

# **Regulatory Perspectives on Including Older Adults in Clinical Trials for Drug Approvals in the United States**

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# Disclaimer

- **This presentation reflects the views and opinions of the presenter and does not represent the views, opinions, and policies of the Food and Drug Administration.**
- **This presenter declares no conflict of interest.**

# Outline

- **Background**
- **Regulatory guidances in the United States**
- **Drug Trials Snapshots**
- **Take-home messages**
- **Acknowledgements**

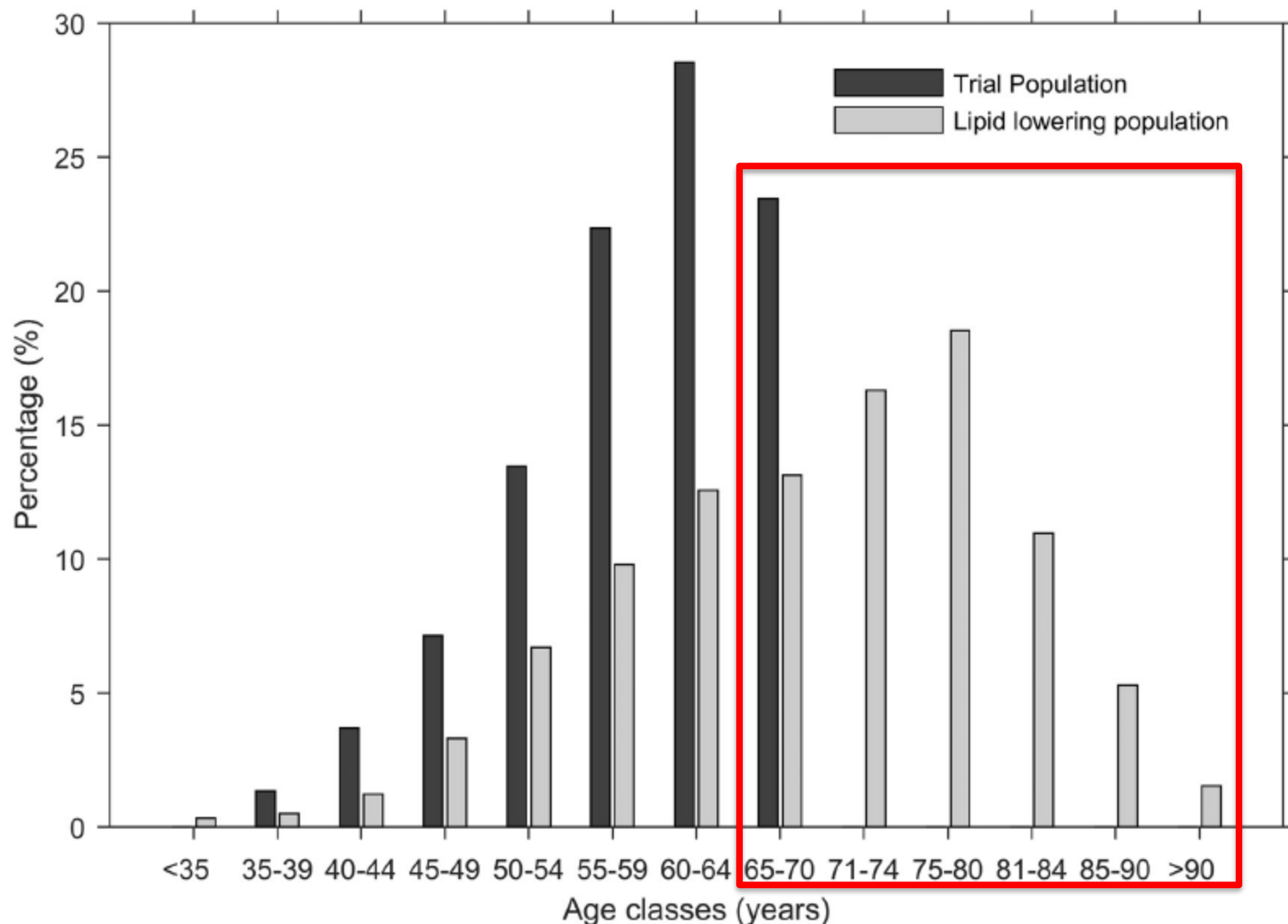
# Background

Older adult patients are the main consumers of medications. This is the fundamental difference between geriatric patients and pediatric patients.

