PROGRESS AND PLANS OF NATIONAL NANOTECHNOLOGY INITIATIVE (NNI) AGENCIES

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Department of Health and Human Services (DHHS)

Food and Drug Administration (FDA)

Summary

The Food and Drug Administration continues to invest in nanotechnology research to help address questions related to the safety, effectiveness, quality, and/or regulatory status of products that contain engineered nanomaterials (ENMs) or otherwise involve the use of nanotechnology; develop models for safety and efficacy assessment; and study the behavior of nanomaterials in biological systems and their effects on both human or non-human animal health. These investments continue to support FDA's mission to protect and promote public health and help support the responsible development of nanotechnology.

The Office of the Commissioner, in partnership with the FDA Nanotechnology Task Force (NTF), continues to facilitate communication and cooperation across the agency on nanotechnology research, both within FDA and with national and international stakeholders. The NTF provides the overall coordination of FDA's nanotechnology research efforts in the following programmatic investment areas: (1) scientific staff development and professional training; (2) laboratory and product-testing capacity; and (3) collaborative and interdisciplinary nanotechnology research.

As needed and appropriate, FDA continues to foster and develop collaborative relationships with other Federal agencies through participation in the National Nanotechnology Initiative (NNI) and the Nanoscale Science, Engineering, and Technology (NSET) Subcommittee of the National Science and Technology Council, as well as with regulatory agencies, healthcare professionals, industry, consumers, and other stakeholders. Most recently, the NTF has increased its international efforts with the goal of strengthening global regulatory research efforts aimed at the development of novel characterization/measurement tools and consensus standards. These collaborations allow information to be exchanged efficiently and serve to identify research needs related to the use of ENMs in FDA-regulated products.

Key Technical Accomplishments by NNI Goal

Goal 1. Advance a World-Class Nanotechnology Research and Development Program

FDA participated in the development of the Nanotechnology for Sensors and Sensors for Nanotechnology Signature Initiative (NSI). The FDA Center for Devices and Radiological Health (CDRH) participated in developing this NSI topic with the goal to support better communication with the *in vitro* diagnostics (IVD) community about the importance of interacting with FDA early in the development process. With this goal in mind, CDRH provided links and information about sensor development for IVDs and presented on this

topic at a webinar on *A Regulatory Case Study for the Development of Nanosensors*,[1] as part of the Sensors NSI webinar series.

Furthermore, CDRH is conducting research to addresses fundamental data gaps and challenges associated with the physico-chemical characterization and safety assessment of nano-objects (nanoparticles) and immobilized surface nanostructures incorporated into medical devices. Research efforts have been focused on evaluating and refining biological test methods for nanoparticle interactions, including genotoxicity and cytotoxicity, and in assessing the toxicologic risk of nanoparticles (NPs) associated with medical devices.

In addition, the FDA Center for Biological Evaluation and Research (CBER) has utilized nanosensors to develop novel and sensitive diagnostic assays for human immunodeficiency virus (HIV), influenza, West Nile virus (WNV), dengue virus, and Zika virus.[2] Additionally, CBER is exploring the use of nanoparticles to track cell therapies *in vivo*.

The National Center for Toxicological Research (NCTR) is conducting collaborative regulatory science research on the advanced characterization, safety, and biodistribution of nanomaterials in FDA-regulated products. The critical scientific data and information generated through this research helps FDA to ensure the safety of FDA-regulated products containing nanomaterials. This information is also utilized in staff training and development, as well as standards development.

Goal 2. Foster the Transfer of New Technologies into Products for Commercial and Public Benefit

The FDA Center for Drug Evaluation and Research (CDER) has worked over the past several years to understand the properties of nanomaterials as they are used in drug products to inform and ensure the development of a regulatory framework that appropriately assesses the impact of their unique physical properties on quality, safety, and efficacy. Initially, this work focused on the role of zinc oxide and titanium dioxide nanomaterials in sunscreens, and whether or not titanium dioxide nanomaterials penetrated normal skin. CDER researchers demonstrated that titanium dioxide nanomaterials did not penetrate the dermis in a pig model. More recently, research projects ongoing within CDER include work focused on nanomaterial characterization and safety assessment in drug products. Ongoing CDER research projects include identifying the limitations of current test methods to assess the quality and safety of nanoparticle-based therapeutics and evaluating the application of nanotechnology on product characteristics, including stability and content uniformity.

CDRH has continued to conduct nanotechnology research to better understand the complex interactions that occur between the body's physiological processes and various types of nanoengineered surfaces. Knowledge gained from this research has allowed FDA to better assess the safety and efficacy of medical products incorporating this novel technology, for premarket review, postmarket assessment, and guidance development.

CDRH nanotechnology research also has resulted in meaningful FDA-related contributions to ASTM and International Organization for Standardization (ISO) standards. In 2017, CDRH added four ASTM E56

[1] http://www.nano.gov/sites/default/files/sapsford_nsi_webinar_nov_2015_slides_with_captions_final.pdf

[2] https://www.ncbi.nlm.nih.gov/pubmed/29528198

standards to its list of recognized consensus standards for nanotechnology, bringing the total number of ASTM standards adopted for the use of nanotechnology in medical devices to six.

Goal 4. Support Responsible Development of Nanotechnology

FDA has announced the availability of draft guidance on *Drug Products, Including Biological Products, that Contain Nanomaterials* for public comment.[3] Nanomaterials in drug products may perform a variety of functions, for example, as active ingredients, carriers loaded with an active ingredient, or inactive ingredients. This draft guidance describes a risk-based approach to the regulation of these products, focusing on the characteristics of the nanomaterial, its intended use and application, and evaluating how its attributes may relate to product quality, safety, and efficacy. The draft guidance provides recommendations to industry engaged in developing human drug products in which a nanomaterial is present in the finished dosage form, including recommendations regarding investigational, premarket, and postmarket submissions for these products.

Plans and Priorities by Program Component Area (PCA)

PCA 5. Environment, Health, and Safety

- CBER and CDER issued joint draft guidance December 18, 2017: *Drug Products, Including Biological Products, that Contain Nanomaterials, Guidance for Industry* (see above).
- CBER has developed highly sensitive diagnostic assays for detection of viral antigens, antibodies, and nucleic acids in an ELISA, microarray, and microfluidics point-of-care format.
- NCTR continues to invest in advanced tools, safety assessment, staff training, standards methods and methodology development in order to better understand emerging issues with nanomaterials in FDA-regulated products.

[3] https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM588857.pdf