FDA CBER OTP Meeting: Leveraging Knowledge to Facilitate the Development and Review of CGTs

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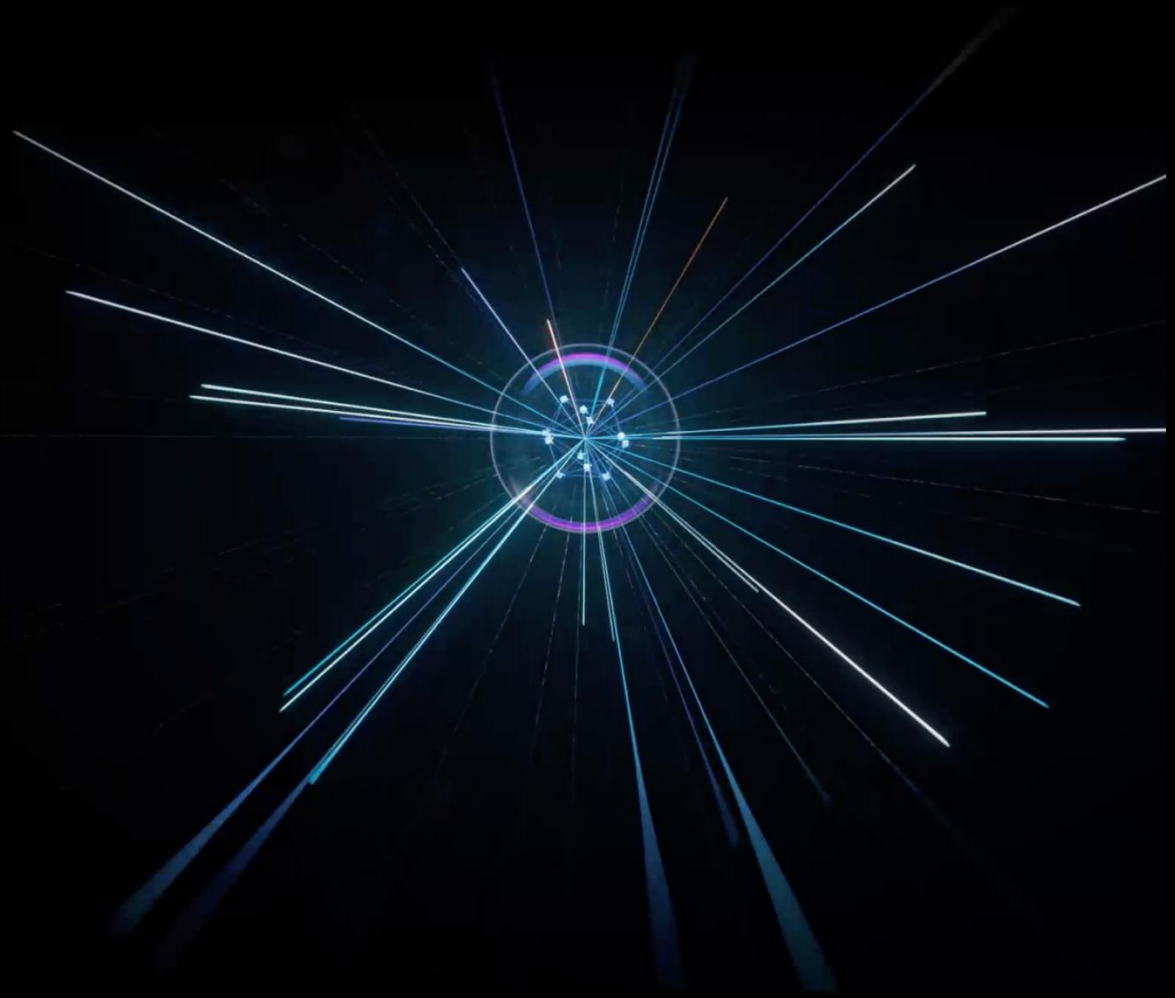
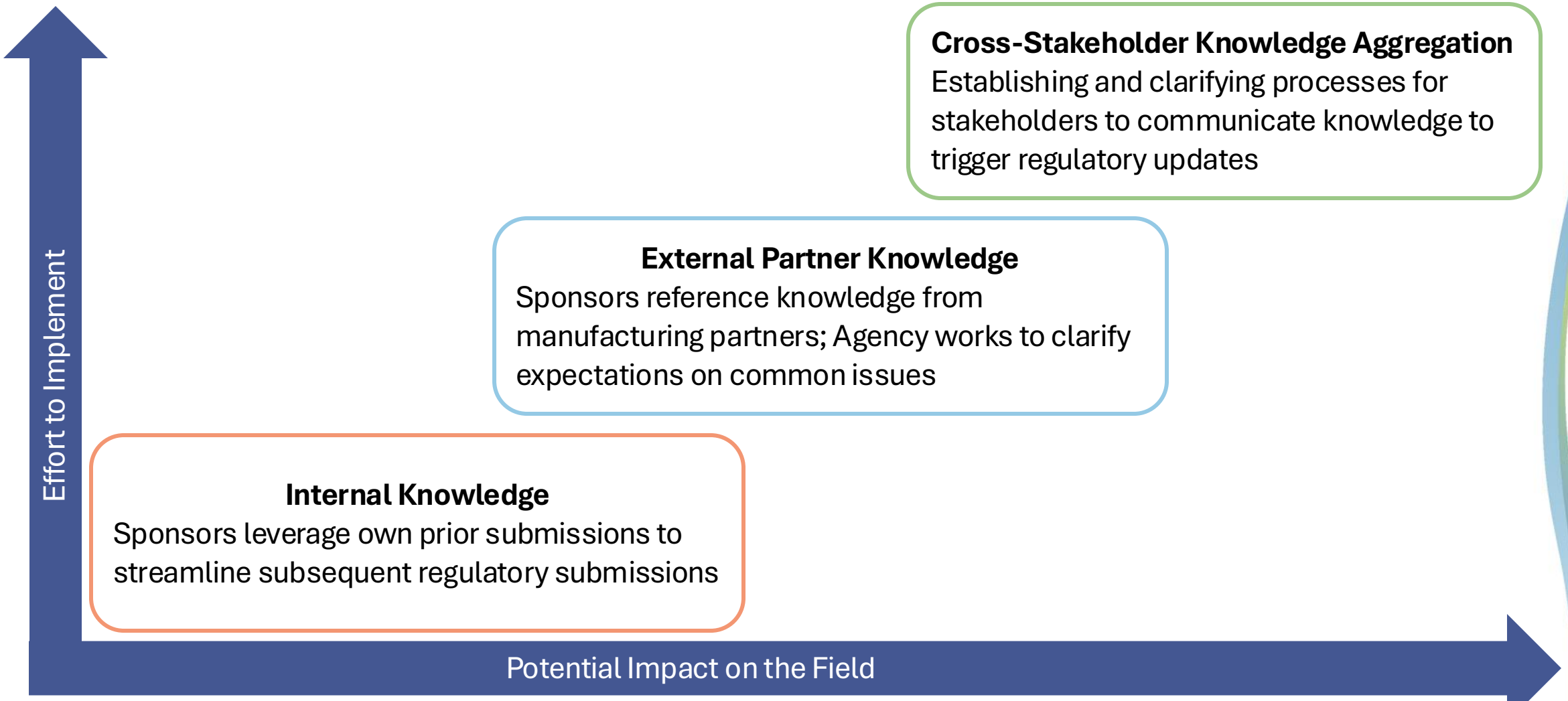
September 18, 2025



