The Importance of Identifying Regulatory Gaps Prior to Tool Development

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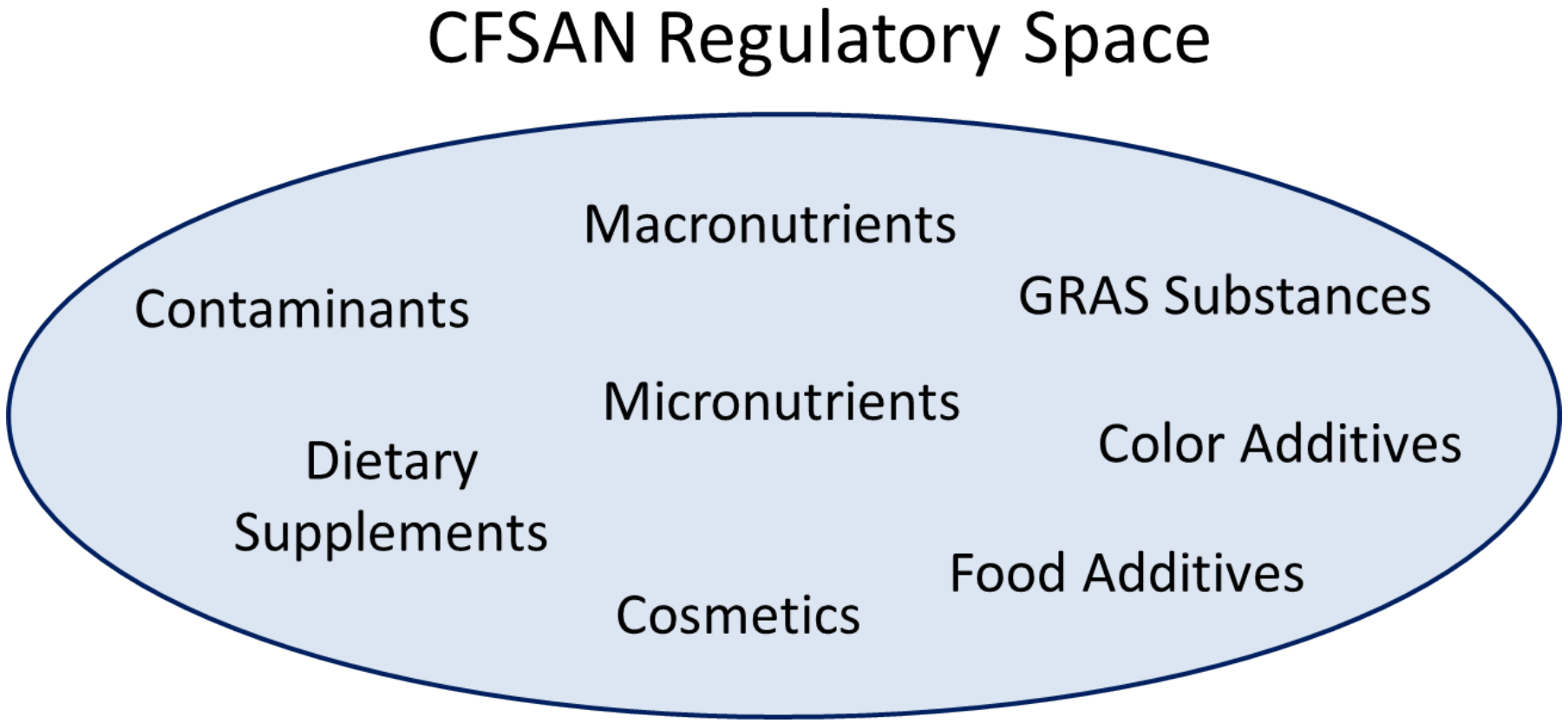
Trust Your Gut: Establishing Confidence in Gastrointestinal Models, An Overview of the State of the Science and Contexts of Use. Preliminary Webinar Series, September 18, 2023