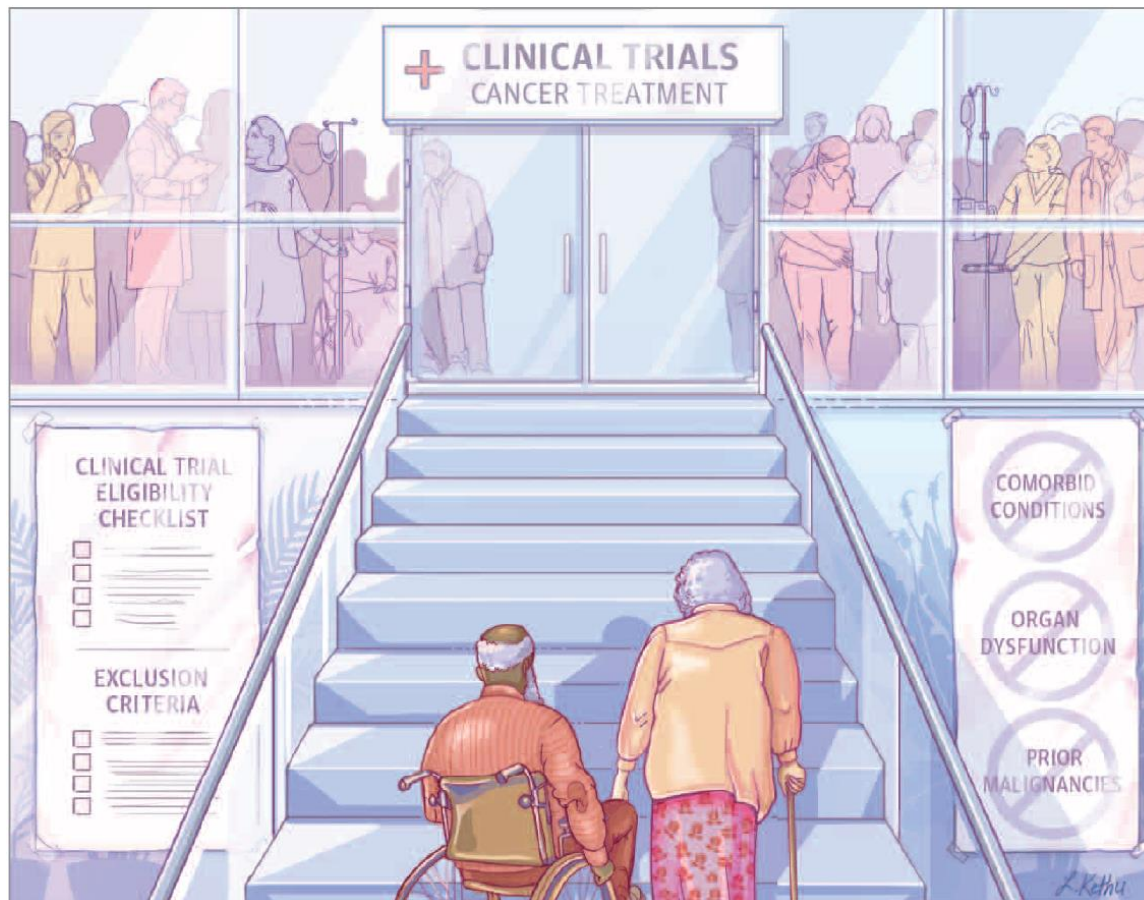
For the current thinking of the FDA on certain topics, the FDA communicates with the stakeholders via guidance documents.

Drug product label or “package insert” is an important tool to communicate critical information of the drug product to prescribers or health-care providers.

# Simvastatin Trial Patients Differ from Actual Patients



# Older Patients (Still) Left Out of Cancer Clinical Trials



# The “Demographic Rule”

**DEPARTMENT OF HEALTH AND  
HUMAN SERVICES**

**Food and Drug Administration**

**21 CFR Parts 312 and 314**

[Docket No. 95N-0010]

## **Investigational New Drug Applications and New Drug Applications**

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Final rule.

