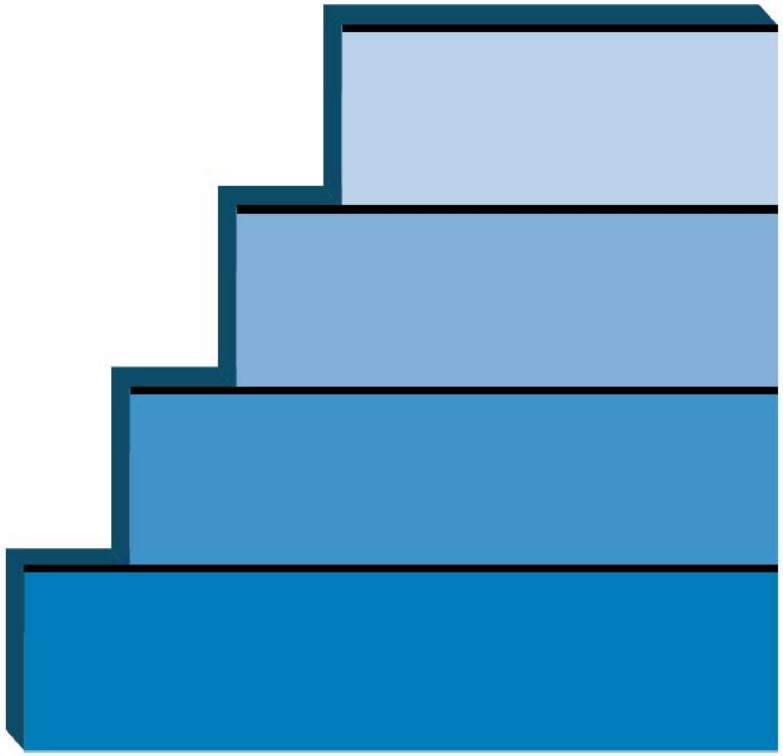
Complex Innovative Trial Designs (CID) Pilot Meeting Program

The Process

U.S. FOOD & DRUG ADMINISTRATION

CID Pilot Meeting Program Benefits



Benefit to Patients

Advancement of CID through Trial Design Transparency

Opportunity for Collaboration

Innovative Medical Product Development

CID Pilot Meeting Program

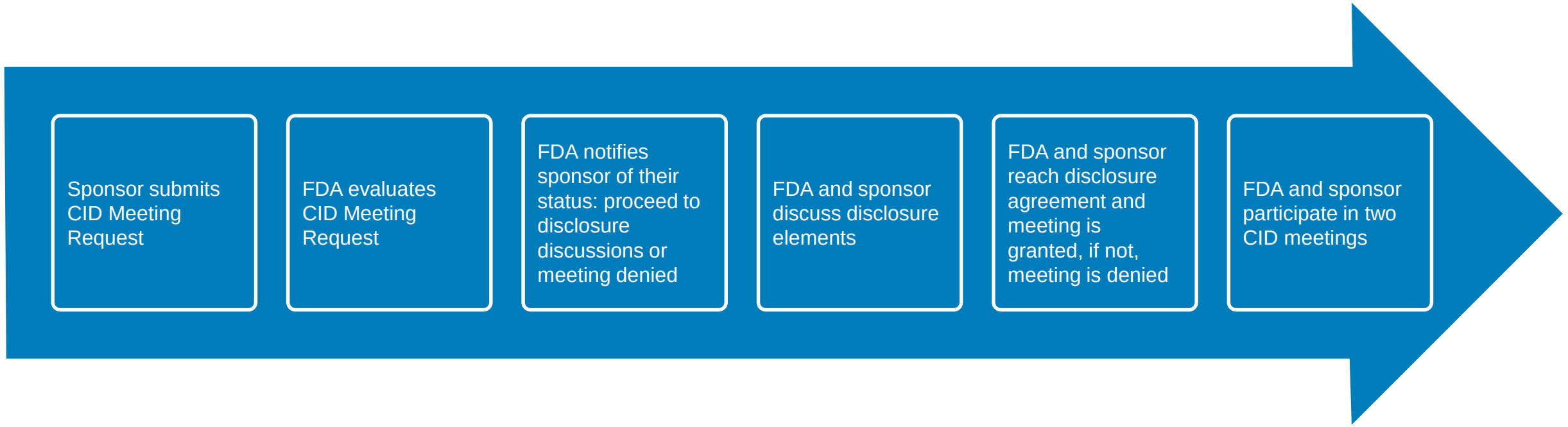
- Five-year program (2018–2022) included in the sixth iteration of the Prescription Drug User Fee Amendments (PDUFA VI)
- Joint effort of the Center for Drug Evaluation and Research and the Center for Biologics Evaluation and Research
- Sponsors have the opportunity to engage with regulatory staff on CID via two meetings approximately 120 days apart
- Meetings are led by statistical review staff with participation from relevant disciplines
- FDA will select up to two CID meeting requests per quarter (with two alternates)
- Under PDUFA VI, FDA will give priority consideration for CID Pilot Meeting Program inclusion to proposals with highly innovative trial designs for which analytically derived properties might not be feasible and for which simulations are necessary to determine design operating characteristics (e.g., type I error*)

