Industry Perspective on Clinical Pharmacology Guidances Advancing Drug Development and Regulatory Assessment

Daniele Ouellet, PhD, FSoP
VP & Global Head Clinical Pharmacology & Pharmacometrics,
Johnson & Johnson

FDA/MCERSI Public Workshop, May 9th, 2024

Welcome Opportunity for Discussion on How to Best Advance Drug Development & Regulatory Assessment

How can regulatory guidance help us achieve those goals?

"At every step of drug development, clinical pharmacology is applied to generate, evaluate, and use knowledge of drug disposition, pharmacology, and disease biology to progressively *reduce regulatory uncertainty and inform public health decision-making*"

In industry

At every step of drug development, clinical pharmacology/MIDD is applied to generate, evaluate, and use knowledge of drug disposition, pharmacology, and disease biology to enable efficient drug development through science-based, data-driven decision-making including dose/dosing regimen rationale at every stage of clinical development with a patient centric focus

"Clinical pharmacology principles form the basis of dosage selection and optimization and promote therapeutic individualization by translating the knowledge of patient diversity into clinical recommendations for safe and effective use of medications"

Clinical Pharmacology Guidances Advancing Drug Development and Regulatory Assessment | Center of Excellence in Regulatory Science and Innovation (umd.edu)

Workshop Goals

- ❑ Provide an overview of scientific recommendations pertaining to clinical pharmacology applications during drug development and regulatory assessment.
- ❑ Discuss the current scientific challenges and gaps in applying clinical pharmacology principles during drug development.
- ❑ Identify potential opportunities and priorities for regulatory research and scientific guidance development from a clinical pharmacology perspective.

<u>Session 6 Objectives</u>

1) Provide an overview of clinical pharmacology guidances that provide recommendations on model based approaches to support drug development and regulatory decision-making
2) Identify gaps and future opportunities

Industry Perspective (sample of 1)

- Clinical Pharmacology & Pharmacometrics ~30 years
  - Need many specialized expertise for each of the guidance
  - Perspective is not meant to be an in-depth look at each available guidance
  - Focus on Clinical Pharmacology but expanded to other relevant guidances
  - Focus on FDA guidance only (although some topics are covered in various ICH guidelines)
- Overview of regulatory guidance (including both draft and final)
  - What is considered core (‘routine’)
  - What are some of the challenges we face in industry
  - What are some of the gaps/opportunities
- Presentation represents 1 industry’s opinion to start conversation and debate

Clinical Pharmacology & Application of MIDD

TOOLS

Translational PK/PD
PopPK, PK/PD, ER
Disease Progression
QSP
MBMA/Landscape
PBPK
ML/AI/RWE

APPLICATIONS

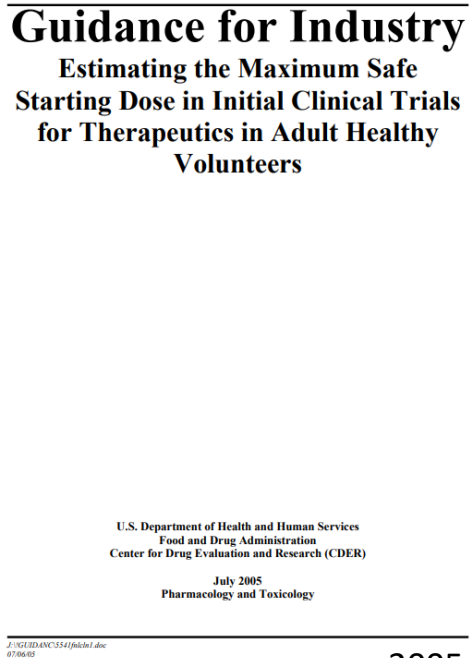
Modified from 'Application of Pharmacometrics in Drug Development' paper submitted To Advanced Drug Delivery Reviews by Y Xiong, M Samtani, D Ouellet

Remit of Clinical Pharmacology (& Pharmacometrics) is broad…8 areas of focus for today

Reviewed many available guidances and summarized as follow:

- Focus #1: Core PK
- Focus #2: Formulation/Product/Route Changes
- Focus #3: Drug-Drug Interactions
- Focus #4: Special Populations
  (including diversity & expanding of clinical trial population)
- Focus #5: New Modalities
- Focus #6: MIDD: Approaches
- Focus #7: MIDD: Clinical Focus
- Focus #8: New Tools & Methodologies

Focus #1 Core PK



Guidance for Industry

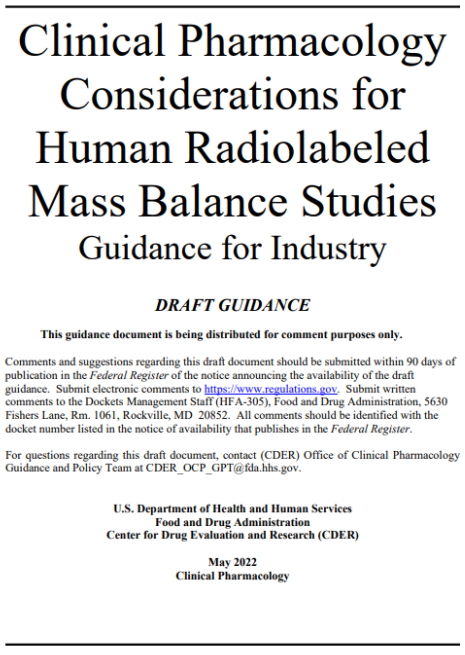
Estimating the Maximum Safe Starting Dose in Initial Clinical Trials for Therapeutics in Adult Healthy Volunteers

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

July 2005
Pharmacology and Toxicology

J:\GUIDANC\5541fnlcln1.doc
07/06/05

2005



Clinical Pharmacology Considerations for Human Radiolabeled Mass Balance Studies

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

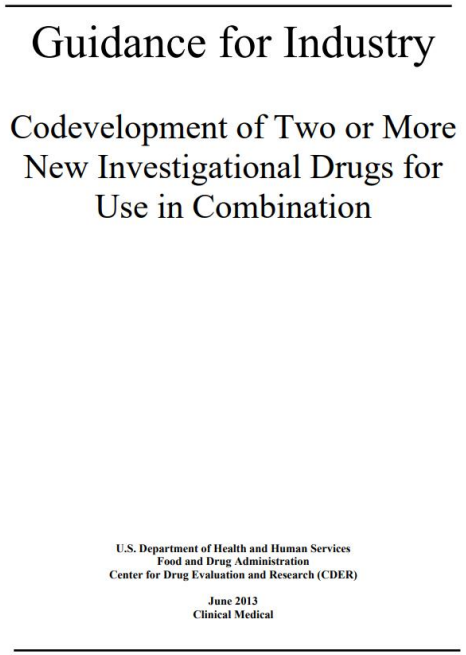
Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Office of Clinical Pharmacology Guidance and Policy Team at CDER_OCP_GPT@fda.hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

May 2022
Clinical Pharmacology

2022



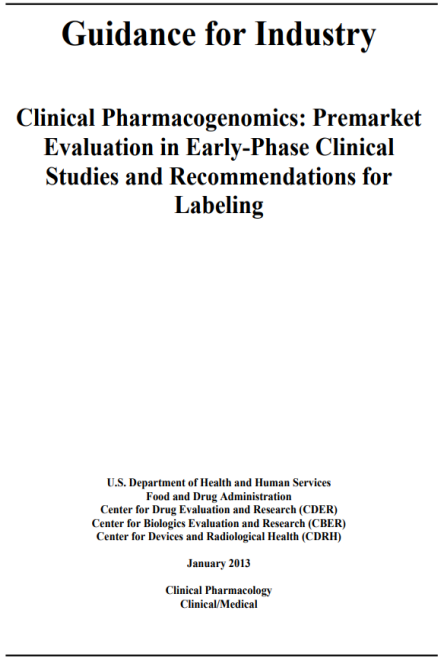
Guidance for Industry

Codevelopment of Two or More New Investigational Drugs for Use in Combination

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

June 2013
Clinical Medical

2013



Guidance for Industry

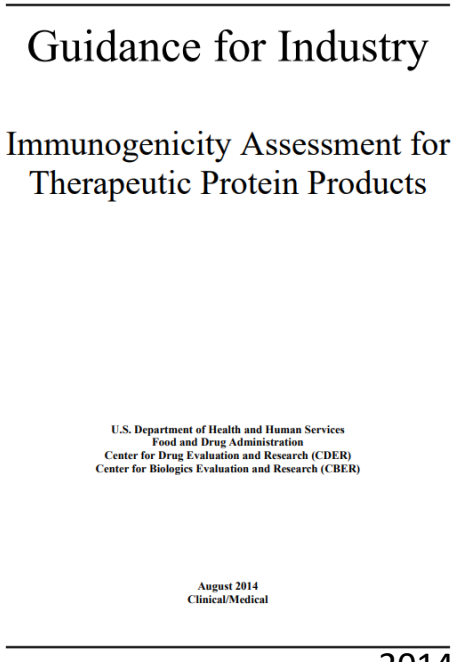
Clinical Pharmacogenomics: Premarket Evaluation in Early-Phase Clinical Studies and Recommendations for Labeling

