Integrating OIVD's 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
  - Clearly 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 requiring additional data

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
- 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?
- Are there new guidances for products of this type, or new expectations not yet included in updated guidance?
- Is the performance characteristic (non-clinical) test plan & data analysis sufficient?
- Do we need FDA feedback on the clinical studies design, sample numbers, patient population, or statistical analysis methods if the device or plan is unique?

Leveraging the FDA Pre-Submission Process

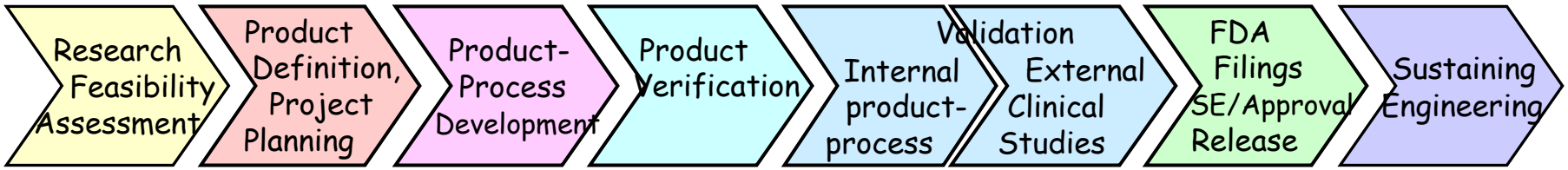
- Are there supplemental data needed should a de novo pathway be agreed upon?
- Are there bundling concerns that need to be worked prior to the submission?
- Does FDA foresee public health issues or concerns surrounding this device or type of device?
- Is the technology particularly complex that FDA should be engaged prior to the submission, outside of the staff college?

Leveraging the FDA Pre-Submission Process

- If no issues are identified, the regulatory strategies can proceed without a pre-IDE; the FDA interaction will be in the context of the submission
- If these type of questions identify potential issues, the Pre-Submission process should be of value
- 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

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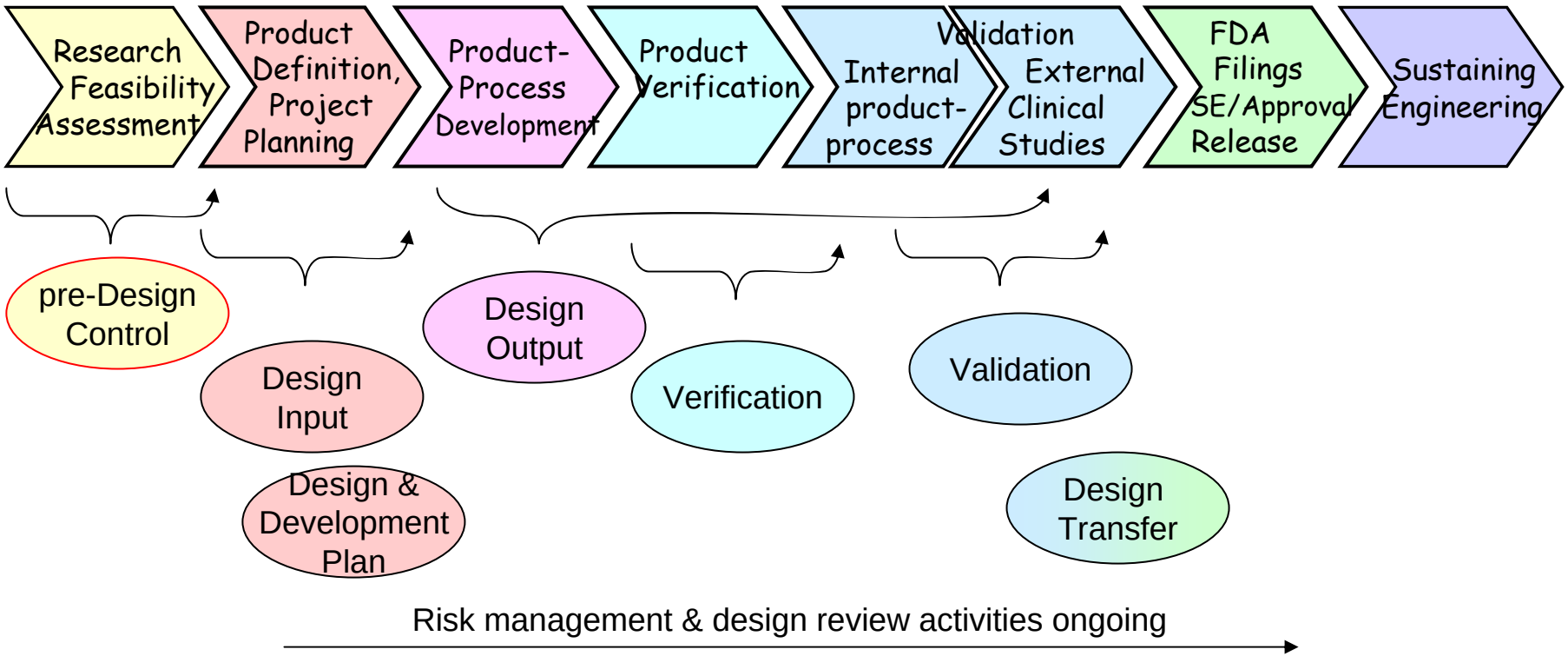
- IVD product phase-gated process
  (in Quality Systems Design Control terms)



