Tattoo Pigments and Inks: Regulation and Challenges U.S. FDA Perspective

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Outline

- Regulatory status of tattoos in the U.S.
- FDA's regulatory authority
- FDA's regulatory challenges
- FDA's activities and actions

Regulatory Status of Tattoos in the U.S.

Tattoo Inks

- Meet the definition of a cosmetic
- FDA defines **cosmetic** as
  - articles (other than soap) intended for
    - Cleansing
    - Beautifying
    - Promoting Attractiveness
    - Altering Appearance
- Federal Food, Drug, and Cosmetic Act, Section 201(i)

Tattoo Pigments

- Meet the definition of a color additive
- FDA defines **color additive** as
  - any material that can impart color to
    - Food
    - Drug
    - Cosmetic
    - Medical device
    - Human body
- Code of Federal Regulations, Title 21, Section 70.3(f)

FDA's Authority for the Regulation of Cosmetics and Color Additives

- 1938 Federal Food, Drug, and Cosmetics Act (FD&C Act)
- 1960 Color Additive Amendments to the Act
- 1966 Fair Packaging and Labeling Act (FPLA)

FDA's Authority Over Color Additives

- Color additives must be pre-**approved** by FDA for use in foods, drugs, cosmetics, and medical devices and must be **safe** for their intended use

- Safe means that there is convincing evidence that establishes with reasonable certainty that no harm will result from the intended use of the color additive

- Approved color additives are listed in the Code of Federal Regulations (CFR):
  - Parts 73, 74, and 82
  - www.ecfr.gov

Color Additive Requirements

Color Additives **Exempt** from Certification

- Manufacturers are responsible for compliance with CFR requirements
- Including purity specifications
- 21 CFR Part 73

Color Additives **Subject** to Certification

- Manufacturers submit a sample to FDA from each new batch
- FDA's Color Certification program analyzes sample
- If requirements are met, FDA issues certificate and FDA lot number
- FD&C, D&C, and Ext. D&C nomenclature is used for certified batches
- 21 CFR Parts 74 and 82

Status of Color Additives for Use in Injections

General restriction on use of color additives

21 CFR 70.5(b) Color additives for use in injections.

No listing or certification of a color additive shall be considered to authorize the use of any such color additive in any article intended for use in injections unless such listing or certification of such color additive specifically provides for such use.

- No color additives have been approved by FDA for injection into the skin for cosmetic purposes
- No tattoo pigments have been approved by FDA for use in tattoo inks

FDA's Authority Over Cosmetics

- Cosmetics must not be adulterated or misbranded
- FDA does NOT have the authority to pre-approve cosmetic products or their ingredients, except for color additives
- **Color additives are the only ingredients in cosmetics subject to FDA pre-market approval**
- Only approved color additives may be used in cosmetics marketed in the U.S.
- Cosmetics should be labeled properly
- FDA authority for cosmetics is post-market

Prohibited Under FD&C Act

Adulterated Cosmetics

- Poisonous/deleterious substance that renders it injurious under labeled or customary conditions of use
- Consists of filthy substance
- Prepared, packed, or held under insanitary conditions that may have contaminated or rendered injurious
- Container is composed of any poisonous substance rendering the product injurious
- Color additive (other than coal tar hair dye) that doesn't conform to applicable regulations under section 721 of the FD&C Act

Misbranded Cosmetics

- False or misleading labeling or doesn't contain all required information
- Labeling improperly placed or inconspicuous
- Misleading container
- Non-compliant packaging (doesn't comply with sec. 3 or 4 of the Poison Prevention Packaging Act of 1970)
- Under FPLA – doesn't contain ingredient declaration so consumers can make informed purchase decisions

FDA's Regulatory Challenges

FDA does not have the **legal authority** to

- Approve cosmetics products before they go on the market
- Require cosmetic manufacturers to provide safety data on their products
- Require mandatory reporting of adverse events related to cosmetics
- Require companies to recall products if problems are identified

Adverse Event Reports

- FDA **monitors** issues related to tattoo inks via adverse event reporting
- FDA **alerts** the public when there is a problem with cosmetics

Katz, L.M. et al. (2016) Reporting cosmetic adverse events to the US Food and Drug Administration, Dermatitis 27, 236-237
https://www.fda.gov/cosmetics/how-report-cosmetic-related-complaint/using-adverse-event-reports-monitor-cosmetic-safety

