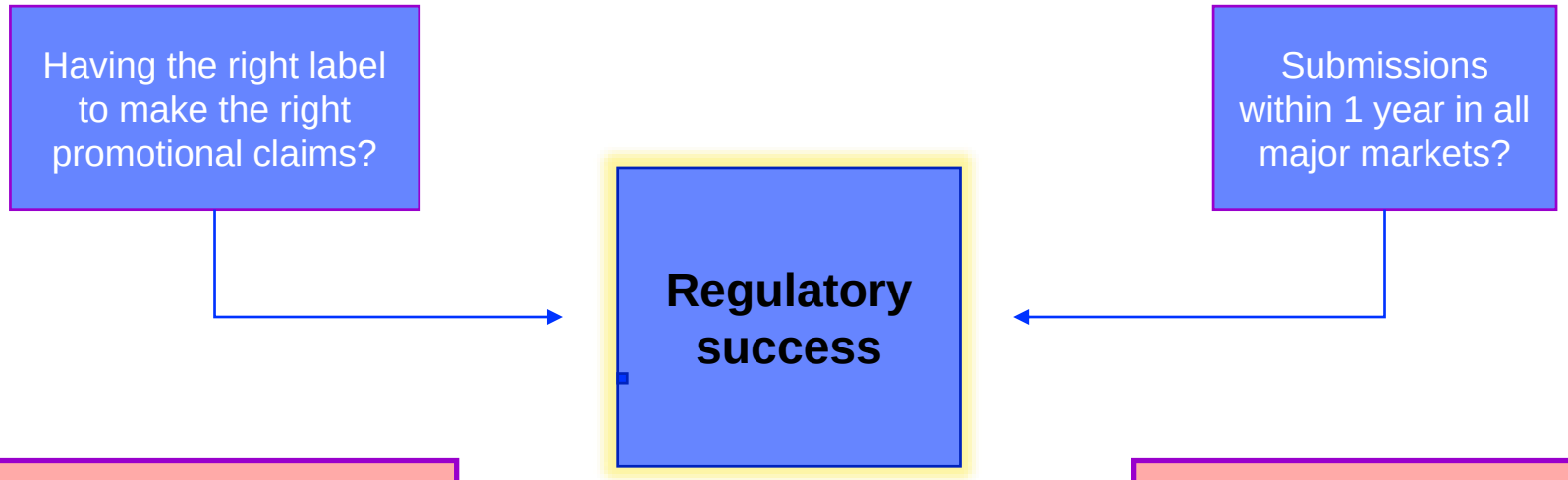
Healthcare Business Summit, Portugal 2019

Breakthroughs that change patients' lives

Agenda

- How do we define global regulatory success?
- Strategic tools
- Preclinical phase
- Clinical phase
- Presubmission and evaluation phase
- Post authorization phase

How to define global regulatory success?



Topics for thought:

- Can we be first to market? Do we want to be first to market?
- Does our organization have the right experts and experience to do this?
- Is it better to be first, or wait on additional data that might support a broader label?
- Do we want to set the price or let others do that work?

Suggestions for regulatory success:

- Build strategic alliances
- Invest more in learning-phase studies
- Obtain early and repeated scientific advice
- Adhere to scientific advice!
- Use innovative regulatory approaches – PRIME, RMAT, conditional approval + post approval commitments