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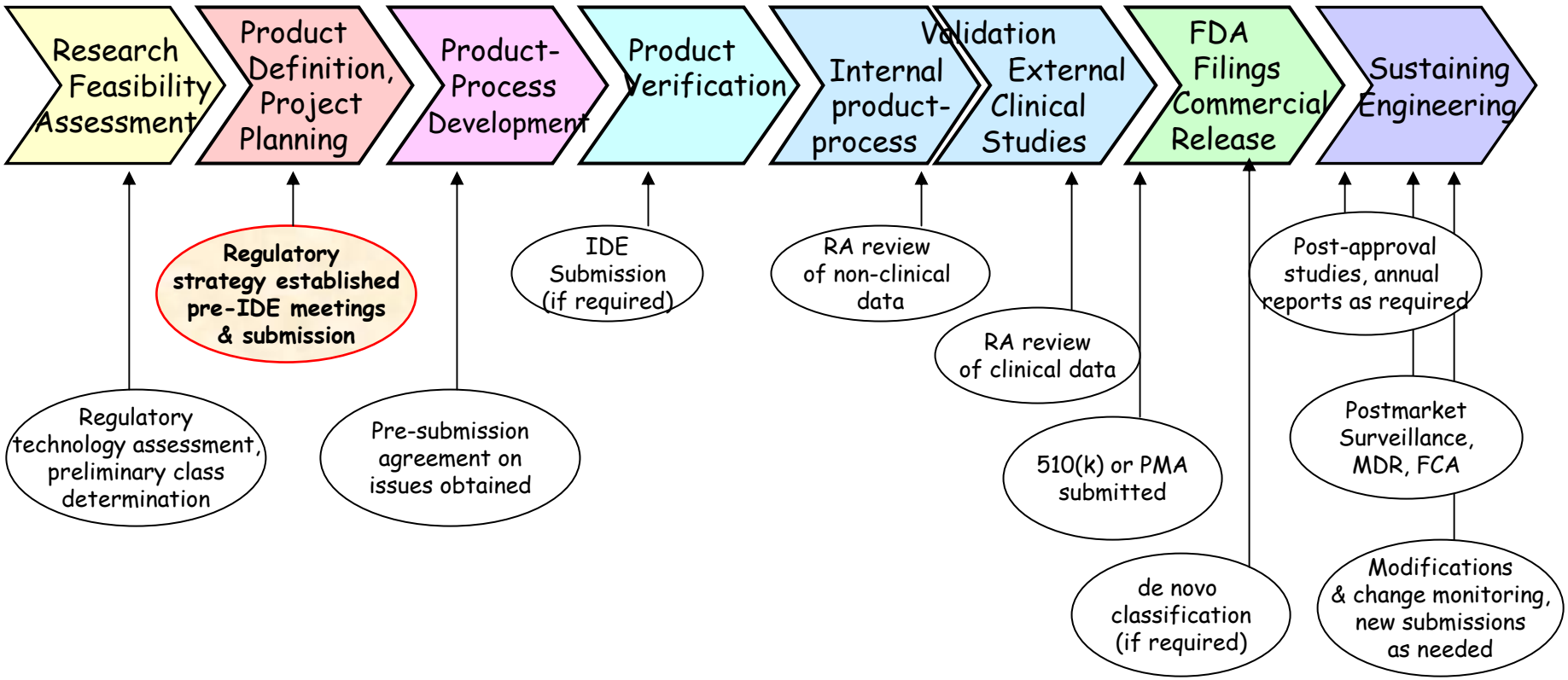