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

January 2013

Clinical Pharmacology
Clinical/Medical

2013



Guidance for Industry

Immunogenicity Assessment for Therapeutic Protein Products

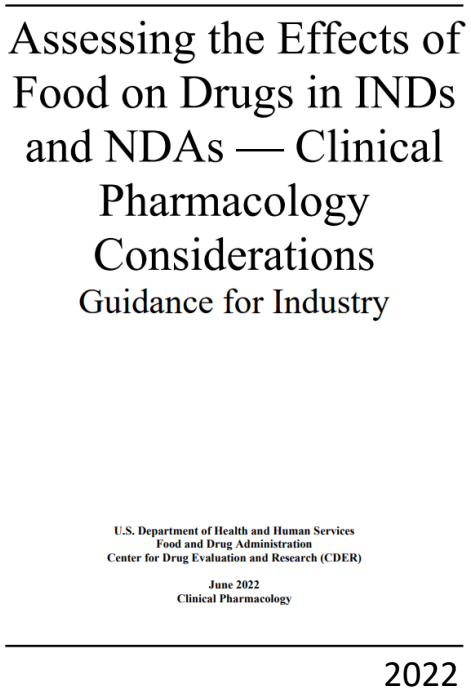
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

August 2014
Clinical/Medical

2014

- Solid foundation on fundamentals with periodic reviews
- Cover wide range of topics supporting core characterization of new drugs & including starting dose
- Challenges with combination development

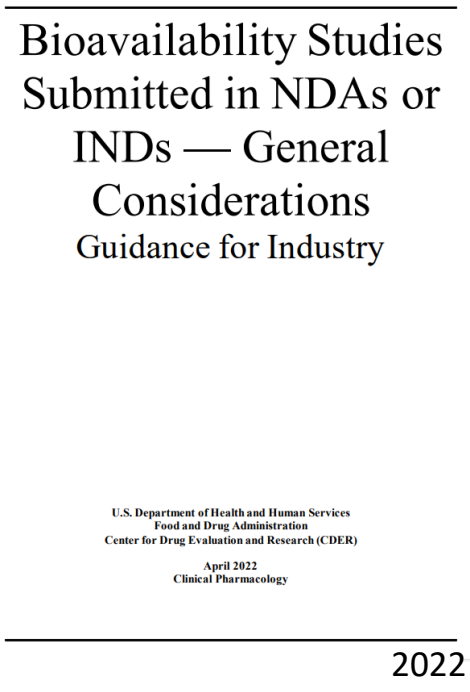
Focus #2 Formulation/Product Change


Assessing the Effects of Food on Drugs in INDs and NDAs — Clinical Pharmacology Considerations
Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

June 2022
Clinical Pharmacology

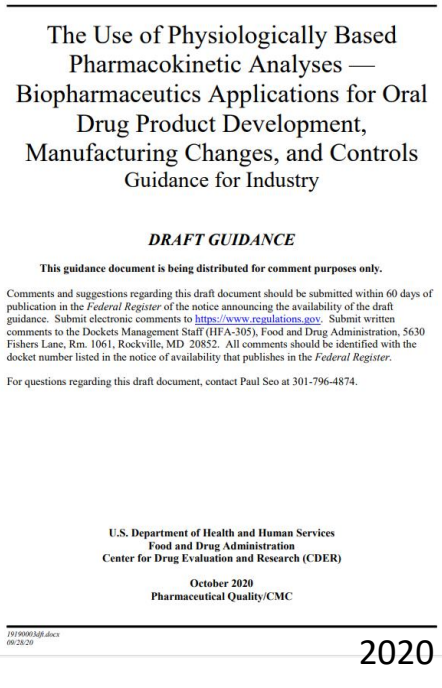
2022


Bioavailability Studies Submitted in NDAs or INDs — General Considerations
Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

April 2022
Clinical Pharmacology

2022


The Use of Physiologically Based Pharmacokinetic Analyses — Biopharmaceutics Applications for Oral Drug Product Development, Manufacturing Changes, and Controls
Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

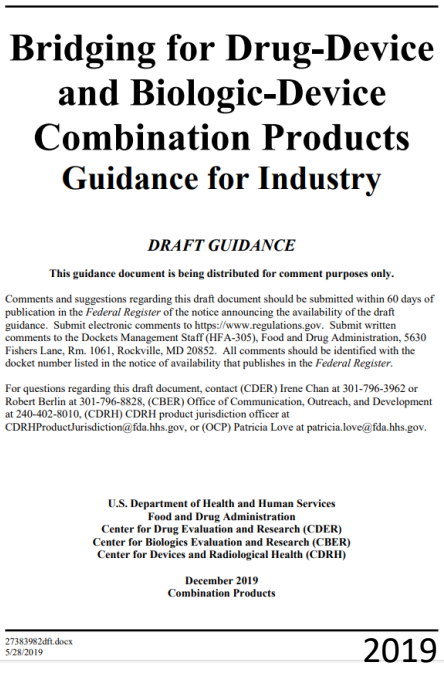
For questions regarding this draft document, contact Paul Seo at 301-796-4874.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

October 2020
Pharmaceutical Quality/CMC

1919090dft.docx
09/28/20

2020


Bridging for Drug-Device and Biologic-Device Combination Products
Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

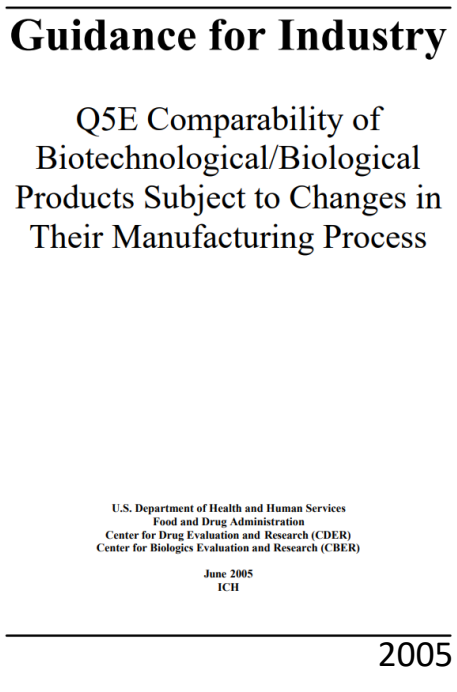
For questions regarding this draft document, contact (CDER) Irene Chan at 301-796-3962 or Robert Berlin at 301-796-8828, (CBER) Office of Communication, Outreach, and Development at 240-402-8010, (CDRH) CDRH product jurisdiction officer at CDRHProductJurisdiction@fda.hhs.gov, or (OCP) Patricia Love at patricia.love@fda.hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

December 2019
Combination Products

27383982dft.docx
5/28/2019

2019


Guidance for Industry

Q5E Comparability of Biotechnological/Biological Products Subject to Changes in Their Manufacturing Process

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

June 2005
ICH

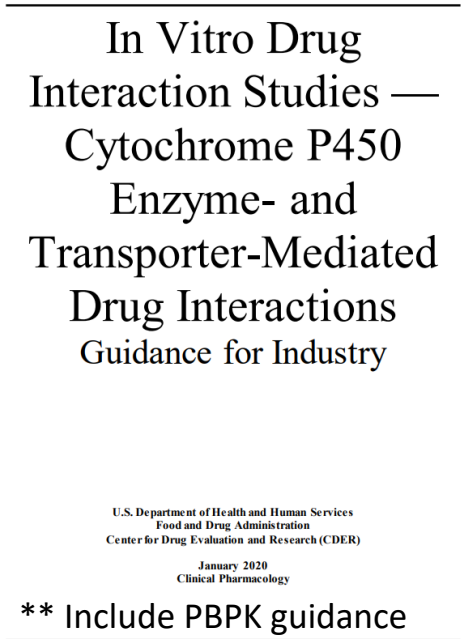
2005

- Rapid development of new drugs leads to inevitable need to change formulation, drug product, cell line, route of administration, etc

Formulation/Product Change – Basics and Opportunities

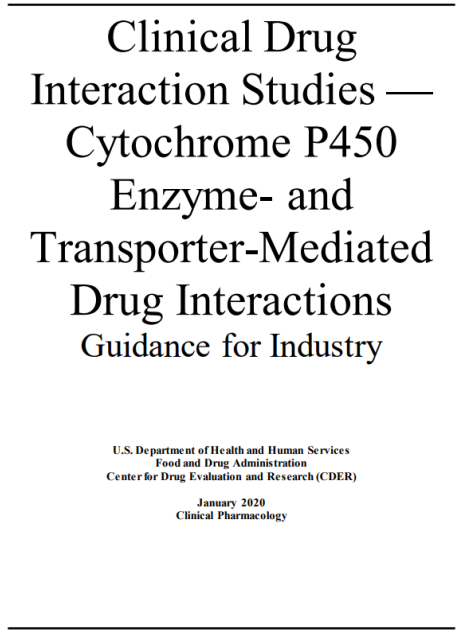
- Core Business
  - Relative BA/BE
  - Path for small molecules
  - Long acting/IVIVC
- Challenges
  - Clinical data package to support change in cell lines relative to stage of development
  - Biopharmaceutic waiver
  - MIDD approaches to support change in route of administration (e.g., IVSC bridging) & other changes
  - Change in manufacturing for new modalities

Focus #3 Drug-Drug Interactions (DDIs)

