CDRH's Draft Guidance: Evaluation and Reporting of Age, Race, and Ethnicity Data in Medical Device Clinical Studies

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Overview

- Objectives
- Background
- Terminology
- Subgroups in Clinical Trials
- Achieving Appropriate Enrollment
- Analysis of Subgroup Data
- FDA and Public Reporting of Subgroup Data

Objectives

- Encourage consideration during study design stage the collection of relevant demographics, (age, race, ethnicity), and other associated covariates (body size, biomarkers, bone density) for devices
- Outline analyses framework for demographic data and interpreting outcomes
- Specify FDA's expectations for reporting demographics in summaries and labeling of medical devices

Background

Section 907, Food and Drug Administration Safety and Innovation Act of 2012

- Required a Report to Congress and the public on the inclusion of demographic subgroups in FDA applications
- Required an Action Plan to improve completeness and quality of data on demographic subgroups
- This Draft Guidance was a commitment by CDRH under the Action Plan!

Terminology: Age

- Subjects should be grouped as appropriate for the disease/condition
- Pediatric population is defined by CDRH as less than 22 years of age
- Geriatric population is not defined, but recommend stratifying age based on relevant disease characteristics

Terminology: Race & Ethnicity

FDA's Guidance for Industry: Collection of Race and Ethnicity Data in Clinical Trials

- Patient self-report of both race and ethnicity
- Preferred method is separate collection of race and ethnicity (i.e. two-question format)

Other considerations:

- Disease/condition may warrant more granular race data
- Categories may not be appropriate outside the U.S.
- In these instances, methodology should be defined in the study protocol

Participation of Subgroups in Clinical Trials

- It is important that clinical trials include diverse populations that reflect the intended population
- Including throughout the enrolling sites, where surgical or operator skill may be important
- Otherwise, differences in device performance or surgical skill may be incorrectly attributed to demographic subgroups
- Therefore, study protocols should include pre-specified statistical plans to address these issues