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**SUMMARY:** The Food and Drug Administration (FDA) is amending its regulations pertaining to new drug applications (NDA's) to clearly define in the NDA format and content regulations the requirement to present effectiveness and safety data for important demographic subgroups, specifically gender, age, and racial subgroups. FDA

also is amending its regulations pertaining to investigational new drug applications (IND's) to require sponsors to tabulate in their annual reports the numbers of subjects enrolled to date in clinical studies for drug and biological products according to age group, gender, and race. This action is intended to alert sponsors as early as possible to potential demographic deficiencies in enrollment that could lead to avoidable deficiencies later in the NDA submission. This rule does not address the requirements for the conduct of clinical studies and does not require sponsors to conduct additional studies or collect additional data. It also does not require the inclusion of a particular number of individuals from specific subgroups in any study or overall. The rule refers only to the presentation of data already collected.

**DATES:** Effective August 10, 1998. Submit written comments on the information collection provisions of this final rule by April 13, 1998.

# ICH E7 Update

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## Guidance for Industry

### E7 Studies in Support of Special Populations: Geriatrics

### Questions and Answers

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 2012  
ICH

- 100 patients are unlikely to be sufficient (aging Baby Boomers); include representative number of older adult patients
- Present data for 4 age groups to assess consistency of treatment efficacy and safety with non-older adult patients:
  - < 65
  - 65 – 74
  - 75 – 84
  - ≥ 85
- Emphasize studying patients ≥ 75 years of age.
- Avoid arbitrary upper age limits in clinical trials.
- Encourage inclusion of patients with concomitant illnesses.
- Prefer inclusion of older adult patients in the pivotal Phase 3 trials, not in separate trials.
- Study PK of older adult patients:
  - Entire spectrum of the older adult patient population to identify age-related differences not explained by other factors (renal and weight)
  - If enough number of patients in different age ranges (including patients ≥ 65 and ≥ 75 years) is included in the clinical trials, then population PK analysis could provide such data.
  - Or, a specific PK study comparing non-older adult and older adult participants in the same study (matched for relevant covariates such as weight and sex) could be performed.

# Enhance Clinical Trial Population Diversity



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

- Inclusive trial practices
  - Relevant population: age, sex, race, and ethnicity
- Trial design and methodology
  - Early characterizing of drug metabolism and clearance
  - Adaptive trial design
- Enrichment strategies
- Inclusion of older adult populations

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)

November 2020  
Clinical/Medical

<https://www.fda.gov/media/127712/download>



# Inclusion of Older Adults in Cancer Trials

## 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

<https://www.fda.gov/media/135804/download>

- Adequate representation of older adults is necessary to determine the benefit-risk profile of cancer therapeutics in this population:
- Early clinical development
  - Enroll older adults in early phase trials, study drug-drug interactions
- Clinical trials
  - Trial design, recruitment strategies, collect additional information, safety monitoring strategies, reporting in discrete age groups
- Collection of post-marketing data thru additional trials, registries, and or real world data

# Guidance on Geriatric Labeling

## Geriatric Information in Human Prescription Drug and Biological Product Labeling Guidance for Industry

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For questions regarding this draft document, contact (CDER) Eric Brodsky at 301-796-0855, 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)

September 2020  
Labeling

<https://www.fda.gov/media/142162/download>

- This guidance discusses:
  - FDA’s initiatives to ↑ quantity and quality of drug information for patients ≥ 65 years of age
  - Geriatric age subgroup:
    - 65 – 74
    - 75 – 84
    - ≥ 85
    - Or continuous function of age
  - 3 examples of drug approval scenarios:
    - Use in adult patients including geriatric patients
    - Geriatric-specific indication
    - Not approved in geriatric patients but approved in younger adults

# Make Available Clinical Trial Data that Supported NDA Approval

## DRUG TRIALS SNAPSHOTS



### WHAT IS THE PURPOSE OF DRUG TRIALS SNAPSHOTS?

Drug Trials Snapshots provide consumers with information about who participated in clinical trials that supported the FDA approval of new drugs. The information provided in these Snapshots also highlights whether there were any differences in the benefits and side effects among sex, race and age groups. Drug Trials Snapshots is part of an overall FDA effort to make demographic data more available and transparent.

