FDA: Application of Nanotechnology to Cosmetics and Foods

Robert L. Bronaugh, Ph.D.
Director, Cosmetics Staff
Office of Cosmetics and Colors

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Outline

- Definitions
- Regulatory authority
- Nanotechnology in food and cosmetics
- Safety/toxicity concerns
- Current research
- Summary
Section I
Definitions
What does nanotechnology mean?

A) Use particles that are larger than 1 nm

B) Use particles that range from 1-100 nm

C) Use particles that have unique properties

D) Answers B&C
Definition

- Nanotechnology
  - No official FDA definition
  - National Nanotechnology Initiative (NNI) definition:
    understanding and control of matter at dimensions of roughly 1 to 100 nm, where unique phenomena enable novel applications
Scope of Products Regulated by FDA’s Center for Food Safety and Applied Nutrition

- Food
  - “Conventional food”
  - Infant formula
  - Medical food
  - Dietary supplements
  - Food additives
  - Food contact substances
  - GRAS substances
  - Prior sanctioned substances
- Color Additives
- Cosmetics
Definitions – Food (201(f))

- Articles used for food or drink for humans or animals (includes pet food and animal feed)
- Chewing gum
- Substances migrating to food from food contact articles
Definition - Dietary Supplements

- Product (other than tobacco) that is intended to supplement the diet
- Contains one or more of the following dietary ingredients:
  - Vitamin
  - Mineral
  - Herb or other botanical
  - Amino acid
  - Other dietary substance used to increase total dietary intake
  - A concentrate, metabolite, constituent, extract, or combination of any of the above dietary ingredients
Definition – Food Additive

- Any substance which may become a component or affect the characteristics of any food
  - Includes substance intended for use in producing, manufacturing, packaging, transporting, or holding food
  - Includes any source of radiation intended for use
  - Under the Food, Drug, and Cosmetic Act and implementing regulations, the use of a food substance may be GRAS either through scientific procedures or, for a substance used in food before 1958, through experience based on common safe use in food.
Definition – Color Additives

- Dye, pigment, or other substance when added or applied to a food, drug, or cosmetic, is capable of imparting color
Definition – Cosmetics

- Articles intended for:
  - Cleansing
  - Beautifying
  - Promoting attractiveness
  - Altering appearance

Excludes soaps
Let’s Pause for Two Questions from the Audience
Section II
Regulatory Authority
Poll Question

- Do you think food, dietary supplements, and cosmetics are subject to approval by FDA?

- Yes
- No
Requirements for market

- Food must not be adulterated or misbranded
- Cosmetics must not be adulterated or misbranded
- No pre-market approval of these products with the exception of food additives and color additives
Question

What do you think might be potential uses of nanotechnology in foods and cosmetics?

1)  

2)  

3)  

Raise your hand to volunteer!
Potential Uses of Nanotechnology in Foods

- Dietary supplements
  - Nanosized mineral supplements which have dramatically increased absorption
  - Nanoemulsions that increase absorption of botanical ingredients
- Enhance flavor and color
Potential Uses of Nanotechnology in Foods (continued)

- Decrease microbial contamination in food and improve packaging
  - Barrier to keep microbes out
  - Kill microbes directly
  - Carrier of antimicrobial compounds
  - Sensor to alert consumers or retailers of potential spoilage
  - Tracer to identify the source of contamination
Section III

Nanotechnology in Cosmetics and Foods
Current Status in Foods

- Titanium nitride was approved as a nanosized recycling aide for polyethylene terephthalate (PET) used as food contact material
Current Reported Uses of Nanotechnology in Cosmetic Products

- Nanodispersed Systems
  - Liposomes (nanosomes)
  - Nanoemulsions
  - Solid lipid nanoparticles

- Other Nanoparticles
  - Polymer systems (nanocapsule, dendrimer)
  - Metal Oxide Nanoparticles
Nanodispersed Systems

- Liposome technology
  - Hydrophilic vesicles with phosphatidylcholine membrane(s) ranging in size from 15-3500 nm
  - Used to alter optical properties, to increase solubility (transport) cosmetic ingredients, and to alter physical properties
- Other nanodispersions used in cosmetics are lipophilic vesicles
  - Nanoemulsions, solid lipid nanoparticles
Nanodispersed Systems

- Liposomes – lipid bilayer
- Nanoemulsion and lipid nanoparticles – lipid monolayer
- Core can be hydrophilic or hydrophobic depending on the number of phospholipid layers
- Deliver water or lipid soluble ingredients

Cosmetic Nanoemulsions

- Useful in typical cosmetic formulations
- Light or oxygen sensitive actives can be protected
  - Vitamin A and Vitamin E
- Low biotoxicity of phospholipid

