Integrating the Pre-Submission/Pre-IDE Process into the IVD Product Development Process

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Regulatory Goals in Product Development

- Our charter as regulatory project leaders and team members is to
  - Develop clear regulatory strategies that guide submission activities
  - Ensure appropriate product classifications
  - Identify FDA regulatory requirements, confirm clinical trial design adequacy, and verify submission content
  - Chart a successful course through the FDA submission process

Key Success Factors for Regulatory Affairs

- Success is defined as
  - Submission content that provides scientific and clinical evidence that the product is safe, effective, substantially equivalent, and fit for the intended use
  - Timely and predictable FDA review cycles and decision outcomes
  - Availability of new products to physicians, healthcare providers, and patients

Business Drivers for Early FDA Interaction

- Time to Market
  - Desire to provide new/innovative diagnostics for doctors and patients
  - Market leadership in key product areas
  - Market windows of opportunity
- Cost of Product Development
  - Product development cycles are long and expensive
  - Inadequate submission content or clinical studies may result in NSE/not approvable decisions, or delays

Leveraging the FDA Pre-Submission Process

- In creating regulatory strategies, we need to evaluate the need for a Pre-IDE for the new assay/instrument/software/system
- Are there elements or issues that could cause problems or delays downstream during FDA review?
- Some points to consider ...
  - Is this a well characterized device for which there is significant history?
  - Is the FDA clearance/approval history predictable?

Leveraging the FDA Pre-Submission Process

- Are there suitable predicate device(s) or would FDA expect a “gold standard” in addition?
- Can multiple predicates be used?
- Are there new guidances for products of this type, or new requirements not yet included in updated guidance?
- Would FDA feedback on the clinical studies design, sample numbers, patient population, or statistical analysis methods enhance the submission?
- Are there CLIA complexity issues or waived trial design to discuss?

Leveraging the FDA Pre-Submission Process

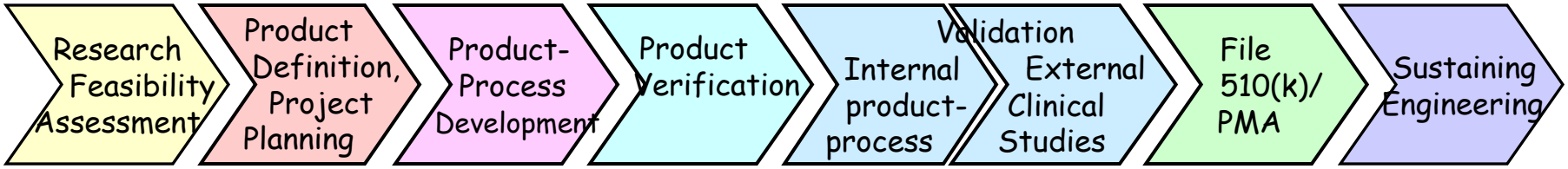
- Are the performance characteristic (non-clinical) test plans & data analyses acceptable?
- Is there other data needed should a de novo pathway be agreed upon?
- Are there bundling concerns that need to be worked prior to the submission?
- Does FDA foresee new public health issues or safety concerns for this device or type of device?
- Is the technology particularly complex that FDA should be engaged prior to the submission?

Leveraging the FDA Pre-Submission Process

- If no special issues are identified, proceed to the submission; the FDA interaction will be in the context of the 510(k)/PMA
- If there are potential issues, the Pre-Submission process should be considered
- The Pre-Submission process now needs to be built into the IVD product development timelines

Concept Model for IVD Product Development*

- IVD product phase-gated process



Research & Feasibility – Market analysis, voice of the customer, feasibility studies Product proposal, high level requirements, reimbursement, Clinical utility & regulatory review

Development – Reiterative design development, subsystem integration, characterization, traceability. Manufacturing process design, MSA, test equipment design/specs

Validation – Rigorous internal &/or external user-focused testing for performance, safety, effectiveness, equivalence. Design transfer, process validation (IQ/OQ/PQ)

Planning – Product/process design & development plans, product definition/design specs, schedules, cost guidelines, regulatory & reimbursement strategy.