### HOW TO USE SNAPSHOTS:

Each Snapshot contains information about the drug in a question and answer format. At the end of each section of the Snapshot, there is a shaded bar with the words “MORE INFO”. Click the “MORE INFO” bar for more technical and detailed content. At the bottom of each Snapshot, there is a link to the drug’s Package Insert as well as the medical review.

### LIMITATIONS OF SNAPSHOTS:

The Snapshot is intended as one tool for consumers to use when discussing a drug’s risks and benefits with their physician. Do not rely on Snapshots alone to make decisions regarding medical care. Do not use Snapshots to substitute for advice from your health care professional.

Conclusions regarding how effective and safe a drug is among different sex, race, and age groups cannot always



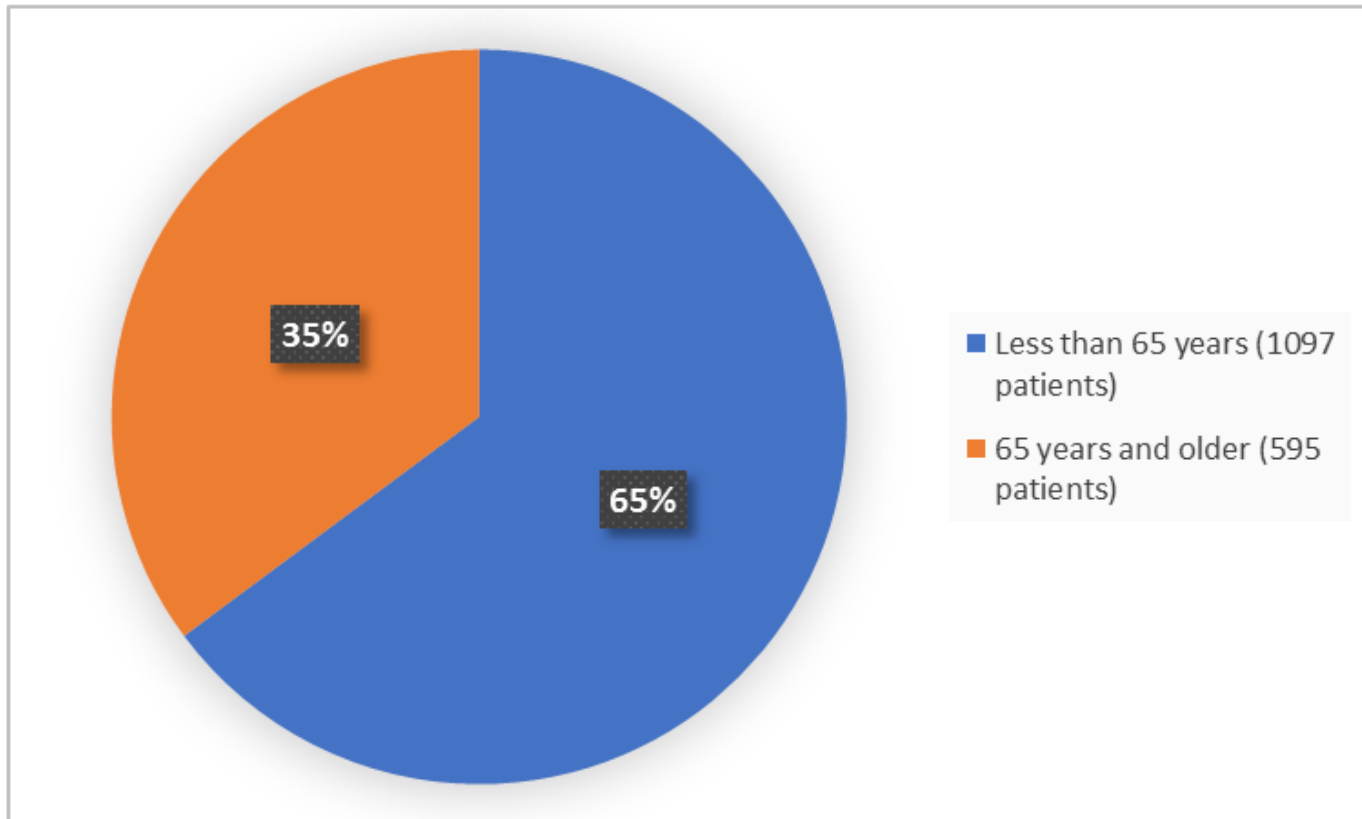
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[Download PDF](#)

