Utilizing the Pre-Submission/Pre-IDE Process to Improve Submission Quality

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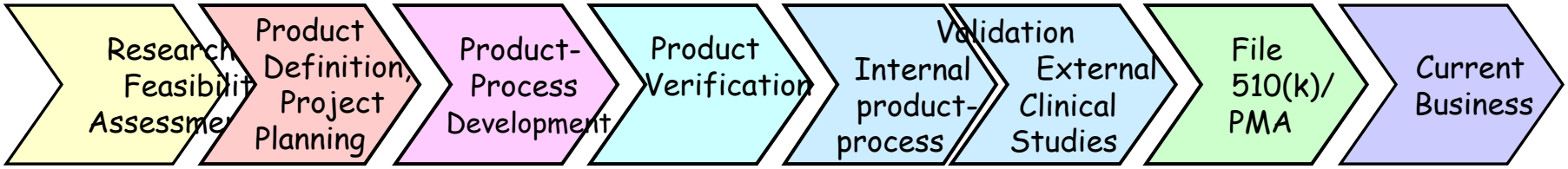
Regulatory Goals in Product Development

- As regulatory project leaders and team members, our mission is to
  - Develop clear US and global regulatory strategies that guide submission activities
  - Identify FDA regulatory requirements, confirm clinical trial and performance data adequacy, and verify submission content
  - Ensure appropriate product classifications
  - Chart a successful course through the FDA submission process

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.

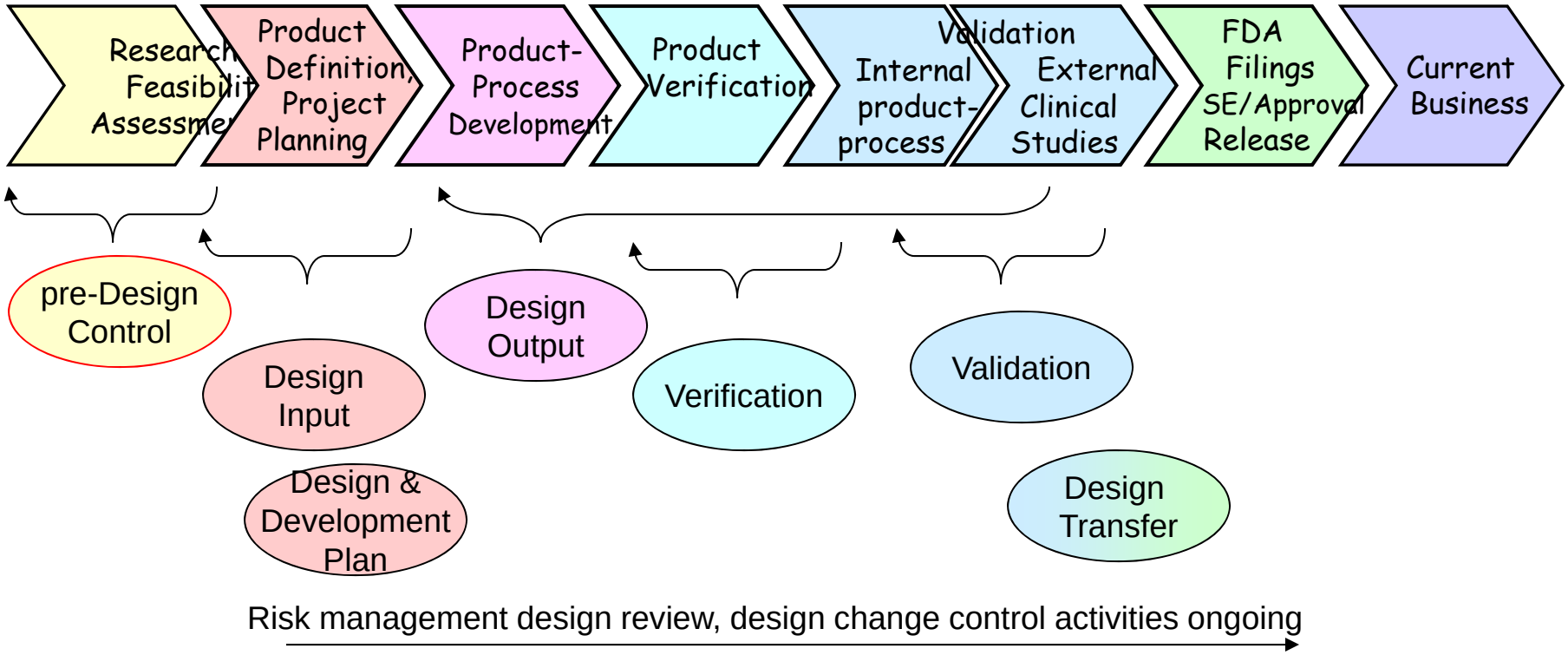
FDA Filing/Product Release – Submit to FDA, EU CE-marking, global registrations, business systems preparation, commercial release upon clearance/approval