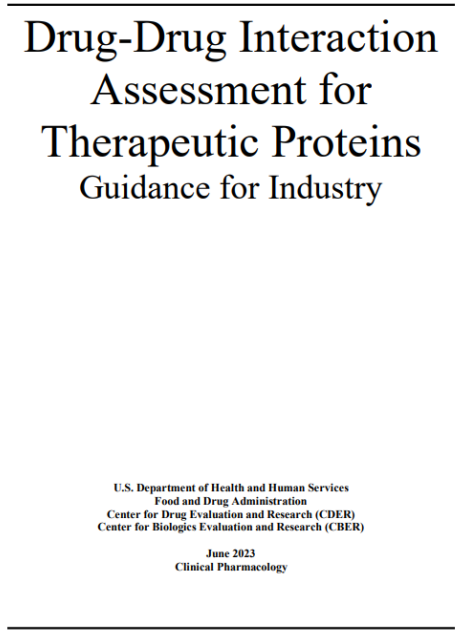


** Include PBPK guidance

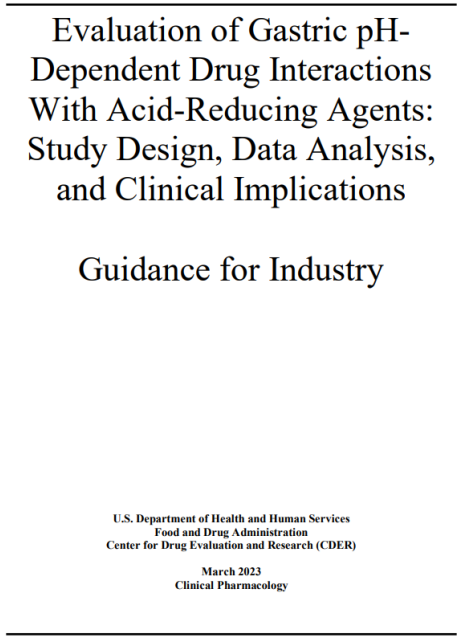
2020



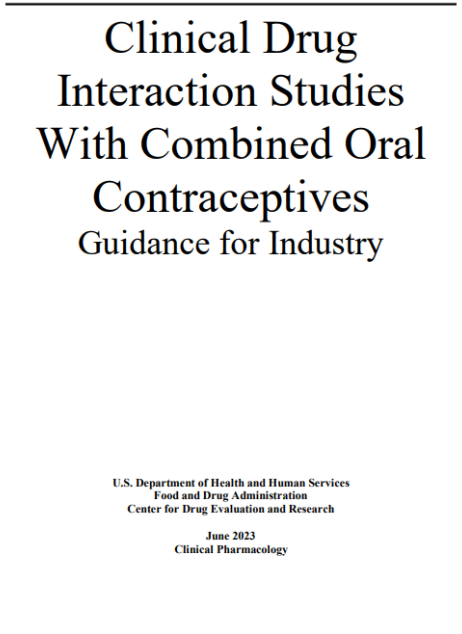
2020



2023



2023



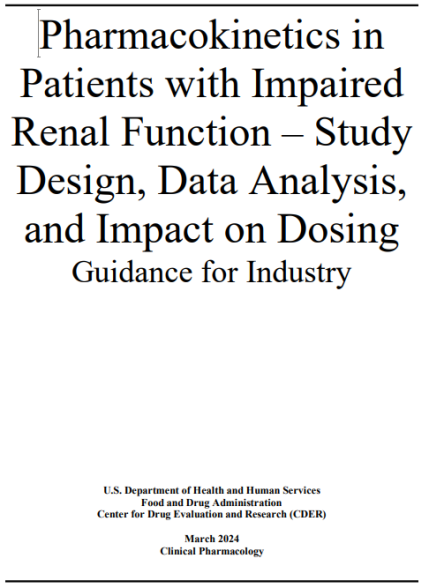
2023

- Well established series of guidance on DDI liability, clinical study requirements & labeling recommendations

DDIs – Basics and Opportunities

- Core Business
  - Solid guidance with explicit decision trees for different types of DDIs
  - Adoption of the use of PBPK to understand DDI risk and dosing/labeling recommendations
  - Increased understanding of risk of DDI with therapeutic proteins
- Challenges
  - Better understanding of impact on transporters and use of endogenous biomarkers
  - How to leverage population PK analysis for DDI questions
  - Use of modeling to address regulatory questions on combination of factors, e.g., DDI with hepatic or renal impairment

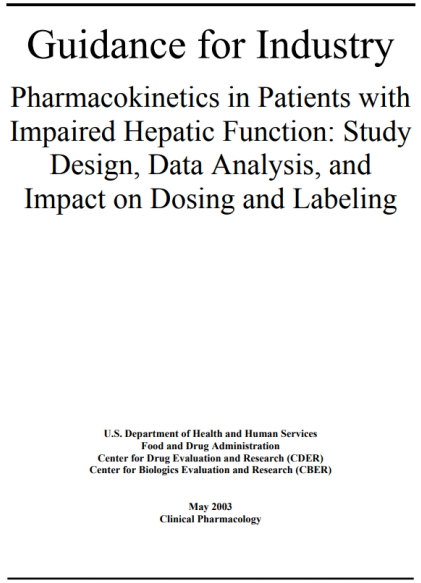
Focus #4 Special Populations


Pharmacokinetics in Patients with Impaired Renal Function – Study Design, Data Analysis, and Impact on Dosing
Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

March 2024
Clinical Pharmacology

2024

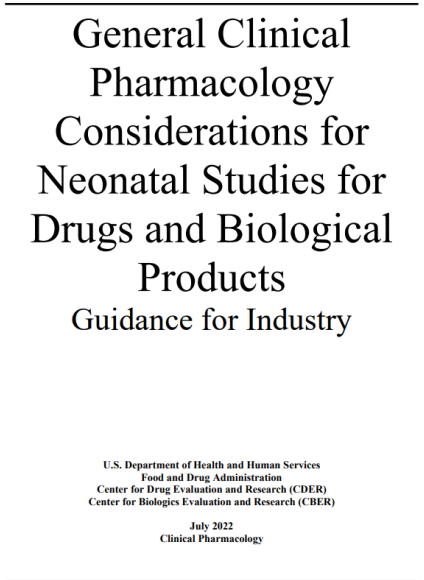

Guidance for Industry

Pharmacokinetics in Patients with Impaired Hepatic Function: Study Design, Data Analysis, and Impact on Dosing and Labeling

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

May 2003
Clinical Pharmacology

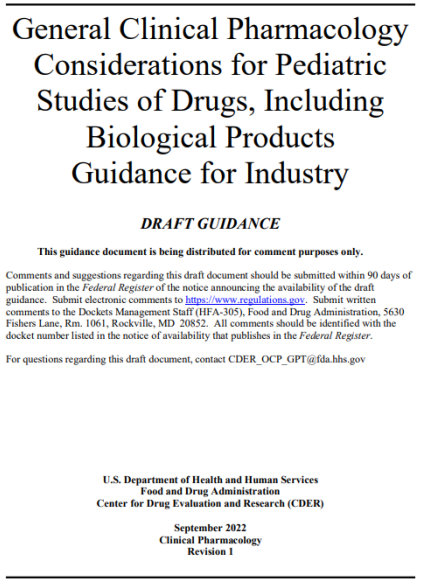
2003


General Clinical Pharmacology Considerations for Neonatal Studies for Drugs and Biological Products
Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

July 2022
Clinical Pharmacology

2022


General Clinical Pharmacology Considerations for Pediatric Studies of Drugs, Including Biological Products
Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

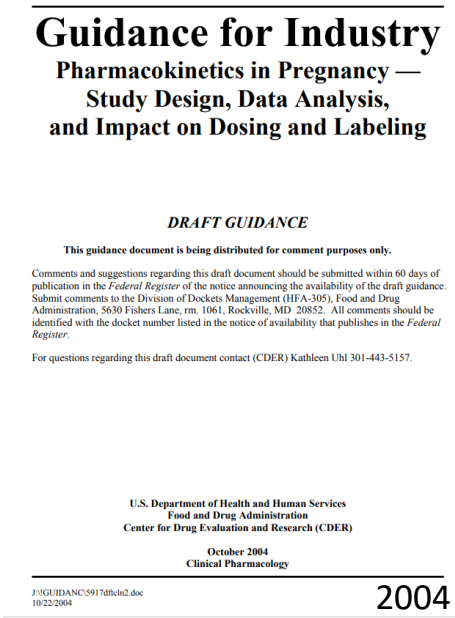
Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact CDER_OCP_GPT@fda.hhs.gov

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

September 2022
Clinical Pharmacology
Revision 1

2022


Guidance for Industry

Pharmacokinetics in Pregnancy — Study Design, Data Analysis, and Impact on Dosing and Labeling

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

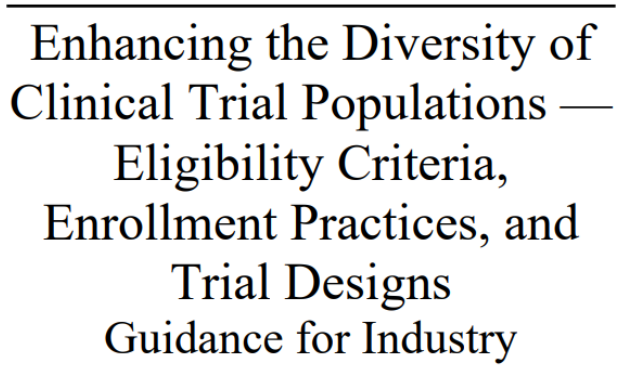
For questions regarding this draft document contact (CDER) Kathleen Uhl 301-443-5157.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