Risks Related to Tattoos

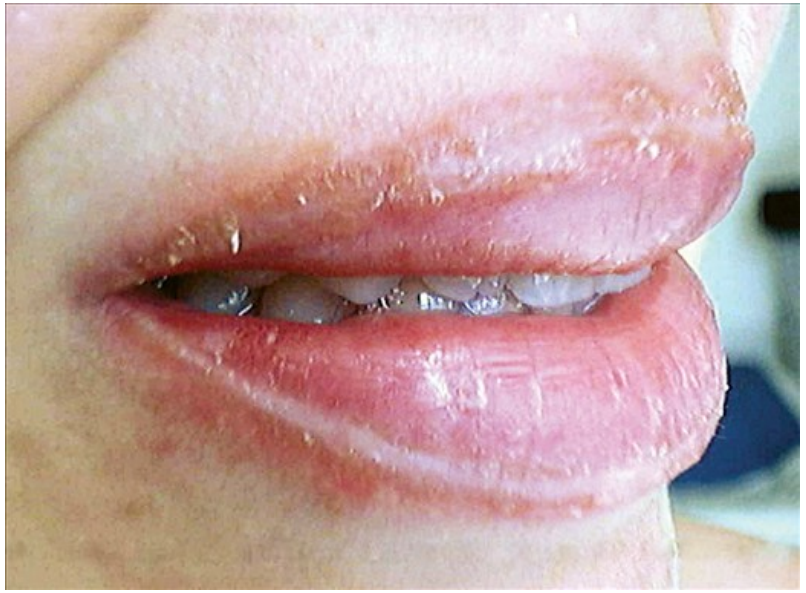
- Infections and inflammatory reactions
- Swelling, cracking, peeling, blistering, scarring
- Granulomas, keloids, and systemic sarcoidosis
- Allergic reactions (acute/delayed)
- Pruritis, local or generalized, acute chronic
- Photosensitivity in tattooed areas
- Disfigurement
- Others

Adverse reactions

Body tattoo

The New England Journal of Medicine, Joel Cook, John Metcalf, Tattoo Allergy, 361, Copyright © (2009) Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

Permanent makeup



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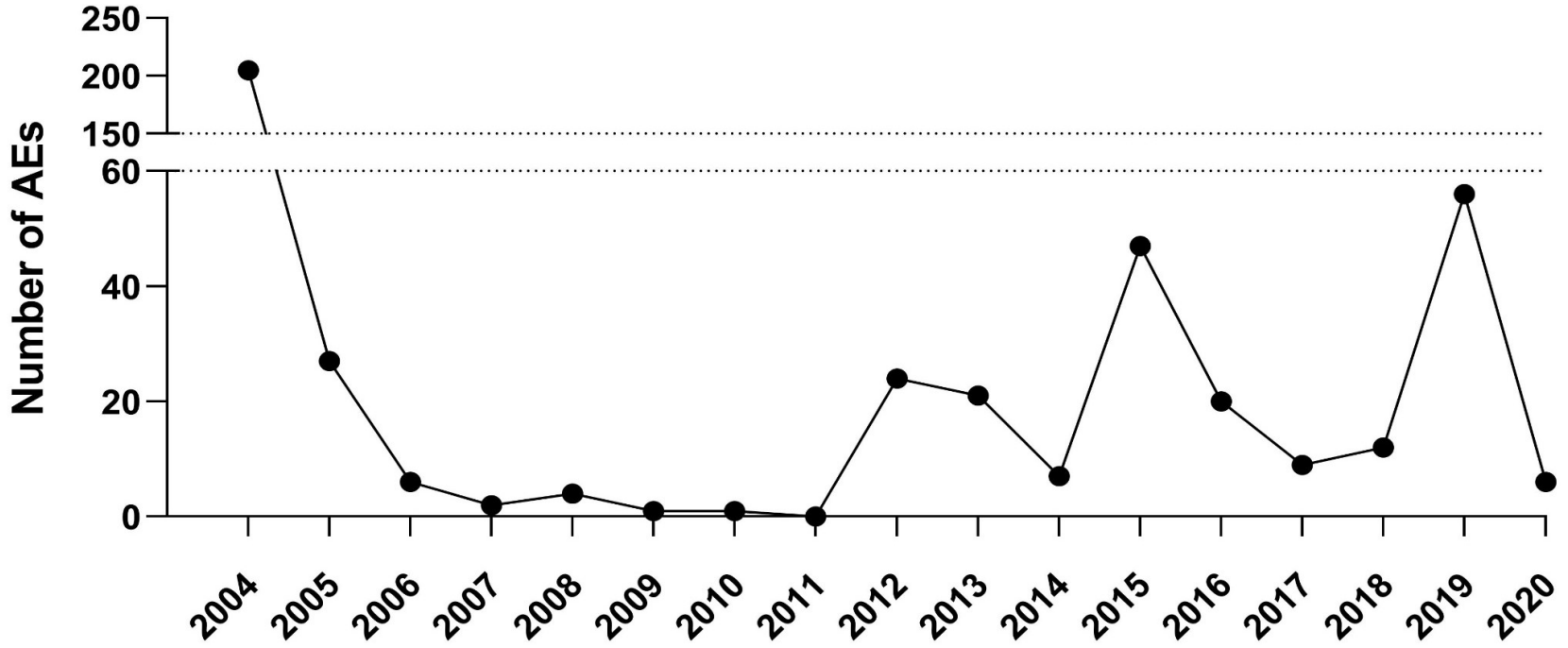
Adverse Events Associated with Tattooing

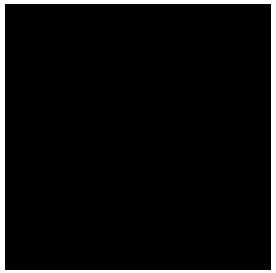
Number of AEs related to tattoo and PMU inks reported to FDA per year from 2004 to Sep 2020 (n = 448).