Knowledge Sharing Pillars

Streamlining innovation by harnessing prior knowledge and regulatory efficiency



Cross-Stakeholder Knowledge Aggregation
Establishing and clarifying processes for stakeholders to communicate knowledge to trigger regulatory updates

External Partner Knowledge
Sponsors reference knowledge from manufacturing partners; Agency works to clarify expectations on common issues

Internal Knowledge
Sponsors leverage own prior submissions to streamline subsequent regulatory submissions

Internal Knowledge Sharing Across CGT Assets

Sponsors are looking for clarity & green lights

A few ideas to consider:

- Allow sponsors to reference/link to their own prior BLAs for products within a Platform Technology Designation (PTD), rather than resubmitting all this information in subsequent BLAs
- Establish a process to define when sufficient data has been reached to reduce the number of required assays in subsequent submissions
- Consider building into FDA meeting advice a standard discussion point to explore if the sponsor has knowledge it can leverage from its own previous work, to demonstrate openness to the concept

Example Application: Off-Target Analysis

Allowing a risk-based approach whereby developers can:

- Reduce the number of assays necessary to produce sufficient and scientifically robust characterization of off-target editing
- Limit the number of tissues analyzed for off-target editing and off-tissue biodistribution
- Maintain agreed upon safety standards while speeding innovation

External Partner Knowledge Sharing

Proposed Sponsor- and FDA-Driven Opportunities

A few ideas to consider:

- Allow BLA sponsors to leverage CMC data from CMO/CDMO master files
- Continue to work with stakeholders to identify opportunities to work together to establish and communicate expectations
    - Sponsors have reported that the OTP Town Halls on CMC expectations in 2023 & 2024 were quite beneficial

Example: CMO Master File

- **Revisit the 2024 final rule**, Biologics License Applications and Master Files
    - BLAs may not incorporate by reference drug substance, drug substance intermediate, or drug product information contained in a master file*
- **Rationale:** Ensuring product quality, as a BLA holder must, can be done while referencing certain CMC attributes of products in DMFs or other mechanisms
- **Benefit:** Would avoid requiring CMO disclosure of confidential information with an application holder, thereby stimulating manufacturing innovation

*Including a drug master file submitted under §314.420, Unless grandfathered, i.e., such information was referenced at the time the application was deemed to be a license

