Roles and Responsibilities of Division of Biopharmaceutics in the Review Process

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OPQ, ONDP, DBP

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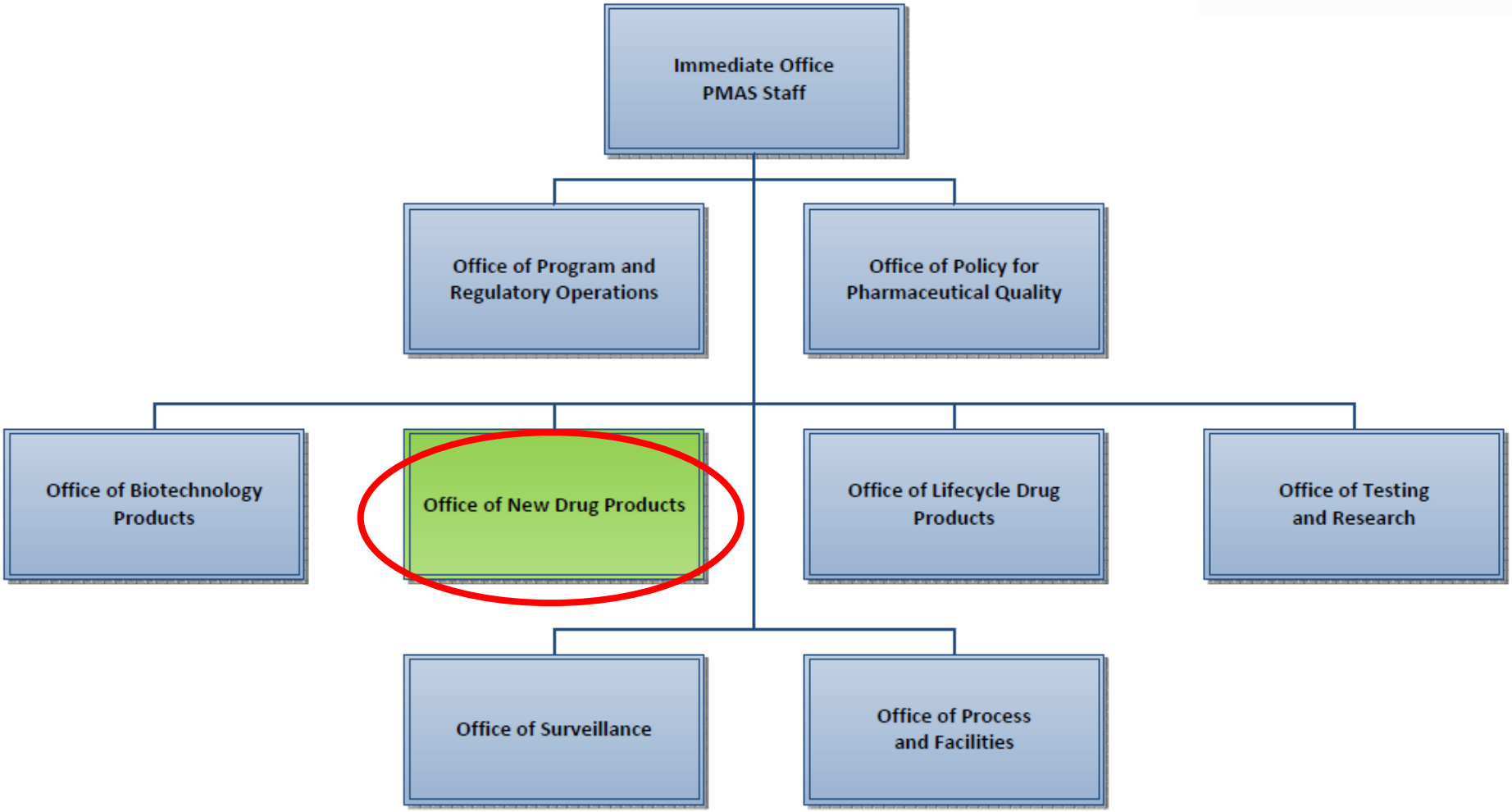
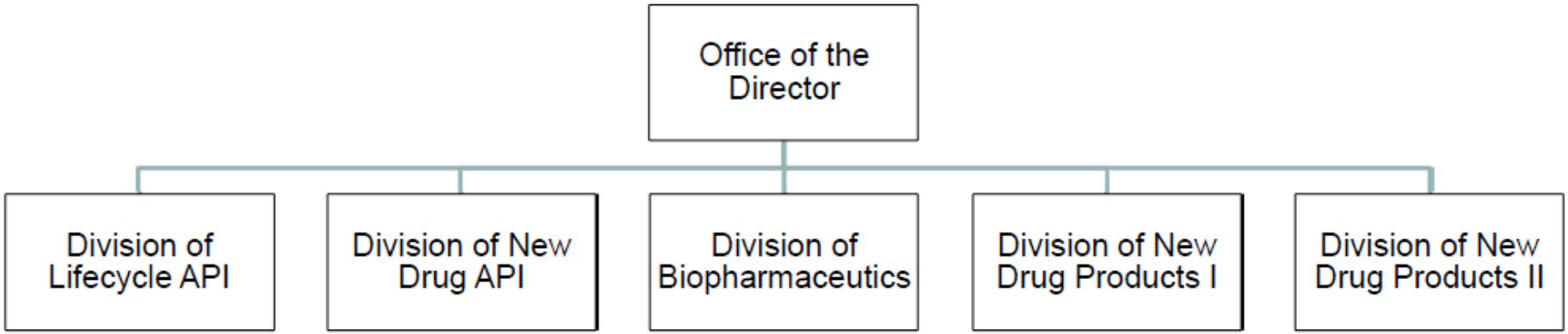
Outline