*Type I error: the probability of falsely concluding that a medical product has an effect when it does not

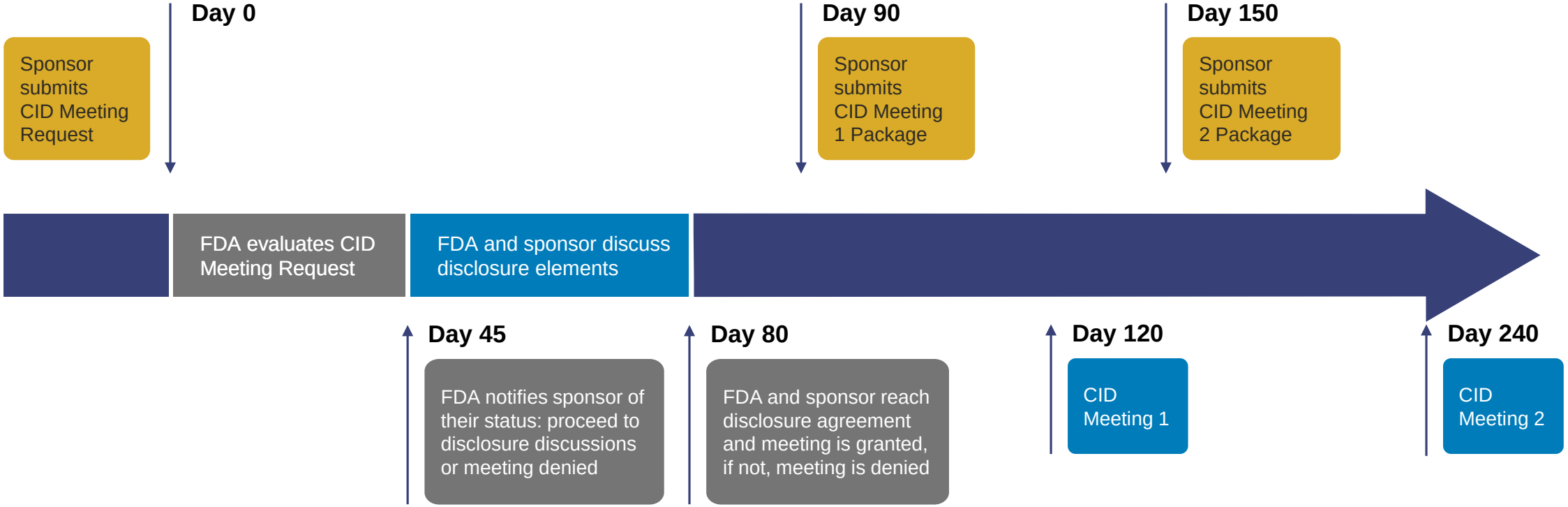
CID Pilot Meeting Program Eligibility Criteria

- The sponsor must have a pre–Investigational New Drug (IND) or IND number for the medical product(s) included in the CID meeting proposal with the intent of implementing the CID in the medical product development program
- The proposed CID is intended to provide substantial evidence of effectiveness to support regulatory approval of the medical product
- The trial is not a first-in-human study, and there is sufficient clinical information available to inform the proposed CID
- **The sponsor and FDA are able to reach an agreement on the trial design information to be publicly disclosed**