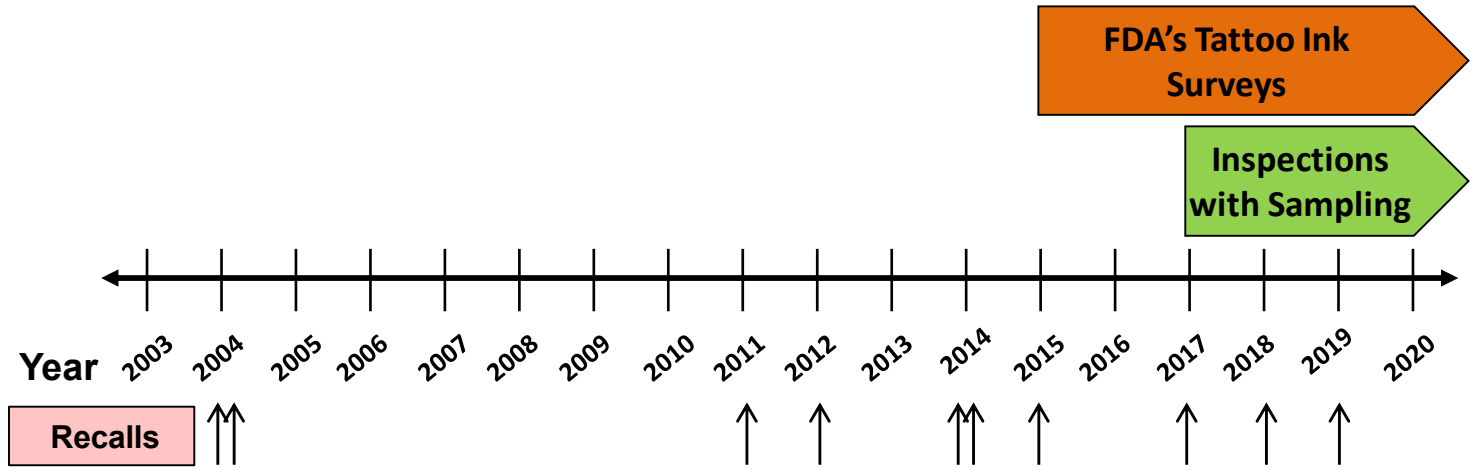
FDA's Activities and Actions

- FDA is testing tattoo inks to
  - Learn more about their compositions
  - Better understand their safety

- Method development and surveys
  - Microbial contamination
  - Tattoo ink ingredients

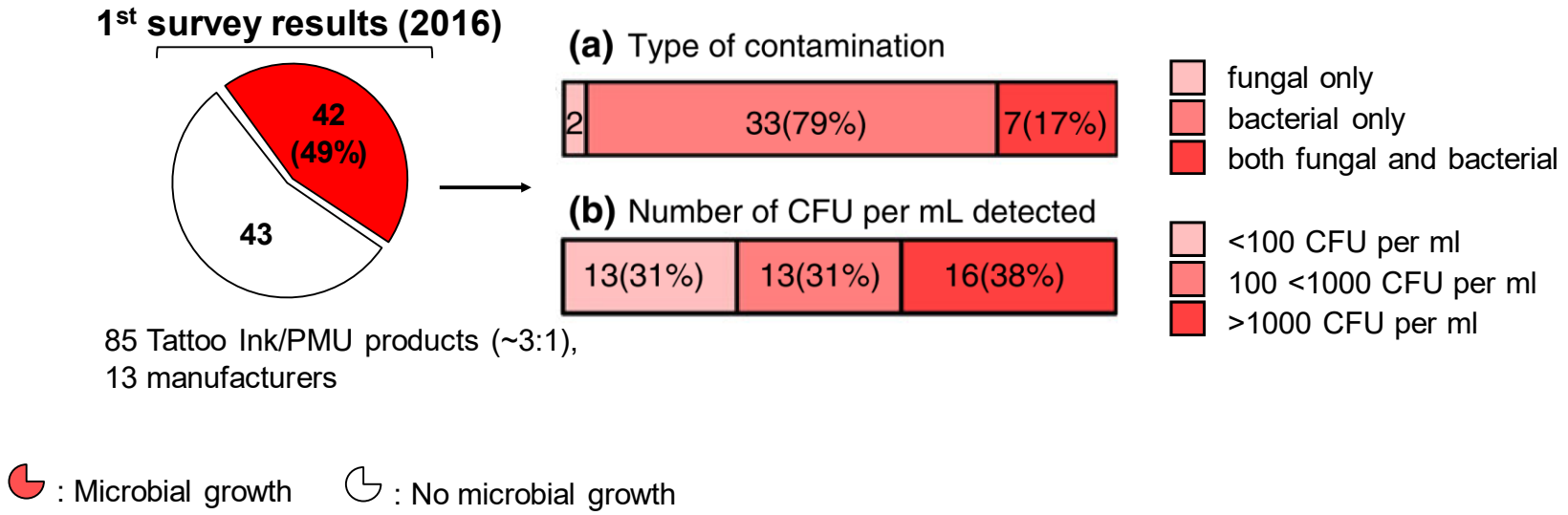


Microbiological Surveys and Inspections



- 2003 - 2015, 7 recalls due to outbreaks and adverse events reported to FDA
- In response, FDA initiated microbiological surveys and inspections with sampling with a goal to
  - Examine prevalence of microbial contamination in TI/PMU products sold in US
  - Examine manufacturing/distribution conditions of TI/PMU products