Cross-Stakeholder Knowledge Aggregation to Inform Regulatory Updates

FDA and Stakeholders Should Jointly Drive Opportunities

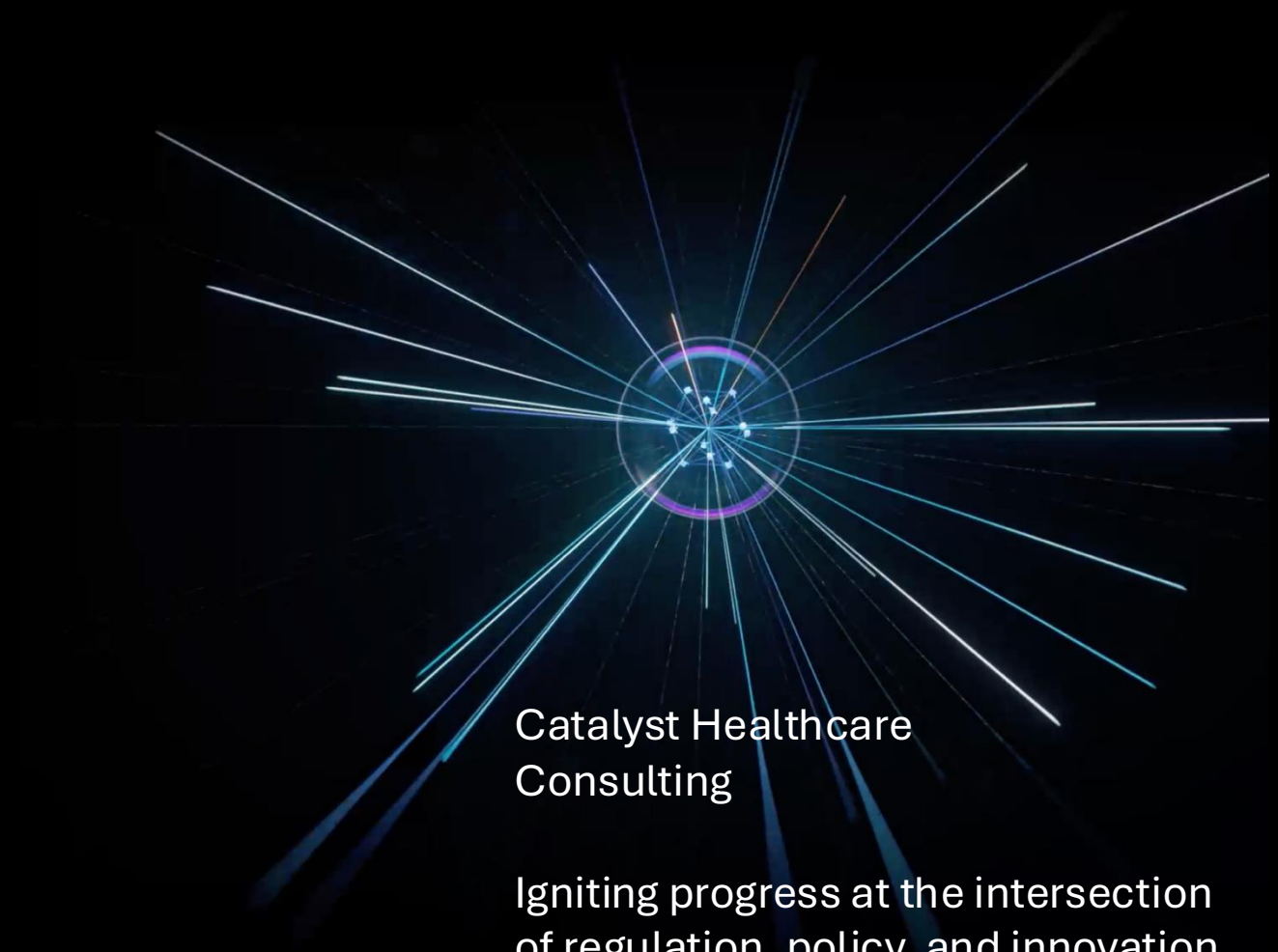
A few ideas to consider:

- US innovators need CBER/OTP to continue encouraging FDA staff/content experts to actively engage with and exchange ideas in collaborative efforts with stakeholders from scientific exchanges, conferences, town hall meetings, workshops and public meetings
- Consider creating a process whereby multiple stakeholders can aggregate data to build a case for updating outdated processes/expectations and submit for regulatory policy discussions and subsequent change considerations

Example Application: CAR-T Long-Term Follow up (LTFU) Requirements

- In guidance from 2020, FDA generally recommend 15 years of long-term follow-up for integrating vectors (e.g., CAR-T cell therapies)
- As the CAR T-cell therapy field has developed (30K patient experiences, 7 approved products, 15 years of data) and new safety data has emerged, patients, sponsors, and other stakeholders have aligned around reducing the length of LTFU to 5 years and modernizing the process of LTFU data collection
- Cross-stakeholder data analysis of safety signals & patient burden support this proposal

Thank you



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Igniting progress at the intersection of regulation, policy, and innovation