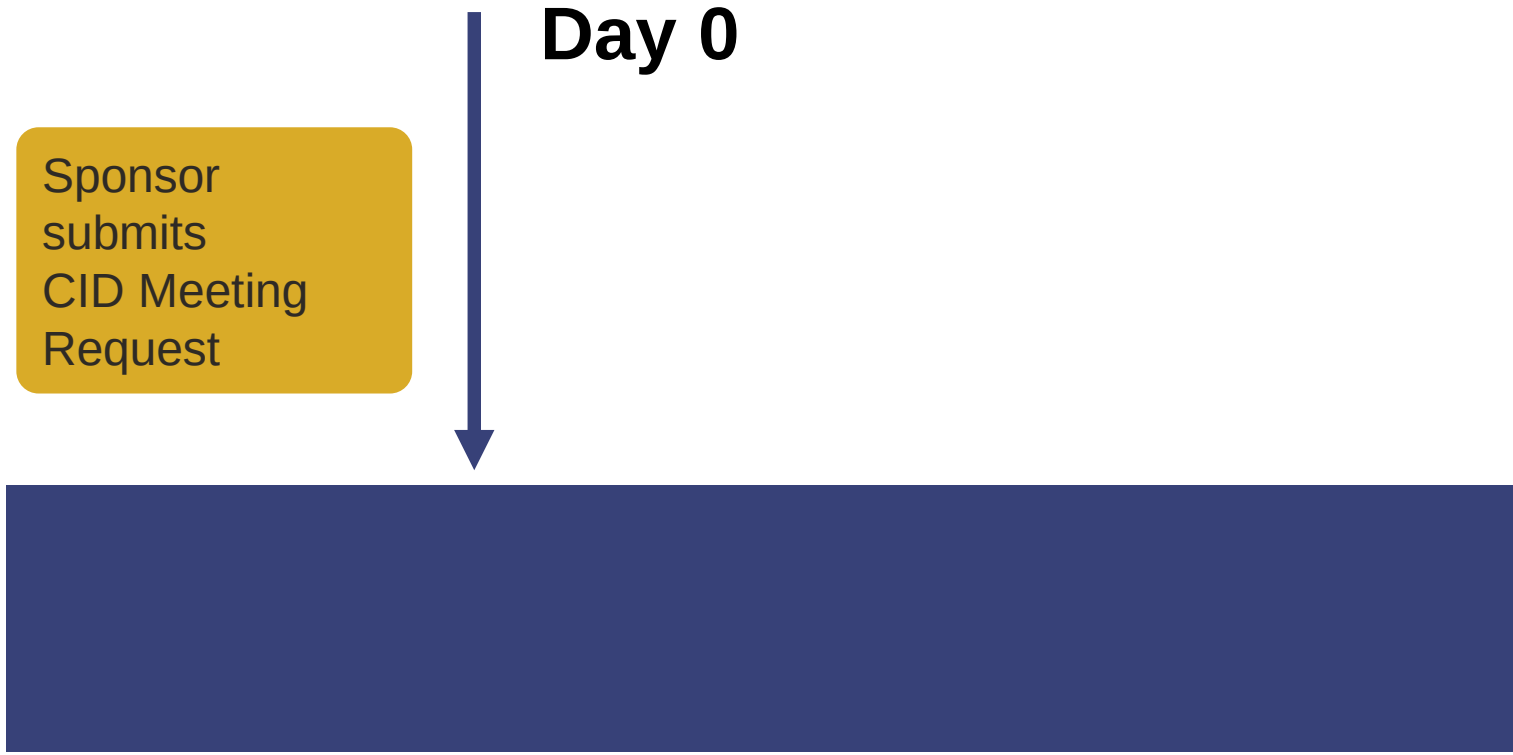
CID Pilot Meeting Process



CID Pilot Meeting Timeline



CID Pilot Meeting Timeline



Sponsor Submits CID Meeting Request

CID Meeting Request contents:

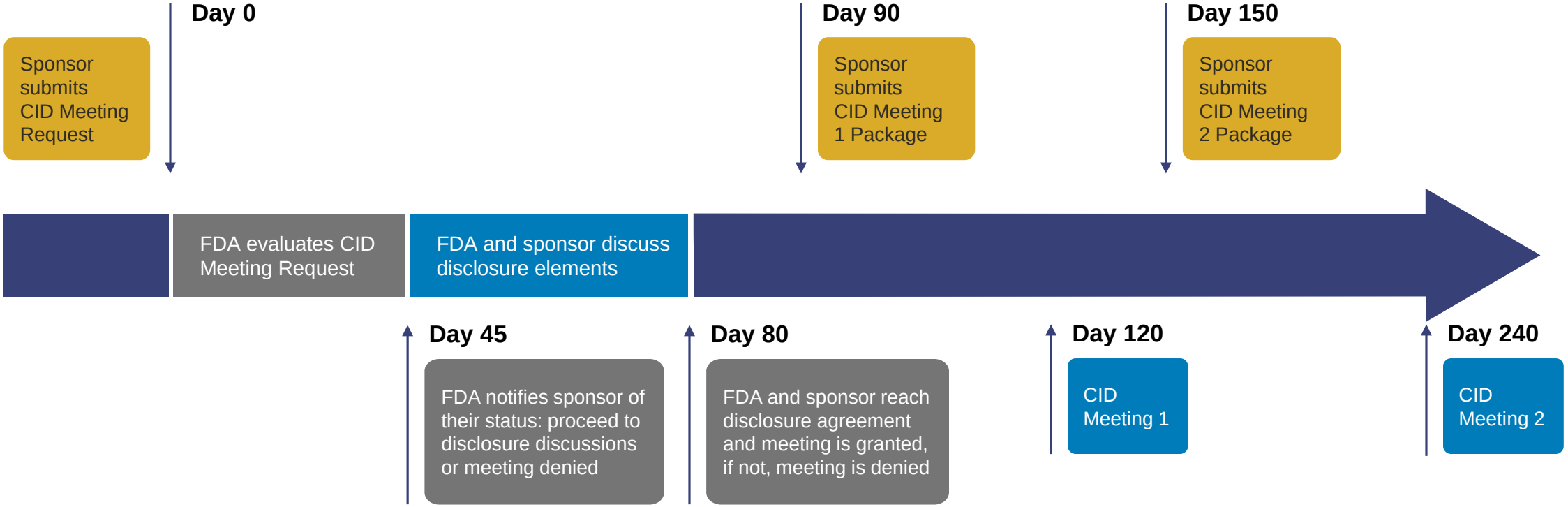
- Product name
- IND or pre-IND number
- Proposed indication(s) or context of product development
- A background section that includes a brief history of the development program and the status of product development
- Trial objectives
- **Brief rationale for the choice of the proposed CID**
- Description of study design, including study schema with treatment arms, randomization strategy, and endpoints

Sponsor Submits CID Meeting Request

CID Meeting Request contents (continued):

- Key features of the statistical analysis plan
- **Simulation plan**
- **Elements of the study design that the sponsor considers non-disclosable, along with a rationale for exclusion**
- A list of issues for discussion with FDA about the specific proposed CID approach for the applicable drug development program and a summarized list of next steps in the regulatory decision-making process, along with any supporting data relevant to the discussion