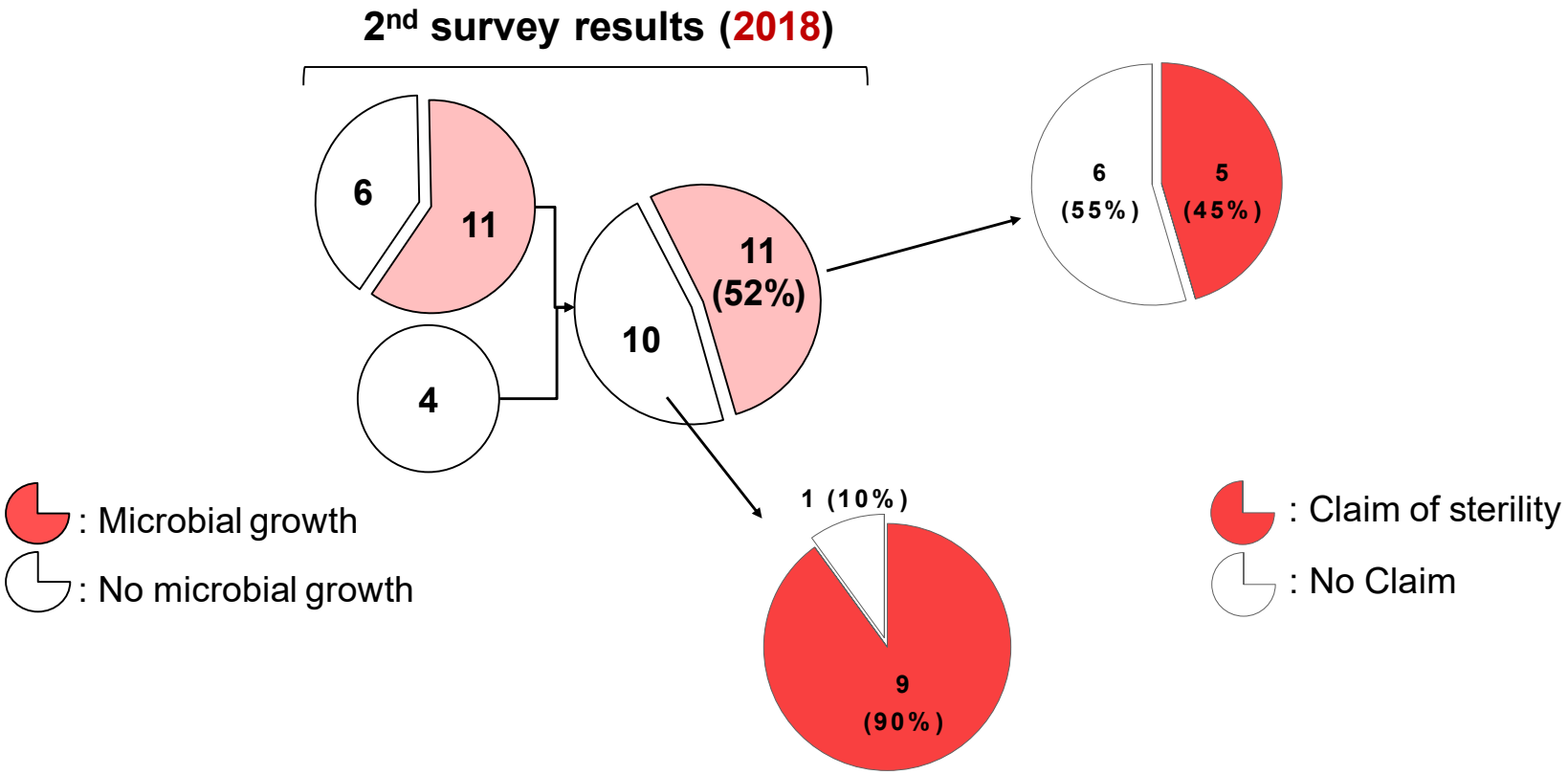
Microbial Contamination: Survey #1 (2016)



A total of 83 bacteria isolates were identified by their 16S rDNA sequences: ***Bacillus* spp. (53%) , *Lysinibacillus fusiformis* (7%), *Pseudomonas aeruginosa* (5%)**