Product Verification – product Performance testing to design specifications, safety testing, risk management, software unit, modular, system tests. Begin design transfer.

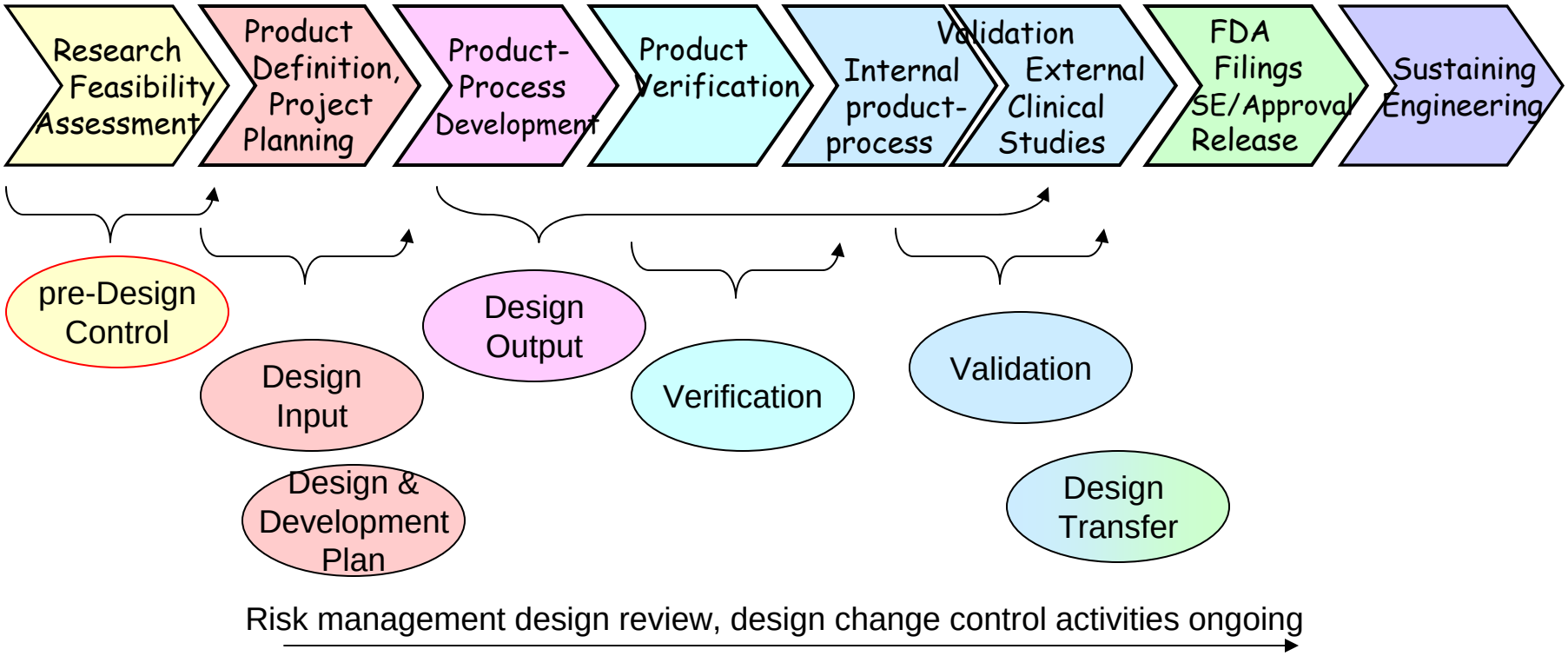
FDA Filing/Product Release – Submit to FDA, EU CE-marking, global registrations, business systems preparation, commercial release upon clearance/approval

Sustaining Engineering - Maintenance, line support, continuous improvement, enhancements, and post market surveillance. Product modification compliance.