- What Division of Biopharmaceutics (DBP) does…

- Tips to you for a bump free ride…


Immediate Office
PMAS Staff
Office of Program and Regulatory Operations
Office of Policy for Pharmaceutical Quality
Office of Biotechnology Products
Office of New Drug Products
Office of Lifecycle Drug Products
Office of Testing and Research
Office of Surveillance
Office of Process and Facilities

Organization-ONDP



Office of Pharmaceutical Quality (OPQ, Michael Kopcha)

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Office of New Drug Products (ONDP, Sarah Pope Miksinski)

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Division of Biopharmaceutics (DBP, Paul Seo)

OFFICE OF
PHARMACEUTICAL QUALITY

Office of New Drug Products (ONDP)

One Team One Quality : Partnered for Patients

API

New Drug Product I

IO

BIOPHARM

New Drug Product II

EXPERTISE-BASED TEAM REVIEW: PATIENT-CENTRIC RISK ASSESSMENT

OPQ

OND

PATIENTS

QUALITY DRUGS

Patients First for Quality Drugs

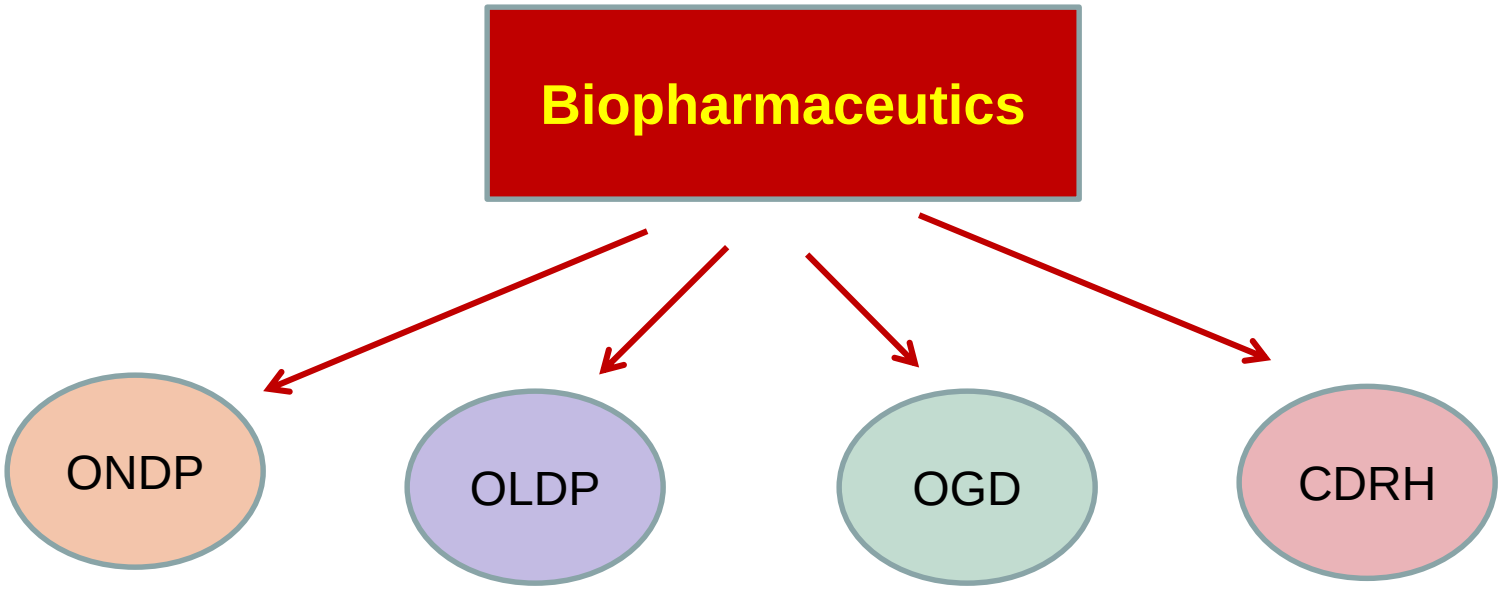
Organization-DBP

- 2 Primary Review Branches
- 1 Support and Research Branch
- Review Branches Organized by Therapeutic Areas
- Support and Research Branch focuses on issues that support review functions (e.g. in silico modelling, IVIVC/R, PKPD, PBPK)