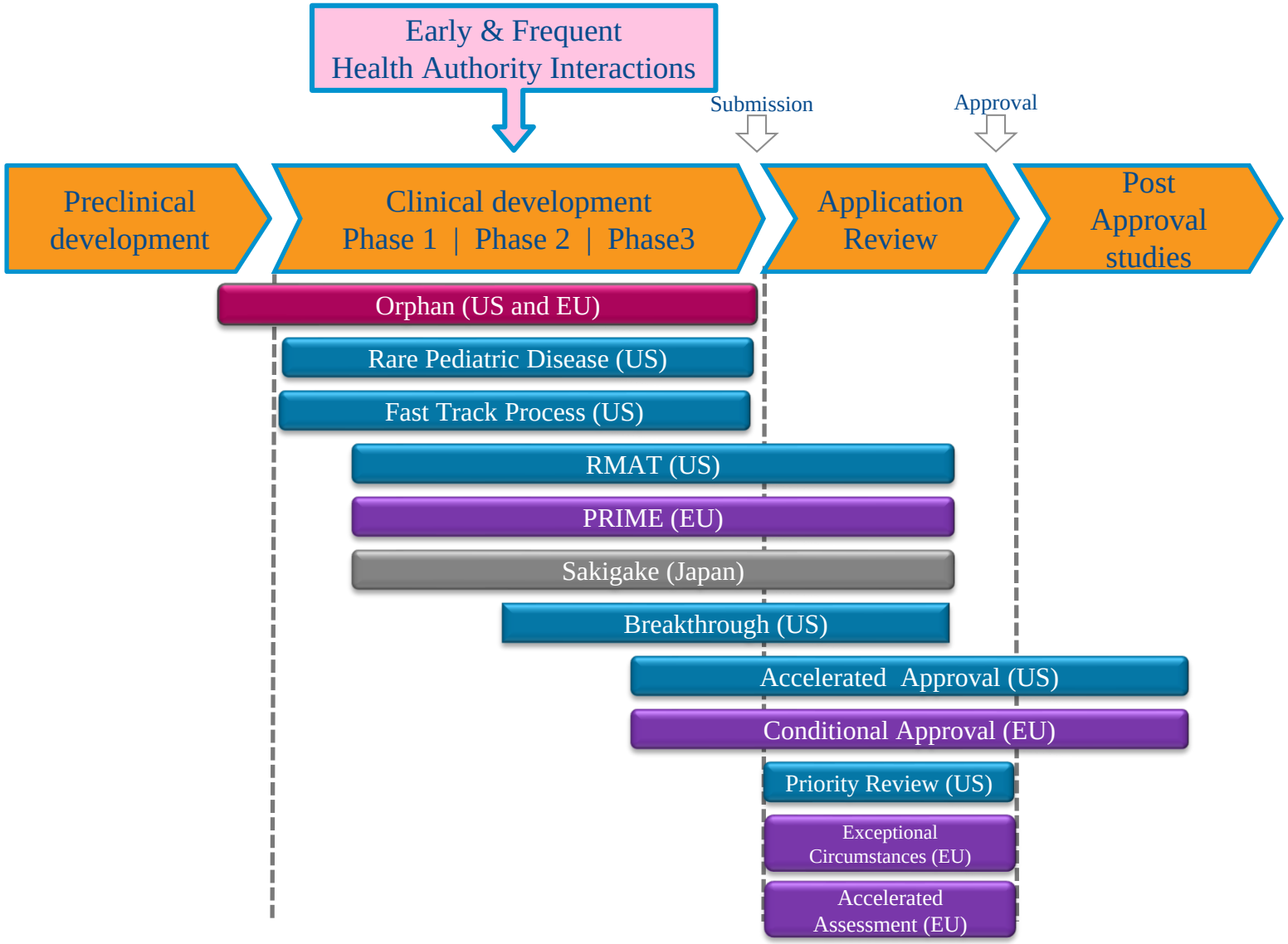
Regulatory success - minimising the 10%

- Attrition rates at key stages of drug development (CMR database 2015)

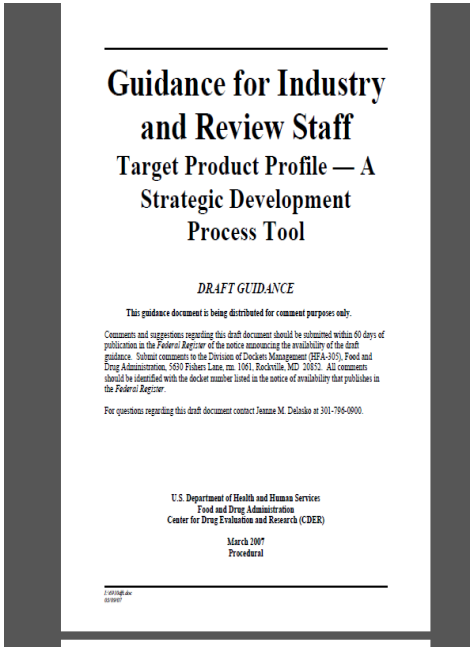
Phase	Failure rate
1	31%
2	56%
3	30%
Regulatory	10%