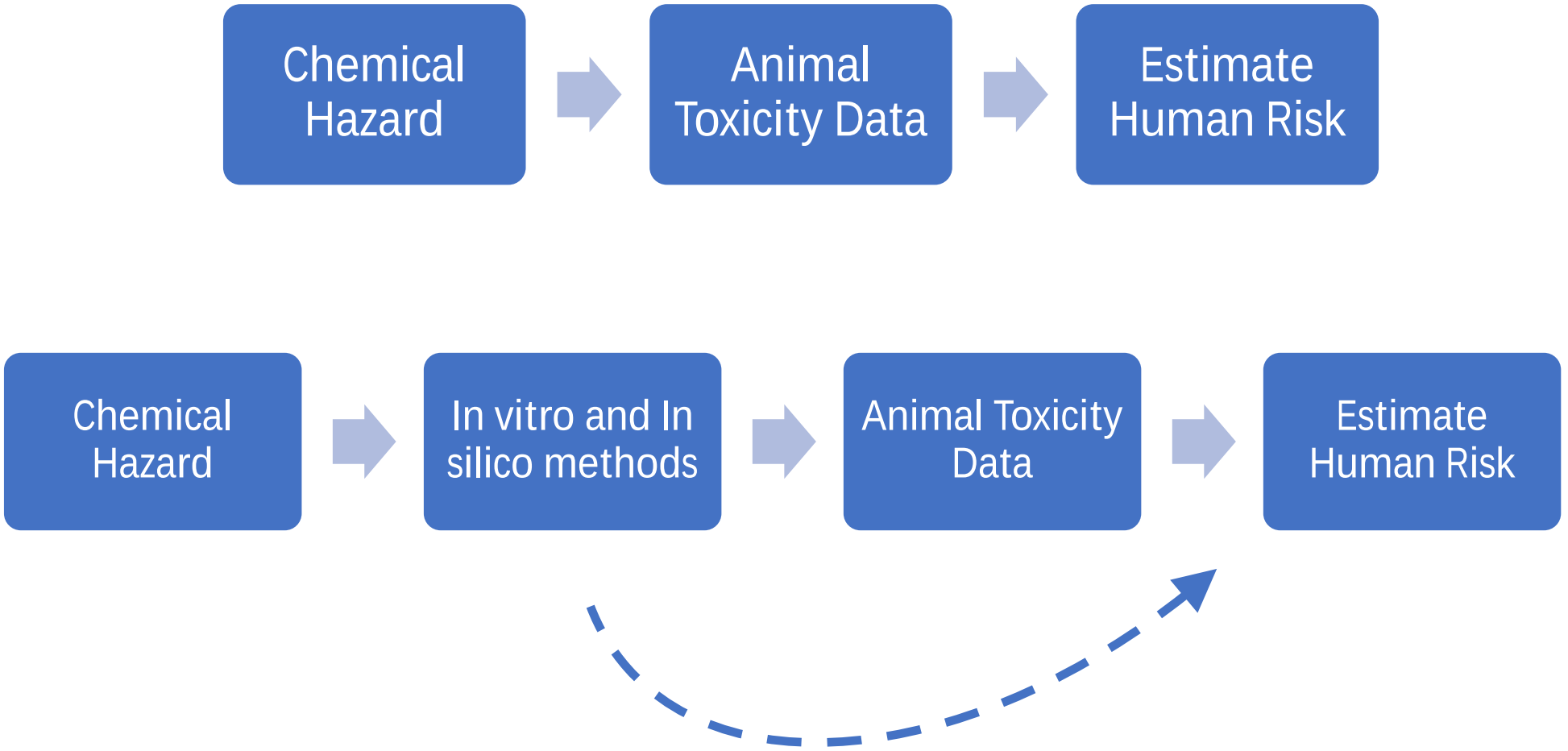
What CFSAN regulates



Some examples of regulatory issues

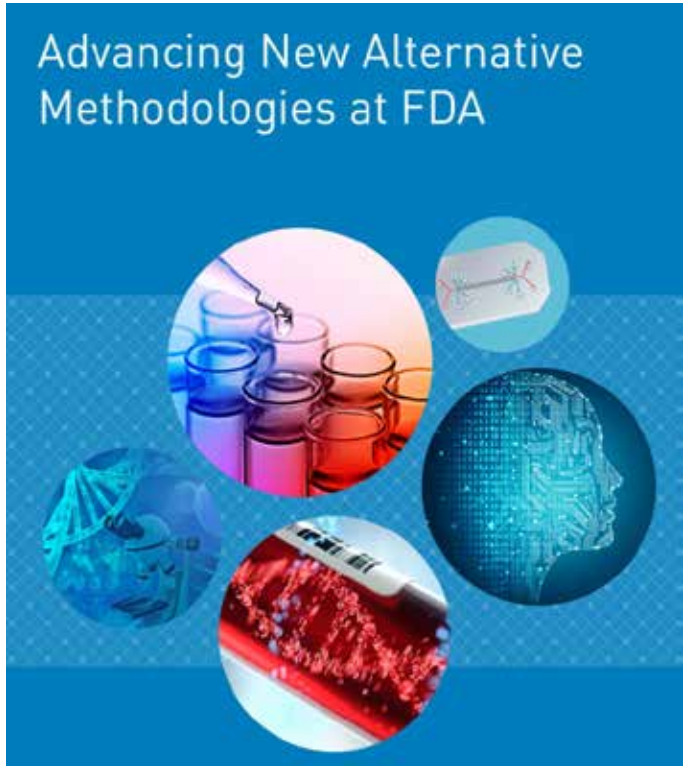
- Novel foods – (new levels of protein)
- New food sources – fungus, insects, etc.
- GE and GMO crops
- Dietary supplement - live microbials
  - Infants and older adults

Food Chemical Safety Evaluation



Advancing new approach methodologies (NAMs)

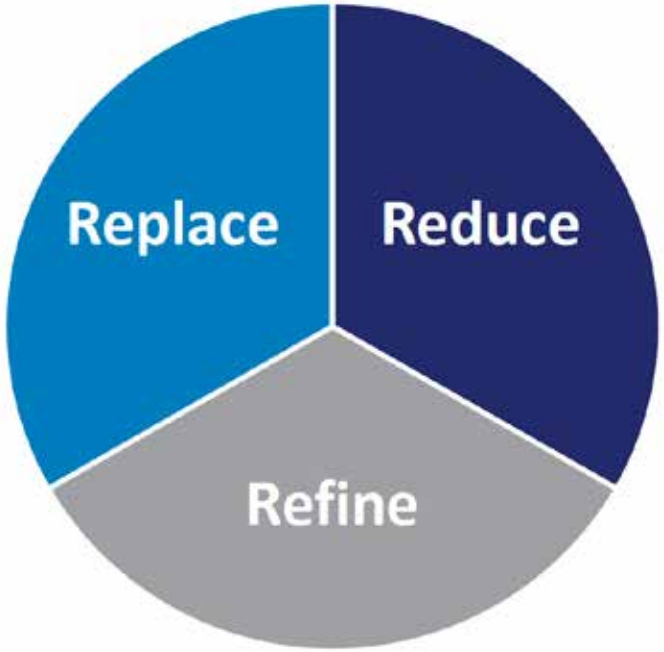
- FDA has had a long-standing commitment to promote the development and use of new technologies to evaluate and predict the safety, effectiveness, and reliable manufacture of regulated products.
- FDA recognizes that new technologies may help bring FDA-regulated products to market faster, with improved efficacy, or prevent products with increased toxicological risk from reaching the market.