* Derived from product development process models from 5 IVD companies with FDA cleared/approved products

Concept Model for IVD Product Development*

- IVD product phase-gated process
  (in Quality Systems Design Control terms)



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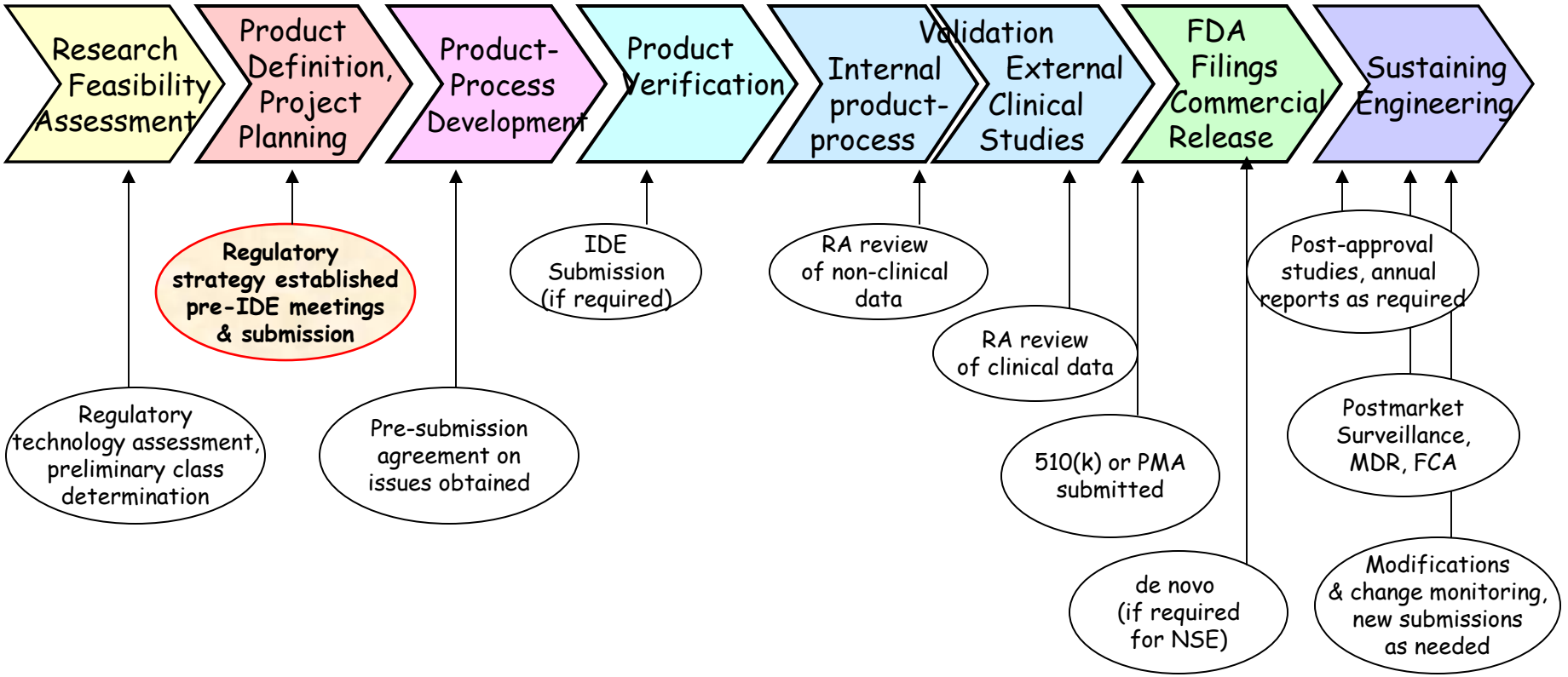
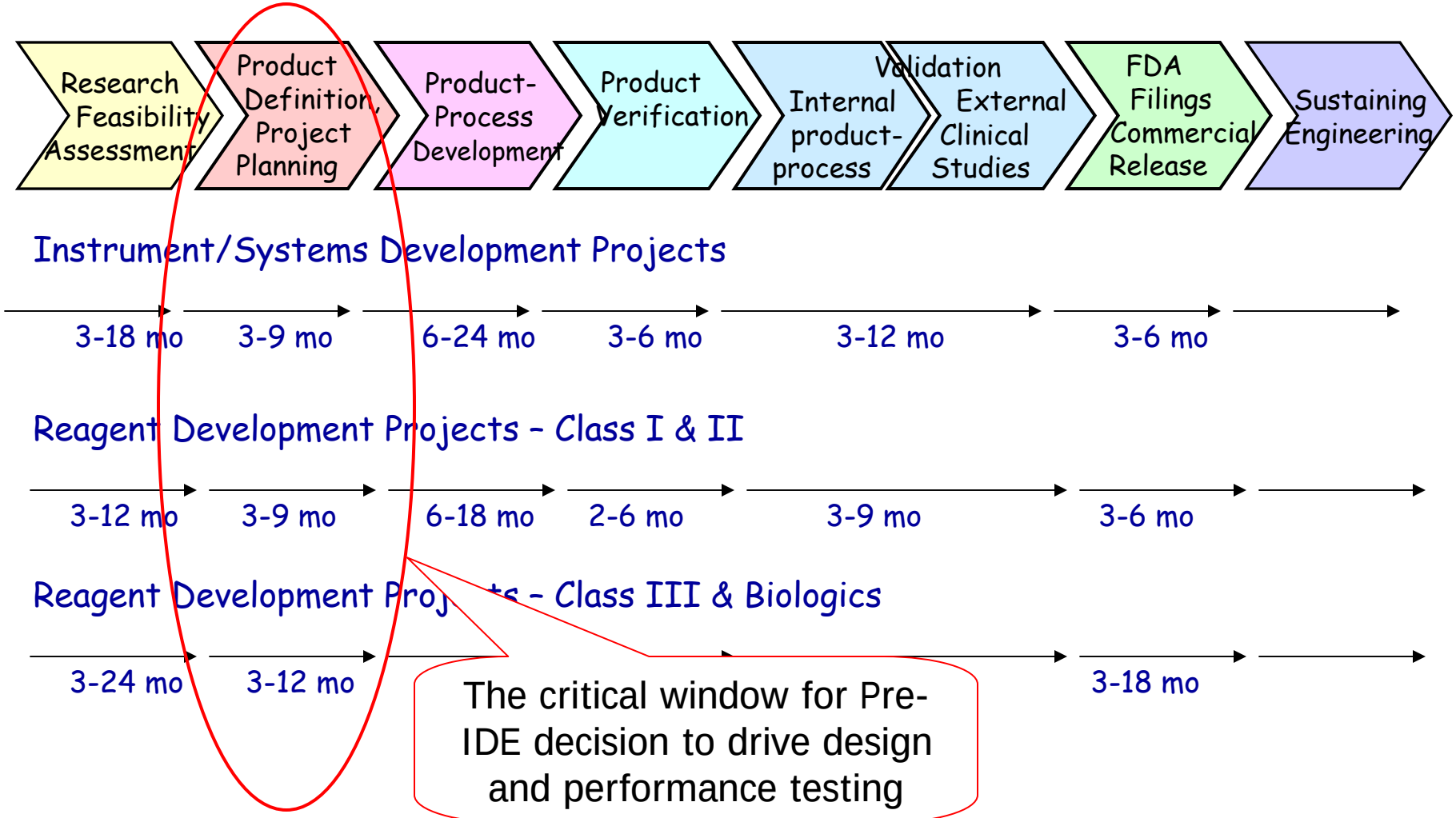
Regulatory Deliverables by Phase