October 2004
Clinical Pharmacology

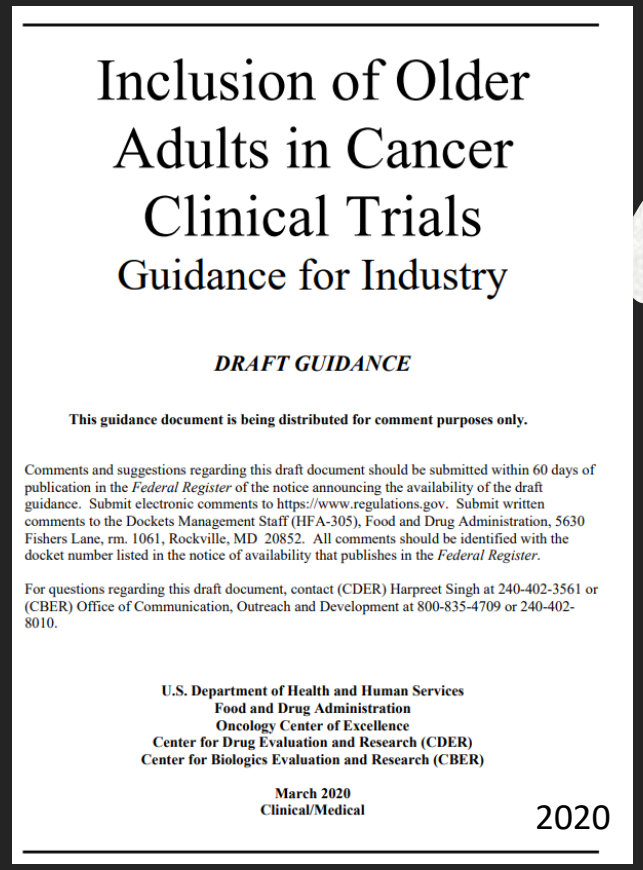
J:\GUIDANC\5917dfcln2.doc
10/22/2004

2004


Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs
Guidance for Industry

2020

Focus #4 Expanding Clinical Trial Population in Oncology



Inclusion of Older Adults in Cancer Clinical Trials

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

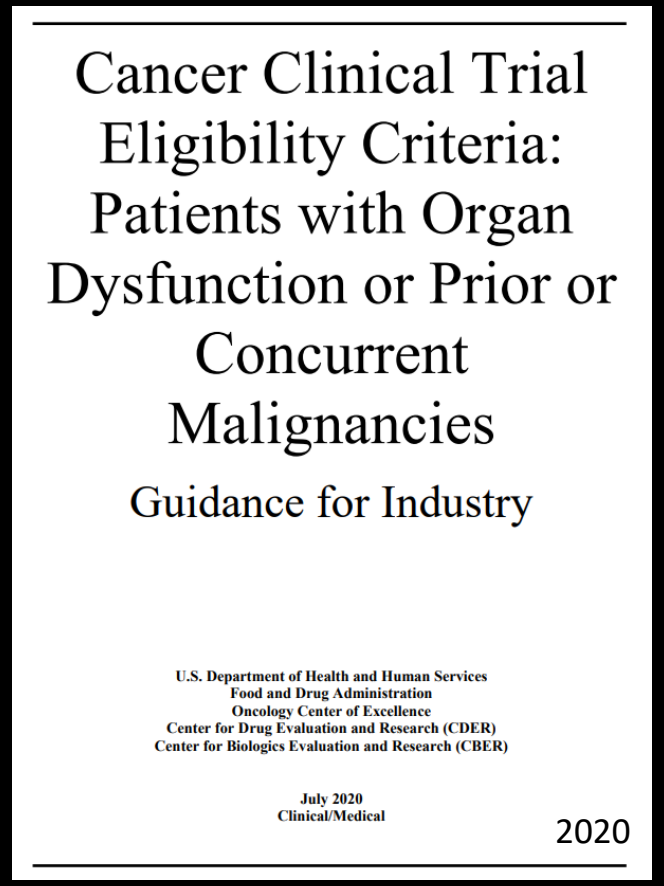
Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Harpreet Singh at 240-402-3561 or (CBER) Office of Communication, Outreach and Development at 800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration
Oncology Center of Excellence
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

March 2020
Clinical/Medical

2020



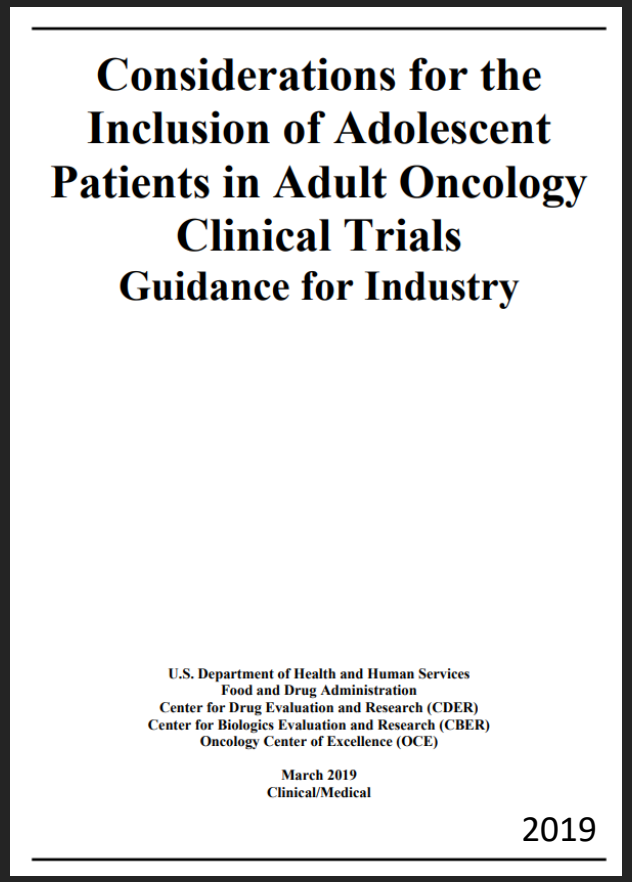
Cancer Clinical Trial Eligibility Criteria: Patients with Organ Dysfunction or Prior or Concurrent Malignancies

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Oncology Center of Excellence
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

July 2020
Clinical/Medical

2020



Considerations for the Inclusion of Adolescent Patients in Adult Oncology Clinical Trials

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Oncology Center of Excellence (OCE)

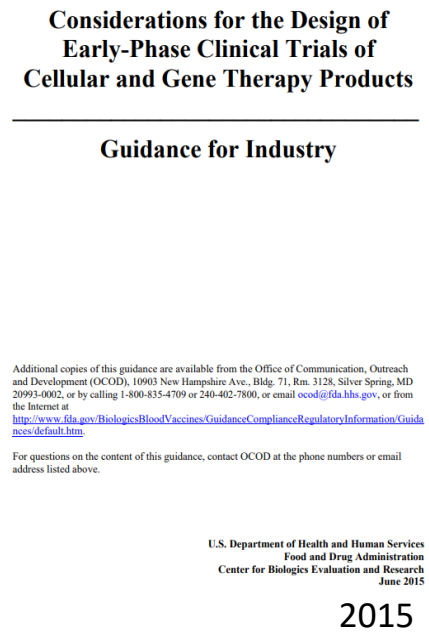
March 2019
Clinical/Medical

2019

Expanding Patient Diversity – Basics and Opportunities

- Core Business
  - Requirement for specialized population (renal, hepatic, pediatric)
  - Need for studies to better reflect patient population
- Challenges
  - Practicality of expanding inclusion/ exclusion criteria (predictions of effects & use of population PK to characterize impact)
  - Better representation of patient population vs. demonstration of benefit risk in a controlled setting
  - Application of PBPK to predict changes with organ dysfunction (early assessment, interpolation/extrapolation) and to support other populations (e.g, transfer to fetus, breast milk)
  - Validity of ‘organs on a chip’
  - Level of evidence required for pediatric assessment including model based approaches

Focus #5 New Modalities



Considerations for the Design of Early-Phase Clinical Trials of Cellular and Gene Therapy Products

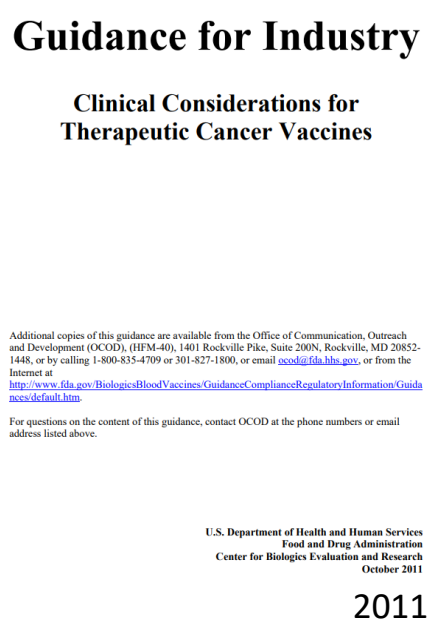
Guidance for Industry

Additional copies of this guidance are available from the Office of Communication, Outreach and Development (OCOD), 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002, or by calling 1-800-835-4709 or 240-402-7800, or email ocod@fda.hhs.gov, or from the Internet at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