Journal of Applied Microbiology, 2018, 124: 1294-1302; doi:10.1111/jam.13713

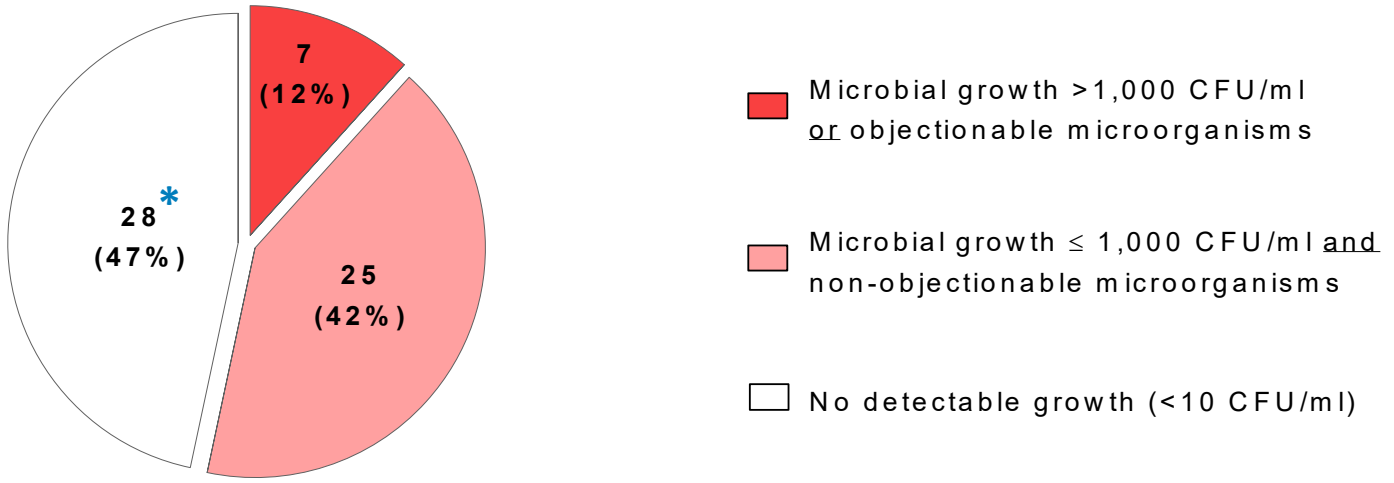
Microbial Contamination: Survey #2 (2018)



Letters in Applied Microbiology, 2020, 71(4): 351-358; doi:10.1111/lam.13353

2018 Tattoo Ink Inspections and Sampling

Microbial Contamination



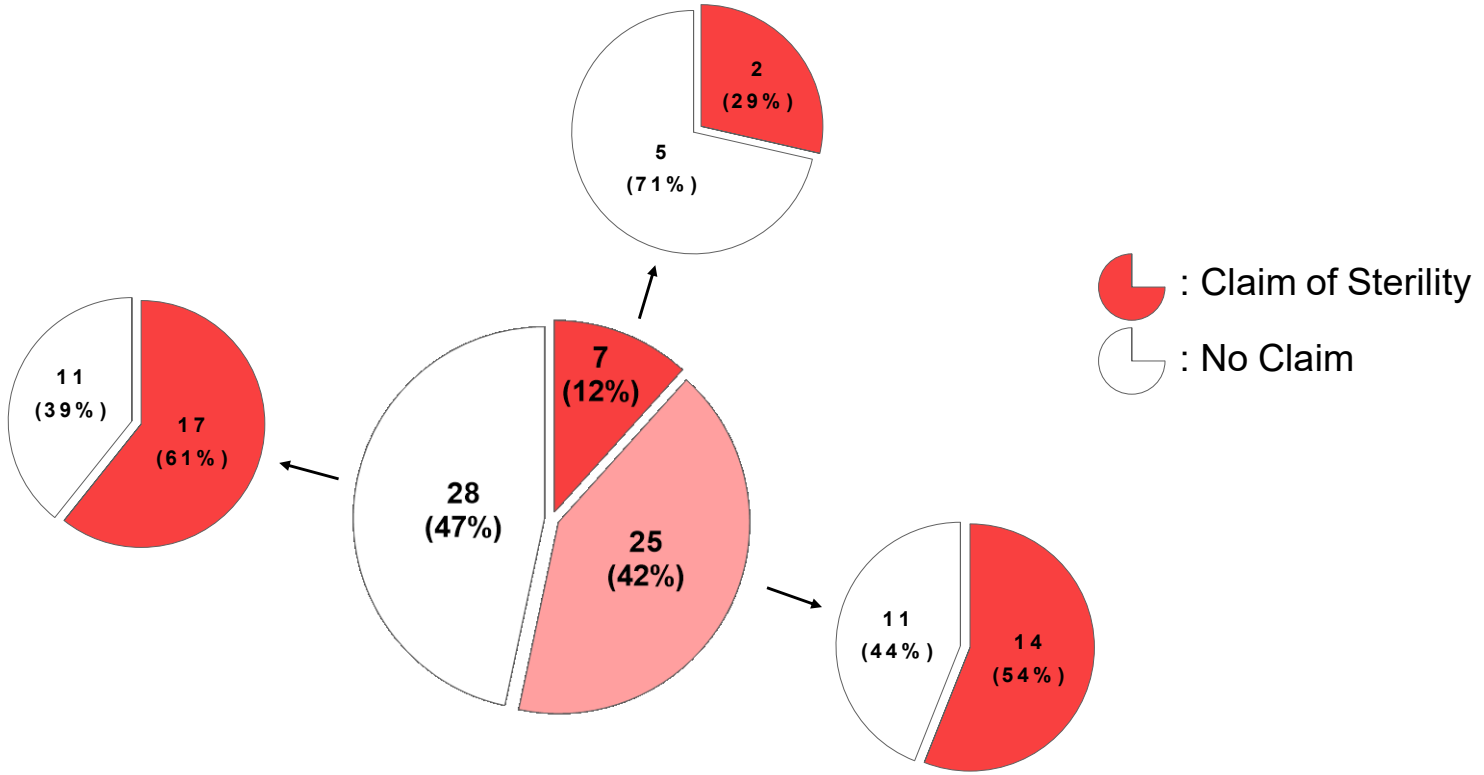
Total = 60 tattoo ink products from 13 manufacturers

