CDER SMALL BUSINESS AND INDUSTRY ASSISTANCE (SBIA)

2023 *NanoDay* Symposium:
Continuous Manufacturing
of Nanomaterials

FDA U.S. FOOD & DRUG ADMINISTRATION

CREATIVE COLLABORATIONS to SPUR INNOVATION

FDA-wide Programs for Regulatory Science Outreach

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Office of the Commissioner (OC)

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8 October 2023

https://www.fda.gov/about-fda/fda-organization-charts/fda-overview-organization-chart

FDA's Office of the Chief Scientist

The National Center for Toxicological Research

THE OFFICE OF
Regulatory Science and Innovation

THE OFFICE OF
Counterterrorism and Emerging Threats

THE OFFICE OF
Scientific Professional Development

THE OFFICE OF
Scientific Integrity

THE OFFICE OF
Laboratory Safety

Advisory Committee Oversight and Management

Technology Transfer Program

- **supports the research foundation, science, and innovation that underpins FDA's regulatory mission;**
- **promotes scientific excellence and innovation to achieve FDA's mission; and**
- **provides research expertise and infrastructure to the FDA product centers.**

ORSI's vision is to improve and advance public health by accelerating innovations through *creative collaborations that harness the best science*.

ORSI's Programs to Advance Regulatory Science

Intramural Programs

- OCS Grants
- Scientific Working Groups
- Standards
- Shared Resources

Extramural Programs

- BAA: Broad Agency Announcement R&D Contracts
- CERSI: Centers of Excellence in Regulatory Science and Innovation

ORSI's Program Impact at a Glance

$100+ Million
in funding from centers/offices to support FDA's regulatory science extramural research portfolio that ORSI facilitates

200+
Technical proposal evaluation and panel reviews

1000+
FDA scientists that utilize ORSI's regulatory science programs

$2.2 Million
for intramural grant awards for FDA Scientists

100+
Regulatory science projects with CERSIs

22
Focus Areas of Regulatory Science

800+
FDA Staff serve on

1000+
consensus standard committees

90+
seminars, training events and workshops ORSI facilitated and launched

Science, Applied Science, Translation Science, and Regulatory Science

Science is the pursuit and application of knowledge and understanding of the natural and social world following a systematic methodology based on evidence.[1]

Applied research results in technology and innovation discovery.[2] New knowledge acquired from applied research has specific commercial objectives in the form of products, procedures or services. And beyond products, technology and innovation can also be used in regulatory science (like tools or standards).

Translational science is the process of turning observations in the laboratory, clinic and community into interventions that improve the health of individuals and the public – from diagnostics and therapeutics to medical procedures and behavioral changes. [NCATS]

Regulatory science is the science of developing tools, standards, and approaches to assess the safety, efficacy, quality, and performance of all FDA-regulated products. [FDA]

1-https://sciencecouncil.org/about-science/our-definition-of-science/
2-https://www.researchgate.net/publication/304364627

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OCS Intramural Grants Program

Four FDA-wide Programs available to FDA Staff who are FTEs

❖ Chief Scientist (OCS) Challenge Grant

The purpose of the Chief Scientist's Intramural Challenge Grants is to enable exceptional and innovative research that FDA might not otherwise conduct, and that shows strong promise in addressing major regulatory science needs that will advance our regulatory mission and the public health.

❖ Office of Women's Health (OWH) Intramural Scientific Research Grant

The Intramural Challenge Grants enables OWH to support regulatory science efforts that advance women's health issues within the Agency through research.

❖ Medical Counter Measures (MCMi) Challenge Grant

MCMi grants are awarded to applicants that offer the greatest potential to address high-priority regulatory science challenges for medical countermeasures and Advanced Manufacturing initiatives.

❖ Office of Minority Health and Health Equity (OMHEE) Intramural Research Grant

The Intramural Challenge Grants enables OMHHE to support regulatory science efforts that advance minority health and health equity research by engaging across all FDA product centers and offices.

https://fda.sharepoint.com/sites/OC-Intranet-OC-OCS-ORSI-Grants-Program

Chief Scientist Challenge Grant

- Since the intramural grant program inception, there were two sponsored programs from the Office of the Chief Scientist that funded 2-year projects:
  - CORES Grant: which focused on nanotechnology
  - Challenge Grant: Broader and novel technology
- As evidenced by our reporting to Congress about ORSI's budget, we have successfully funded more than 70 projects in the area of Nanotechnology, with relevant outcomes of interest to inform the regulatory process (e.g., consensus standards)
- Moreover, we yearly report on these to the Office of Science and Technology Policy's National Nanotechnology Coordination Office