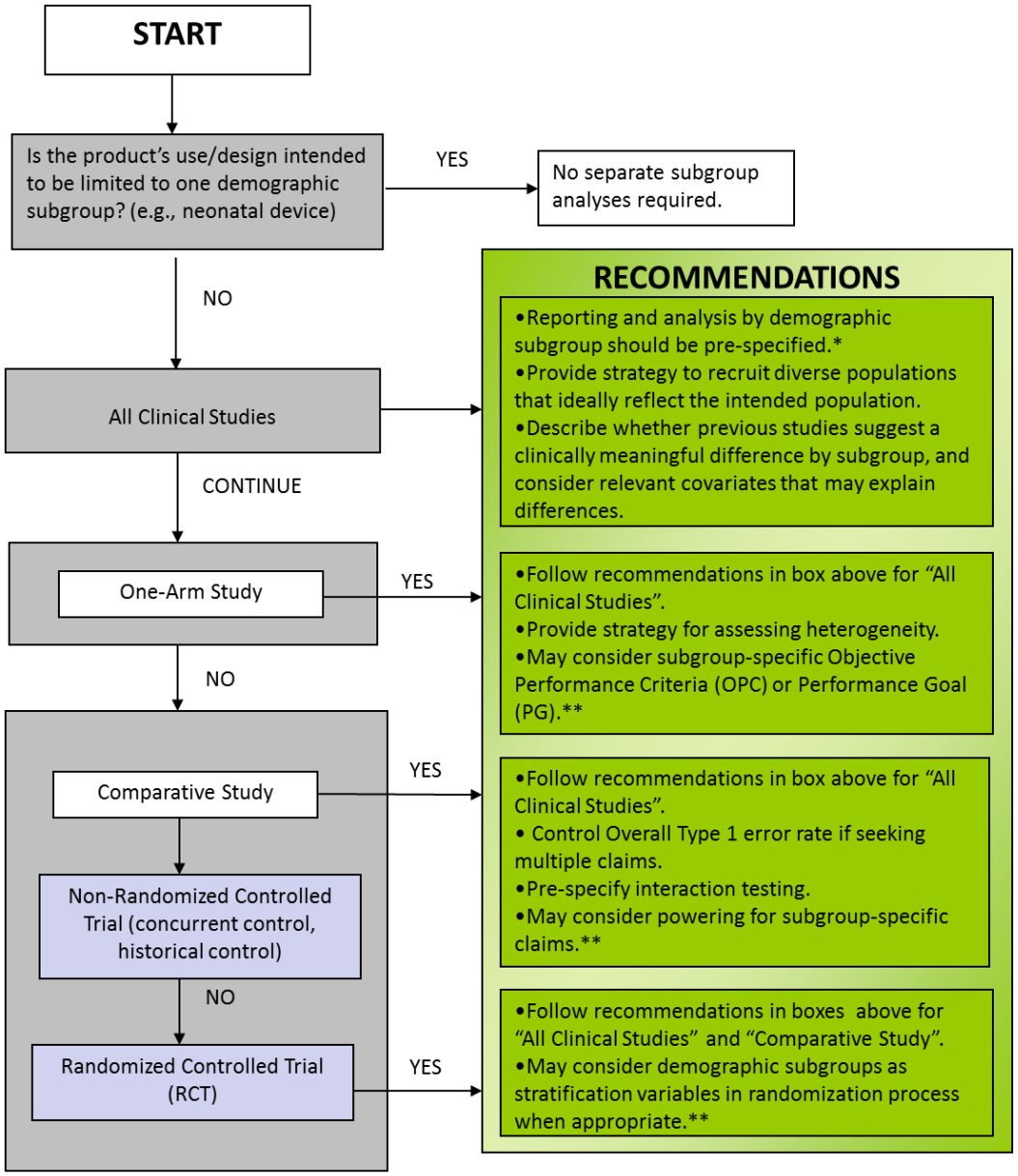
Consideration of Subgroup Differences

For potential age, race, and ethnicity differences relevant to the evaluation of the device for the disease/condition, consider

- Prevalence
- Diagnosis and treatment patterns
- Previous subgroup inclusion in past studies for target indication
- Any clinically meaningful subgroup differences in safety or effectiveness

Recommendations for Demographic Subgroup-Specific Statistical Design

Follow recommendations associated with study design type.



*For ongoing studies, provide descriptive statistics. For new studies, provide statistical inferences

**Applicable when subgroup differences are anticipated

Achieving Appropriate Enrollment

To enhance enrollment of relevant subgroups:

- Wide variety of investigational sites
- Alternate communication strategies
- Revise enrollment criteria
- Establish parallel cohorts or registries
- Investigate no or low inclusion of key demographic subgroups
- Involve community or local providers in recruitment
- Compensation for transportation costs
- Flexible scheduling and on-site child care and elder care

Investigator Tools & Techniques for Enrollment

- Cultural competency training
- Stress the importance of follow-up at time of informed consent and subsequent visits
- Reminder calls for upcoming visits
- Attempt to locate and return patients lost to follow-up
- Record reason for patient withdrawals
- Demonstrate patient interest with post-op and follow-up visit calls

Recommendations for Analysis of Subgroup Data

Data should be examined for clinically meaningful age, race, and ethnicity specific differences in:

- Primary effectiveness endpoints
- Primary safety endpoints
- Key secondary endpoints

