New Approach Methodologies for Use in FDA Food Safety Assessments

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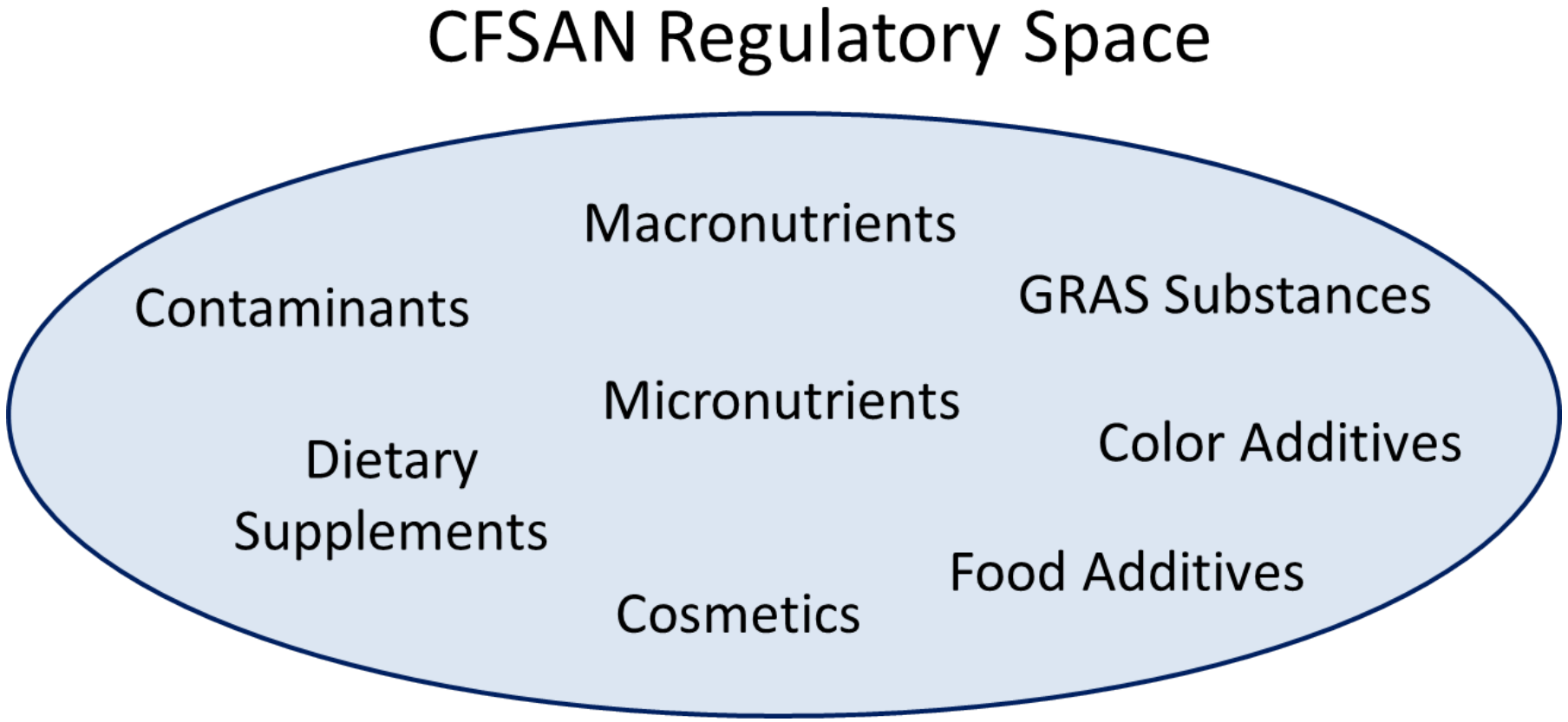
Advancing new alternative methodologies at FDA

- 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.
- FDA supports the development of new regulatory tools that can help improve predictivity and potentially replace, reduce, and/or refine animal testing.
- FDA recognizes that each of its product centers are unique and encourages development of Center-specific Qualification Programs that can then share knowledge across the agency.