Promote innovation and predictability in the development of safe and effective nanotechnology-based products by establishing scientific standards and evaluation frameworks to guide nanotechnology-related regulatory decisions. (Outcome)	FY 2022: 70 CORES projects with completed annual milestones Complete review of 100% of Medical Product nanotechnology standards (Target Met)

FDA Standards Program

https://fda.sharepoint.com/sites/OC-Intranet-OC-OCS-ORSI-Standards-Program

FDA Standards Program

FDA's Standards Representatives Activity Report

Center Code	Center Full Name	Unique Representative for Activities	Active Committee
CBER	Center for Biologics Evaluation and Research	115	127
CDER	Center for Drug Evaluation and Research	241	210
CDRH	Center for Devices and Radiological Health	371	609
CFSAN	Center for Food Safety and Applied Nutrition	62	102
CTP	Center for Tobacco Products	7	21
CVM	Center for Veterinary Medicine	54	23
NCTR	National Center for Toxicological Research	10	0
OC	Office of the Commissioner	17	5
Total		877	1,097

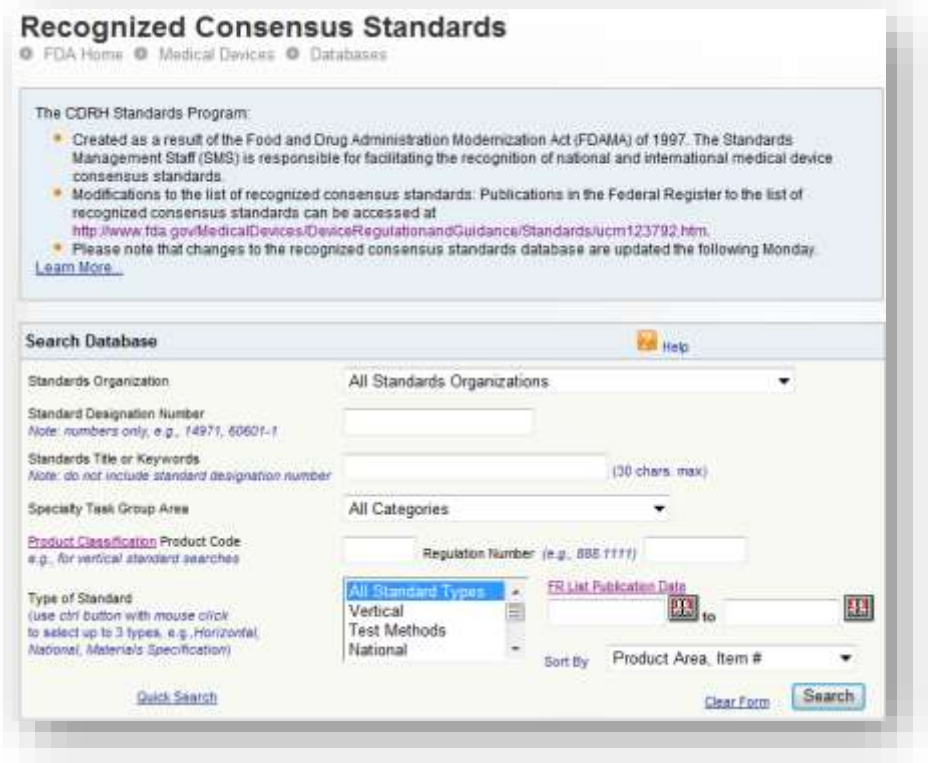
Report as of April 1, 2023

https://www.fda.gov/regulatory-information/standards

Standards in Nanotechnology

Nanotechnology Subcommittee

- Reviewed 75 and commented on over 49 draft consensus standards
  - Find these in the FDA Standards Database
  - http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm
- 23 nanotechnology standards recognized by CDRH in 2023



Standards in Nanotechnology

There are seven active work items in the ASTM Standards Development Organization:

You can get involved!