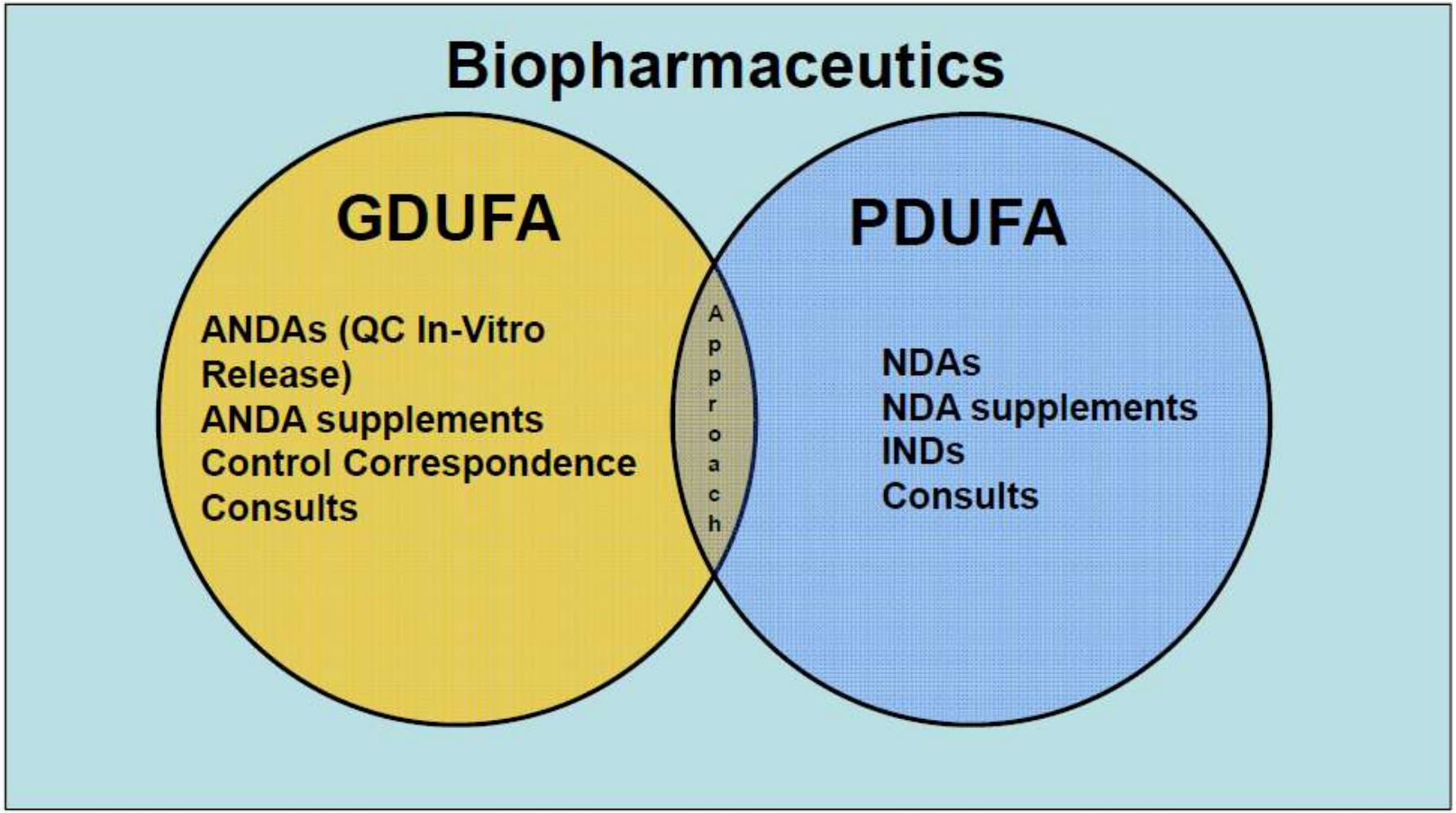
Program Responsibilities

- **PDUFA** related Biopharmaceutics Reviews
  - NDAs
  - NDA supplements
  - INDs
- **GDUFA** related Biopharmaceutics Reviews
  - ANDAs (QC In-Vitro Release)
  - ANDA supplements
  - Consults (OGD, Citizen Petitions, Control Documents)
- **CDRH** Consults