Current Business - 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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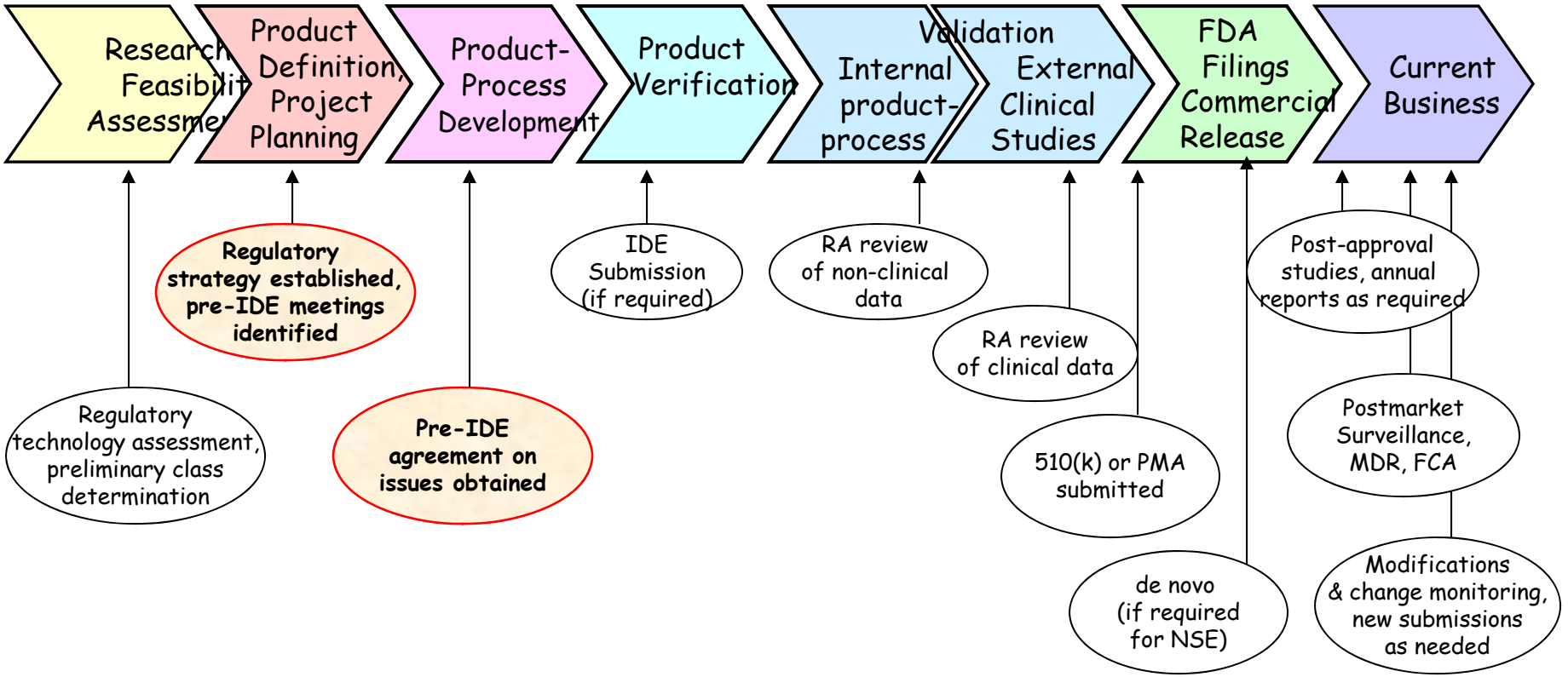
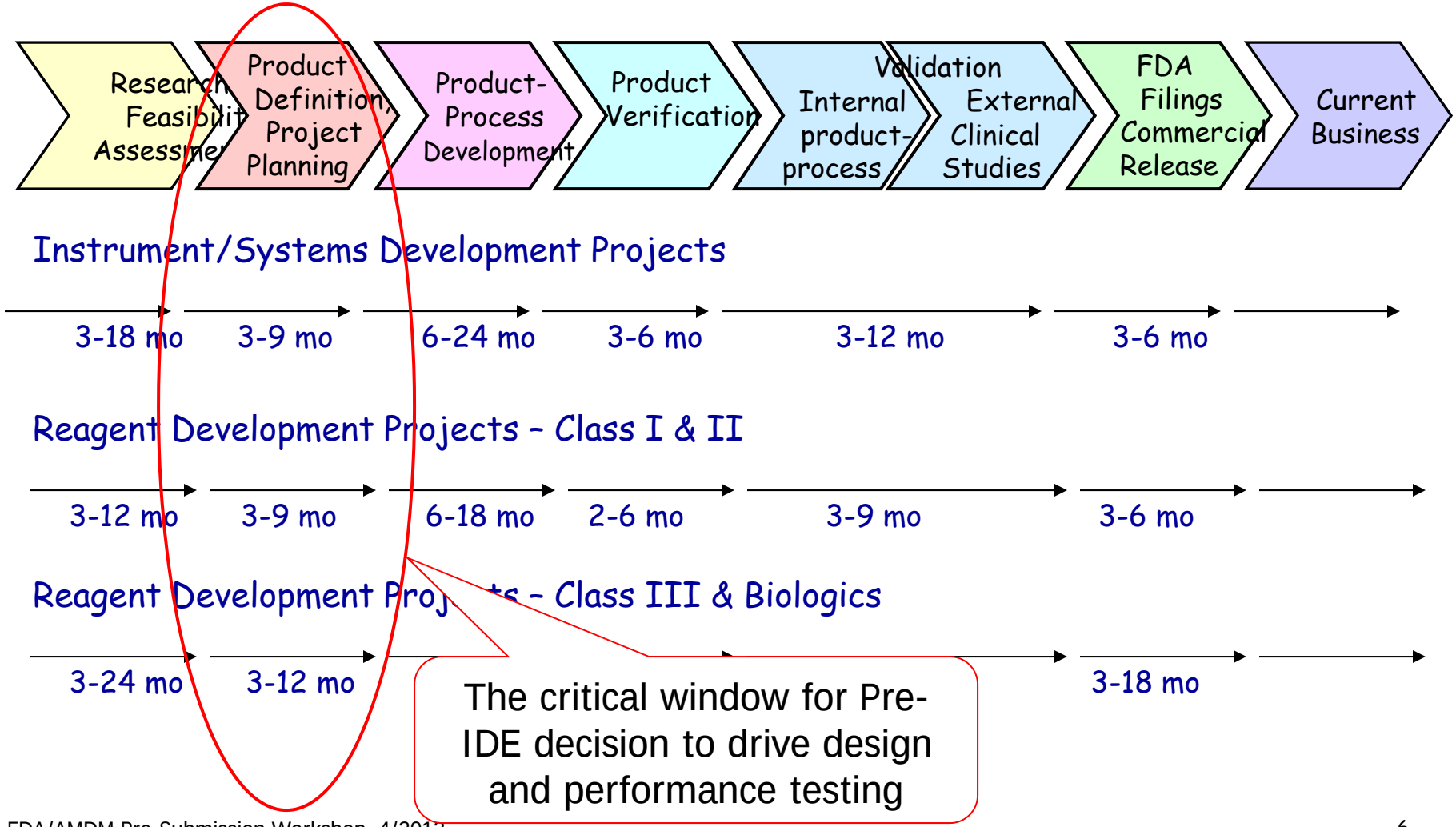
Regulatory Deliverables by Phase