ASTM E56

Evaluation of Nanoparticulate Material Internalization by Phagocytic Cells In Vitro	WK60553
Quantifying Poly(ethylene glycol) Coating on the Surface of Gold Nanostructured Materials Using High Performance Liquid Chromatography with Evaporative Light Scattering Detection	WK67980
Assessing the Activation of the Complement System in Human Plasma Through Quantification of iC3b Concentration by ELISA	WK69051
Standard Guide for the Analysis of Nanoparticles by Single Particle Inductively Coupled Plasma Mass Spectrometry	WK54613
Characterization of Graphene Flakes Produced by Exfoliation	WK56764
Analysis of Liposomal Drug Formulations using Multidetector Asymmetrical-Flow Field-Flow Fractionation (AF4)	WK68060
the Determination of the Mass Fraction of Particle-Bound Gold in Colloidal Gold Suspensions	WK68377

FDA Standards Executive – Hany Demian hany.demian@fda.hhs.gov
Director - FDA Nanocore – Anil Patri, Ph.D. anil.patri@fda.hhs.gov

FDA Scientific Working Groups

To achieve the Office of the Chief Scientist (OCS) mission and to help implement the FDA strategic plan to advancing regulatory science, the Office of Regulatory Science and Innovation (ORSI) established the Scientific Working Groups Program (SWG), an agency-wide collaborative platform to:

- Promote communication and dissemination of information across FDA centers
- Coordinate educational activities, training, and scientific projects
- Exchange scientific expertise and resources
- Identify scientific and regulatory challenges

The current FDA-wide working groups that are part of this program are:

- Advanced Manufacturing Technologies Working Grou...
- Alternative Methods Working Group (AMWG)
- Artificial Intelligence Working Group (AIWG)
- Biomarker Working Group (BWG)
- [INACTIVE] Emerging Sciences Working Group (ESWG)
- FDA Statistical Association (FDASA)
- Microbiome Working Group (MWG)
- Modeling and Simulation Working Group (ModSimWG)
- Nanotechnology Task Force (NTF)
- Omics Working Group (OWG)
- Social and Behavioral Science Working Group (SBSWG)
- Toxicology Working Group (TWG)

https://www.fda.gov/science-research/nanotechnology-programs-fda/nanotechnology-task-force

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Regulatory Science Framework

Product Areas

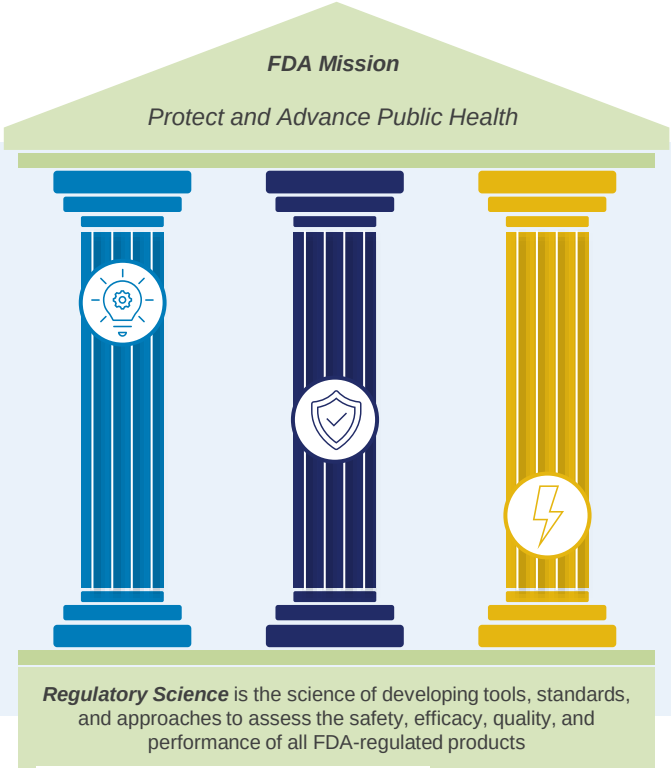
devices, drugs, biologics, combination products, veterinary medicine, food, cosmetics, dietary supplements, & tobacco products

Populations

racial & ethnic minorities, sex & gender minorities, women, children & adolescents, older adults, persons from rural geographies, immunocompromised persons, pregnant and lactating persons, persons with HIV infection, persons receiving gender-affirming medical interventions, persons with disabilities, persons with cancer, persons with rare diseases, & populations that include patients from multiple groups

https://www.fda.gov/science-research/advancing-regulatory-science/**regulatory-science-framework**

Regulatory Science Framework



The goal of the framework is to harness regulatory science to advance FDA's mission.

