Tattoo Pigments:
Regulation, Chemistry, Photostability, and Potential Complications in the Human Body

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Outline

• Regulatory status of tattoo inks and tattoo pigments
• Chemistry of tattoo pigments
• Potential impurities in tattoo pigments
• Photostability of tattoo pigments
• Tattoo marketplace
• Potential complications from tattooing and FDA responses
Regulatory status of tattoo inks in the U.S.

• Tattoo inks are mixtures of pigments and other components intended for introduction into the skin
  – Tattoo inks fall under the definition of a cosmetic
  – Pigments are regulated as color additives
  – Other components include water, isopropyl alcohol, glycerine, and witch hazel

• FDA traditionally has not exercised its regulatory authority over tattoo inks
  – Safety information is posted on FDA’s website

• The practice of tattooing is regulated by state and local jurisdictions
Regulatory status of tattoo pigments in the U.S.

- Tattoo pigments impart color to tattoo inks and the human body
  - FDA defines *color additive* as any material that can impart color to a food, drug, cosmetic, or medical device, or to the human body
  - Therefore, tattoo pigments meet the definition of a color additive

- Color additives must be pre-approved by FDA for use in foods, drugs, cosmetics, and medical devices
  - Approved color additives are listed in the Code of Federal Regulations
  - 21 CFR Parts 73, 74, and 82

- **No** color additives have been approved for injected use
  - See 21 CFR 70.5(b)
  - Therefore, tattoo pigments are considered unapproved color additives
Types of tattoo pigments

• Inorganic pigments
  – Natural mineral or synthetic sources
  – E.g., metal oxides

• Organic pigments
  – Synthesized from carbon, hydrogen, nitrogen, sulfur, and oxygen
Classification of tattoo pigments

• Colour Index (C.I.) categories and numbers

• Example: C.I. Pigment Red 170
Inorganic tattoo pigments

- **Black**
  - Charcoal (C) ...................... Pigment Black 7
  - Magnetite (FeO•Fe$_2$O$_3$) ........ Pigment Black 11
- **Red**
  - Hematite (Fe$_2$O$_3$) ................. Pigment Red 102
- **Yellow**
  - Limonite (FeO•OH•$n$H$_2$O) ........ Pigment Yellow 43
- **White**
  - Anatase or rutile (TiO$_2$) ............ Pigment White 6
  - Barium sulfate (BaSO$_4$) .............. Pigment White 21
- **Blue**
  - [Phthalocyaninato (2-)] copper .... Pigment Blue 15
Limitations of inorganic tattoo pigments

- Iron oxides fade or change color
- Historically used mercury and cadmium salts are toxic
Potential impurities in inorganic tattoo pigments

• Elemental impurities
  – Lead (Pb)
  – Arsenic (As)
  – Mercury (Hg)
  – Cadmium (Cd)

• Can be determined by inductively coupled plasma (ICP) or atomic absorption (AA) techniques
Organic tattoo pigments

• Typically more intense colors than inorganic pigments

• Wider range of colors

• Some are removable by laser treatments
Potential impurities in organic tattoo pigments

- Polycyclic aromatic hydrocarbons (PAHs)
- Primary aromatic amines (PAAs)

- Many of these are known carcinogens
- PAHs can be determined by liquid chromatography or gas chromatography techniques
Marketplace – inks and implements
Tattoo inks

• Suspensions of non-soluble pigments with binders and solvents
  – Binders include polymers and shellac
  – Solvents include water, ethanol, isopropyl alcohol, and glycerine

• Finely dispersed pigment mixtures are stabilized
  – Stabilizers include surfactants and thickening agents
  – Otherwise the pigments will agglomerate

• Preservatives can be added to prevent microbiological spoilage
General body tattooing
Permanent makeup

• Until late 1970’s, most tattoo artist avoided tattooing the face.
• Permanent makeup inks
  – Applied to face including eye area, lips
• Replaces traditional makeup
  – Eyeliner
  – Eyebrows
  – Lipliner
  – Full lips
  – Blusher
• Also called “micropigmentation”
Examples of permanent makeup

Eyebrows

Lips
Tattoo/permanent makeup industry

- Technicians diverse
  - Amateurs to RNs and MDs
- Salons/tattoo parlors regulated by state and local health departments
- Tattoos/permanent makeup in salon, home, workshop settings
  - No injected anesthesia
  - Varying sterile techniques
- Permanent makeup in medical setting
  - Injected anesthesia
  - Varying artistic ability
Complications from tattoos and permanent makeup

- Swelling, cracking, peeling, blistering, scarring
- Granulomas (small nodules of inflamed skin)
- Keloids (scars that grow beyond normal boundaries)
- Allergic reactions
- Photosensitivity
- Serious disfigurement
- MRI complications
Allergic reaction
Adverse reactions to permanent makeup
Adverse reactions to permanent makeup