For questions on the content of this guidance, contact OCOD at the phone numbers or email address listed above.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
June 2015

2015



Guidance for Industry

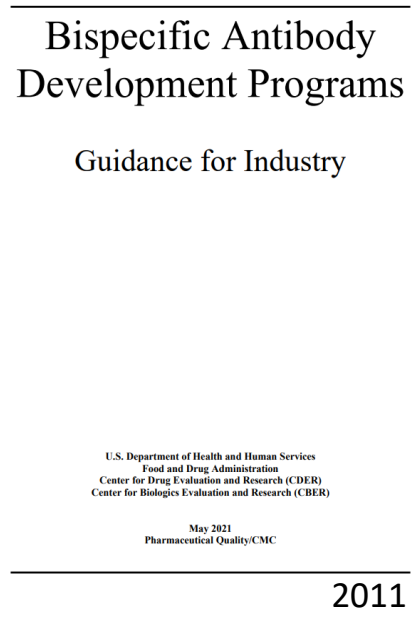
Clinical Considerations for Therapeutic Cancer Vaccines

Additional copies of this guidance are available from the Office of Communication, Outreach and Development (OCOD), (HFM-40), 1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448, or by calling 1-800-835-4709 or 301-827-1800, or email ocod@fda.hhs.gov, or from the Internet at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

For questions on the content of this guidance, contact OCOD at the phone numbers or email address listed above.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
October 2011

2011



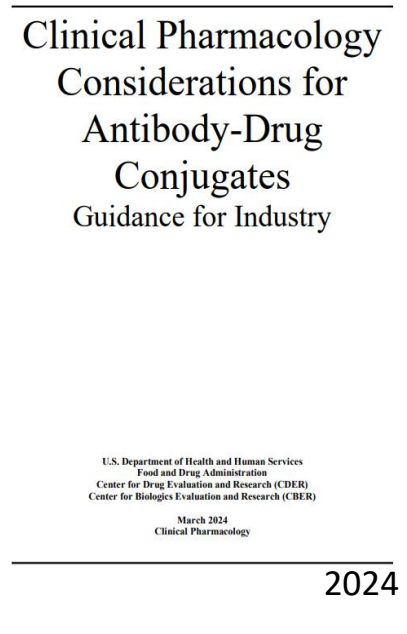
Bispecific Antibody Development Programs

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

May 2021
Pharmaceutical Quality/CMC

2011



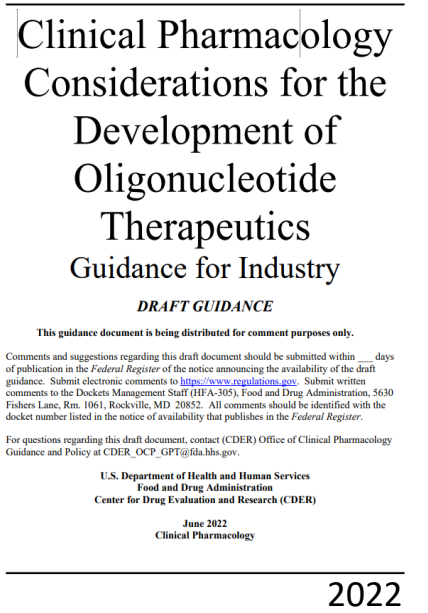
Clinical Pharmacology Considerations for Antibody-Drug Conjugates

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

March 2024
Clinical Pharmacology

2024



Clinical Pharmacology Considerations for the Development of Oligonucleotide Therapeutics

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

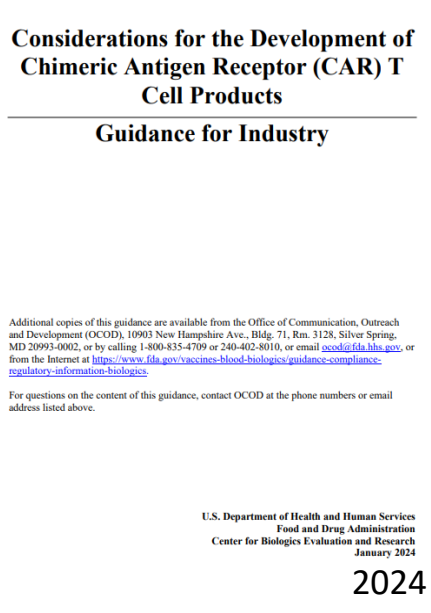
Comments and suggestions regarding this draft document should be submitted within ___ days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Office of Clinical Pharmacology Guidance and Policy at CDER_OCP_GPT@fda.hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

June 2022
Clinical Pharmacology

2022



Considerations for the Development of Chimeric Antigen Receptor (CAR) T Cell Products

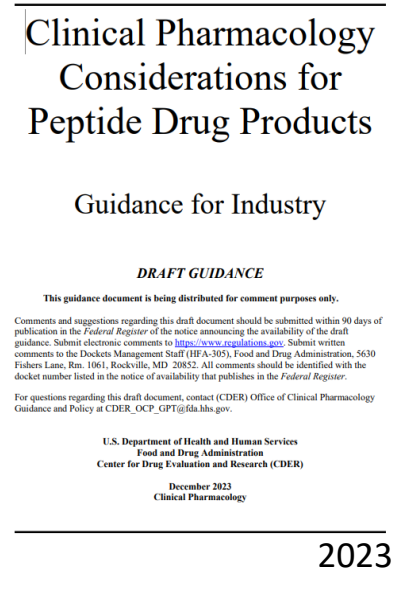
Guidance for Industry

Additional copies of this guidance are available from the Office of Communication, Outreach and Development (OCOD), 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002, or by calling 1-800-835-4709 or 240-402-8010, or email ocod@fda.hhs.gov, or from the Internet at https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics.

For questions on the content of this guidance, contact OCOD at the phone numbers or email address listed above.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
January 2024

2024



Clinical Pharmacology Considerations for Peptide Drug Products

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

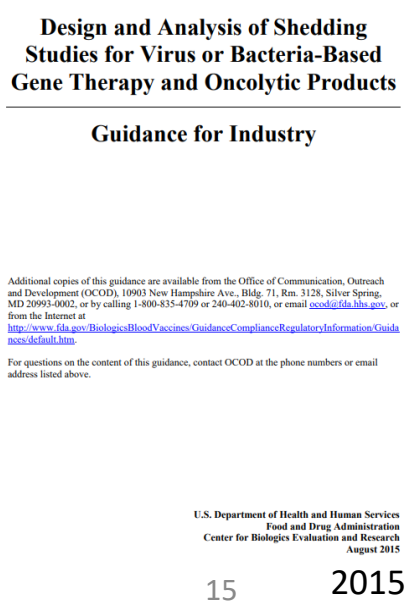
Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Office of Clinical Pharmacology Guidance and Policy at CDER_OCP_GPT@fda.hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

December 2023
Clinical Pharmacology

2023



Design and Analysis of Shedding Studies for Virus or Bacteria-Based Gene Therapy and Oncolytic Products

Guidance for Industry

Additional copies of this guidance are available from the Office of Communication, Outreach and Development (OCOD), 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002, or by calling 1-800-835-4709 or 240-402-8010, or email ocod@fda.hhs.gov, or from the Internet at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

For questions on the content of this guidance, contact OCOD at the phone numbers or email address listed above.

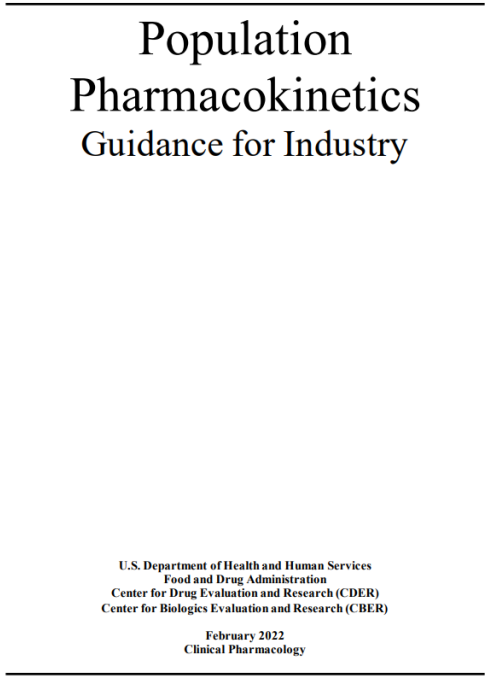
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
August 2015

2015

New Modalities – Basics and Opportunities

- Core Business
  - Valuable insight on different modalities
  - Inform industry's thinking based on agency's broad experience
- Challenges
  - What defines clinical pharmacology characterization
  - Dose/dosing regimen optimization for new modalities
  - Translation of new modalities including more complex assumptions and modeling approaches from preclinical studies