* **No-growth** was found by BAM Ch.23 methods, but samples may or may not be sterile. BAM Ch.23 methods are not designed to test for sterility assurance of cosmetics, including tattoo ink; however, they can detect and enumerate microorganisms, if present, at >10 CFU/g or ml.

Letters in Applied Microbiology, 2020, 71(4): 351-358; doi:10.1111/lam.13353

2018 Tattoo Ink Inspections and Sampling

Sterility Claims



Approximately one-half (16/33) of samples labeled "sterile" or "sterilized" were found to contain microorganisms upon testing by FDA using BAM Ch. 23 method.

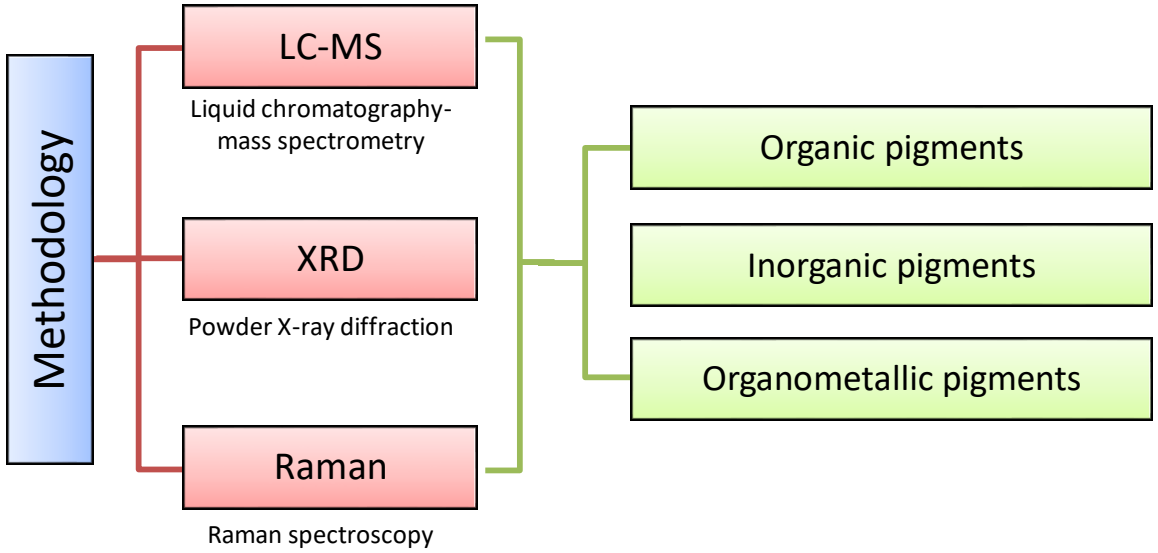
Letters in Applied Microbiology, 2020, 71(4): 351-358; doi:10.1111/lam.13353

2018 Tattoo Ink Inspections and Sampling Results

- Three firms recalled their tattoo inks
- Three firms receive Warning Letters (2019)
- FDA met with the tattoo industry to discuss
  - FDA findings of some microorganisms below the current level of regulatory concern (<1,000 CFU/ml and non-objectionable microbes)
  - Sterility testing of tattoo inks including timing of testing (ingredients vs. final product) and methods used
  - Misbranding issues identified in the FDA sampling assignment

FDA's Activities: Method Development

- Analysis of pigments in tattoo inks is difficult because of
  - Low solubility of pigments
  - Interferences from other tattoo ink components
- Qualitative methodology
  - Considers the chemistry of individual pigments when screening for pigments in tattoo inks
  - Uses a combination of chromatography and spectroscopy techniques