CID Pilot Meeting Timeline



CID Pilot Meeting Timeline

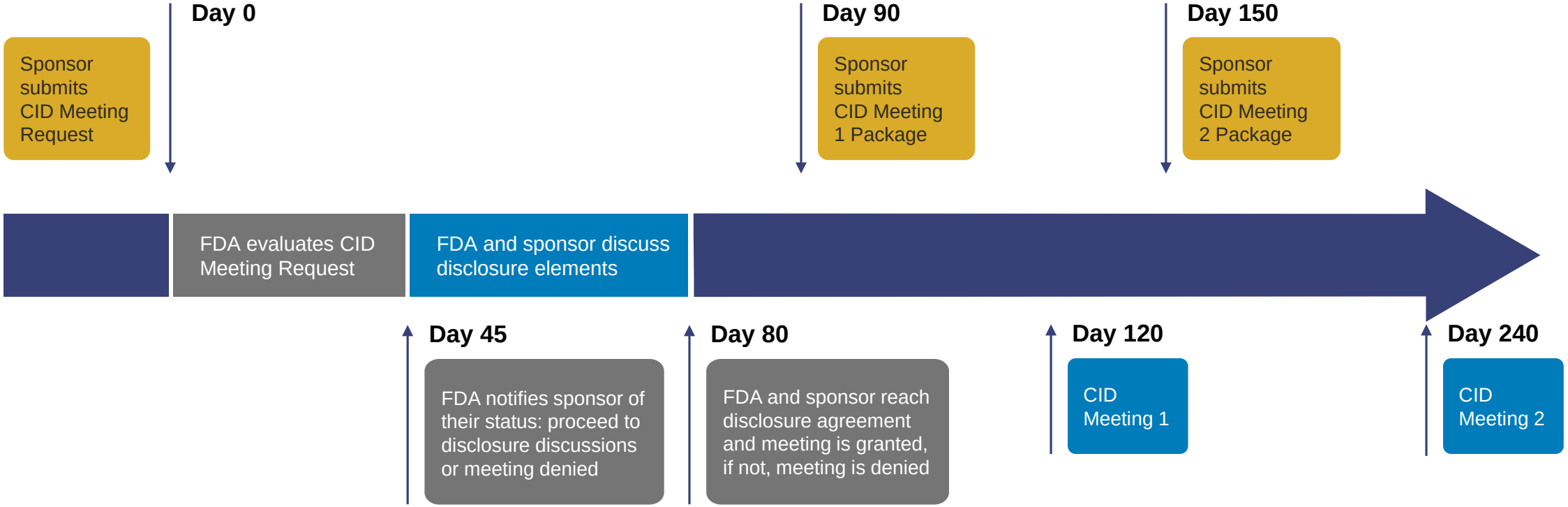
FDA evaluates CID Meeting Request

FDA Evaluates CID Meeting Request

FDA considers the following factors:

- Need for simulations to assess trial design operating characteristics (FDA will give initial priority to this factor)
- Therapeutic need
- Trial design appropriateness for CID Pilot Meeting Program
- Level of innovation of the trial design
- Value proposition of the CID

CID Pilot Meeting Timeline



CID Pilot Meeting Timeline

FDA and sponsor discuss disclosure elements

Day 45

FDA notifies sponsor of their status: proceed to disclosure discussions or meeting denied

Day 80

FDA and sponsor reach disclosure agreement and meeting is granted, if not, meeting is denied

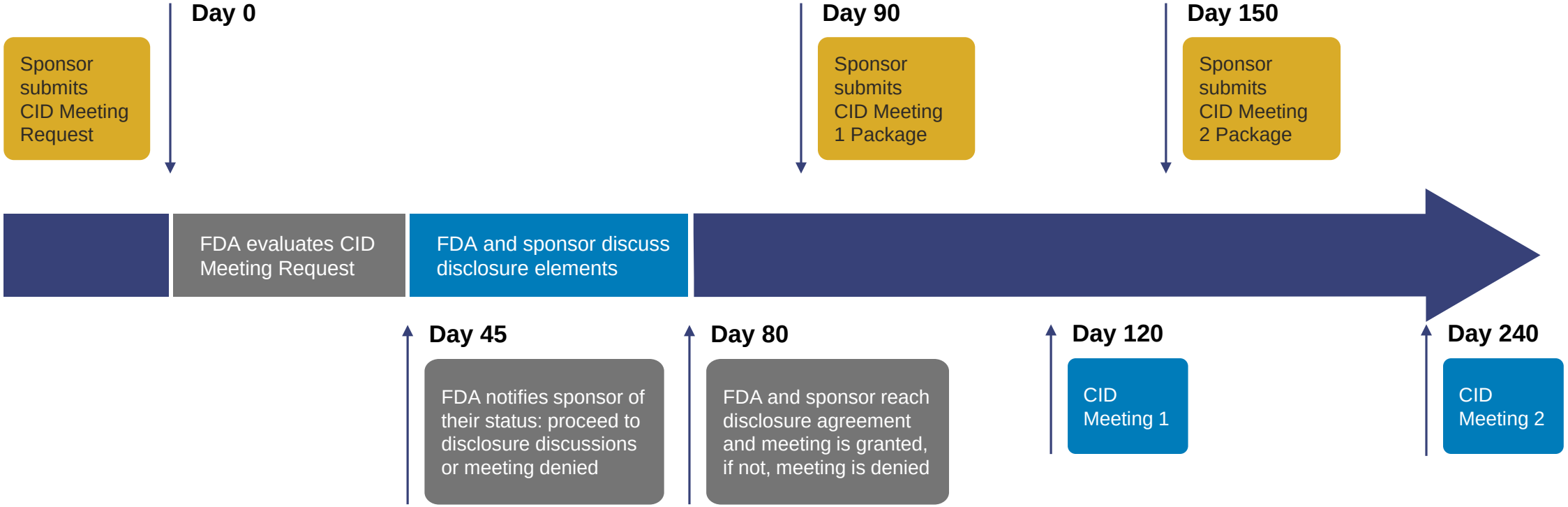
FDA and Sponsor Discuss Disclosure Elements