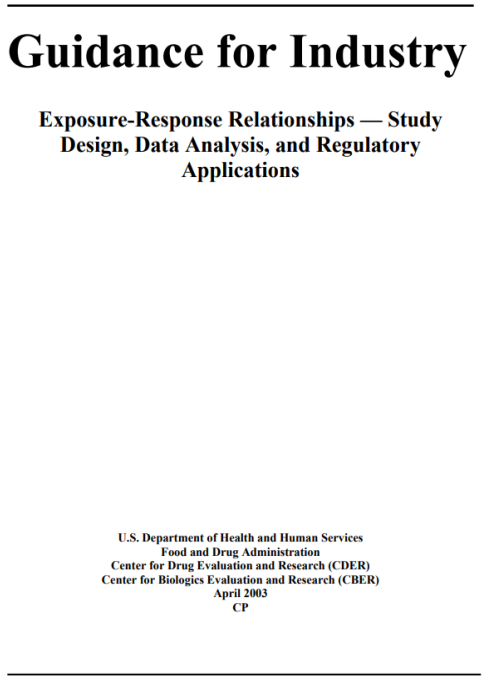
Focus #6 MIDD/Approaches


Population Pharmacokinetics
Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

February 2022
Clinical Pharmacology

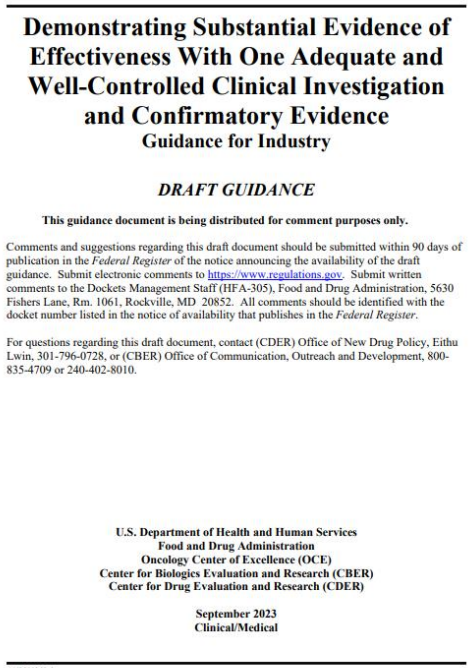
2022


Guidance for Industry

Exposure-Response Relationships — Study Design, Data Analysis, and Regulatory Applications

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
April 2003
CP

2003


Demonstrating Substantial Evidence of Effectiveness With One Adequate and Well-Controlled Clinical Investigation and Confirmatory Evidence
Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

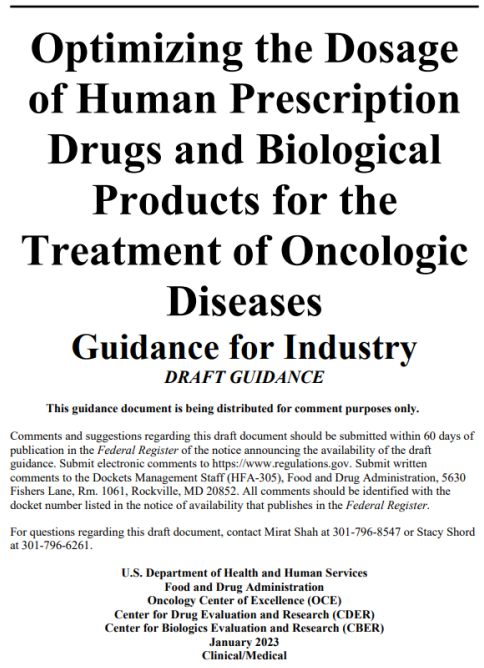
For questions regarding this draft document, contact (CDER) Office of New Drug Policy, Eithu Lwin, 301-796-0728, or (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration
Oncology Center of Excellence (OCE)
Center for Biologics Evaluation and Research (CBER)
Center for Drug Evaluation and Research (CDER)

September 2023
Clinical/Medical

4462509 2dft.docx
09/11/23

2023


Optimizing the Dosage of Human Prescription Drugs and Biological Products for the Treatment of Oncologic Diseases
Guidance for Industry
DRAFT GUIDANCE

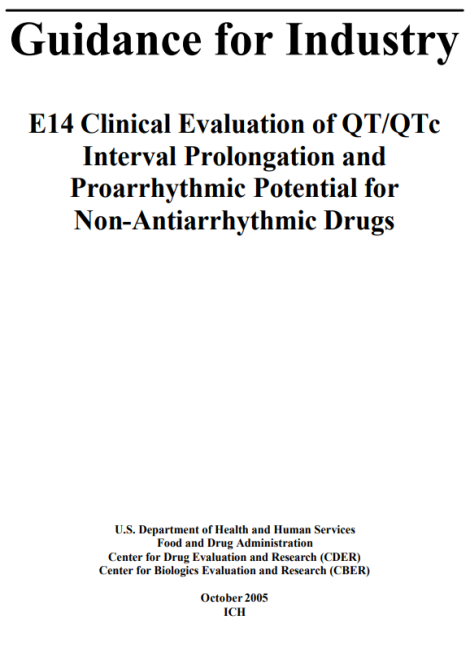
This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact Mirat Shah at 301-796-8547 or Stacy Shord at 301-796-6261.

U.S. Department of Health and Human Services
Food and Drug Administration
Oncology Center of Excellence (OCE)
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
January 2023
Clinical/Medical

2023

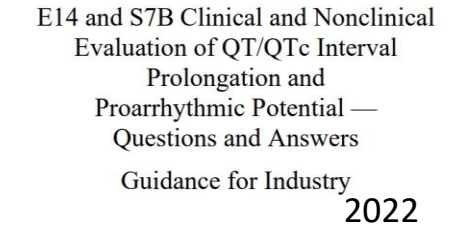

Guidance for Industry

E14 Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

October 2005
ICH

2005


E14 and S7B Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential — Questions and Answers

Guidance for Industry

2022

- Provides fundamentals around modeling principles
- Application of MIDD expanded & solidified with MIDD paired meetings (+ globalization with draft ICH M15 guidance)

FDA guidance on methodology + paired MIDD meetings provide huge opportunity for innovation & additional framework for interactions with multi-disciplinary team

Goals of MIDD Paired Meeting Program:

- ❑ Provide an opportunity for drug developers and FDA to discuss the application of MIDD approaches to the development and regulatory evaluation of medical products in development, and
- ❑ Provide advice about how a particular MIDD approach can be used in a specific drug development program

MIDD Success Stories

The US Food and Drug Administration's Model-Informed Drug Development Meeting Program: From Pilot to Pathway

Rajanikanth Madabushi[1,*], Jessica Benjamin[1], Hao Zhu[1] and Issam Zineh[1]

CPT 2024, doi:10.1002/cpt.3228

WHITE PAPER

Considerations for Industry—Preparing for the FDA Model-Informed Drug Development (MIDD) Paired Meeting Program

Gerald R. Galluppi[1], Malidi Ahamadi[2], Souvik Bhattacharya[3], Nageshwar Budha[4], Ferdous Gheyas[5], Chi-Chung Li[6], Yuan Chen[6], Anne-Gaëlle Dosne[7], Niels Rode Kristensen[8], Mindy Magee[9], Mahesh N. Samtani[7], Vikram Sinha[10], Kunal Taskar[9], Vijay V. Upreti[11], Jianning Yang[3] and Jack Cook[12,*]

CPT 2024, doi:10.1002/cpt.3245

Industrial Perspective on the Benefits Realized From the FDA's Model-Informed Drug Development Paired Meeting Pilot Program

Gerald R. Galluppi[1,*], Satjit Brar[2], Luzelena Caro[3], Yuan Chen[4], Nicolas Frey[5], Hans Peter Grimm[5], Deanne Jackson Rudd[3], Chi-Chung Li[6], Mindy Magee[7], Arnab Mukherjee[8], Lee Nagao[9], Vivek S. Purohit[10], Amit Roy[11], Ahmed Hamed Salem[12,13], Vikram Sinha[3,†], Ahmed A. Suleiman[14], Kunal S. Taskar[15], Vijay V. Upreti[16], Benjamin Weber[17] and Jack Cook[18,*]

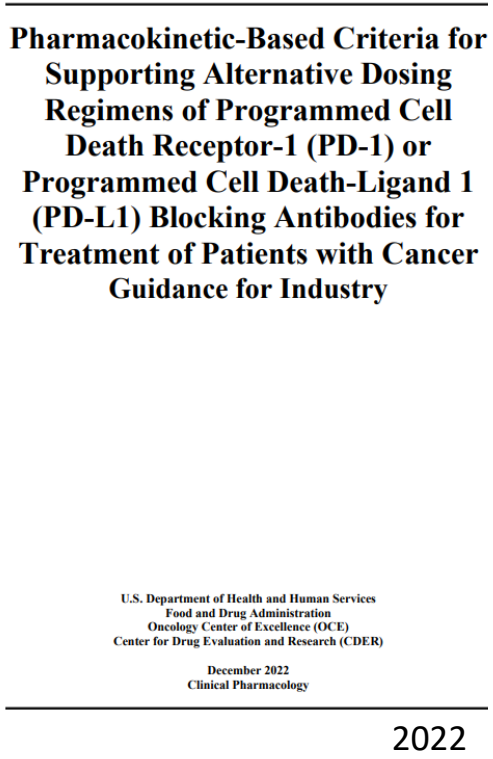
CPT 2021, 110(5): 1172-5

The US Food and Drug Administration's Model-Informed Drug Development Paired Meeting Pilot Program: Early Experience and Impact