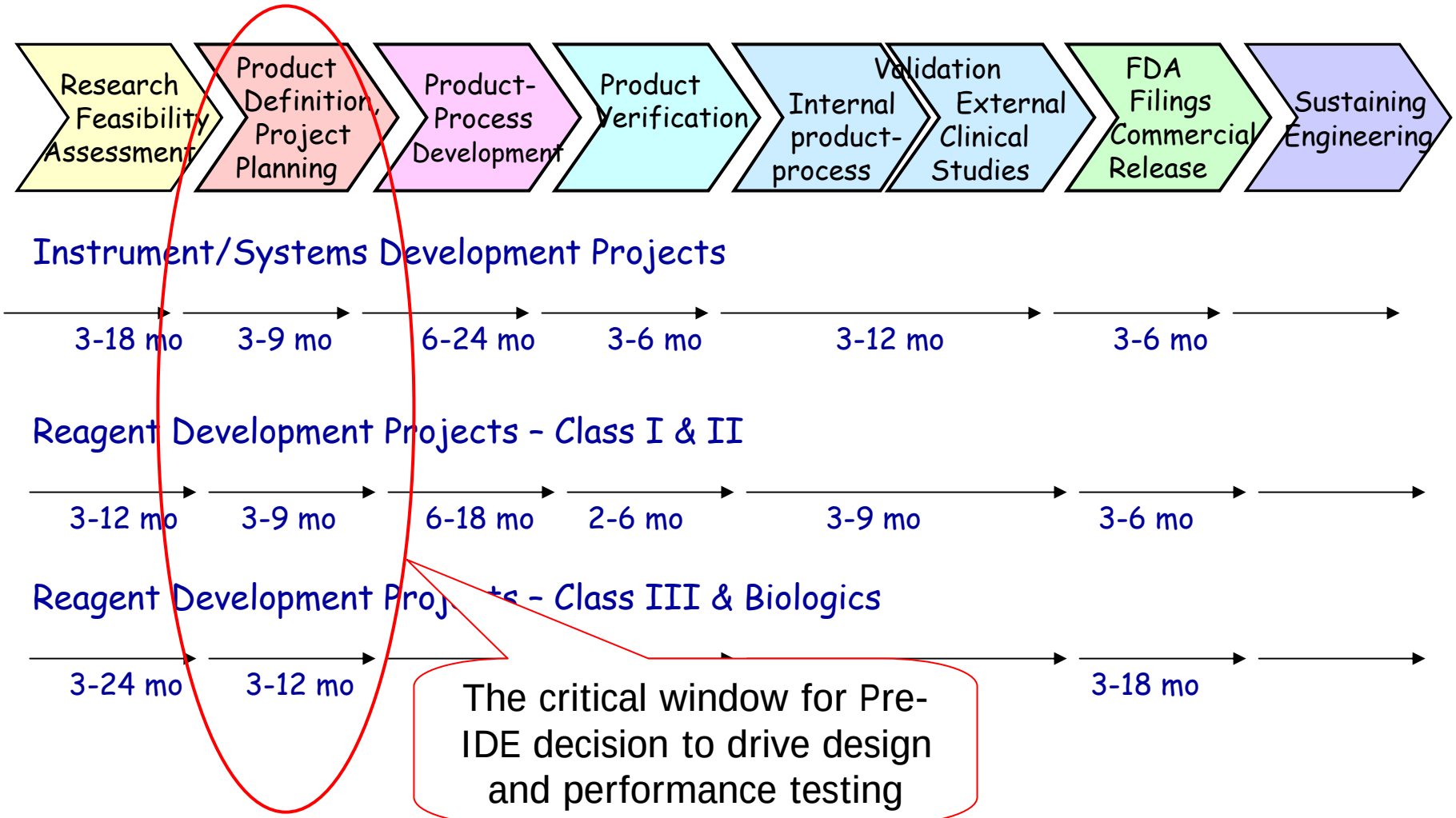
Regulatory Deliverables by Phase

