Regulation of Tattoo Inks in the US

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Tattoo Ink: FDA’s Evolving Regulatory Policy and Overview of Color Additive Regulation
Tattoo Ink Overview

- Role of tattoo ink in recent outbreaks
- Factors contributing to contamination
- What can industry do?
- FDA’s current actions and future goals
Tattoo Ink Current Regulatory Authority

- Tattoo inks are cosmetics regulated under:
  - Section 601 – Adulteration
  - Section 602 – Misbranding
  - Section 801 – Imports
Tattoo Inks and Tattoo Pigments

- **Tattoo inks** are a mixture of pigments and diluents intended for introduction into the skin.
- FDA traditionally has not exercised its color additive regulatory authority over tattoo inks or tattoo pigments.
- The **practice** of tattooing is regulated by state and local jurisdictions.
How Safe Are Tattoos?

- Tattoos growing in popularity – 25% of population sports a tattoo!
- Reports of adverse reactions linked to tattoos and permanent makeup reported in Medwatch have steadily increased over past decade
- Reactions sometimes hard to control
- Recovery can be painful, effects long-lasting
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
Adverse Reaction to Permanent Makeup
Allergic Reaction
Non-tubercular Mycobacterium (NTM) in Tattoo Ink

- In 2011 there were several outbreaks in US possibly linked to bottled tattoo ink
- Non-tubercular mycobacterium (NTM) isolated from bottled ink
- Other pathogens have been isolated
- New England Journal of Medicine Article
NTM Infection
Contamination Sources

• NTM 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
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
FDA is Reconsidering Its Regulatory Position on Tattoo Ink

- 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 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
Current Regulatory Status of Tattoo Pigments

- **Tattoo pigments** are unapproved color additives
- **No** color additives have been listed for injected use
  - See 21 CFR 70.5(b)
Color Additive Overview

- Definition of color additive
- Petition process for listing color additives
- Certified color additives
- Color additives exempt from certification
- FDA’s color certification process
- Common color additive violations
Definition of Color Additive

- A substance that imparts color to a food, drug, cosmetic, medical device, or human body
- Color additives used in FDA-regulated products must be pre-approved (listed)
- Individual color additives may only be used as allowed by regulation
- Does not include colorants used in packaging
Color Additive Petition Process

- FDA receives about 3 petitions per year for review
- If approved, color additives are listed in the CFR specifically for use in
  - Food, drugs, devices and/or cosmetics
Requirements for Listing Color Additives

• Probable exposure from use
• Cumulative effect in the diet (applies to color additives in food and drugs)
• Evaluation of safety by qualified experts
• Analytical methods to assure purity
• Particle size (for eye area use only)
Listed Color Additives

• Exempt from certification - 21 CFR Part 73
• Subject to certification - 21 CFR Part 74
• “Lakes” subject to certification - 21 CFR Part 82
• Most other color additive requirements
  – 21 CFR Parts 70, 71, 80, and 81
Certified Color Additives

- Synthetic organic dyes and pigments
  - "Synthetic" means man-made
  - "Organic" means made of carbon, hydrogen, nitrogen, oxygen, and sulfur
- Not much dye needed to achieve desired coloring
  - Dyes have high absorptive values
<table>
<thead>
<tr>
<th>Common name</th>
<th>Certifiable as</th>
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<tr>
<td>Allura Red AC</td>
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<tr>
<td>Tetrabromofluorescein</td>
<td>D&amp;C Red No. 21</td>
</tr>
</tbody>
</table>
FDA’s Color Certification Program

- FDA’s oldest user fee program – color additive amendments of 1960
- Manufacturers submit samples from each new batch
  - OCAC’s Color Certification Branch conducts analyses
  - Certificate and lot number issued if all specifications are met
  - Average 5-day turnaround
- New web-based certification system
  - Online certification requests and results
Certification Analyses

- **Total color**
  - Spectrophotometry
  - TiCl$_3$ titration
  - Gravimetric analysis
- **Volatile matter**
- **Insoluble matter**
- **Soluble matter**
- **Extractable matter**
- **Salts**
- **Soluble barium**
- **Leuco base**
- **Intermediates**

- **Subsidiary colors**
- **Component colors**
- **Reaction by-products**
- **Aromatic amines**
- **Heavy metals**
  - Lead, arsenic, mercury
  - Manganese, chromium
- **Surface area**
- **Polynuclear aromatic hydrocarbons**
- **Sulfur and carbon**
Certification-exempt Color Additives

- Manufacturers are responsible for compliance with CFR specifications
- Must conform to purity requirements
- Mostly metal oxides or mineral origin
- Some are derived from animal or plant sources
- Less coloring power than synthetic
Common Color Additive Violations

- **Adulteration**
  - Color additive use violations
  - Uncertified color additive used in a product
  - Non-permitted color additives used in a product

- **Misbranding**
  - Color additives not declared by their listed names
  - Food labeling requirements not followed
Summary: Important Color Additive Requirements

- Only approved and listed color additives may be used in food, drugs, cosmetics, and medical devices marketed in the U.S.
- All color additives must comply with the requirements in their listing regulations
  - Including purity requirements
- Color additives must be used appropriately
  - Manufacturers must consult the listing regulation
- Batch-certified material must be used in products when required
Summary/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
Acknowledgements

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Resources for Color Additives

- FDA’s web site
  - http://www.fda.gov
  - http://Industry@fda.gov
- Summary of Color Additives for Use in United States in Foods, Drugs, Cosmetics, and Medical Devices
  - http://www.fda.gov/ForIndustry/ColorAdditives/ColorAdditiveInventories/ucm115641.htm
- Companies That Have Requested Color Certification Within the Last Two Years,
  - http://www.fda.gov/ForIndustry/ColorAdditives/ColorCertification