Disclosure discussion facilitates FDA and sponsor agreement regarding which elements of the study design may be disclosed

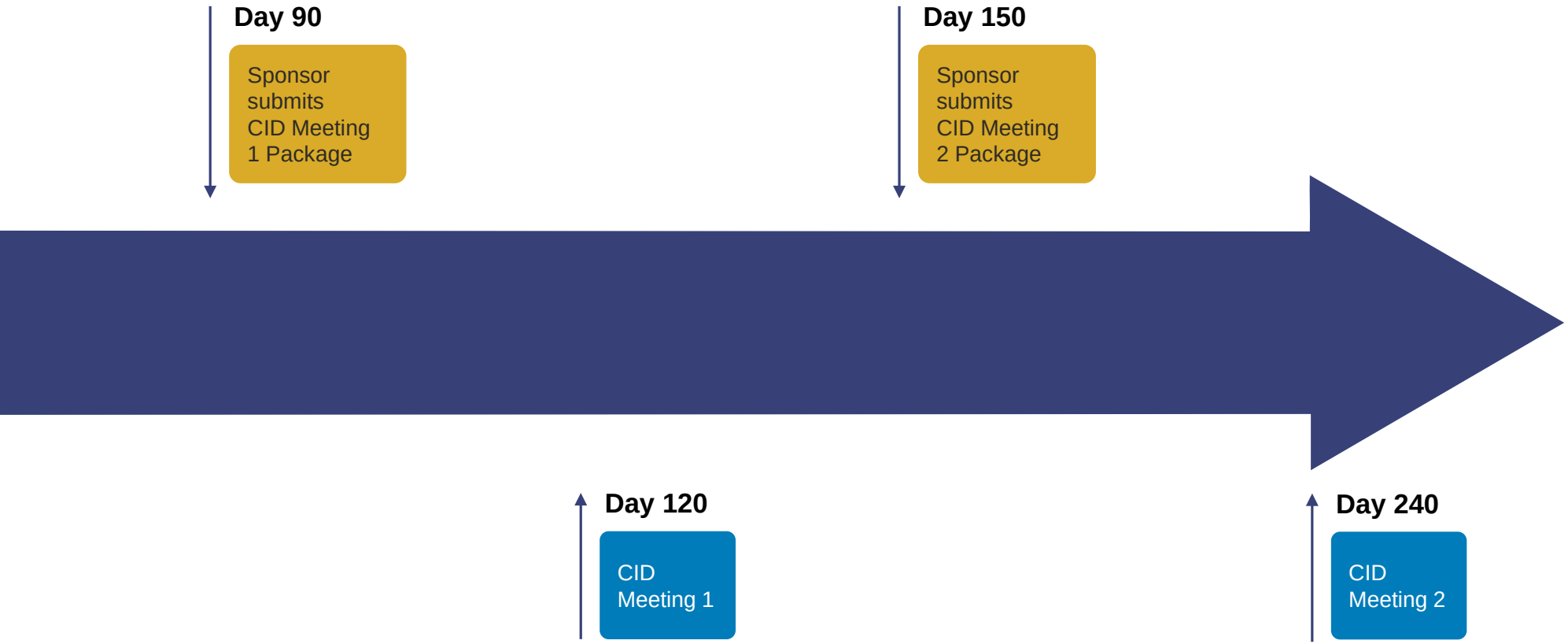
Potential elements for disclosure:

- Study endpoints, to the degree necessary to describe the design
- Target population
- Sample size and power determination
- Null and alternative hypotheses
- Key operating characteristics
- Assumed rates for dichotomous outcomes, or mean and variance for continuous outcomes
- Simulation objectives, simulation scenarios, assumptions, and modeling characteristics
- Critical study design characteristics, including any adaptive elements and, if a Bayesian approach is used, how Bayesian methods are being used for design and/or analysis purposes, how prior distributions are obtained and discounted, and what Bayesian decision rule is considered

CID Pilot Meeting Timeline



CID Pilot Meeting Timeline



FDA and Sponsor Participate in Two CID Meetings

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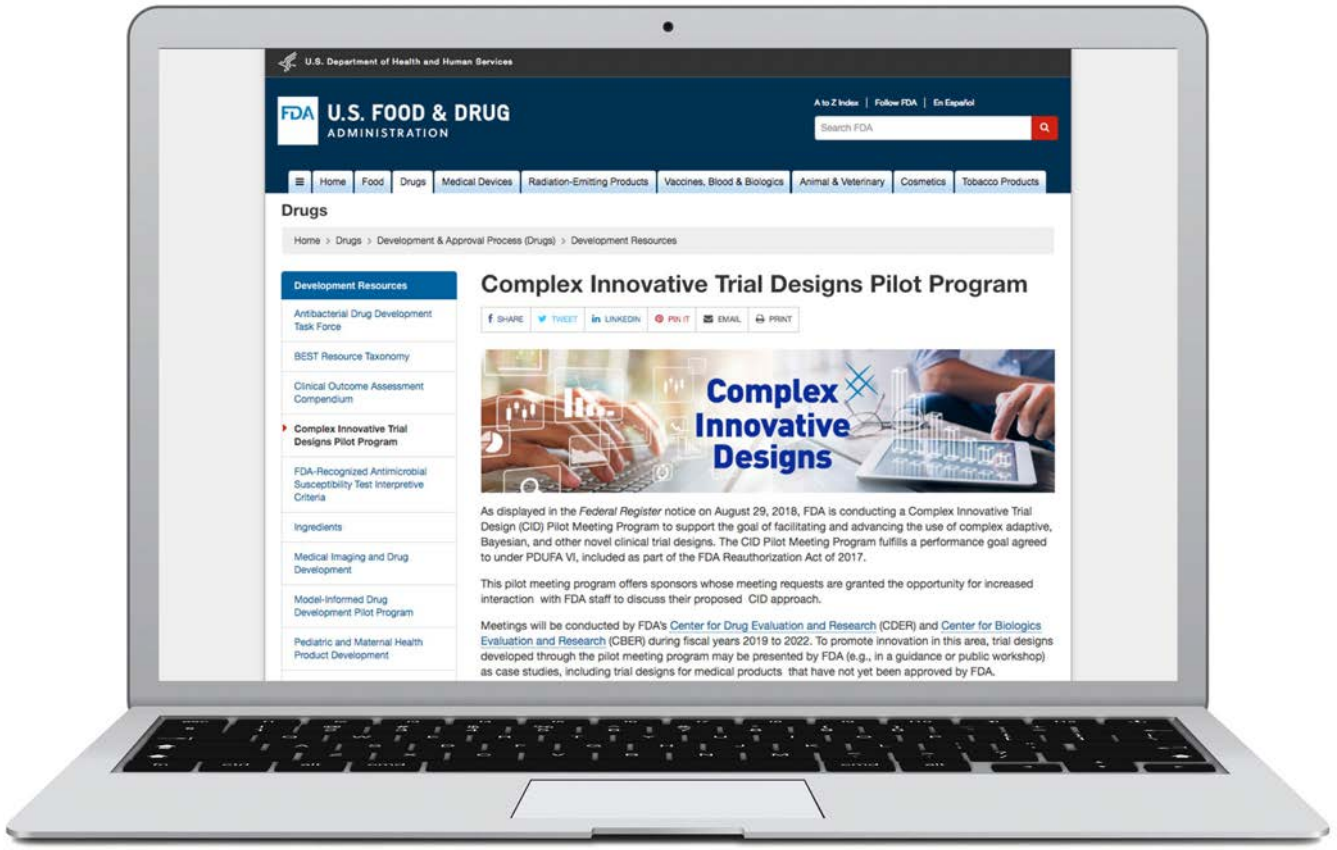
CID Meeting One Package Contents

- Product name (initial and follow-up meeting packages)
- IND or pre-IND number
- Proposed agenda, including time estimates for discussion of each agenda item
- List of discussion questions, along with a brief rationale for the questions
- Detailed description of the statistical methodology
- **Detailed simulation report***
- **Overall conclusions, including:**
  - **A brief summary of the simulated operating characteristics, based on design features and analyses**
  - **A discussion of the utility of the CID, given the simulation results**

*The CID Pilot Meeting Program *Federal Register* notice describes the required components of the simulation report.