# Drug Trials Snapshots: Lemborexant

Figure 3. Demographics by Age (efficacy population)



# Take-home Messages

- **Older adults are the main consumers of medications.**
- **The ICH E7 Questions and Answers and FDA guidances guide the conduct of clinical trials for product registration for older adults.**
- **The 2020 FDA geriatric labeling guidance guides the labeling for the use of prescription drug and biological products in older adults.**

# Acknowledgements

- **Office of Clinical Pharmacology's Geriatrics Scientific Interest Group**
- **OCPers (current and former)**
- **Friends in the geriatrics field**
- **Older adult relatives and friends**



# Please attend this free workshop.

## FDA Roadmap to 2030 for New Drug Evaluation in Older Adults

by The Food and Drug Administration, Office of Clinical Pharmacology/OTS/CDER

[Follow](#)

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[Register](#)

### FDA Roadmap to 2030 for New Drug Evaluation in Older Adults

#### About this Event

This workshop will bring together stakeholders from academia, industry, and regulatory agencies in a virtual setting to discuss the current status of inclusion of older adults in clinical trials and strategies to ensure the safe and effective use of drugs in this population.

#### Date And Time

Tue, March 23, 2021  
10:00 AM – 4:30 PM EDT  
[Add to Calendar](#)

#### Location

**Online Event**

[https://www.eventbrite.com/e/fda-roadmap-to-2030-for-new-drug-evaluation-in-older-adults-registration-137460709683?utm\\_medium=email&utm\\_source=govdelivery](https://www.eventbrite.com/e/fda-roadmap-to-2030-for-new-drug-evaluation-in-older-adults-registration-137460709683?utm_medium=email&utm_source=govdelivery)

# Backup

# US Guideline



GUIDELINE FOR THE STUDY OF DRUGS  
LIKELY TO BE USED IN THE ELDERLY



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
PUBLIC HEALTH SERVICE  
FOOD AND DRUG ADMINISTRATION

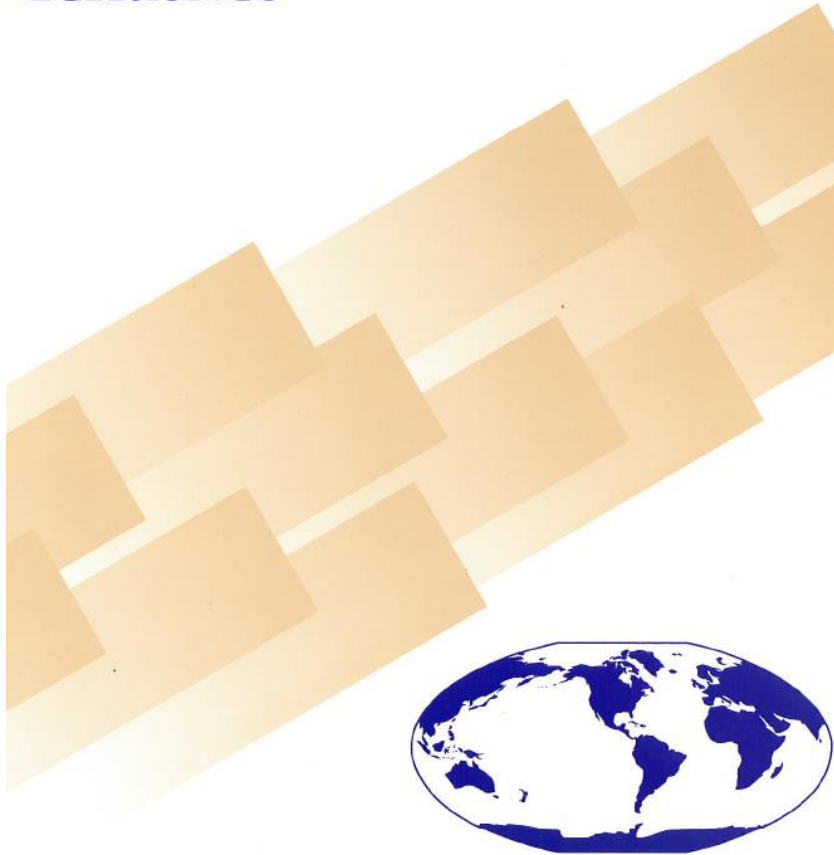
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<https://www.fda.gov/media/71114/download>