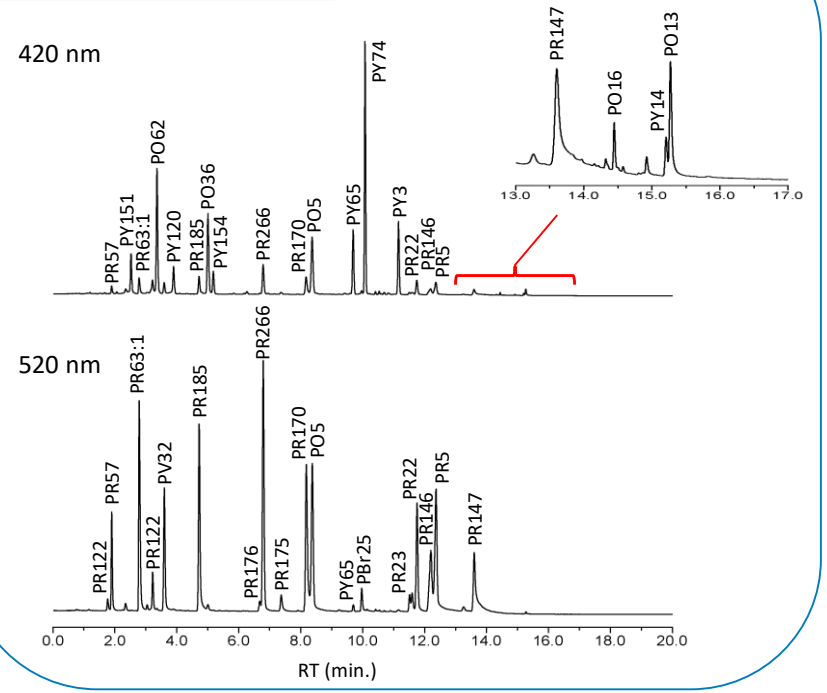
254th ACS National Meeting & Exposition, Washington, DC, USA, August 20-24, 2017, ANYL-193.
129th AOAC Annual Meeting & Exposition, September 27-30, 2015.
J. Raman Spectrosc., 2017, 48: 736– 743.

Tattoo pigment identification methodology

- One method may be **confirmatory** for another method
- This is important due to the complexity of tattoo inks mixtures