- Significant activity in the R&D phase, several years in advance of the eventual BLA/MAA is needed
  - Good regulatory framework is critical to maximise success
  - Effective and efficient drug development starts with the end in mind
  - Well considered regulatory strategies should be employed at each stage of development, and should ideally incoroporate the perspective of payers and patients where possible

Regulatory tool kit



Strategic tools: Target Product Profile (TPP)



Guidance for Industry and Review Staff

Target Product Profile — A Strategic Development Process Tool

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact Jeanne M. Delasko at 301-796-0900.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

March 2007
Procedural

- From the guidance: *"A TPP is a format for a summary of a drug development program described in terms of labelling concepts. A TPP can be prepared by a sponsor and then shared with the appropriate FDA review staff to facilitate communication regarding a particular drug development program. Submission of a TPP is voluntary."*
- TPP forces us to star with the end in mind – it will eventually evolve into the label
- Provides continual focus on the goals of the drug development programme
- Communication tool that can be used internally and externally
- TPP spans the entire scope of drug development

Preclinical phase → Clinical phase → Pre-submission → Evaluation phase → Post authorisation phase

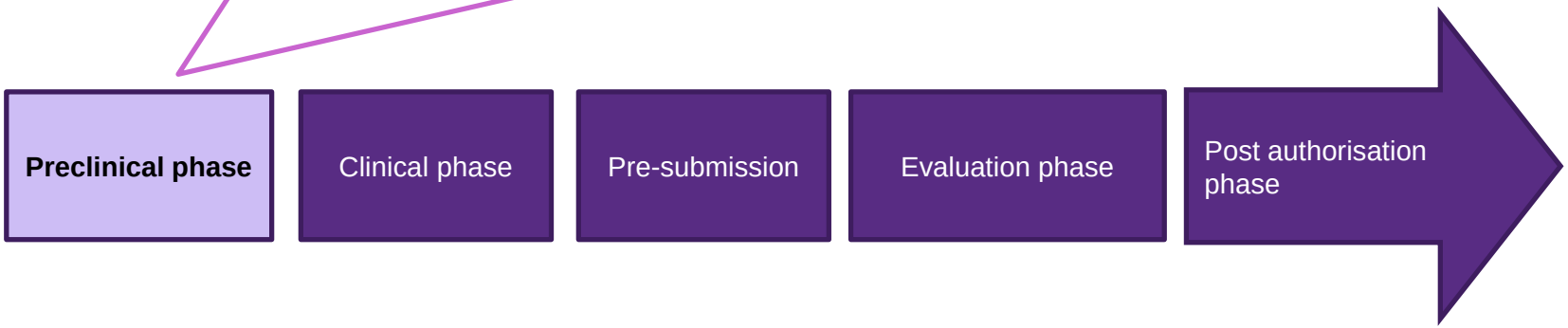
Preclinical phase

Scientific Advice

- Early and frequent interactions are key to success, especially in novel areas like ATMPs
- Its possible to have scientific advice before you've even selected a candidate i.e. general advice on novel class of medicinal products
- Other early phase topics might include appropriateness of toxicological and pharmacological tests and choice of animal models, and interpretation and implementation of FDA/EMA/PMDA guidance's

Orphan Drug Designation for rare diseases

- Treatment, prevention or diagnosis of a disease that is life-threatening or chronically debilitating
- Prevalence criteria defined by EMA and FDA
- Period of market exclusivity, fee reduction, and tax credits are among the benefits of orphan drug designation