modernize development and ***evaluation*** of FDA-regulated products

strengthen post-market surveillance and ***labeling*** of FDA-regulated products

invigorate public health preparedness and ***response*** of FDA, Patients & Consumers

https://www.fda.gov/science-research/advancing-regulatory-science/**regulatory-science-framework**

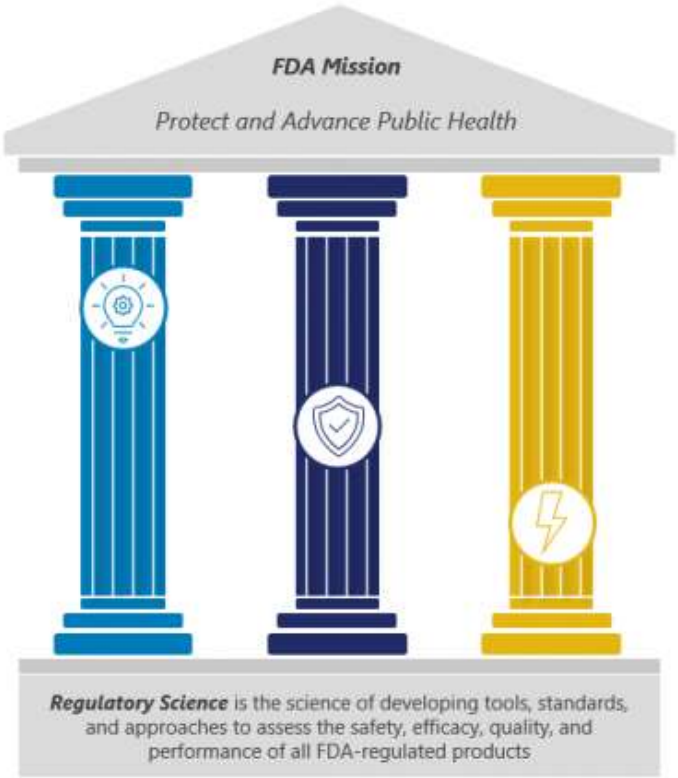
Research & Development Contracts (Extramural)

Advancing Regulatory Science Broad Agency Announcement

To spur innovation in regulatory science, FDA funds extramural research using various contract mechanisms and grants to address broad Agency challenges within FDA's ***scientific priority areas***.

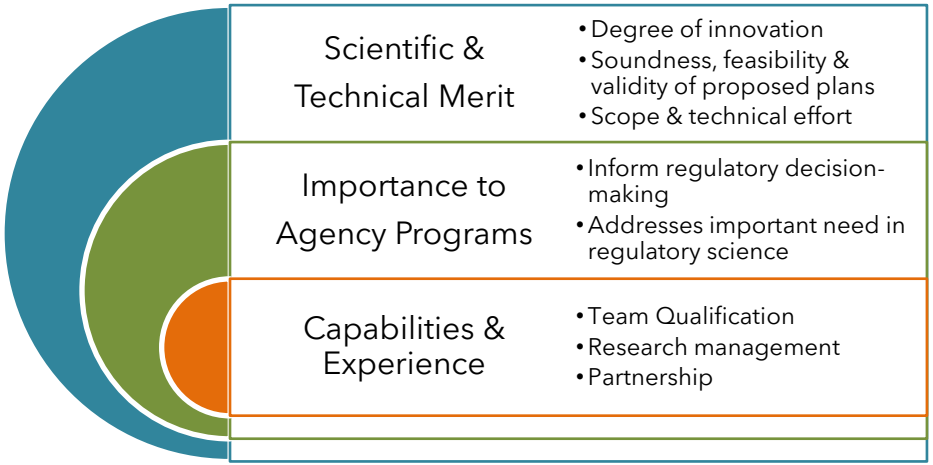
The BAA makes it possible for FDA to solicit innovative ideas and approaches to developing and evaluating FDA-regulated products by tapping into ***external*** knowledge and infrastructure in areas where FDA has limited expertise or capacities.

https://www.fda.gov/science-research/advancing-regulatory-science/regulatory-science-framework



SAM.gov website here.

BAA Rigorous Review Process and Evaluation Criteria



Award information is public knowledge each fiscal year. Check out the **SAM.gov** website.

