CAPITOL STREET

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FDA Monoclonal Antibody Guidance Excludes Oncology

Recommendations Seek to Eliminate Longer Term Animal Toxicity Studies

Relevant Companies

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Our Take & Next Up

FDA's new guidance aims to eliminate longer term, preclinical animal safety studies for monoclonal antibodies. Today, the FDA released draft guidance on reducing testing on non-human primates for monoclonal antibodies (here). The guidance provides multiple alternative methods for longer-term, nonclinical safety assessments, however, animal testing itself is not eliminated with the guidance still requiring 3 month nonrodent animal studies. Notably, the guidance does not apply to any monoclonal antibodies being developed for oncology indications.

The guidance is part of the FDA's current efforts to phase out animal testing, however, progress is limited. We believe manufacturer uptake of alternatives methods will be limited at first, due to concerns of validity and ongoing uncertainty at the FDA. Clearly there is a role for animal models.

Key Points

The guidance is meant to reduce longer term animal testing for monospecific antibodies in any indication except for oncology. Oncology-specific guidances will still apply for oncology indications.

This guidance does not address the following:

- toxicology studies related to multispecific antibodies
- conjugated antibodies (e.g., antibody-drug conjugates)
- antibody constructs (e.g., single-chain variable fragments).

Animal testing is reduced but not replaced. FDA will rely on shorter term (3 months) animal studies and weight-of-evidence (WoE) risk assessment to review toxicities from chronic administration. In general, studies longer than 3 months in nonrodent animals (e.g., non-human primates, dogs, and mini-pigs) are not warranted when data from 3-month studies are supplemented with a WoE risk assessment.

Recommendations are voluntary, but the FDA wants to phase out animal models over time. The recommendation is a step in the FDA's ongoing efforts at phasing out animal testing requirements, starting with monoclonal antibodies. The science is not yet developed to eliminate animal testing wholesale. We note that the FDA continues to collaborate with the NIH and the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) to validate and expand new approach methodologies (NAMs).

The FDA announced its intention to phase out animal testing in April 2025. While the FDA has outlined a long-term roadmap, widespread adoption is likely to stall with ongoing uncertainty at the agency and lack of validated methods. The transition is viewed as a 3–5 year goal.

We believe most companies (if they pursue this alternative nonclinical design) will use a mix of sources to generate safety data. Companies may also heavily rely on pre-published research. Acceptable WoE risk assessment methods include pre-published papers/research, NAMs, tissue level data, toxicity finding in humans, and other pharmacologically relevant specifics. A WoE risk assessment may include the following data:

- Mechanism of action and pharmacology data generated with the monospecific antibody
- A literature-based assessment of potential toxicities associated with the molecular target
- Results of toxicology and pharmacokinetic (PK) data in pharmacologically relevant species
- Results of an assay to detect human-relevant off-tissue binding and potential secondary effects
- Clinical safety and PK data generated with the monospecific antibody (e.g., phase 1 or 2 data)
- Toxicity findings in animals and humans, such as when extensive information is published on toxic effects based on other monospecific antibodies against the same target.
- Other nonclinical data as scientifically justified (e.g., NAMs, transgenic models, data using surrogates).

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