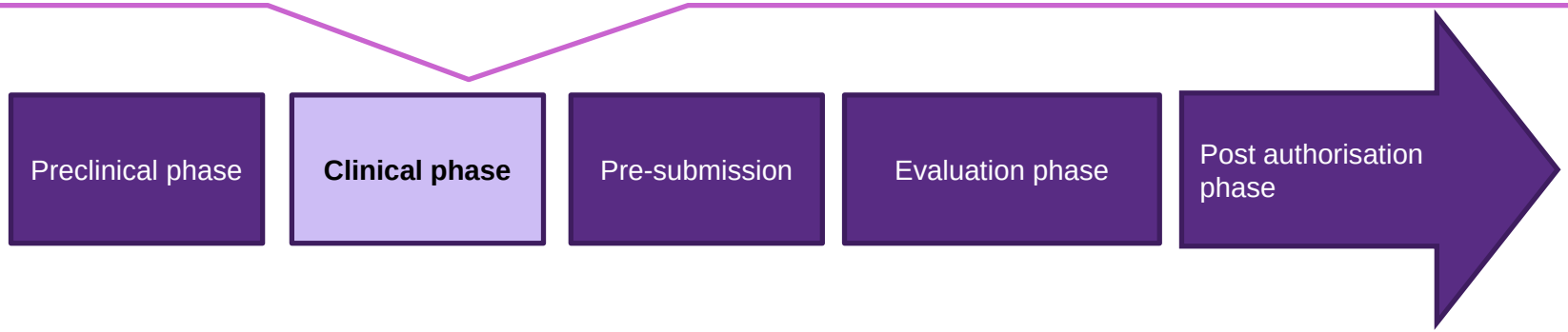
Clinical phase

Scientific Advice

- Early and frequent interactions are key to success – in clinical development the **TPP will be the driver** of areas for advice.
- Potential topics include: choice of endpoints, comparator, sample size. Manufacturing release, stability, comparability
- Regulatory topics include applicability of programme for either MAA under conditional or exceptional circumstances
- Scientific advice available in many forms:
  - FDA only, EMA only, National EU agency
  - Parallel EMA and FDA advice to try and reach consensus on key topics
  - EMA/HTA parallel advice for the early perspective of reimbursement bodies

Innovation Task Force (ITF), EMA

- A multidisciplinary group that includes scientific, regulatory and legal competences.
- The ITF holds meetings with applicants covering regulatory, technical and scientific issues arising from the development of innovative medicines, new technologies and borderline products.
- Recent areas of ITF engagement have included nanomedicines, pharmacogenomics, synthetic biology, biomaterials, modelling and simulation, and m-health ('mobile health', the use of mobile devices to support healthcare).
- Meetings are free of charge and are intended to facilitate the informal exchange of information and the provision of guidance early in the development process. Briefing meetings are intended to complement and reinforce existing formal regulatory procedures e.g. CHMP advice



Clinical phase

Complex Innovative Trial Design (FDA)

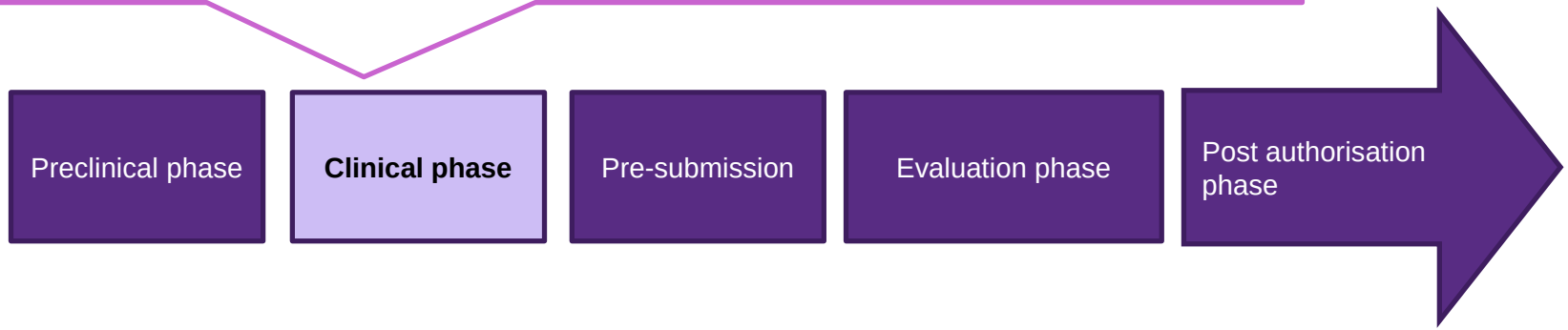
- Program designed to support the goal of facilitating and advancing the use of complex adaptive, Bayesian, and other novel clinical trial designs.
- Promote innovation by allowing FDA to publicly discuss the trial designs considered through the pilot program, including trial designs for medical products that have not yet been approved by FDA