- Drugs should be studied in all age groups, including the geriatric, for which they will have significant utility.
- Attempt to include > 75 years and concomitant illnesses
- Pharmacokinetic (PK) studies for:
  - renal impairment
  - hepatic impairment
  - PK screen
  - drug-disease and drug-drug interactions
- Pharmacodynamic studies

# ICH E7 Guideline

## Studies in Support of Special Populations: Geriatrics



ICH - E7  
August 1994

- Arbitrary geriatric population  $\geq 65$  years; important  $\geq 75$  years
- Suggested to include “meaningful number” of geriatric patients in Phase 3 (and Phase 2 optional) trials
- Disease not unique to, but present in older adults, a **minimum of 100 patients** to detect difference
- Drug interaction studies (CYP isozymes)
- Updated with Q&A

# Selected Guidances on Developing Drug Products for Older Adults



- Food and Drug Administration: Guidance for Industry: Guideline for the Study of Drugs Likely to Be Used in the Elderly. 1989. <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072048.pdf>
- International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use: ICH E7: Guideline for Industry: Studies in Support the of Special Populations: Geriatrics. 1994. <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073131.pdf>
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- 52. Food and Drug Administration Safety and Innovation Act. Public Law 112–144, July 9, 2012. [www.gpo.gov/fdsys/pkg/PLAW-112publ144/pdf/PLAW-112publ144.pdf](http://www.gpo.gov/fdsys/pkg/PLAW-112publ144/pdf/PLAW-112publ144.pdf)
- FDA Report: Collection, analysis, and availability of demographic subgroup data for FDA-approved medical products. 2013. [www.fda.gov/downloads/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/FDASIA/UCM365544.pdf](http://www.fda.gov/downloads/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/FDASIA/UCM365544.pdf)
- FDA report: FDA action plan to enhance the collection and availability of demographic subgroup data. 2014. [www.fda.gov/downloads/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/FDASIA/UCM410474.pdf](http://www.fda.gov/downloads/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/FDASIA/UCM410474.pdf)
- Drug Trials Snapshots <https://www.fda.gov/Drugs/InformationOnDrugs/ucm412998.htm>
- Food and Drug Administration: Webpage on Guidances for Drugs <https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>
- Food and Drug Administration: Guidance for Industry: Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products. 1998. <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072008.pdf>
- Food and Drug Administration: Guidance for Industry: Exposure-Response Relationships — Study Design, Data Analysis, and Regulatory Applications. 2005. <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072109.pdf>
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- Food and Drug Administration: Guidance for Industry: Bioavailability Studies Submitted in NDAs or INDs — General Considerations. Draft Guidance, 2019. <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM631943.pdf>
- Food and Drug Administration: Guidance for Industry: Bioanalytical Method Validation. 2018. <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070107.pdf>
- Food and Drug Administration: Biologics development <https://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/General/default.htm>
- Food and Drug Administration: Guidance for Industry: Assay Development and Validation for Immunogenicity Testing of Therapeutic Protein Products. Draft Guidance 2016. <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM192750.pdf>
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- Food and Drug Administration: Guidance for Industry: Pharmacokinetics in Patients with Impaired Renal Function — Study Design, Data Analysis, and Impact on Dosing and Labeling. Draft Guidance, 2010. <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM204959.pdf>
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- Food and Drug Administration: Human Factors and Medical Devices <https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HumanFactors/default.htm>