CID Meeting Two Package Contents

- Product name (initial and follow-up meeting packages)
- IND or pre-IND number
- Updated background section, including a brief history of development program and status of product development and clinical data to date
- Proposed agenda, including estimated times needed for discussion of each agenda item
- List of discussion questions, along with a brief rationale for the questions
- **Updated programs/shells for simulations, if applicable**
- Summary of new information that is available to support discussions



Complex Innovative Trial Designs (CID) Pilot Meeting Program
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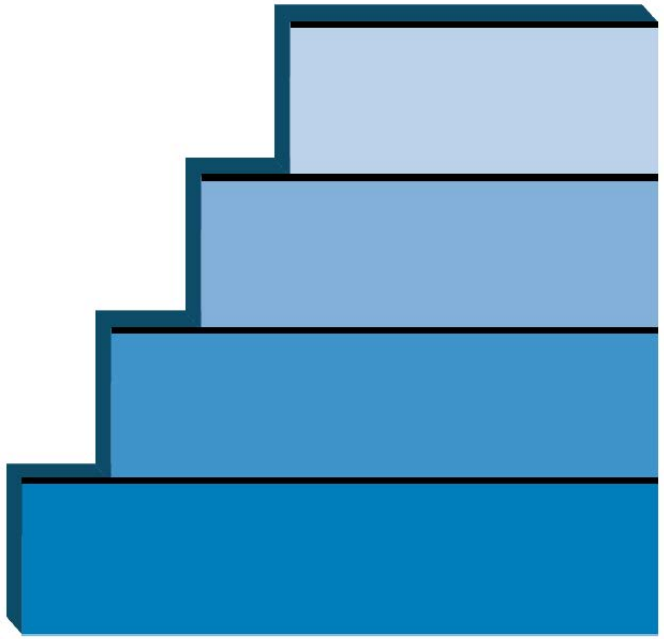
CID Pilot Meeting Program Success

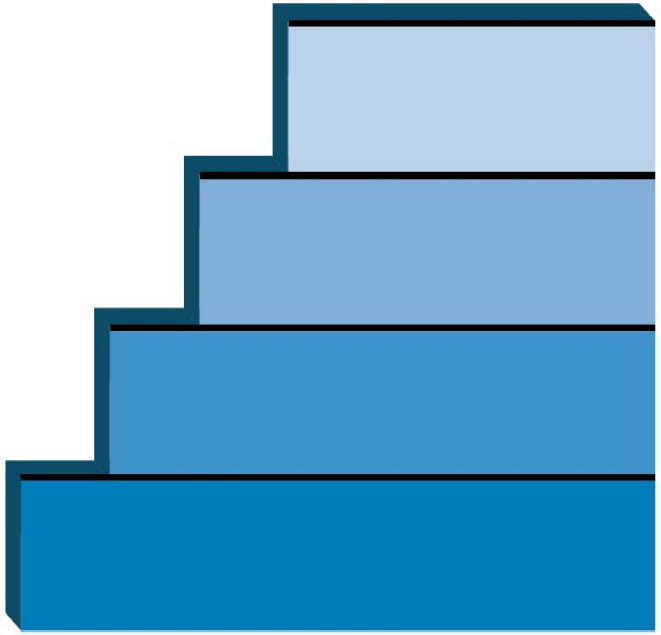
Advances the use of complex adaptive, Bayesian, and other novel clinical trial designs



CID Pilot Meeting Program Success

Patients Benefit

Promotes development of new therapies across a diverse range of therapeutic areas where a need exists



Thank you!

For more information, visit: https://www.fda.gov/CIDpilot

For questions, please email:
CID@fda.hhs.gov