• 1988 to 2003 – FDA received only five reports of adverse reactions

• 2003 to 2004 – FDA received more than 150 reports of adverse reactions

• FDA and CDC – identified 101 patients with adverse reactions

• Adverse reactions – tenderness, swelling, itching, and bumps

• Clinical diagnoses – allergic reactions or granulomas
FDA and CDC actions

• July 2, 2004 – FDA alerted public to concerns with Premier Pigment brand of ink shades
  – “FDA Talk Paper” (press release) on FDA’s website

• Sept. 27, 2004 – Product line recalled by manufacturer

• July 2005 – Case study in Archives of Dermatology

• June 28, 2007 – Publication in New England Journal of Medicine
Adverse reactions to tattoo inks without preservatives

• “Starbrite Colors” website bragged that no preservatives or other additives were used in their tattoo inks

• Claims included
  – The inks are made with sterilized distilled water
  – The ink is not an alcohol-based tattoo ink
Starbrite Ink microbial contamination

- 2004: Belgium withdrew “Starbrite Colors” tattoo ink from market because of microbial contamination

- FDA analyses found bacteria (*Pseudomonas aeruginosa*) and mold (*Acremonium*)

- Resulted in manufacturer recall of Starbrite ink

- Starbrite ink became contaminated because the manufacturer removed the alcohol preservative from their ink formula
More microbial contamination of tattoo inks

• In 2011 there were several outbreaks in the U.S. possibly linked to bottled tattoo ink
• Non-tubercular mycobacterium (NTM) was isolated from bottled ink
• Other pathogens have been isolated
• New England Journal of Medicine article
Contamination sources

• NTM is commonly found in public water supplies
• Cannot be removed by filtration
• Spores can only be destroyed by sterilization
  – Problem: sterilization may affect pigments
• NTM and other pathogens may be introduced by the user
  – Diluting with water, pouring back unused ink, storing open containers
Recent example of microbial contamination

- FDA issued a Safety Advisory on May 15, 2019 warning consumers, tattoo artists, and retailers about using or selling certain tattoo inks contaminated with microorganisms.
- Five tattoo ink products were voluntarily recalled:
  - Four black inks and one red ink
Misleading websites

• Website claim by tattoo ink manufacturer:
  – FDA has approved polymethylmethacrylate (PMMA) for medical uses
  – Website claims FDA’s approval of PMMA makes the ink safe for use in tattooing

• Problem: false claim!
  – FDA has NOT approved PMMA for use in tattooing
  – FDA has NOT approved any pigments for use in tattooing
Problems with tattoos and permanent makeup

• Tattoo pigments have not been approved by FDA for cosmetic purposes
  – Safety for skin injection has not been demonstrated
• No color additives have been listed for injected use
  – See 21 CFR 70.5(b)
• Adverse reactions have occurred
• Removal can be difficult
Tattoo removal

Laser treatments
- Painful
- Expensive
- Time consuming
- May result in discoloration of skin
- May not be complete
- Iron oxide and titanium dioxide pigments turn black

Surgery
- Painful
- Expensive
- Scarring
Current issues

- NTM contamination in sealed bottles of tattoo ink
- Alcohol preservation may not be bactericidal
- Sterilization methods are untested
- Industry has not demonstrated microbiological expertise
- FDA’s rapport with industry is limited
Questions for Industry Consideration

• Single vs. multiple use?
• Preservation requirements?
• Sterilization treatment options?
• Required labeling statements?
More information is needed

• Tattoo ink ingredients
  – FDA is in the process of sampling and testing tattoo inks to learn more about ingredients and contaminants

• Processing methods
  – FDA is planning to inspect more manufacturers to learn more about prevailing practices
FDA’s future goals

• Better understanding of composition, methods of preservation and safe use
• Development of better tools to assess human health risks from tattoo inks and pigments
• Better understanding of the tattoo industry
• Continued outreach with all stakeholders
• Consideration of changing color additive enforcement policy
Summary of challenges

• Regulatory oversight
• Development of better tools to assess human health risks from tattoo inks and pigments risk
• Improvement in recognition of problems (both clinically and scientifically)
• Communication and outreach with stakeholders and constituents
Conclusions

• Marketplace – wide variety of pigments in tattoos and permanent makeup

• Adverse reactions – FDA has responded

• Misleading websites!!!

• Tattoos are difficult to remove!

• No pigments have been approved by FDA for tattooing for cosmetic purposes
Further information

• Current website “Tattoos and Permanent Makeup”
  https://www.fda.gov/cosmetics/cosmetic-products/tattoos-permanent-makeup-fact-sheet
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