- Regulatory Affairs engagement through the product development process



Timeline Models for IVD Product Development

- Timelines vary by project & complexity



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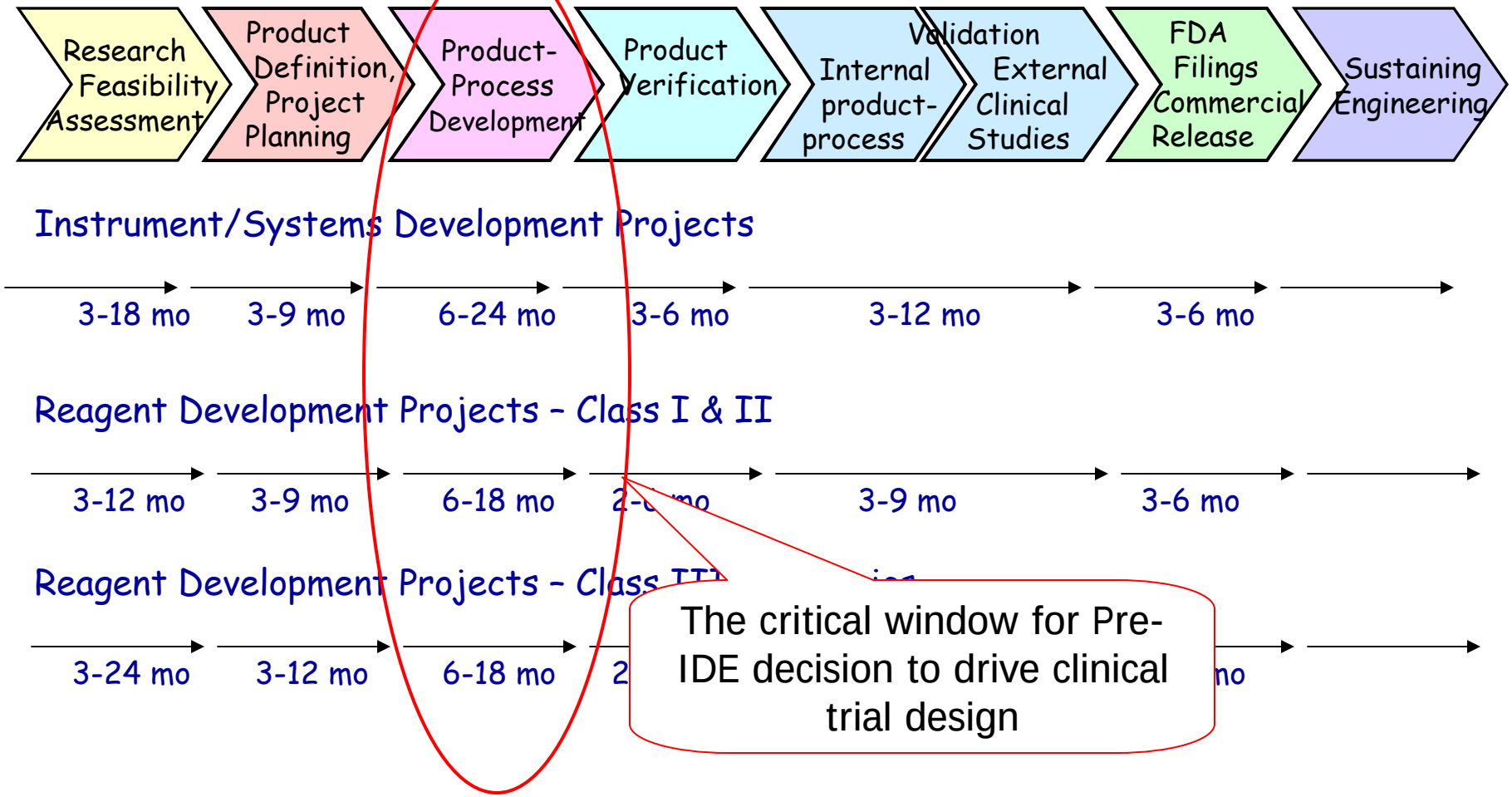

Importance of Timeline Efficiency

- A goal of this workshop is to efficiently and effectively use the Pre-submission process to get answers to our questions about performance and clinical protocols, technology concerns, public health or safety issues, supplemental data sets, or concerns about intended use prior to submission
- So, let's hear from FDA on methods to navigate the process most successfully