Rajanikanth Madabushi[1], Jessica M. Benjamin[1], Renmeet Grewal[1], Michael A. Pacanowski[1], David G. Strauss[1], Yaning Wang[1], Hao Zhu[1] and Issam Zineh[1,*]

CPT 2019, 106(1): 74-8

Focus #7 MIDD/Clinical Focus

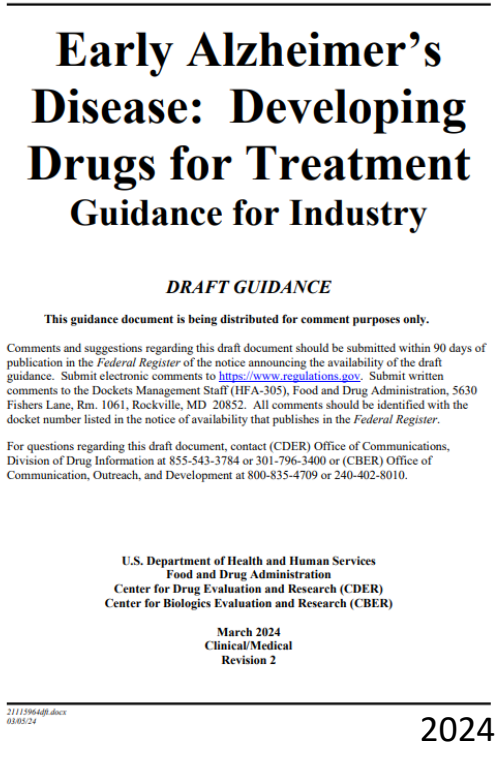


Pharmacokinetic-Based Criteria for Supporting Alternative Dosing Regimens of Programmed Cell Death Receptor-1 (PD-1) or Programmed Cell Death-Ligand 1 (PD-L1) Blocking Antibodies for Treatment of Patients with Cancer
Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Oncology Center of Excellence (OCE)
Center for Drug Evaluation and Research (CDER)

December 2022
Clinical Pharmacology

2022



Early Alzheimer's Disease: Developing Drugs for Treatment
Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

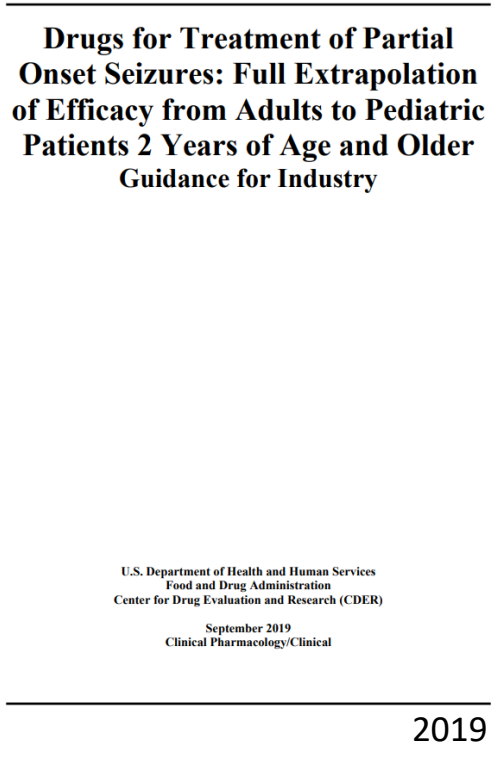
For questions regarding this draft document, contact (CDER) Office of Communications, Division of Drug Information at 855-543-3784 or 301-796-3400 or (CBER) Office of Communication, Outreach, and Development at 800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

March 2024
Clinical/Medical
Revision 2

211159644dft.docx
03/05/24

2024

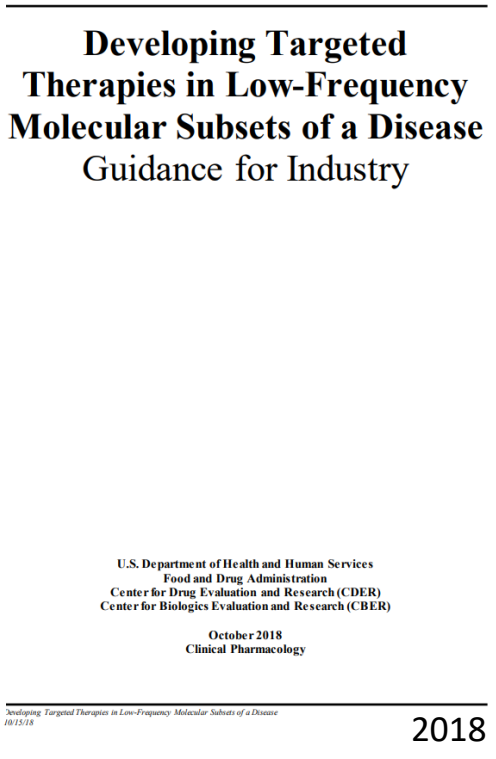


Drugs for Treatment of Partial Onset Seizures: Full Extrapolation of Efficacy from Adults to Pediatric Patients 2 Years of Age and Older
Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

September 2019
Clinical Pharmacology/Clinical

2019



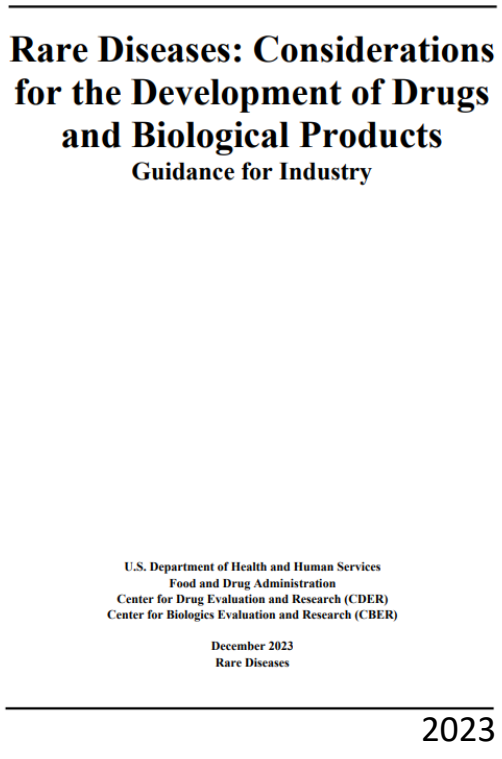
Developing Targeted Therapies in Low-Frequency Molecular Subsets of a Disease
Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

October 2018
Clinical Pharmacology

Developing Targeted Therapies in Low-Frequency Molecular Subsets of a Disease
10/15/18

2018



Rare Diseases: Considerations for the Development of Drugs and Biological Products
Guidance for Industry

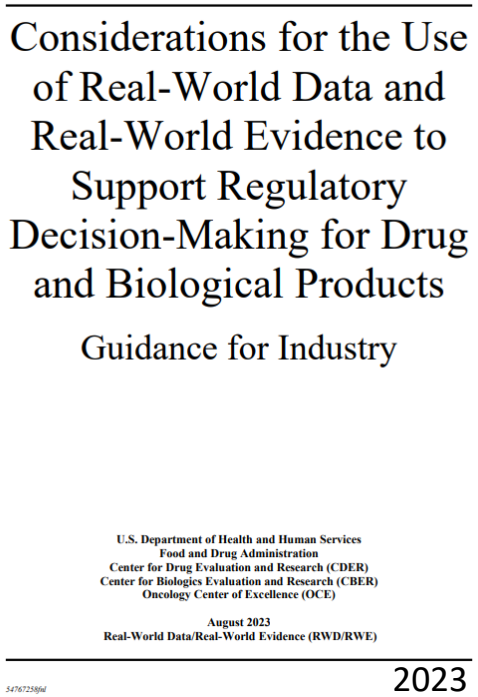
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

December 2023
Rare Diseases

2023

MIDD – Basics and Opportunities

- Core Business
  - Applications are broad and key in internal decision making and drug development decisions
  - Get agency's insight on what is considered clinically relevant (broad experience across multiple compounds)
  - QTc characterization
  - Methodology & reporting requirements
- Challenges
  - Further bridging opportunities, e.g., cross indications, cross patient populations
  - Use of exposure-response for optimization of dose in oncology
  - Modeling disease modification over time or novel endpoints (e.g., longer trials)
  - QSP applications
    - Level of credibility for intended use


Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision-Making for Drug and Biological Products

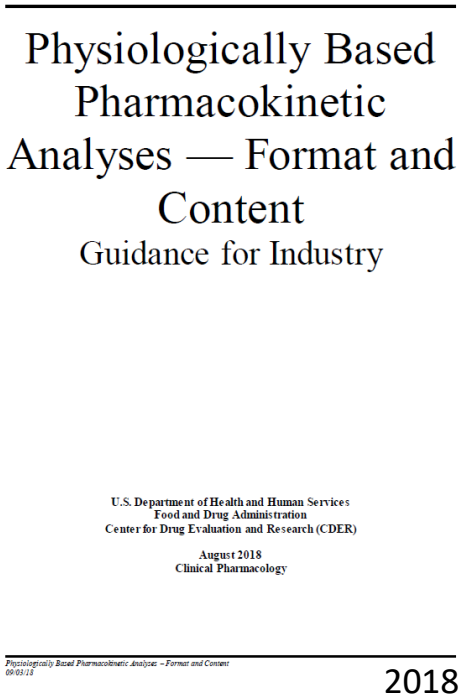
Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Oncology Center of Excellence (OCE)