Report available on the FDA webpage

What CFSAN regulates- For most of these products CFSAN lacks pre-approval authorities



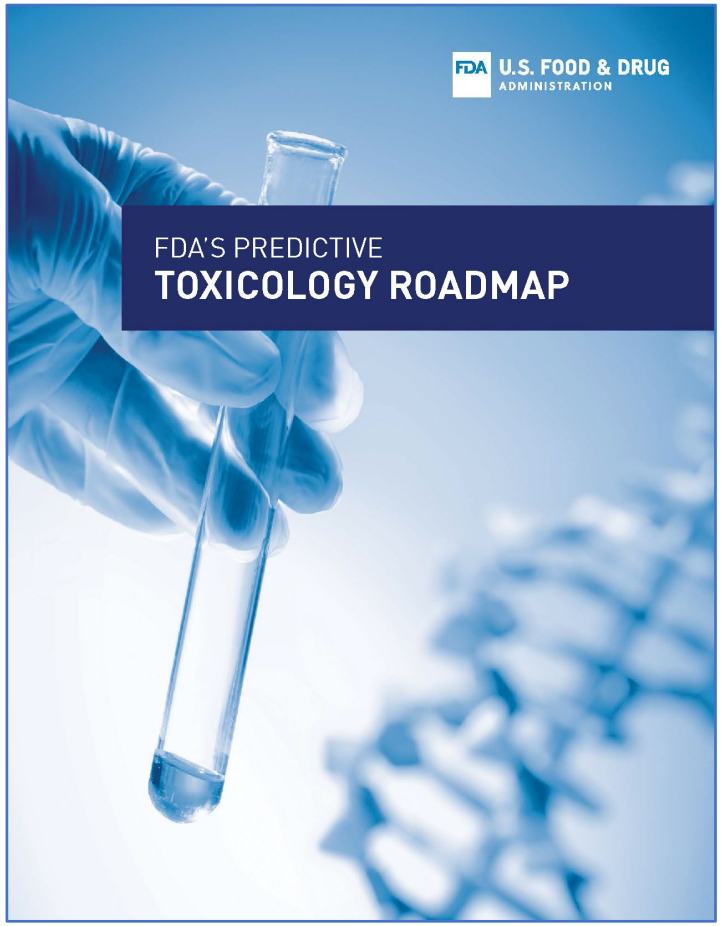
CFSAN Vision: Advancing Toxicology

Transition to 21st century technologies to enhance chemical risk management

CURRENT APPROACH	FUTURE DIRECTION
• Heavy reliance on animal studies • Evaluation of multiple apical endpoints • Based on traditional toxicity tests	• Less reliance on animal studies • Tailored data generation • Based on toxicity pathways

FDA Predictive Toxicology Roadmap Announced December 6, 2017

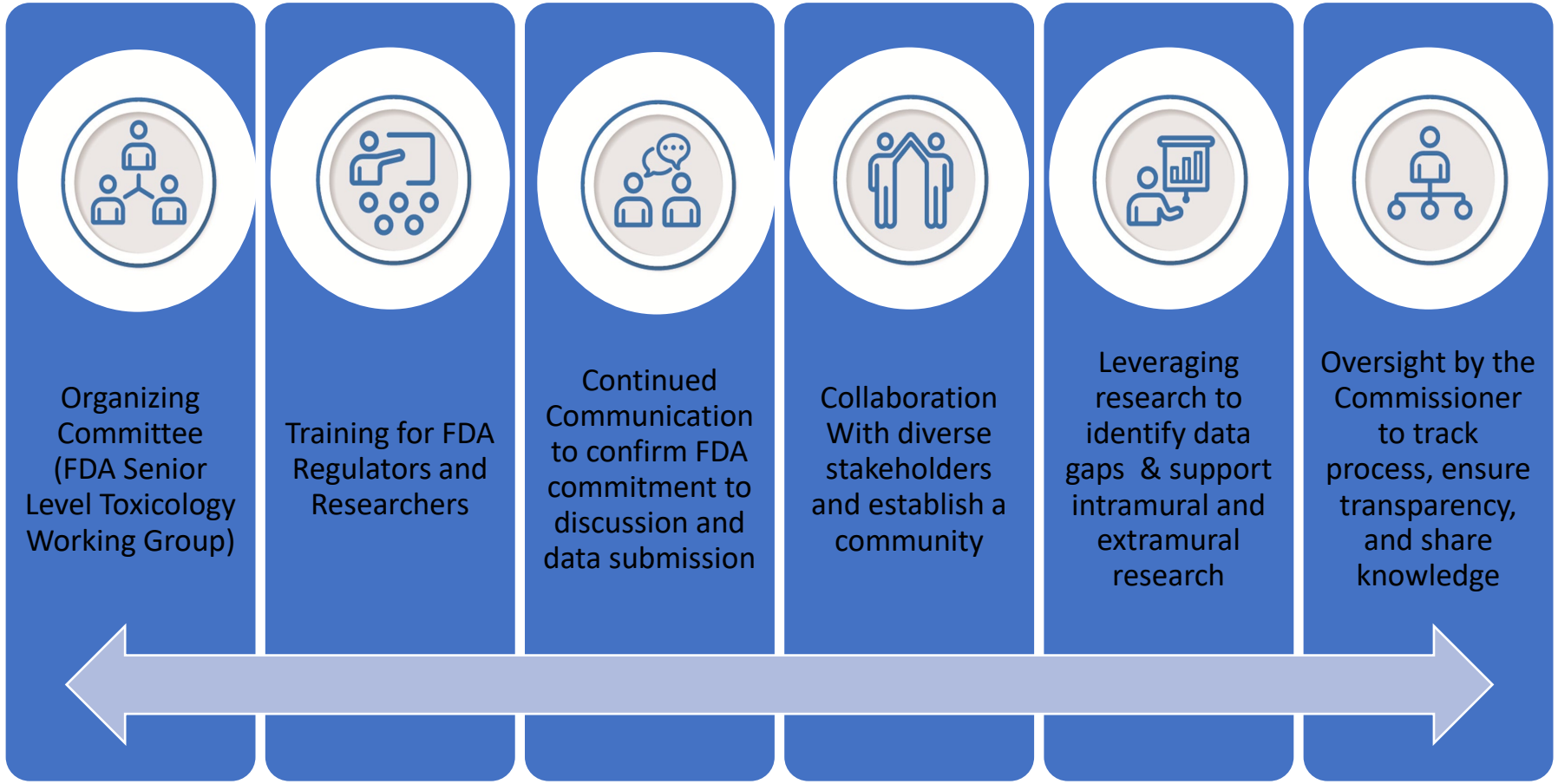
- https://blogs.fda.gov/fdavoice/index.php/2017/12/fda-launches-predictive-toxicology-roadmap-to-enable-advances-in-toxicity-testing/