- Regulatory engagement during the product development process



Timeline Models for IVD Product Development

- Timelines vary by project & complexity



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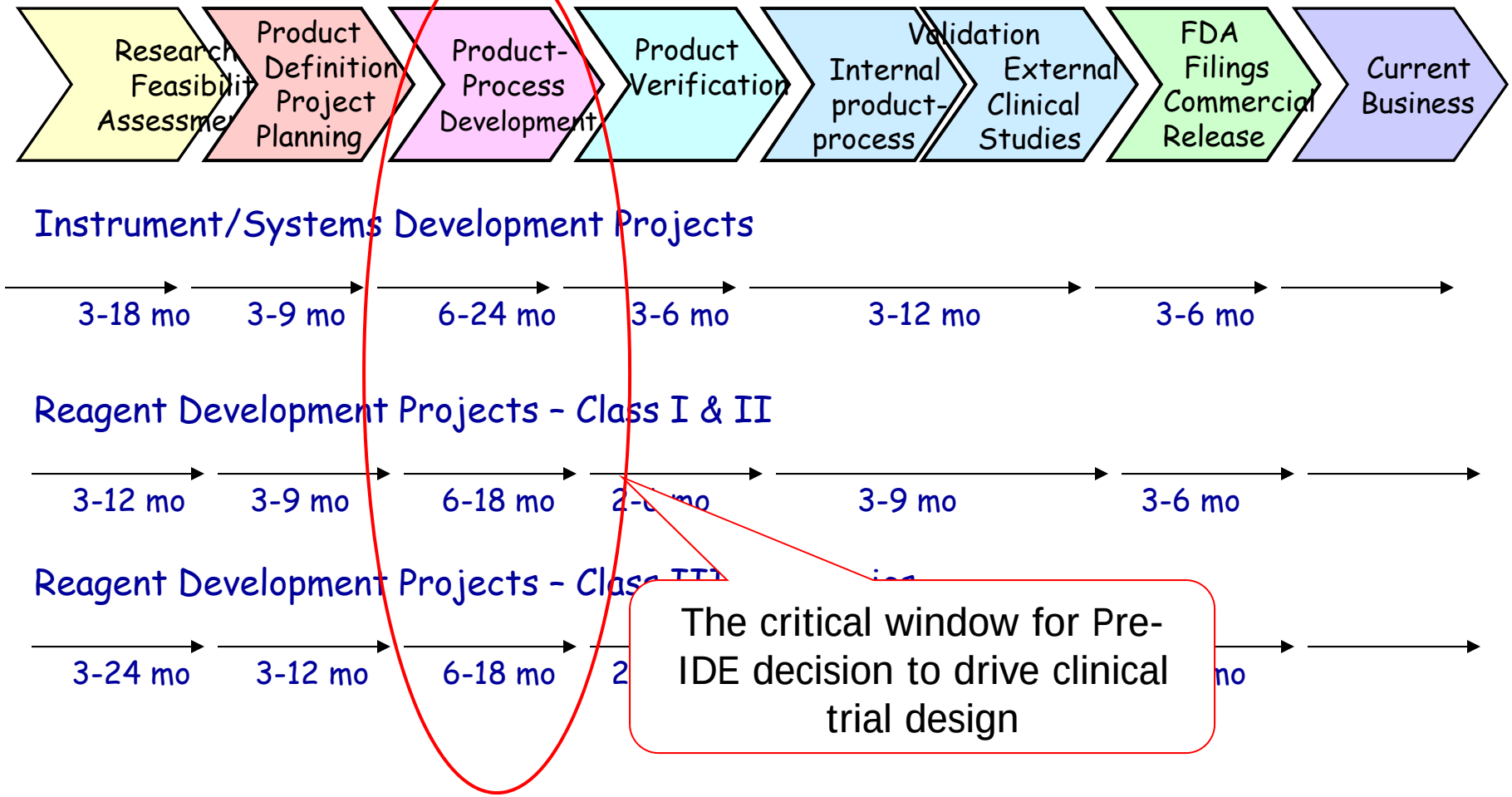

Business Drivers for Early FDA Interaction

Business Drivers for Pre-IDE

- 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 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 with history of predictable FDA clearance/approval?
  - Or, are there questions we want asked and answered now rather than during review?

Leveraging the FDA Pre-Submission Process

- A Pre-IDE/Pre-Submission activity may be needed if your team has questions around regulatory strategy:
  - Are there bundling concerns that need to be worked prior to the submission?
  - Is there other data needed should a de novo pathway be agreed upon?
  - Is the technology new or particularly complex that FDA will have concerns that could change the classification, data, or submission content?

Leveraging the FDA Pre-Submission Process

- A Pre-IDE/Pre-Submission activity may be needed if your team has questions around intended use:
  - Are there anticipated issues with our intended use versus the classification regulation?
  - Does FDA foresee new public health issues or safety concerns for this device or type of device that would change our intended use?
  - Can the intended use be general or will FDA require specifics (population, instrument, setting, etc.)

Leveraging the FDA Pre-Submission Process

- A Pre-IDE/Pre-Submission activity may be needed if your team has questions around predicate devices:
  - Can multiple predicate devices be used?
  - Are there devices that OIVD has determined are “not suitable” as predicates?
  - Is there a “gold standard” that FDA expect in addition to predicate device data?

Leveraging the FDA Pre-Submission Process

- A Pre-IDE/Pre-Submission activity may be needed if your team has questions around guidance documents or standards:
  - Are there new guidances for products of this type, or new requirements not yet included in updated guidance?
  - Can we use CLSI standards as the “base” of our performance tests or do they have to be as written?

Leveraging the FDA Pre-Submission Process

- A Pre-IDE/Pre-Submission activity may be needed if your team has questions around clinical trials/studies or performance characteristic testing:
  - Will FDA provide feedback on the clinical study design, sample numbers, patient population, or statistical analysis methods enhance the submission?
  - Are there CLIA complexity issues or waived trial design to discuss?
  - Are the performance characteristic (non-clinical) test plans & data analyses acceptable?

Leveraging the FDA Pre-Submission Process

- If no specific issues are identified necessitating a pre-IDE, 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
- Should you decide to submit a pre-IDE, build the time to submit, conduct Q&A, and reach agreement into the IVD product development timeline

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
  - FDA clearance for global registrations
  - Availability of new products to physicians, healthcare providers, and patients

Importance of Timeline Efficiency

- Many companies have successfully utilized the pre-IDE process to obtain early agreement with FDA in the areas of regulatory strategy, intended use, predicate devices, performance and clinical data, statistical analysis, and other areas
- Planning and incorporation of the pre-IDE timing into the product development process is essential to maximize the process benefit