FY24 Process Changes *Coming Soon!*

Contracts awarded in Nanotechnology

Fiscal Year	Contract Number	Amount Obligated	Total Estimated Contract Value	Center	Awardee Name	Description of Requirement
FY19	75F40119C10139	$447,236	$1,788,939	CDER	Institute of Quantitative Systems Pharmacology	MIDD Approach to Identify Critical Quality Attributes and Specifications for Generic Nanotechnology Products
FY20	75F40120C00201	$349,364	$349,364	CDER	University of Connecticut	Continue Processing of Liposomal Nanoparticles as Materials for Drug Product Development
FY22	75F40122C00202	$764,285	$764,285	CDER	University of Sydney	Identification of Drug Distribution in Aerosols: A Nanospectroscopy and NanoThermal Analysis
FY22	75F40122C00186	$2,692,771	$2,692,771	CBER	Trustees of Princeton University	An Integrated Platform for Continuous RNA Nanoparticle Formulation and Drying
FY22	75F40122C00203	$6,523,977	$47,223,590	CDRH	Nanobiosym INC.	Gene-RADAR Mobile Device & Nanobiosym Digital Dx Platform for Precision Mobile Diagnosis
FY23	75F40123C00118	pending	pending	CDER	University of Connecticut	Investigating the Impact of API Purity, Lipid Source and Manufacturing Process on Performance and Quality of Complex siRNA Lipid Nanoparticles

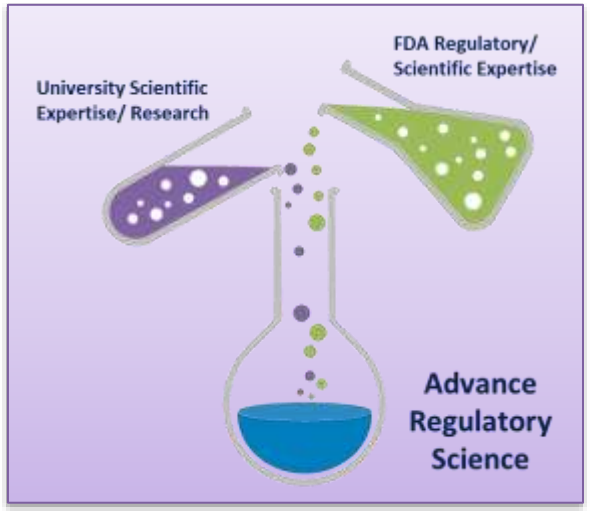
FY24 Solicitation for new R&D contracts – coming soon.

Cooperative Agreement Grant (Extramural)

Centers of Excellence in Regulatory Science and Innovation

FDA's CERSIs are collaborations between FDA and academic institutions to advance regulatory science through innovative research, training, and scientific exchanges:

- Regulatory Science Research with FDA Subject Matter Experts
- Workshops and Lectures
- Training courses
- Fellowships and CERSI Scholars programs