The FDA Predictive Toxicology Roadmap -A Six-Part Framework for New or Enhanced FDA Engagement in the Science of Toxicology

- The key goal of the roadmap is to invigorate and strengthen FDA's long commitment to promoting the development and use of new technologies to better predict human, animal, and environmental
- CFSAN has incorporated the principles of the FDA Predictive Toxicology Roadmap into its program on New Approach Methodologies for Food Safety Assessments.

FDA's Roadmap: Framework for Incorporating Emerging Predictive Toxicology Methods in Regulatory Reviews



CFSAN Senior Level Toxicology Working Group

CFSAN's Office of the Center Director has created a NAMS working group to leverage CFSAN resources to advance the integration of emerging predictive toxicology methods into regulatory food safety and risk assessments.

The NAMS WG includes senior and junior scientists from both CFSAN regulatory and research programs and has liaisons from ORA and NCTR.

Charter of the CFSAN NAMS Working Group

Goal : To develop criteria for developing confidence in NAMs for use in human food safety assessments and regulatory decisions and to test these criteria using case studies

- Identify which NAMs are currently being used in the food industry, academia and other government agencies (nationally and internationally).
- Develop a plan to evaluate NAM's for applicability to human food safety evaluation that includes qualification criteria, feasibility, cost, how far the method is in the development stage (early vs commercially available).
- Develop a draft qualification guidance. Consider where a separate guidance is needed for different categories of NAMs (e.g., microphysiological systems vs. *in silico* models vs. biomarkers).
- Conduct stakeholder workshops on Qualification criteria, NAMs status, gaps and use at CFSAN.

Training of CFSAN regulators and researchers

- Continuing ongoing education in new predictive toxicology methods is essential priority for both CFSAN regulators and researchers
- CFSAN has establish a Center-wide education calendar of courses, events and publications as a resource for all its scientists
- CFSAN incorporates the principles of “Training by Doing”- Includes Junior Scientists in the planning and implementation of all NAMS activities.

Collaborations with Stakeholders

- CFSAN encourages collaborations across sectors and disciplines nationally and internationally.
- CFSAN supports the importance of collaborations in identifying the needs, maintaining momentum, and establishing a food safety community to support delivery of new predictive toxicology methods.

Potential Partnerships Avenues to Work with CFSAN on NAMS

- Public-private partnerships (PPP)
  - FDA invited to participate
  - Increased access to resources and expertise
- Memorandum of understanding (MOU)
  - Relationship between federal agencies
  - Share information and resources
- Research collaboration agreement (RCA)
  - Share resources, methods, technology during research project
  - Both parties get something out of the agreement

INTERNATIONAL LIAISON GROUP ON METHODS FOR RISK ASSESSMENT OF CHEMICALS IN FOOD (ILMERAC)

Created through partnership with CFSAN/FDA and EFSA.

