

OVERVIEW OF FDA'S ACTIVITIES AT THE NANO-BIO INTERFACE

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Risk Management Approach

- FDA regulates products on a product-by product basis
 - Pre-market approval
 - Pre-market “acceptance”
 - Post-Market
- FDA does not regulate “technologies”
- Product Review process is not static – As we learn more, we evolve the process
- Assistance to industry we regulate

FDA REGULATED PRODUCTS

- Foods
 - All interstate domestic and imported, including produce, fish, shellfish, shell eggs, milk (not meat or poultry)
 - Bottled water
 - Wine (<7 alcohol)
 - Infant formula
- Food additives
 - Colors
 - Food containers
- Cosmetics
- Dietary Supplements
- Animal Feeds
- Pharmaceuticals
 - Human
 - Animal
 - Tamper resistant packaging
- Medical devices
- Radiation emitting electronic products
- Vaccines
- Blood products
- Tissues
- Sterilants
- Counter-terrorism products

APPLICATION OF NANOPARTICLES TO DRUG DISCOVERY AND BIOLOGY

- Fluorescent biological markers
- Detection proteins
- Probing of DNA structures
- Separation and purification of biological molecules and cells
- MRI contrast enhancement
- Tumor destruction via heating
- Tissue engineering
- Drug and gene delivery

NANOTECHNOLOGY AND DRUG DELIVERY

- Enhanced drug properties:
 - Solubility
 - Rate of dissolution
 - Oral bioavailability
 - Target ability
- Enhanced dosing requirements:
 - Lower dose administered
 - Better side effect profile
 - More convenient dosage forms

SAFETY CONSIDERATIONS

- Access to cells and tissues
- Time in cells and tissues
- Clearance
- Effects on cells and tissue functions
- ADME questions

PRECLINICAL TESTS FOR SAFETY EVALUATION

- Pharmacology
- Toxicology
- ADME
- Genotoxicity
- Developmental toxicity
- Immunotoxicity
- Carcinogenicity
- Other

ADEQUACY OF CURRENT BATTERY OF PRECLINICAL TESTS

- High dose multiples
- 2 animal species
- Histopath on most organs
- Functional tests (cardiac, neurologic, respiratory, reproductive, immune system, etc)
- Extended dosing periods

ENVIRONMENTAL CONSIDERATIONS

- Release into environment following human and animal excretion
- Determining environmental impact
- Methodology to determine nature and quantify release

NANO CHARACTERIZATION CONSIDERATIONS

- Forms in which particles are presented to cells
- Standard tools used for characterization of nano particles
- Validated assays to detect and quantify nano particles
- Stability of nanomaterials
- Critical and physical properties
- Scale-up and manufacturing processes

NANO PRODUCTS ASSESSMENT CONSIDERATIONS

- Safety assessment
 - Adequacy of current toxicology screens
 - Potential for novel, unanticipated reactions
 - Environmental considerations
- Medical utility
 - Experience with clinical testing
- Industrialization
 - Physical/chemical properties and product performance
 - Test methods and specifications for product/process control
 - Scale-up
 - Reference material and standards

NANO-REGULATORY ISSUES

- FDA expects many “Combination Products”
- FDA only regulates to “claims” by a sponsor – FDA may be unaware that nanotechnology is being employed
- FDA has only limited authority for potentially high risk nano-products
 - Cosmetics
- Existing pharmtox tests are probably adequate for most nano-products
- Nomenclature – What is a nano-particle? What are properties of nano-particles? Same chemical – smaller size – new formal definition? (ASTM E56)
- For new nano-materials, new “tools” may be needed

FDA NANO ACTIVITIES

- Member of NSET, NEHI, NPEG, and GIN
- External collaboration with NCI and NIEHS
- Internal coordination, ex., NTIG
- Agency web site
- Policy of external relations on nanotechnology

CHALLENGES!!

- New technology - unknown risks
- Communication with new manufacturers
- Stakeholder involvement
 - Early involvement of all parties
 - Risk communication
- Timely reporting of relevant scientific findings

THANK YOU

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