Special Review Designations & Approval Pathways

- Special Designations
  - Fast Track
  - Breakthrough Therapy
  - Priority Review (including voucher programs)
  - Orphan Drug

- Special Approval Pathways
  - Accelerated Approval
  - Animal Rule
Special Review Designations

- **Fast Track Designation**
  - Where: §506(b) of the FD&C Act, part of FDAMA in 1997, amended by Section 901 of the Food and Drug Safety and Implementation Act (FDASIA)
  - Qualifying Criteria:
    - Drug intended to treat a serious condition AND non-clinical or clinical data demonstrate the potential to address an unmet medical need or a drug has been designated as a qualifying infectious disease product (QIDP).
    - Request w/ IND, no later than pre-NDA/BLA meeting, FDA response w/in 60 days
  - Features: expedited development and review through rolling review process.
Special Review Designations

- Breakthrough Therapy Designation
  - Where: §506 (a) of the FD&C Act, added by §902 of FDASIA
  - Qualifying Criteria:
    - Drug intended to treat a serious condition AND preliminary clinical evidence indicates that the drug may demonstrate substantial improvement on a clinically significant endpoint(s) over available therapies.
  - Request: w/ IND, no later than End of Phase 2 Mtg., FDA response w/in 60 days
  - Features: all fast-track features, intensive guidance on efficient drug development during IND, as early as Phase 1, organizational commitment w/ senior leadership (“all hands on deck approach”)

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Special Review Designations

- **Priority Review**
  - Where: Prescription Drug User Fee Act (PDUFA) of 1992
  - Qualifying Criteria:
    - Application (original or efficacy supplement) for drug that treats a **serious condition** AND if approved *would provide a significant improvement in safety or effectiveness* OR
    - Supplement for labeling change pursuant to a report on a pediatric study under Pediatric Research Equity Act OR QIDP OR any application or supplement submitted with a Priority Review Voucher
  - Request with BLA, NDA or efficacy supplement, FDA response in 60 days
  - Features: 6 month review clock vs. normal 10 month
Special Review Designations

- Orphan Drug Designation
  - Qualifying criteria:
    - Sponsor must submit documentation demonstrating that “the disease or condition for which the drug is intended affects fewer than 200,000 people in the United States or, if the drug is a vaccine, diagnostic drug, or preventative drug, the persons to whom the drug will be administered in the United States are fewer than 200,000.”
  - Features: no PDUFA fee, 7 years of marketing exclusivity (active ingredient + indication), will typically receive fast track and/or priority review but this is not automatic.
Special Approval Pathways

- **Accelerated Approval**
  - Where: 21 CFR 314, Subpart H (for drugs); 21 CFR 601, Subpart E (for biologics); §506(c) of the FD&C Act as amended by §901 of FDASIA.
  - Qualifying Criteria:
    - A drug that treats a **serious condition** AND provides **meaningful advantage** over available therapies AND demonstrates an effect on a **surrogate endpoint** that is reasonably likely to predict clinical benefit OR on a **clinical endpoint** that can be measured earlier than an effect on irreversible morbidity or mortality (IMM) that is reasonably likely to predict an effect on IMM or other clinical benefit (i.e., intermediate clinical endpoint).
  - Discuss w/ review division as early as possible
  - Features: based on surrogate; Post-marketing study commitments to verify (Phase IV)

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Special Approval Pathways

- Animal Rule
  - Where: 21 CFR §314.600 (Subpart I)
  - Qualifying Criteria:
    - new drug or biologic that intended to “treat or prevent serious or life threatening conditions causes by exposure to lethal or permanently disabling toxic biological, chemical, radiological, or nuclear substances” and where “human efficacy studies cannot be conducted because it would be unethical….and field trials…have not been feasible.” 21 CFR 314.600
  - Discuss w/ review division as early as possible
  - Features:
    - FDA will rely on animal studies to show efficacy when, *inter-alia*, effect is demonstrated in more than 1 animal species predictive of the response in humans; Animal study endpoint is related to the desired endpoint in humans,
    - Post-market studies when exigency emerges. See 21 CFR 314.610.(b)(1)
Review

- **DRUGS**
  - OTC Monograph (over-the-counter drugs)
  - 505(b)(1) NDA (full-scale product application)
  - 505(b)(j) ANDA (generic drugs)
  - 505(b)(2) NDA (reliance on studies without a right of reference)
  - Supplemental NDA (sNDA) (for changes to approved NDA)

- **BILOGICS**
  - 351(a) PHSA Biologics License Application
  - 351(k)(1) Biosimilar
  - 351(k)(2) Interchangeable
  - Supplemental BLA (sBLA) (changes to approved BLA)

- **DEVICES**
  - Exempt
  - 510(k)
  - PMA
  - Determine if Class I II or III

- **Applicable to All**
  - IND or IDE
  - Registration and Listing
  - Good Manufacturing Practices/Quality System Regulation
  - Compliance