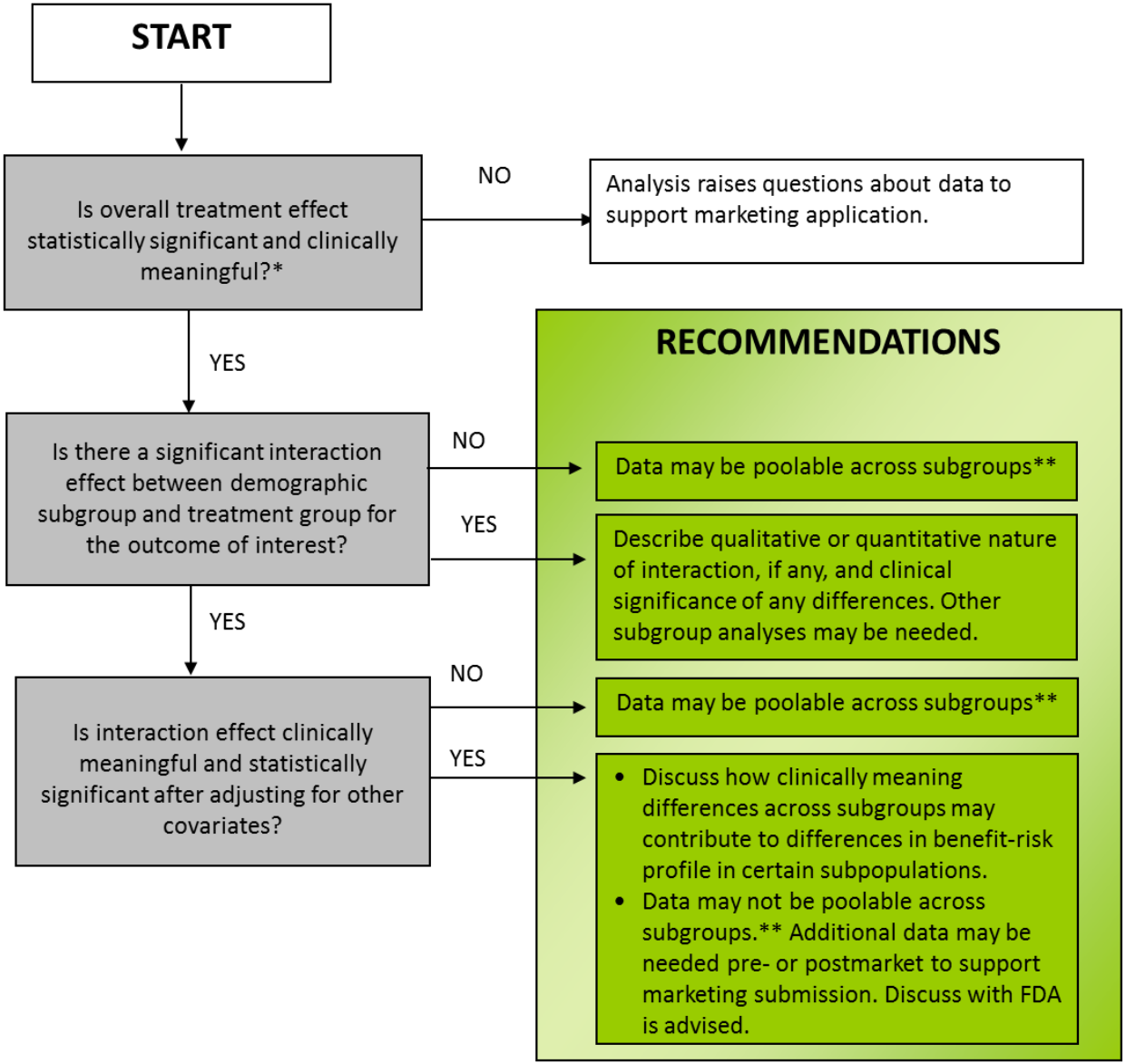
Regardless of the potentially limited statistical power of these subgroup analyses!

Other Considerations of Subgroup Analyses

- Inadequate sample size and unplanned subgroup analyses are generally not considered adequate for statements in labeling
- Sometimes effect can be statistically significant but not clinical meaningful and vice versa
- Observed heterogeneity could be explained by other covariates
- Discussion with FDA is recommended if difference(s) remain clinically meaningful and/or statistically significant

Additional FDA Actions on Subgroup Analyses

- FDA may request additional subjects from one or more subgroups pre or post-market if data is insufficient to determine clinically meaningful differences
- Or request additional confirmatory studies, implement specific pre or post-approval conditions, and/or subsequent study modifications where clinically meaningful subgroup differences are observed



*Unplanned subgroup analyses are generally not considered to be adequate to support statements in the labeling regarding the safety or effectiveness of the device if overall treatment effect is not statistically significant and clinically meaningful.

