U.S. FOOD & DRUG ADMINISTRATION

Human Foods Program

# Engaging NAMs for Toxicant REgulation and Effects

## ENTRÉE

An HFP Pilot Program

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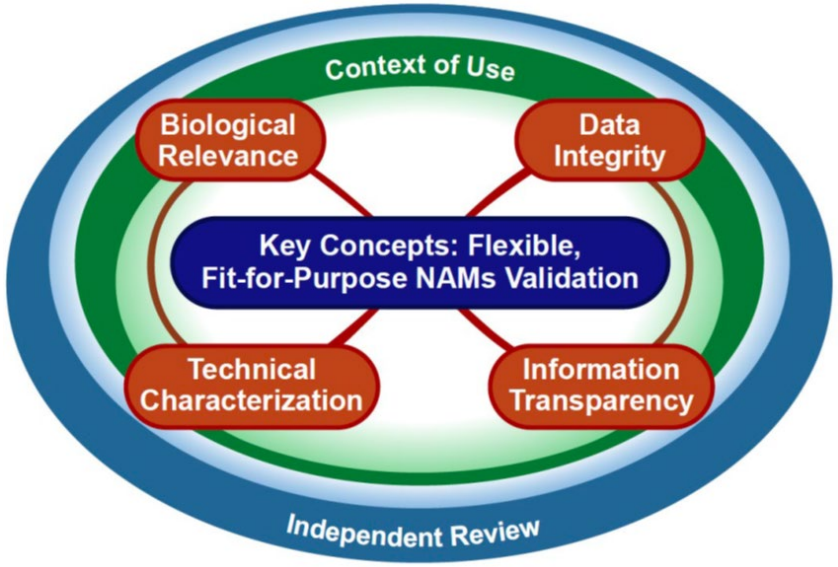
# ENTRÉE is HFP's Pilot Qualification Program

**E**ngaging **N**AMs for **T**oxicant **RE**gulation and **E**ffects

It is based on the parameters set forth in the 2024 ICCVAM report and CDER's ISTAND program.




*Validation, Qualification, and Regulatory Acceptance of New Approach Methodologies, ICCVAM, March 2024*
*doi: 10.22427/NICEATM-2*
https://ntp.niehs.nih.gov/whatwestudy/niceatm/iccvam


Innovative Science and Technology Approaches for New Drugs (ISTAND)

https://www.fda.gov/drugs/drug-development-tool-ddt-qualification-programs/innovative-science-and-technology-approaches-new-drugs-istand-pilot-program

# What is Qualification?

A process that allows for an alternative method to be endorsed for regulatory use by FDA in advance for a specific **context of use**.

Qualification is a conclusion that within the stated **context of use**, an alternative method can be relied upon to have a specific interpretation and application in regulatory review (FDA).

Once an alternative method is qualified through ENTRÉE, resulting data generated using the method according to the **context of use** can be submitted to FDA HFP without providing data to justify the use of the method.

- ***Qualification begins with the regulatory question or gap – not the tool, method, or test***

# What is Context of Use?

The manner and purpose of use for an alternative method; the specific role and scope of an alternative method to address the question of interest. ***When FDA qualifies an alternative method, it is qualified for a specific context of use or COU*** (FDA).

- The COU defines the questions that need to be answered and the specific purpose of the NAM.
- The COU will determine the amount of data required to support the qualification process and defines limits.
- If the alternative method involves evaluation of food (and not just a purified chemical), the mechanism of introducing food to the test system should be considered as part of the COU.

# ENTRÉE – Next Steps

- ENTRÉE is a pilot program. Expect evolution as needed and NAMs are evaluated case-by-case.
- First HFP use of NAMs qualified through this pilot program will be to support the post-market assessment of chemicals in food.
- Interested participants (e.g., test method sponsors) should reach out to FDA via email to HFPNAMS@fda.hhs.gov
- Start with an informal discussion. Sponsors of new methods will be asked to send a **Letter of Intent** to the FDA HFP ENTRÉE program.
- After receiving and reviewing the **Letter of Intent**, HFP will schedule a formal meeting with the sponsor to discuss the proposed method and address any additional information that may be needed.

# ENTRÉE – Letter of Intent

The Letter of Intent should discuss the following:

- Context of Use
- Biological Relevance
- Technical Characterization
- Data Integrity and Information Transparency
- Qualification Plan
- Independent Review
- Training Plan Once Qualified

- The Letter of Intent to the FDA/HFP will be submitted to HFPNAMS@fda.hhs.gov

- HFP requests a discussion with sponsors before they submit a Letter of Intent.

# ENTRÉE
## Essential Steps to be Successful

1. Informal Discussion
2. Letter of Intent (LOI)
3. Outline the Qualification Plan
4. Submit the Full Qualification Package

# ENTRÉE – Proprietary Information

- Per the ICCVAM Model of Qualification, HFP requires disclosure of all relevant methodological and supporting scientific data.
- HFP recognizes that sponsors may have a financial stake in the method and may desire to protect some information from public disclosure.
- **Sponsors should clearly state what information and data are (or will be) considered Confidential Business Information (CBI).**
- HFP will discuss internally and follow up with the sponsor describing the extent to which the information can be protected from public disclosure.
- The sponsor can use this information to decide if they wish to proceed with a Letter of Intent to HFP for evaluation via ENTRÉE.

# Integration of ENTRÉE into HFP

- During the pilot program, ENTRÉE submissions will be managed through the review and feedback process by a designated point of contact within HFP in collaboration with FDA subject matter experts
- Once all criteria outlined in the Letter of Intent are complete and supporting data received, the submission package will be reviewed for acceptance by subject matter experts within HFP and/or across FDA*
- HFP may choose to convene a group of subject matter experts outside the FDA to advise on the acceptability of the NAM within the COU
- As the NAM proceeds through the review process, the HFP designated point of contact will work with the Sponsor to develop training materials
- At the end of the process, HFP will post the final acceptance of the method including COU and results of the review to its website

*Note that subject matter experts reviewing a data package for qualification will be independent of those involved in the submission process.