Pediatric Regulations 2012: Permanent Laws and New Provisions under FDASIA

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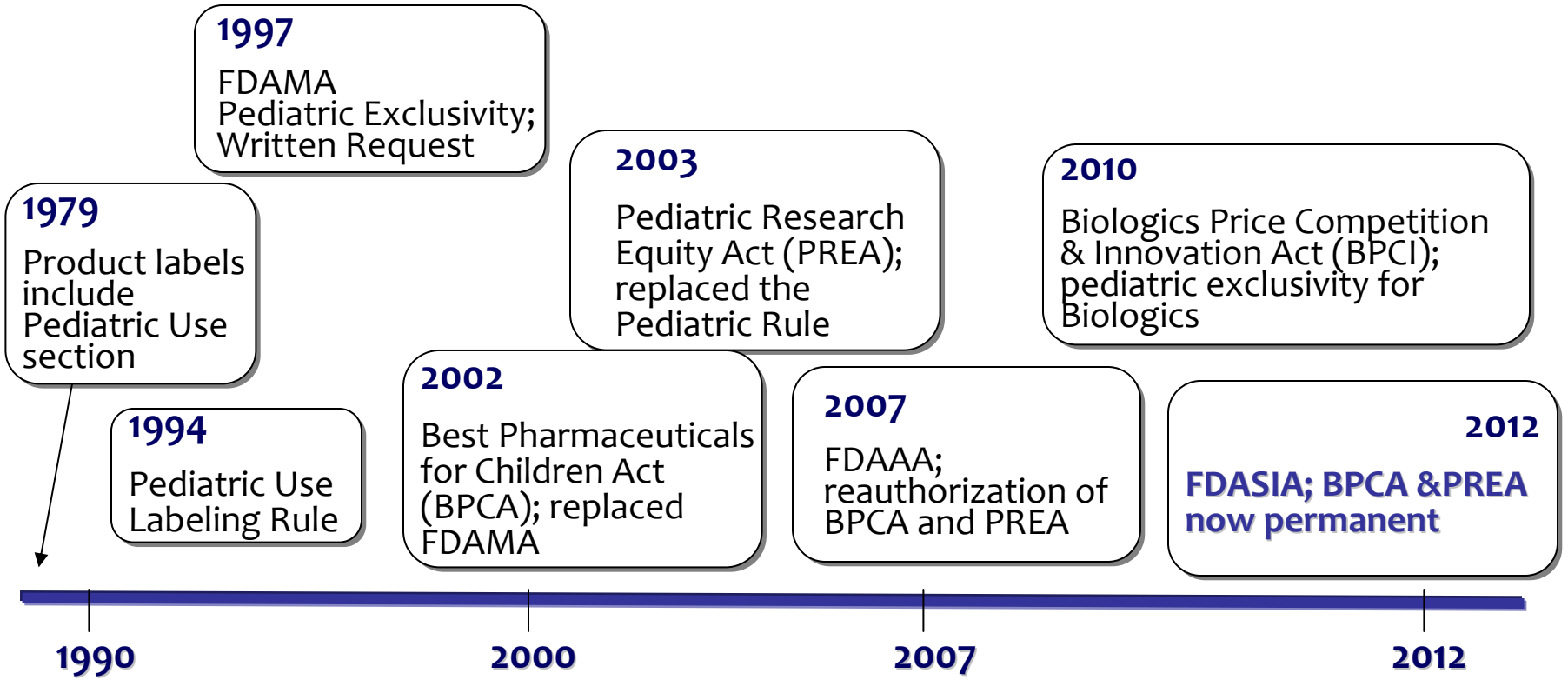
Pediatric Regulatory History



Acronyms

- BPCA – Best Pharmaceuticals for Children Act
- FDAAA – Food and Drug Administration Amendments Act
- FDASIA – Food and Drug Administration Safety and Innovations Act
- PAC – Pediatric Advisory Committee
- PeRC – Pediatric Review Committee
- PPSR – Proposed Pediatric Study Request
- PREA – Pediatric Research Equity Act
- PSP – Pediatric Study Plan
- WR – Written Request