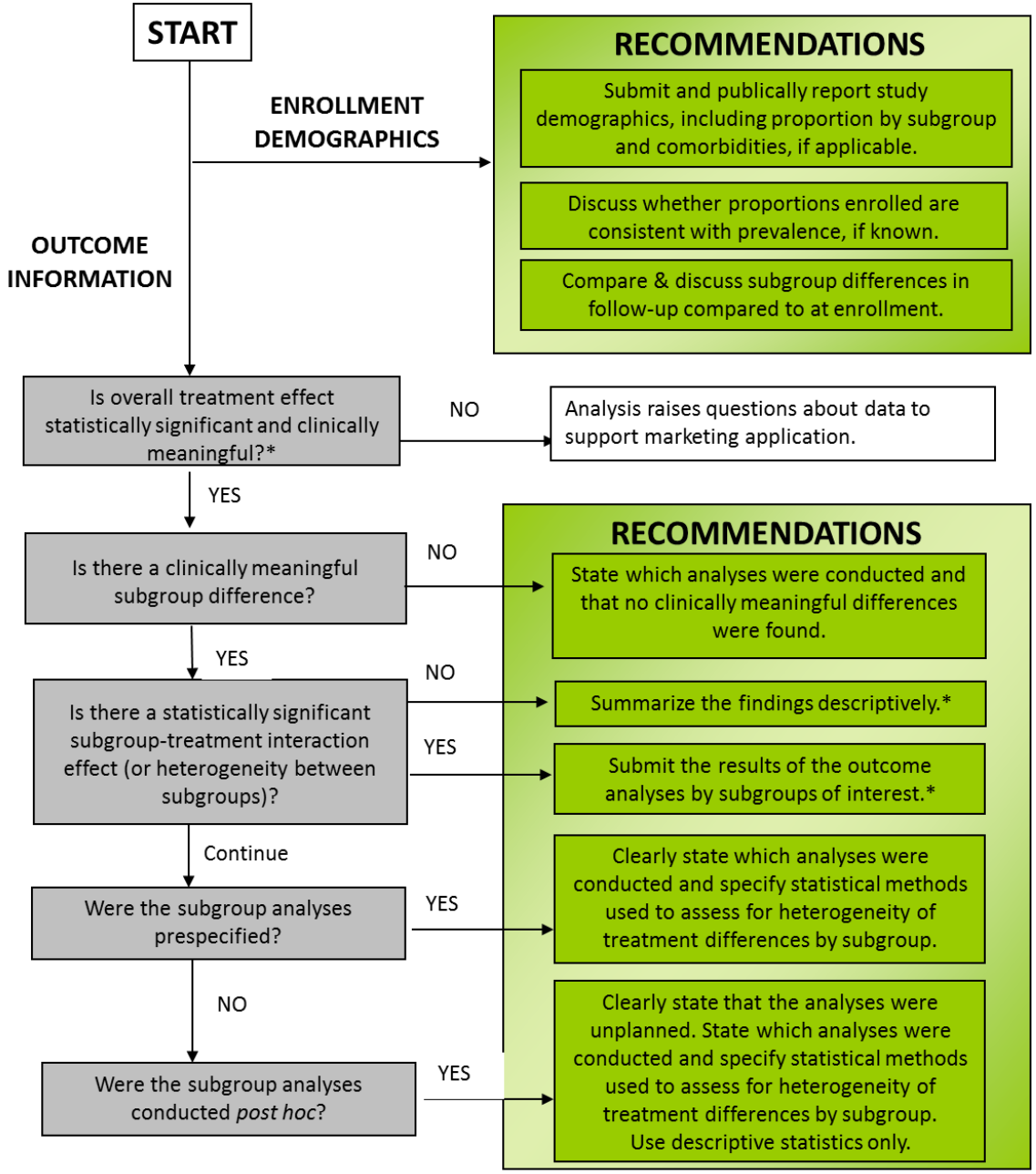
**Provide justification for pooling data across subgroups, if applicable.

Note: In some cases, the subgroup-specific difference could be statistically significant but not clinically meaningful or clinically meaningful but not statistically significant. In these cases, discussion with FDA is advised.

Subgroup Data in Submissions to FDA and Public Reporting

Report the number and proportion of subjects by age, race, and ethnic groups treated/diagnosed with device:

- Proportion enrolled and completed
- Subgroup proportions consistent or not with prevalence
- Discuss generalizability of results when enrollment is substantially different than prevalence
- Co-morbidities and baseline characteristics for subgroups should be analyzed and submitted
- Discuss subgroups with disproportionate loss, by time points and study arm(s)



* Discuss how clinically meaning differences across subgroups may contribute to differences in benefit-risk profile in certain subpopulations.

Note: The term "submit" refers to information submitted to the FDA for analysis. The term "report" refers to information that should be included in publically available documents (e.g., labeling, SSED).

Comments to the Docket

Stakeholders should submit comments on the draft guidance by September 19, 2016

- Federal eRulemaking Portal: http://www.regulations.gov. Comments are public and appear unchanged, including attachments
- Mail/Hand delivery/Courier (for written/paper submissions): Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

Comments & Questions

Thank you!

U.S. Food and Drug Administration

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