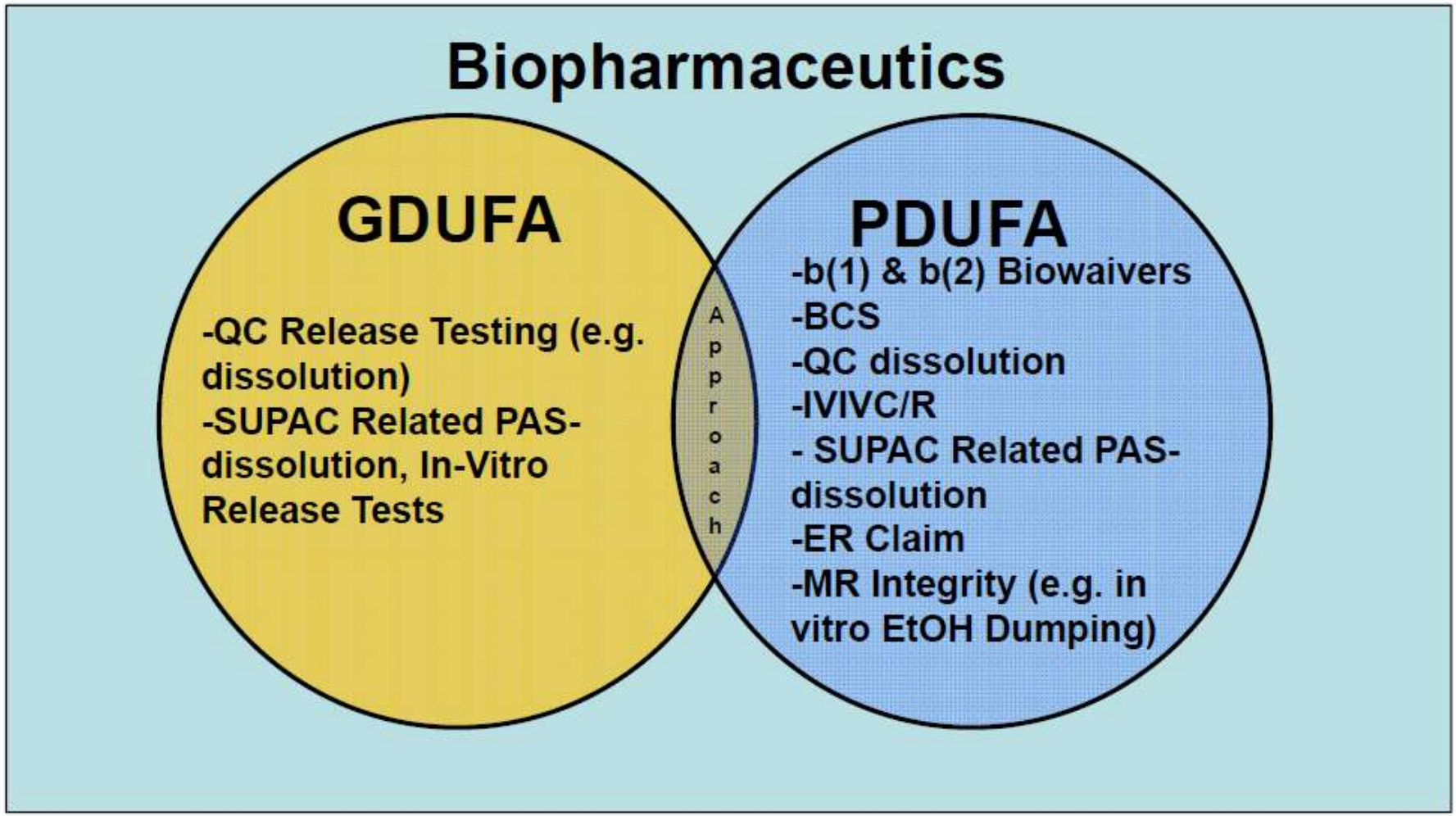
Biopharm Responsibilities



Current State



Generally Covered Areas



OCP- ONDP INTERACTION
Guiding Principles and Responsibilities

- Both pre-approval and post-approval product quality is evaluated in ONDP
- OCP reviews all *in vivo* clinical pharmacology studies
- OCP and ONDP work with other offices in:
  - Granting biowaivers;
  - Developing clinically relevant quality specifications
  - Revision or development of biopharmaceutics-related guidances
- All BE clinical protocols or sponsor questions are reviewed by OCP
- IVIVC/R, IVRT are reviewed by ONDP

OGD- ONDP INTERACTION

Review of Biopharmaceutics-Related Issues: Guiding Principles and Responsibilities for new ANDAs

- DBP reviews all ANDAs for QC release testing for dissolution
- OGD/DBEs reviews all waivers (e.g. DESI, BCS)
- IVIVC is reviewed by OGD/DBEs but consulted to DBP
- Dissolution Review:
  - QC Testing/Multi Media Testing (Dose Dumping) is reviewed by DBP
  - F2, EtOH Dose Dumping is reviewed by OGD/DBEs

OGD - OLDP (DBP) INTERACTION

Guiding Principles and Responsibilities for A/NDA Supplements

DBP reviews:

- API supplier changes that need only dissolution documentation
- SUPAC changes (IR, ER, and TDS) that need only dissolution documentation, SUPAC changes (for non-sterile semisolids) supplements containing comparative IVRT data

OGD reviews:

- BE in vivo or BE in vitro studies
- BE in vitro studies pertaining to nasal and inhalation product post-approval changes

Boiler Plate Language

Solid IR Products:

- **Dissolution Test:** Include the dissolution method development and validation report supporting the selection of the proposed dissolution test with discriminating ability. (This is not the analytical method!!!)
- **Dissolution Acceptance Criterion:** the specification time point should be around where Q=80 % dissolution occurs.

Solid ER/TDS Products:

- **Dissolution Acceptance Criterion:** A minimum of three time points is recommended to set the specifications. The last time point should be the time point where at least 80% of drug has released.

ER Products only:

- Conduct a drug-alcohol interaction study with your ER product.

Boiler Plate Language

IVIVC

Consult: ***Guidance for Industry: Extended Release Oral Dosage Forms: Development, Evaluation, and Application of In Vitro/In Vivo Correlations***

Applications of an IVIVC:

A. Aid in formulation and process development

B. Biowaivers for Changes in the Manufacturing of a Drug Product

C. Setting Dissolution Specification

Boiler Plate Language

IVIVC

- Generally at least 3 release rates are required for the IVIVC development along with selected formulation Information compared to the target
- Detailed *in vitro* method and *in vitro* dissolution profile data including f2 test
- *In vivo* study design and clinical study report including individual and mean plasma concentration versus time profiles
- Approach for IVIVC model development and detailed procedures including the software and modeling data
- Model validation data to show model robustness

Boiler Plate Language

Non-sterile Semisolid Products:

- **IVRT:** develop an *in vitro* release test (IVRT) methodology and propose *in vitro* release acceptance criteria (range) for your drug product to be used systemically at release and during stability as a quality control parameter.
- **IVRT Acceptance Criterion:** Plan to report acceptance criteria (i.e., *specification value with range*) as the rate of release (*slope value*) with proper units (e.g., µg/cm2/hr1/2).
- Presence of an established IVRT method and specification will be useful in bringing back a discontinued product in the absence of a current reference product.

Acknowledgements

- Paul Seo, Ph.D.
- Sarah Pope Miksinski, Ph.D.

Thank you!

Please evaluate this session:

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