US Pediatric Laws: PREA and BPCA

John Singer Sargent

PREA

Studies mandatory

Required studies for adult indication under review

Applies to drugs and biologics

Not required for orphan indications

BPCA

Studies voluntary

Studies for entire active moiety (all relevant indications)

Applies to drugs and biologics

WR may be issued for orphan indications

BPCA: Written Request (WR)

- A description of pediatric studies
  - issued by a Review Division
  - Can be in response to a PPSR
  - Can be for indications and conditions other than the adult indication
- Considerations
  - What is the public health benefit?
  - Are the study designs feasible; sufficient to support dosing, safety and efficacy?
  - Have all populations and conditions been addressed?
  - Are there other products already approved for the condition?
- Successful completion results in an award of 6 months exclusivity attached to the patent

FDASIA 2012

- New requirements for Pediatric Study Plans
- Provision for extension for deferred studies
- Neonates and the Written Request
- Pediatric Priority Review Voucher

Changes under FDASIA

- Pediatric Study Plans - PSPs
  - Sponsors required to submit plans at End of Phase 2
- Must include:
  - Outline of the pediatric study or studies that the applicant plans to conduct *(including, to the extent practicable study objectives and design, age groups, relevant endpoints, and statistical approach)*
  - Any request for a deferral, partial waiver or waiver, along with supporting information

Developing the Pediatric Study Plan

- Overview of the disease in the pediatric population for the product under development
- Potential plans and justification for use of extrapolation
- Plans and justification for full or partial waiver
- Plans for pediatric specific formulation development
- Nonclinical data, complete or planned, to support studies in children
- Synopsis/summary of all clinical studies planned
- Timeline for the Pediatric Study Plan
- Provide any agreements with other Health Authorities (e.g., PIP for EMA)

Pediatic Investigation Plan [PIP] ; European Medicines Agency [EMA]

Timeline for Review

- Sponsor must submit initial PSP within 60 days of End of Phase 2 meeting — Day 0
- Review Division and PeRC must review this initial PSP within 90 days
- Review Division must discuss the initial PSP with Sponsor by day 90 (meeting or written comments)
- Sponsor must incorporate recommendations and submit "Agreed Initial PSP" within 90 days from the meeting
- PeRC must review "Agreed Initial PSP" within 30 days of submission of Agreed Initial PSP
- Letter to confirm agreement with "Agreed Initial PSP" must be sent to sponsor within 30 days of submission of Agreed Initial PSP — Day 270

PREA Under FDASIA

- New provision to allow extension for deferred studies under PREA
- General criteria for acceptance of extension requests
  - Provide general consistency with reasons for delayed FDAAA Post Marketing Requirements [PMRs]
  - Delay in development could not have been prevented or could not have been foreseen
  - Sponsor will still be able to complete the studies

FDASIA and the Written Request

- No changes in the process
  - PPSR submitted by sponsor or WR generated by FDA
- Inclusion of neonates (birth – 28 days)
  - All age groups must be considered and included where appropriate
  - If inclusion of neonates is not warranted a justification must appear in the WR
    - Disease does not occur in this age group
    - Studies are not feasible or safe