PRIME - PRIority Medicines (EMA)

- Enhanced support for medicines that target unmet medical need through enhanced interaction and early dialogue to optimise development plans so medicines reach patients earlier
- Access to accelerated assessment
- Application based on early clinical data

RMAT – Regenerative Medicine Advanced Therapy (FDA)

- Increased access/interaction with FDA
- Eligible for priority review and accelerated approval
- Application based on preliminary clinical evidence:



Pre-submission and evaluation phase

Accelerated assessment (FDA)

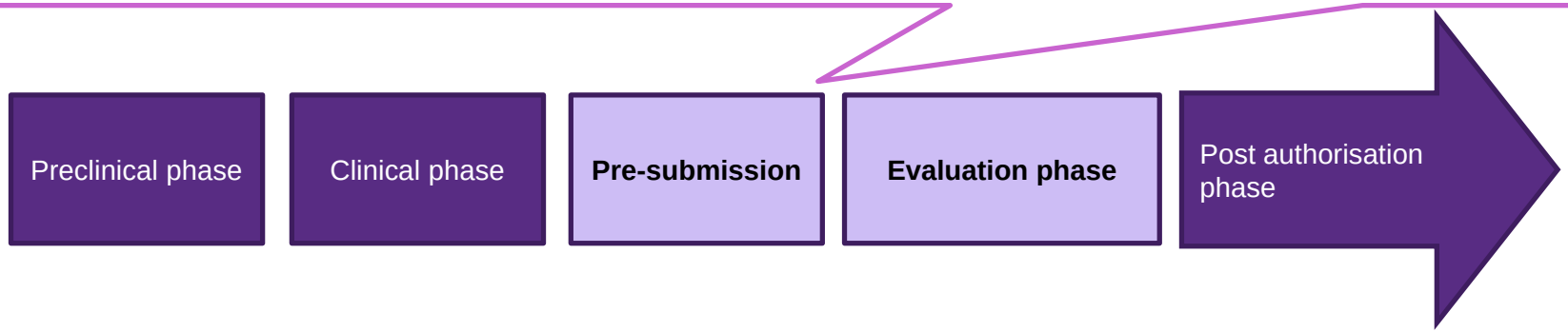
- FDA takes action within 6 months of a BLA submission
- Qualifying criteria are that medicine must treat a serious or life threatening condition and demonstrate significant improvement over existing therapies

Exceptional Circumstances (EMA)

- Products for which the applicant can demonstrate comprehensive data cannot be provided. Justifications include
  - Inability to provide comprehensive efficacy and safety data due to rarity of the indication, OR due to present state of scientific knowledge OR because it would be contrary to medical ethics.

Exceptional Circumstances (EMA)

- In order to meet unmet medical needs of patients and in the interests of public health it may be necessary to grant marketing authorisations on the basis of less complete data. Must fall into one of these categories:
  - Seriously debilitating or life threatening diseases OR products to be used in emergency situations OR orphan medicinal products
- Risk-benefit balance must still be positive
- Once the post approval commitments are fulfilled, the license will become a 'normal' one.



Post authorisation phase

- Effective and efficient drug development starts with the end in mind!
- Post approval commitments should not really be a surprise – a well designed regulatory strategy should have uncovered these in the course of scientific advice
- Reimbursement – in the EU possible to solicit parallel scientific and HTAB advice so that the development programme delivered meets the needs of regulators and reimbursement bodies.

Conclusions

- Effective and efficient drug development starts with the end in mind
- Good regulatory framework is critical to maximise success
- Well considered regulatory strategies should be employed at each stage of development, and should ideally incorporate the perspective of payers and patients where possible
- The target product profile is the tool that should be used to drive discussions both within your organization and externally with regulators