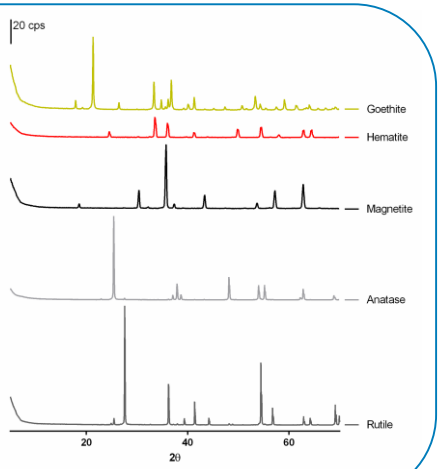
LC-MS method

- organic pigments moderately soluble in select organic solvents



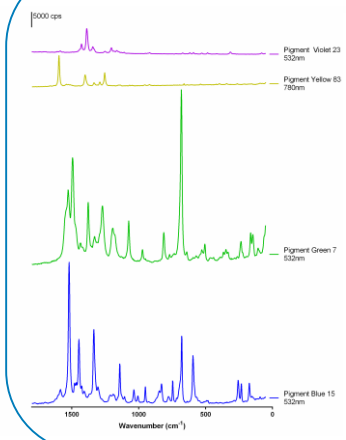
XRD method

- inorganic pigments
- organic pigments not identifiable by LC-MS
- confirmatory



Raman method

- carbon black
- confirmatory



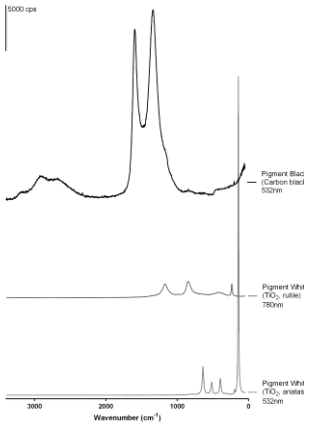


Photo: DXRxi System, courtesy of Thermo Fisher Scientific

2019 Survey of Pigments in Tattoo Inks

Sampling

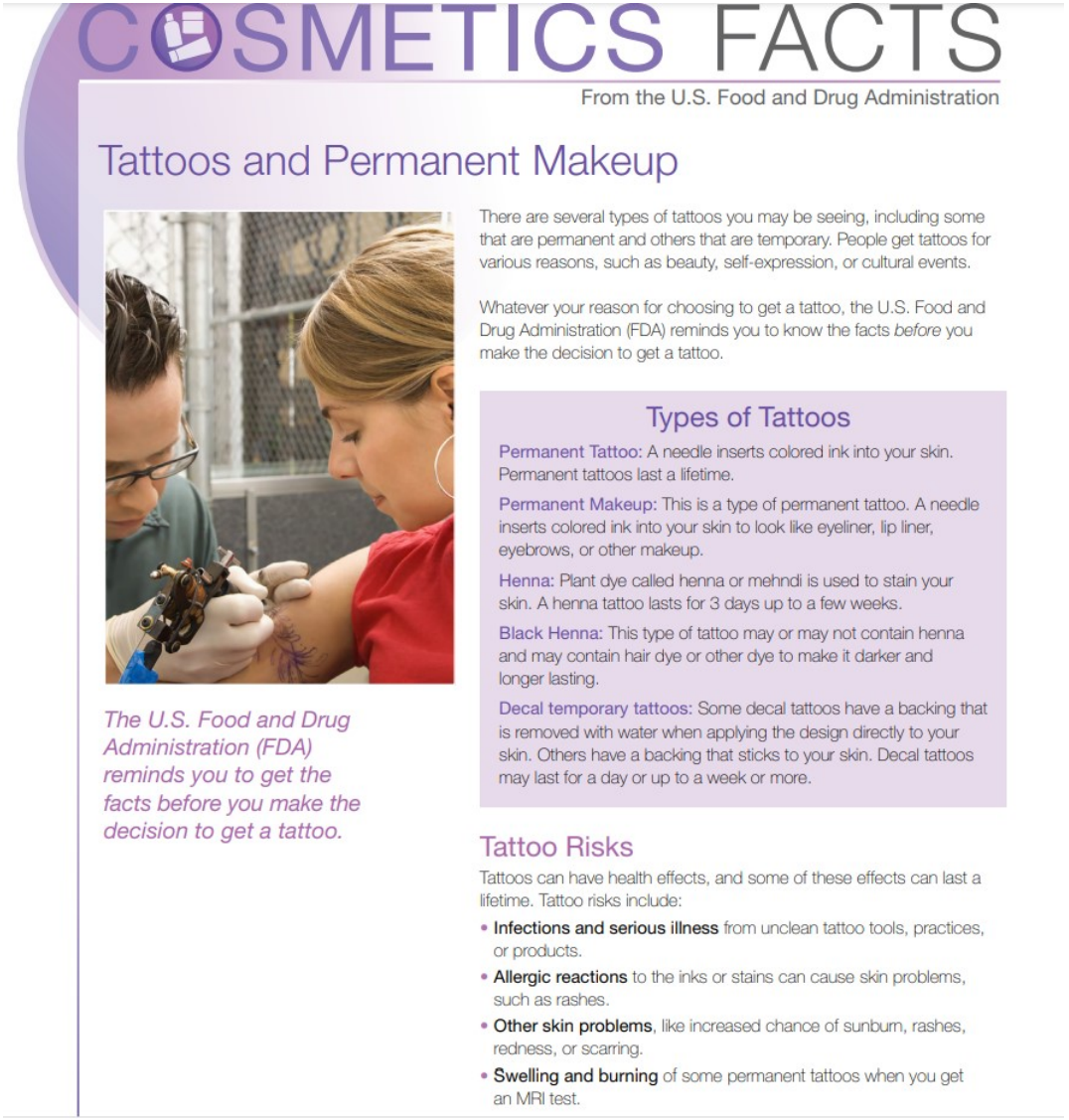
- Surveyed ca. 200 tattoo inks
- Samples obtained from 2004-2017
- 14 tattoo ink manufacturers
- Targeted organic pigments
- Analyzed only by LC-MS
- Analysis by XRD and Raman on-going

Findings

- Commonly identified organic pigments
  - Pigment Yellow 74
  - Pigment Yellow 14
  - Pigment Red 170
  - Pigment Red 22
  - Pigment Red 122
  - Pigment Violet 19
  - Pigment Orange 13
  - Pigment Orange 16
- Organic pigments identified not always included on ingredient list, when available

FDA's Activities: Information for Consumers

- "Tattoos and Permanent Makeup" https://www.fda.gov/cosmetics/cosmetic-products/tattoos-permanent-makeup-fact-sheet



COSMETICS FACTS

From the U.S. Food and Drug Administration

Tattoos and Permanent Makeup

The U.S. Food and Drug Administration (FDA) reminds you to get the facts before you make the decision to get a tattoo.

There are several types of tattoos you may be seeing, including some that are permanent and others that are temporary. People get tattoos for various reasons, such as beauty, self-expression, or cultural events.

Whatever your reason for choosing to get a tattoo, the U.S. Food and Drug Administration (FDA) reminds you to know the facts *before* you make the decision to get a tattoo.

Types of Tattoos

Permanent Tattoo: A needle inserts colored ink into your skin. Permanent tattoos last a lifetime.

Permanent Makeup: This is a type of permanent tattoo. A needle inserts colored ink into your skin to look like eyeliner, lip liner, eyebrows, or other makeup.

Henna: Plant dye called henna or mehndi is used to stain your skin. A henna tattoo lasts for 3 days up to a few weeks.

Black Henna: This type of tattoo may or may not contain henna and may contain hair dye or other dye to make it darker and longer lasting.

Decal temporary tattoos: Some decal tattoos have a backing that is removed with water when applying the design directly to your skin. Others have a backing that sticks to your skin. Decal tattoos may last for a day or up to a week or more.

Tattoo Risks

Tattoos can have health effects, and some of these effects can last a lifetime. Tattoo risks include:

- **Infections and serious illness** from unclean tattoo tools, practices, or products.
- **Allergic reactions** to the inks or stains can cause skin problems, such as rashes.
- **Other skin problems**, like increased chance of sunburn, rashes, redness, or scarring.
- **Swelling and burning** of some permanent tattoos when you get an MRI test.

Summary

- FDA's regulatory authority
  - Tattoo inks are considered cosmetics
  - Tattoo pigments are considered color additives

- FDA's regulatory challenges
  - Limited regulatory authority over cosmetics; post-market
  - Color additives are the only cosmetic ingredients subject to pre-market approval

- FDA's actions and activities
  - Monitor adverse events via MedWatch
  - Surveys and inspections
  - Issue safety alerts to consumers
  - Issue warning letters to tattoo manufacturers that led to voluntary recalls
  - Research to better understand the composition of tattoo inks

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