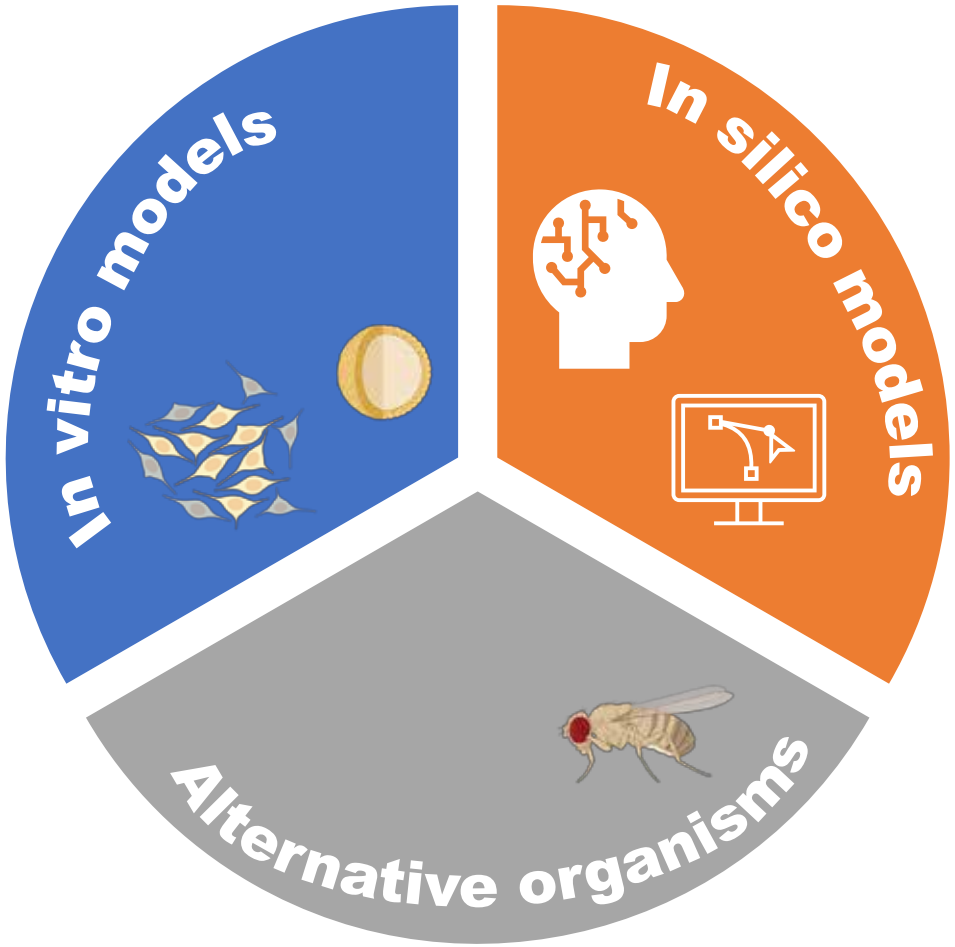
Report available on the FDA webpage

Basis for NAMs investment

- Replace, reduce, and/or refine animal testing
- Faster and more efficient identification of toxicity and associated pathways
- Better modeling of human toxicity
- Lower overall costs?



Alternative Methods – Lots of them



Tox-GAN: An Artificial Intelligence Approach Alternative to Animal Studies—A Case Study With Toxicogenomics

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ffect of ketamine on gene expression in zebrafish embryo

Jiang Gu, Jyotshna Kanungo

First published: 17 May 2021 | https://doi.org/10.1002/jat.4199

Reevaluation of the embryonic stem cell test

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[Publications Co-authored by FDA on Alternative Methods | FDA]