Facilitating and coordinating research and regulatory efforts on NAMs through an international framework will provide the best path to harmonized outcomes.

ILMERAC created a working group on New Approach Methods.

ILMRERC NAMS WG is new but already has selected the first list of priority actions for increasing the use of NAMs in food safety assessments.

International Liaison Group for Methods on Risk Assessment of Chemicals in Food (ILMERAC)

Organisation	Contact person
US FDA – Food and Drug Administration	Suzanne Fitzpatrick (co-chair) Goncalo Gamboa Steven Hermansky Jason Aungst Paul South
EFSA – European Food Safety Authority	Jose Tarazona (co-chair) Maria Chiara Astuto Irene Cataneo Jean-Lou Dorne Yann Devos Georges Kass Maria Bastaki
HC - Health Canada	Tara Barton-Maclaren Sonya Billiard John Field David Lefebvre Zoe Gillespie Marc Beal

Organisation	Contact person
RIVM	Esther de Jong Astrid Bulder Anne Kienhuis Ellen Hessel
JRC - Joint Research Centre	Sandra Coecke
BfR - German Federal Institute for Risk Assessment	Philip Marx-Stoelting Majlinda Lahaniatis
NVWA - the Netherlands Food and Consumer Product Safety Authority	Michiel den Braver
CFSA -China National Center for Food Safety Risk Assessment	Haixia Sui
OECD - Organisation for Economic Co-operation and Development	Patience Brown
NZFS - New Zealand Food Safety	Jeane Nicolas
KIT - Korean Institute of Toxicology	Yu WookJoon Lee Seung-Jin

Experts from non-ILMERAC organizations are invited for specific topics.

Priorities of the ILMERAC Work Group on NAMS

First challenge: To cover key data gaps with NAMs, minimizing requests for additional *in vivo* studies. Mixtures were identified as a global problem. The mixtures themselves could be different but hopefully the tools to assess the toxicity of them could be harmonized.

Second challenge: To provide guidance for using non-guideline studies (i.e., peer-reviewed publications), including harmonized reporting, and to explore the "context of use qualification" approach.

Third challenge: (R)evolution of the risk assessment paradigm, facilitating the integration of mechanistic information rather than apical endpoints at the end of a study.. Mechanistic information includes AOPS and IATAs.

Continued Communication

- CFSAN is committed to incorporating data from newly qualified toxicology methods into regulatory assessments
- CFSAN encourages discussions with stakeholders as part of the regulatory submission process.
- CFSAN encourage sponsors to submit a scientifically valid approach for using a new method early in the regulatory process

Food Chemical Toxicology Public Private Partnership

Goal is to provide the food toxicology community with a repository and credible source of science-based information on food toxicology.

The Institute for Food Safety and Health agreed to serve as the designated convener of the FTPPP.

Open to anyone in the food toxicology community

CFSAN has several members

Agenda is being developed

Leveraging Research

CFSAN's research programs will use regulatory gaps and needs identified by the NAMS WG to direct and support all intramural and extramural research to ensure that the most promising technologies are identified, developed, validated, and integrated into the product pipeline.

CFSAN Research Principles Governing Both In House and Collaborative Research Projects

Recognize that regulators have to be included up front in new method development.

Regulators will identify gaps for additional research.

Regulators will delineate what tools were needed.

New CFSAN toxicology research must answer regulatory questions.

Continued ongoing training for regulators in new methods is required.

Oversight Senior Management at CFSAN and FDA

- CFSAN NAMS Work Group updates its progress directly to CFSAN Senior Management on a monthly basis.
- CFSAN collaborates with other Center/Programs thru its role as Co-Chair of the FDA Alternative Methods Work Group.
- CFSAN works thru its public NAMS website to contiually ensure transparency, to foster opportunities to share ideas and knowledge, showcase technologies, and to highlight collaborations on developing and testing new methods

Collaboration on the Roadmap Principles Across FDA

- Greater FDA cross-center collaboration can help accelerate the use of emerging predictive toxicology methods in various programs and in the regulatory arena.
- One size may not fit all; each of FDA's product centers has different legal authorities for product safety evaluations.
- CFSAN's incorporation of key roadmap principles helps to assure the continued success of it NAMS programs.
- CFSAN will work to assure that its toxicology testing is applied across the breadth of FDA-regulated products.

FDA
CFSAN