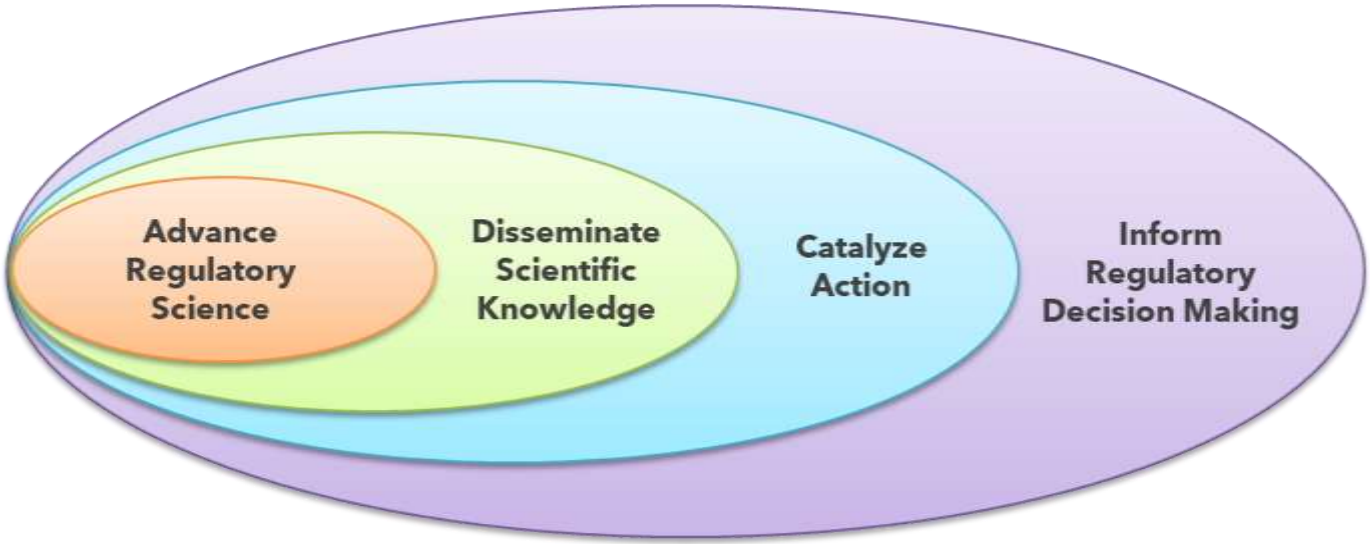


CERSI Johns Hopkins University | CERSI UCSF - Stanford | Triangle CERSI | CERSI University of Maryland | CERSI Yale-Mayo Clinic

We renewed the four existing CERSIs and funded a new CERSI at University of North Carolina, Chapel Hill in a partnership with Duke University (Research Triangle CERSI) under cooperative agreement (RFA-FD-23-004). CERSIs received awards for 5 years (9/1/23-8/31/28).

https://www.fda.gov/science-research/advancing-regulatory-science/centers-excellence-regulatory-science-and-innovation-cersis

Regulatory Science Projects:
Outcomes of Interest were established as a step toward aligning on how we measure impact



Advancing Public Health from left to right

Outcomes of Interest for Regulatory Science Projects

ADVANCE PUBLIC HEALTH			
Advance Regulatory Science	**Disseminate Scientific Knowledge**	**Catalyze Action**	**Inform Regulatory Decision Making**
Project aligns with FDA's Regulatory Science Framework and Science Priorities	To FDA via reports, presentations and/or training	Create partnerships	Present outcomes at FDA Advisory Meeting
		Enhance communications	Outcomes used by FDA for regulatory application
Project enhances FDA resources/ expertise/ capacity	To scientific stakeholders via manuscriptions, presentations, platforms/databases, and/or training	Industry utilizes outcomes in regulatory submission	Development or change in: - Reference materials/ standards - Surveillance strategies - Guidelines/guidance
		Patient and/or consumer groups use outcomes	
Projects address an unmet need or regulatory science challenge	To Public via media coverage	Technology transfer to stakeholder Outcomes subject of a professional meeting	- Regulations - Compliance/ enforcement strategies - inspection/sampling strategies
		Outcomes subject of FDA public meeting	- External communication strategies
		Future research funding	- Labeling - Agency policy
		Inclusion into clinical practice or medical guidelines	

https://www.fda.gov/science-research/advancing-regulatory-science/outcomes-interest-regulatory-science-research-projects

CERSI Project in Nanotechnology

CERSI P.I. and Collaborator:

- Taylor Woehl, Ph.D., UMCP Department of Chemical and Biomolecular Engineering

FDA SMEs and Collaborators:

- Bin Qin, Ph.D., CDER FDA,
- Yan Wang, Ph.D., CDER FDA,
- Stephanie Choi, Ph.D., CDER, FDA

First publication:

- M. Licausi, A. Vervier, S. Nikfarjam, T. Woehl, "Interferometric scattering microscopy of albumin-bound paclitaxel nanoparticles," Microscopy & Microanalysis, 28 (Suppl 1) 1424-1426.

Two additional manuscripts underway

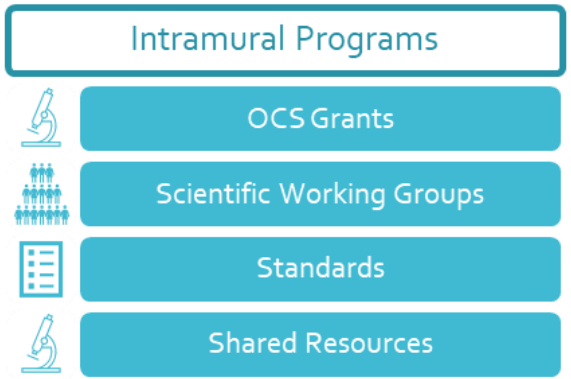
Dr. Woehl also presented the recent findings at the Microscopy & Microanalysis meeting, 2022, Portland, OR