- Regulatory Affairs engagement is significant all through the product development process



Timeline Models for IVD Product Development

- Timelines vary by project & complexity



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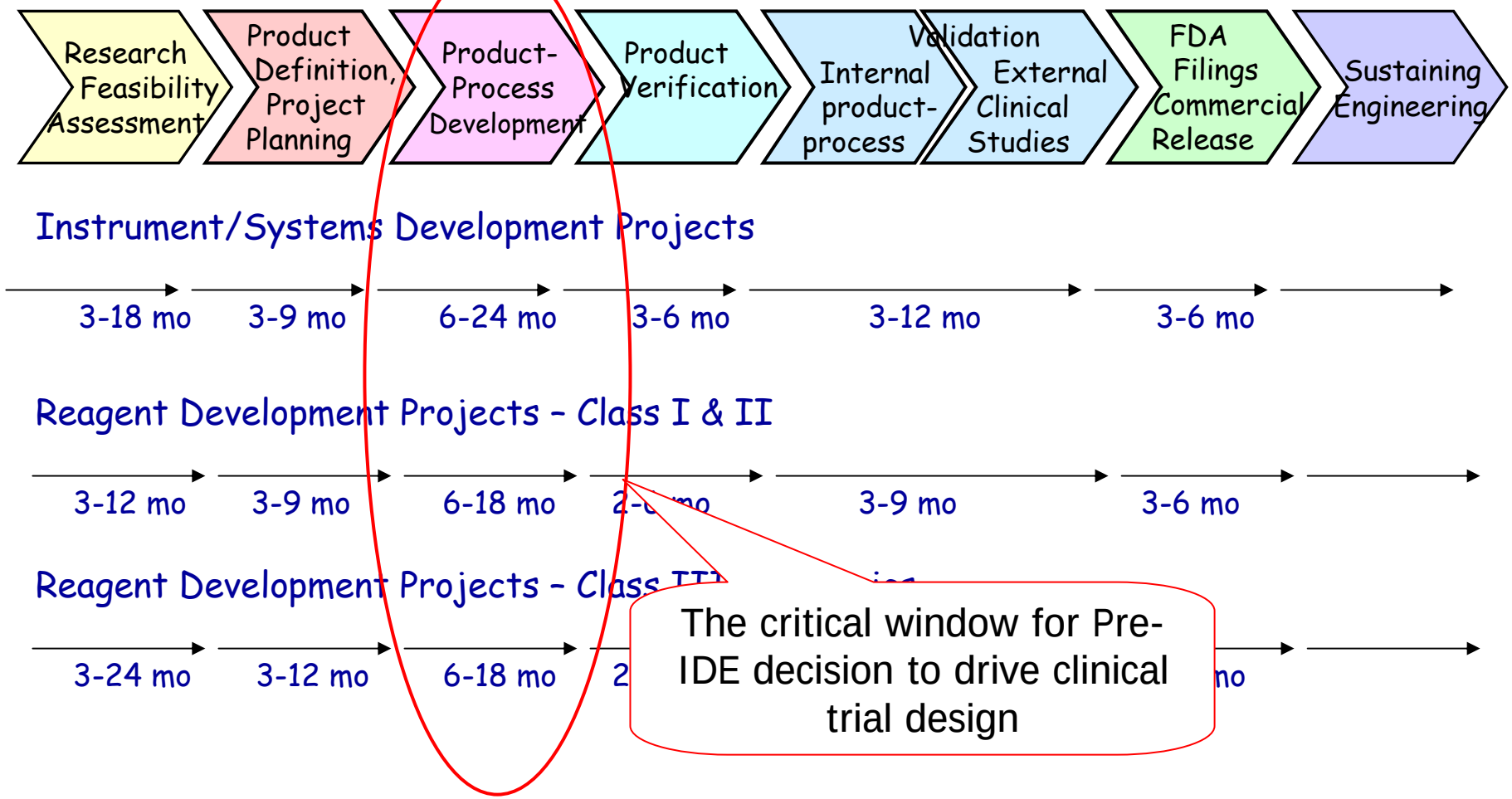

Importance of Timeline Efficiency

- 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 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