Nanoencapsulation of ingredients

May be found in skin and hair care preparations

US Patent 6335022; Simonnet; J._T., Sonneville; O., Legret; S.; L’Oreal, 1999.
Potential Lipid Nanoparticle Advantages

- Improved stability of ingredients
- Controlled release of ingredients
- Improved skin hydration
- Incorporation of lipophilic ingredients
- No or low carrier biotoxicity
Solid Hydrophobic Nanospheres

- Highly cationic charge density of surface layer leads to strong interaction with skin/hair
- Solid hydrophobic core protects water soluble and volatile ingredients
- Found in fragrances, vitamins
Polymer Nanoparticles

- Can lead to burst or controlled release of active ingredient
- Robust compared to liposomal formulations
- Great number of natural and synthetic sources
- Stable in both liquid and powder form
- Nanocapsules, dendrimers
Metal Oxide Nanoparticles

- Metal oxides, such as TiO$_2$ and ZnO, are found in many commercial applications.
Poll Question

- What advantages would titanium dioxide or zinc oxide nanoparticles have for use as sunscreens?
  - A) Transparent on the skin
  - B) Protection against UVB rays only
  - C) Helps increase penetration of sunscreen deep within the skin
Potential Advantage of Metal Oxides

- Small crystal size and controlled particle size give excellent dispersibility, make skin feel attractive, and is transparent on the skin
- May increase protection against both UVA and UVB rays
Let’s Pause for Two Questions from the Audience
Section IV
Safety/Toxicity Concerns
Toxicity Concerns

- Similar to that of other FDA regulated products that are not nanoparticles
- Potential for toxicity related to type of nanoparticle used
  - Nanotubes
  - Fullerenes (Buckyballs)
Section V
Current Research
On-going Research in Cosmetics

Skin Absorption Studies
Barrier Layer of Skin
Upper Hair Follicle

- Hair canal
- Infundibulum of the sebaceous gland
- Area of the sebaceous gland
- Outer root sheath
- Isthmus
Image shows penetration of microspheres into hair follicle. Authors concluded that penetration was between cuticula of hair shaft and inner root sheath.
Preparation of Skin with Dermatome
Percutaneous Absorption Studies

In Vitro Diffusion Cell

Skin
Receptor Fluid
Input
Receptor
Let’s Pause for Two Questions from the Audience
Quantum Dot Study

- Good model compound for topical products
  - Relatively stable
  - Highly fluorescent
Skin Penetration Study Details

- Human cadaver or surgical specimen skin
- Applied to skin in a borate buffer or in an oil/water emulsion for 8 or 24 hr.
- Skin surface was either washed with soap and water at the end of the study or left unwashed
- Generally, frozen sections made with a cryostat, fixed with formaldehyde vapor and examined for fluorescence at 40X with a Laser Scanning Confocal Microscope
Evaluation of Quantum Dot Penetration – Human Skin

Liposome Study

- Liposome Formulations
  - Phosphatidyl choline (egg)
  - Tween 80
  - Oil dye
- Skin absorption studies conducted with hairless guinea pig skin for 24 hr.
- Frozen skin sections examined using confocal microscope
“Flexible” liposome formulations contain a mixture of liposomes and micelles. Increased concentration of micelles may promote skin penetration.

O. Ogunsola et al., ACS Colloid and Surface Science Symposium, June 2007
G4 PAMAM Dendrimer

48 surface groups, 4.4 nm diameter
Effect of Dendrimers on Rat Skin Penetration of Indomethacin from a Transdermal Patch

Chauhan et al., J. Control Release, 90, 335-343, 2003
Penetration of G5 PAMAM Dendrimers into Human Skin

Let’s Pause for Two Questions from the Audience
Research – Safety of Cosmetic Products Using Nanoparticles

- In vitro penetration studies
  - Little or no penetration into viable skin of 20 nm or 37 nm diameter quantum dots
  - Nanoscale sized liposomes may deliver a fluorescent dye into viable skin tissue
    - Stability
- Using dendrimer nanoparticles to assess skin absorption
Some Potential Research Needs

- Types of instrumentation and methods needed to characterize aspects such as the size, stability, and solubility in different solutions/formulations
- Battery of toxicological studies to compare properties of nanoparticles vs. macroparticles
- Toxicological properties of nanoparticles following different routes of administration
- Information on absorption into and through skin

For a more comprehensive list refer to http://www.nano.gov/html/news/EHS_research_needs.html
Summary

- Information available on nanoparticles in foods and cosmetics is scant
- Information is needed regarding methodology for detection and for monitoring safety
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