

Introductory FDA Remarks

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Virtual Public Workshop: Drug Development Considerations

for the Prevention of Health Care Associated Infections

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Welcome

- Innovation in drug development to prevent health care associated infections will be critical to reduce morbidity and mortality and address AMR.
- CDC and FDA have partnered to host this workshop - what we hope will be the first of a number of public dialogues to address drug development challenges in this space.
- Special thanks to our CDC colleagues, national thought leaders, and industry development leaders that are here with us today.

Today's Program



Session 1: Background and Epidemiology

- A state of the art review of prevention science and the major health care associated infections
- Patient impact and perspective
- Formal public comments

Session 2: Regulatory Perspective and Trial Design Challenges/Considerations

- Regulatory considerations for drugs, antiseptics, and microbiome based therapeutics
- Clinical, statistical, and operational considerations
- Moderated panel discussion

Cross-Cutting Regulatory Considerations

Endpoints – form the basis of labeling claims

- Clinical endpoints:
 - Endpoints that describe or reflect how an individual feels, functions, or survives
- Surrogate endpoints:
 - Endpoints used as a substitute for a direct measure of how a patient feels, functions or survives and thought to predict such effects
- Accelerated approval can be supported by trials establishing an effect on a surrogate endpoint reasonably likely to predict clinical benefit.
- Traditional approval can be supported by trials establishing an effect on a clinical endpoint or a validated surrogate endpoint with very persuasive data demonstrating its ability to predict clinical benefit (e.g., HIV-1 plasma viral load).

Cross-Cutting Reg. Considerations



21 CFR Part 314 Subpart H, Section 314.510: Approval based on a surrogate endpoint or on an effect on a clinical endpoint other than survival or irreversible morbidity

“FDA may grant marketing approval for a new drug product on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely, based on epidemiologic, therapeutic, pathophysiologic, or other evidence, to predict clinical benefit or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. Approval under this section will be subject to the requirement that the applicant study the drug further, to verify and describe its clinical benefit, where there is uncertainty as to the relation of the surrogate endpoint to clinical benefit, or of the observed clinical benefit to ultimate outcome. Postmarketing studies would usually be studies already underway.”

Cross-Cutting Reg. Considerations



- Use of decolonization as a surrogate endpoint in clinical trials would have pros and cons.
- In addition to other endpoint regulatory requirements, sponsors would need to discuss the data with the Agency that supports that the endpoint is reasonably likely to predict clinical benefit for the particular pathogen and clinical situation.
- If accelerated approval, sponsors would need to discuss with the Agency the plan to verify the clinical benefit.

Cross-Cutting Reg. Considerations



Bundles

- Prevention strategies usually involve bundles (evidence-based practices implemented collectively).
- For a new product that is part of a bundle, data are needed to understand the contribution of the new product to the benefit demonstrated in the trial.
- Standardization between study sites needs to be addressed.

Cross-Cutting Reg. Considerations



Other Design Considerations

- There are unique statistical issues for cluster randomized trials to discuss with the Agency as the trial is being designed.
 - E.g., the cluster level risk difference may not be equivalent to the individual level risk difference. Individual patient benefit will be a review consideration.



Thank you for joining us today and for your commitment to prevention of health care associated infections.