August 2023
Real-World Data/Real-World Evidence (RWD/RWE)

5476725f6d

2023


Physiologically Based Pharmacokinetic Analyses — Format and Content

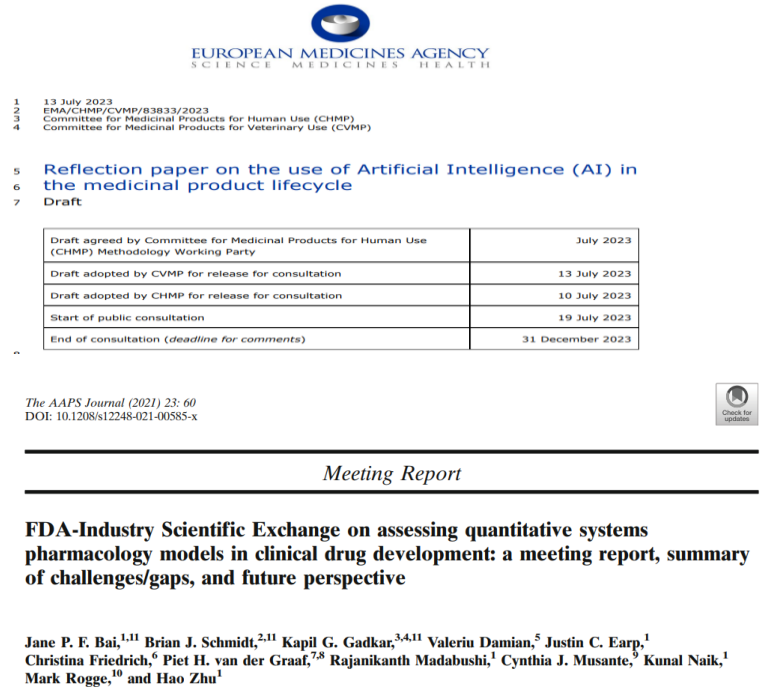
Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

August 2018
Clinical Pharmacology

Physiologically Based Pharmacokinetic Analyses – Format and Content
09/03/18

2018


EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

13 July 2023
EMA/CHMP/CVMP/83833/2023
Committee for Medicinal Products for Human Use (CHMP)
Committee for Medicinal Products for Veterinary Use (CVMP)

Reflection paper on the use of Artificial Intelligence (AI) in the medicinal product lifecycle
Draft

Draft agreed by Committee for Medicinal Products for Human Use (CHMP) Methodology Working Party	July 2023
Draft adopted by CVMP for release for consultation	13 July 2023
Draft adopted by CHMP for release for consultation	10 July 2023
Start of public consultation	19 July 2023
End of consultation (*deadline for comments*)	31 December 2023

The AAPS Journal (2021) 23: 60
DOI: 10.1208/s12248-021-00585-x

Meeting Report

FDA-Industry Scientific Exchange on assessing quantitative systems pharmacology models in clinical drug development: a meeting report, summary of challenges/gaps, and future perspective

Jane P. F. Bai,[1,11] Brian J. Schmidt,[2,11] Kapil G. Gadkar,[3,4,11] Valeriu Damian,[5] Justin C. Earp,[1] Christina Friedrich,[6] Piet H. van der Graaf,[7,8] Rajanikanth Madabushi,[1] Cynthia J. Musante,[9] Kunal Naik,[1] Mark Rogge,[10] and Hao Zhu[1]

Focus #8 New Tools & Methodologies

- Opportunity in providing guidance on use of QSP
- RWE to support certain therapeutic areas difficult to study (e.g., rare disease, oncology)
- How to embrace AI/ML in clinical pharmacology/drug development
- Use of virtual twin/virtual control group

Fit for Purpose Tools

Drug Development Tools: Fit-for-Purpose Initiative

Share | Post | Linkedin | Email | Print

Background

The Fit-for-Purpose (FFP) Initiative provides a pathway for regulatory acceptance of dynamic tools for use in drug development programs. Due to the evolving nature of these types of drug development tools (DDTs) and the inability to provide formal qualification, a designation of 'fit-for-purpose' (FFP) has been established. A DDT is deemed FFP based on the acceptance of the proposed tool following a thorough evaluation of the information provided. The FFP determination is made publicly available in an effort to facilitate greater utilization of these tools in drug development programs.

Contact Us

For more information about the FFP Initiative, please contact DrugDevelopmentTools@fda.hhs.gov

Fit-For-Purpose Tools and Supporting Information:

Disease Area	Submitter	Tool	Trial Component	Issuance Date and Supporting Information
Alzheimer's disease	The Coalition Against Major Diseases (CAMD)	Disease Model: Placebo/Disease Progression	Demographics, Drop-out	Issued June 12, 2013 • Determination Letter
Multiple	Janssen Pharmaceuticals and Novartis Pharmaceuticals	Statistical Method: MCP-Mod	Dose-Finding	Issued May 26, 2016 • Determination Letter • Statistical Review • Pharmacometric Review
Multiple	Ying Yuan, PhD The University of Texas MD Anderson Cancer Center Department of Biostatistics	Statistical Method: Bayesian Optimal Interval (BOIN) design	Dose-Finding	Issued: December 10, 2021 • Determination Letter • Statistical Review • Publication Erratum
Multiple	Pfizer	Statistical Method: Empirically Based Bayesian Emax Models	Dose-Finding	Issued: August 5, 2022 • Determination Letter • Multidisciplinary Review

Drug Development Tools: Fit-for-Purpose Initiative | FDA

Summary of Opportunities

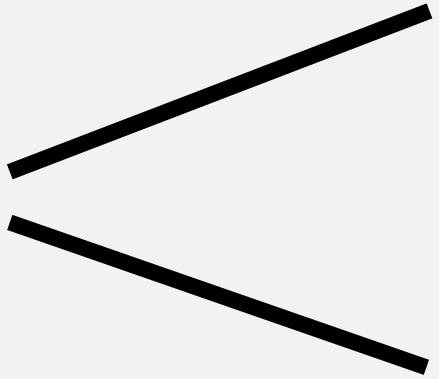
Embracing New Science & Application to Core Guidance

Embracing New Methodology

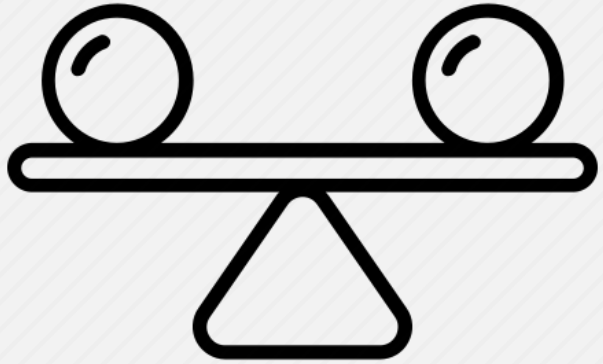
Embracing MIDD to Enhance New Drug Development Strategies

FDA Guidance – Key to Successful Implementation

Iterative
(Learn & Adjust)



Expand to Global Acceptance



Balance Between Intent & Practicality

Need for guidance and continued interaction with agency

Thank you!

Session Participants: Raj Madabushi, Hao Zhu, Joga Gobburu, and Karen Rowland Yeo
Colleagues at J&J

Acknowledgments

Others….

Guidance for Industry

E11 Clinical Investigation of Medicinal Products in the Pediatric Population

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

ICH
December 2000

Human Prescription Drug and Biological Products — Labeling for Dosing Based on Weight or Body Surface Area for Ready-to-Use Containers — "Dose Banding"

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

October 2023
Labeling

54099102fnl09-26-23.docx

Pregnant Women: Scientific and Ethical Considerations for Inclusion in Clinical Trials

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact the Division of Pediatric and Maternal Health (CDER) at (301) 796-2200 or the Office of Communication, Outreach, and Development (CBER) at 800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

April 2018
Clinical/Medical
Revision 1

Clinical Lactation Studies: Considerations for Study Design

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Jian Wang at 301-796-3846 or (CBER) the Office of Communication, Outreach, and Development at 800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

May 2019
Clinical/Medical

248065fdft.docx
05/01/19

Guidance for Industry

Codevelopment of Two or More New Investigational Drugs for Use in Combination

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

June 2013
Clinical Medical

Physiologically Based Pharmacokinetic Analyses — Format and Content

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

August 2018
Clinical Pharmacology

Physiologically Based Pharmacokinetic Analyses – Format and Content
09/03/18

Pregnancy, Lactation, and Reproductive Potential: Labeling for Human Prescription Drug and Biological Products — Content and Format

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact the Division of Pediatric and Maternal Health (CDER) at 301-796-2200 or the Office of Communication, Outreach, and Development (CBER) at 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

July 2020
Labeling
Revision 1

50762dft.docx
7/15/2020