Hyperspectral Interferometric Scattering Microscopy for Characterizing Nanoparticle-based Therapeutics | Center of Excellence in Regulatory Science and Innovation (umd.edu)

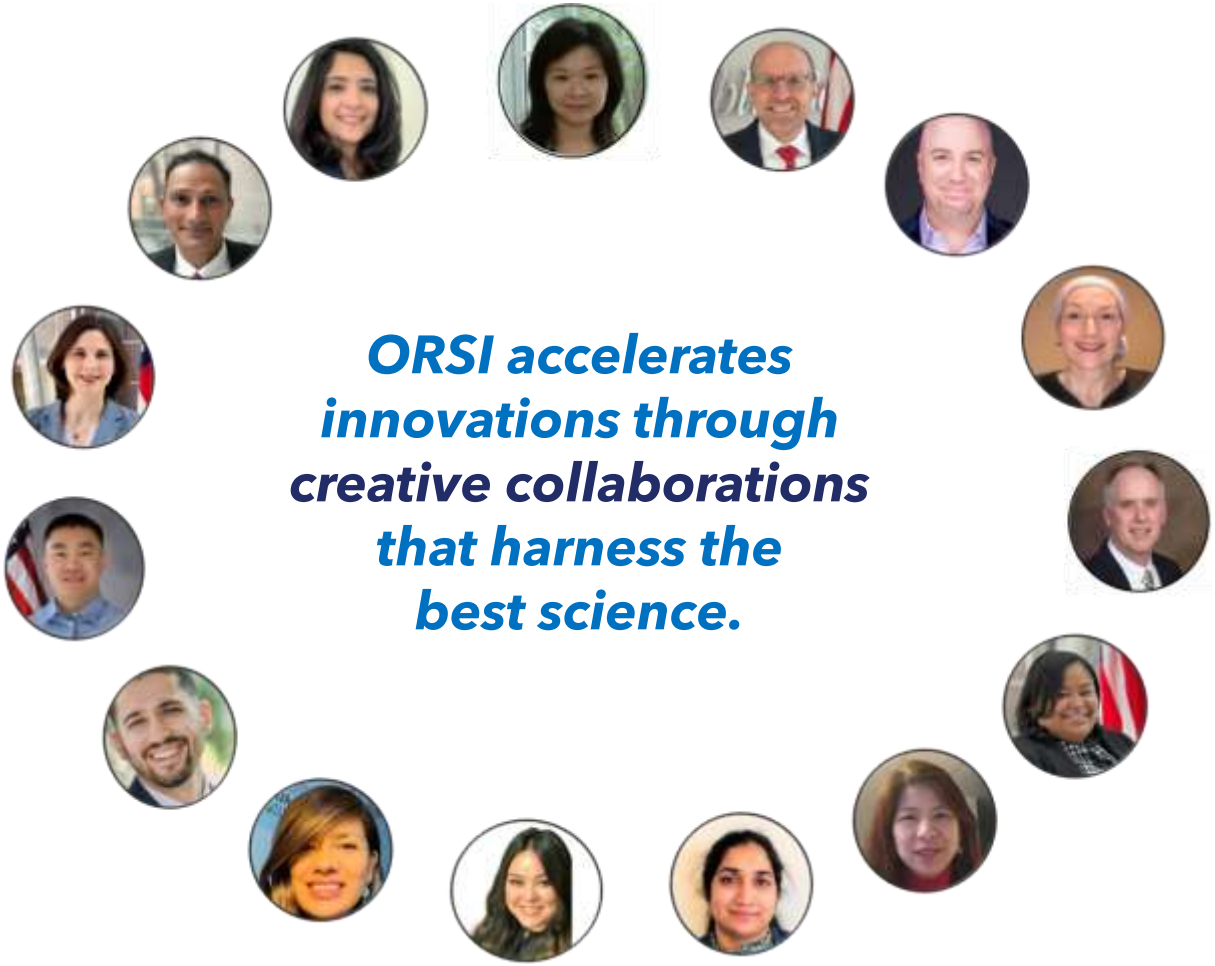
Read project summary here:

Summary

- ORSI aims to improve and advance public health by accelerating innovations through *creative collaborations that harness the best science*.
- Our FDA-wide programs help to advance regulatory science in dozens of cross-cutting areas, like nanotechnology.



- We have a small but nimble team to support the FDA's scientists and their collaborators!



ORSI accelerates innovations through creative collaborations that harness the best science.

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