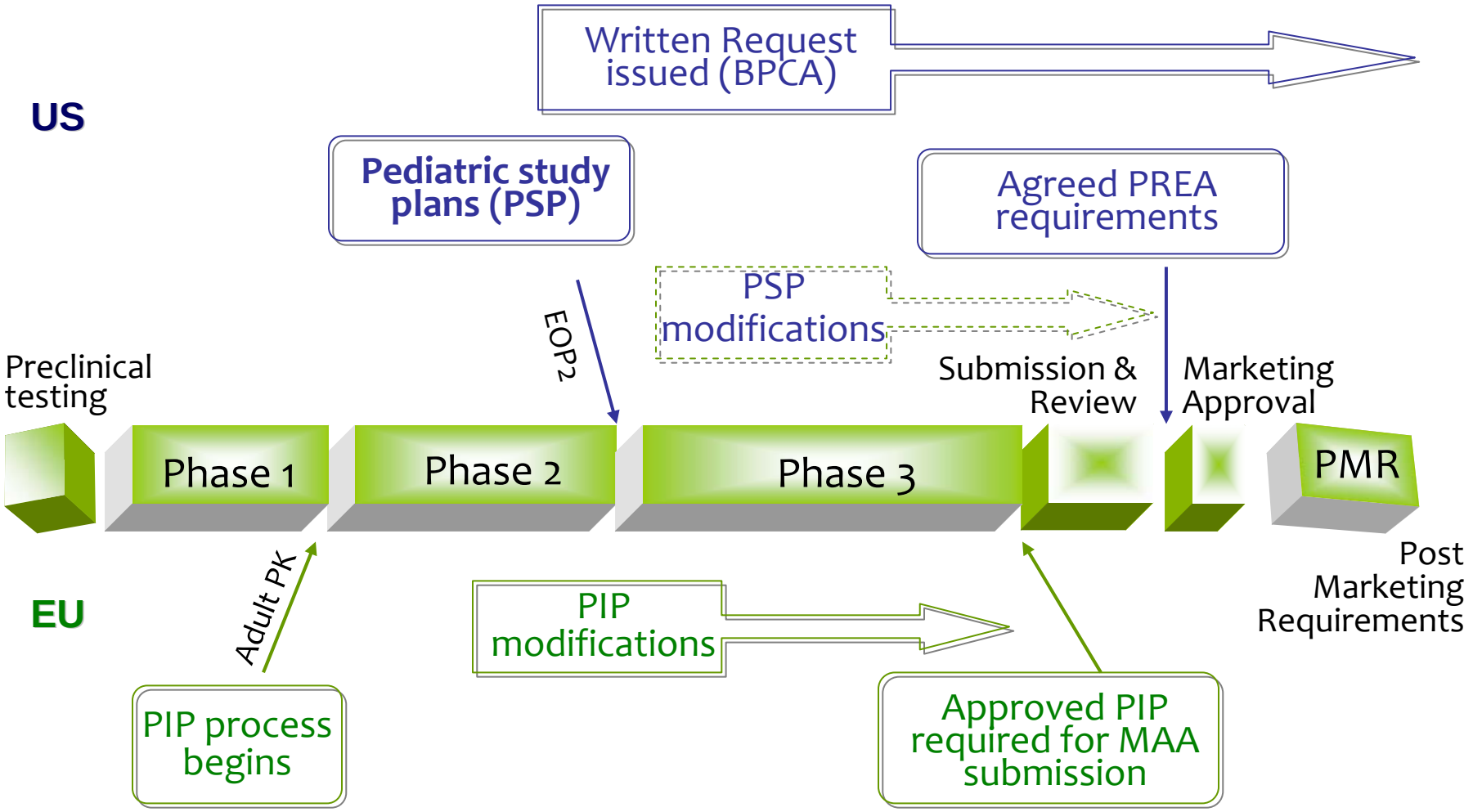
FDASIA - Pediatric Priority Review Voucher

- For development of products for rare pediatric disease
- Provides a voucher for 'priority review' of any subsequent human drug application.

FDASIA - Pediatric Priority Review Voucher

- Definition of a rare pediatric disease
  - "disease that primarily affects individuals aged from birth to 18 years, including age groups often called neonates infants, children and adolescents"
  - meets the definition of 'rare disease or condition' as set forth in the Orphan Drug Act
- 3 pronged requirement
  - Meet definition above
  - Provide clinical data from studies in the intended pediatric population – including dosing information
  - Are not seeking approval for an adult indication in the original rare pediatric disease product application

Pediatric Planning in the Drug Development Process



Marketing Application Authorization [MAA]

FDASIA and Drugs for Pediatric Cancers

- Goal of an Oncology Pediatric Plan is to develop drugs that provide a meaningful advance in the treatment of children with cancer with the potential to
  - Prolong life
  - Improve the quality of life
  - Reduce toxicity
  - Improve efficacy
- Small numbers of patients demand thoughtful approaches and prospect of direct benefit

FDASIA and Drugs for Pediatric Cancers

- Same regulatory expectations
  - Procedural provisions under PREA for waivers when appropriate
  - PPSR for a WR under BPCA
- Earlier review and discussion of the Pediatric Study Plan
  - Coordination with EMA
  - Engagement with the Committee
- Attention to the youngest patients with focus on neonates
- New incentive in the Voucher Program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