Challenges for regulatory decision making

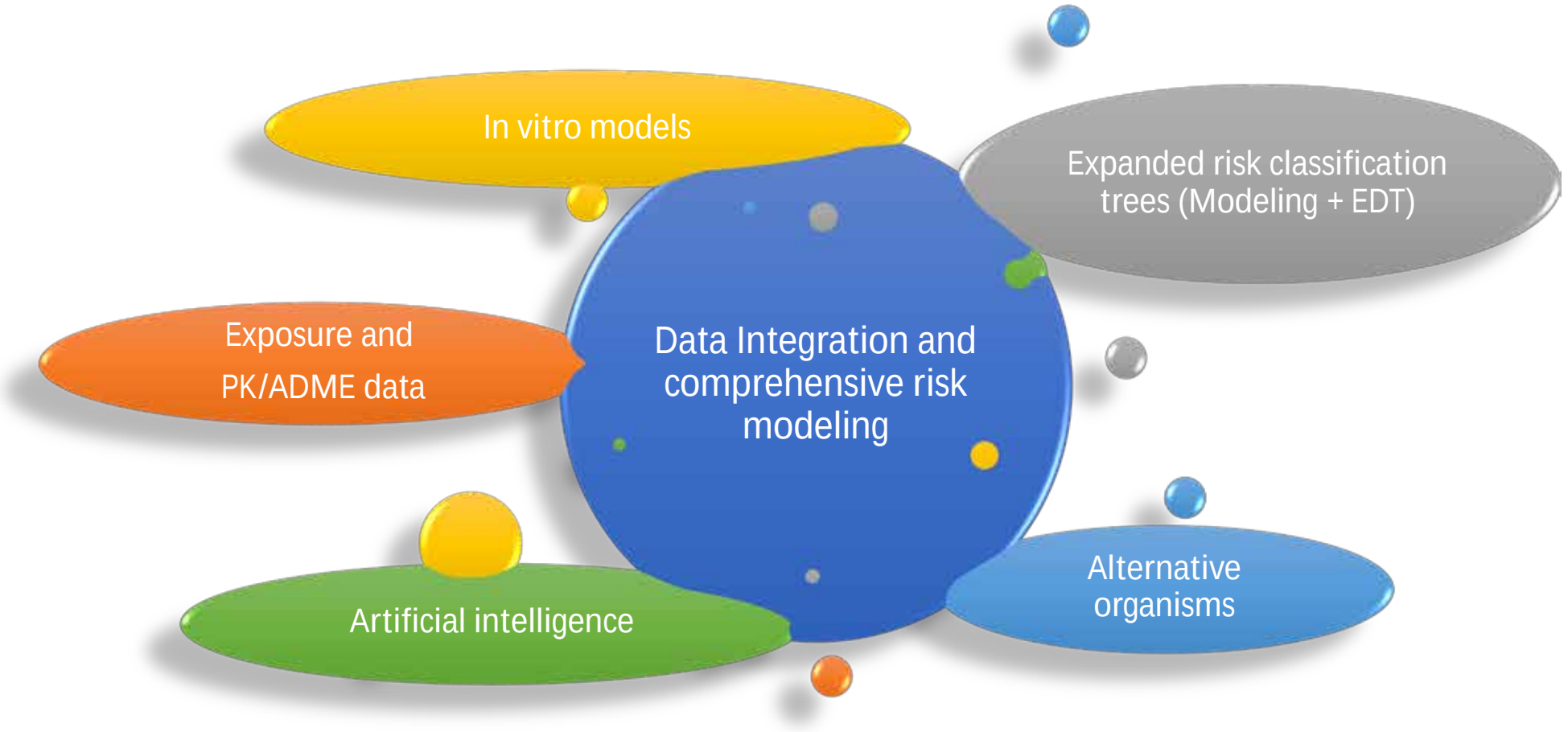
Relevance!

- What endpoints are being measured?
- Are they predictive of in vivo effects?
- Do the results account for relevant PBPK and exposure estimates?
- Translatable to human and at-risk groups?

Moving toward regulatory use

- Is the assay mature enough?
  - Stable platform, cell lines, reagents and supplies
- Qualification/validation?
  - Is it reproducible?
  - What test compounds have been assessed?
    - Need compounds with in vivo data
    - Positives and negatives
- Applicability domain
  - Define compounds the assay can assess and not assess
- Define limitations of the assay
  - What are sensitivity and specificity?

Integration of multiple data streams



Conclusion

- Significant need for modeling and new approaches to accessing human toxicity
- Greater emphasis on qualification
- Collaboration and comparison across laboratories
- More work on data integration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