Regulation of Cosmetics in the United States

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Overview

- Cosmetics and Colors:
  - Laws, Regulations, Scope, Definition, and FDA's authority
- Cosmetics Labeling and Claims
- Compliance and Enforcement
- Microbiome and Cosmetics

U.S. Laws and Regulations of Cosmetics

1938 – Legislation

- Injuries led to inclusion of cosmetics in consumer legislation
- Federal Food, Drug, and Cosmetic Act (FD&C Act) of 1938

Cosmetics – Scope

- Used by most consumers daily
- Examples:
  - Moisturizers, other skin preparations
  - Hair care, hair dyes, hair straighteners
  - Makeup, nail polishes
  - Shaving preparations
  - Perfumes
  - Toothpastes, mouthwashes
  - Face and body cleansers, deodorants
  - Tattoos

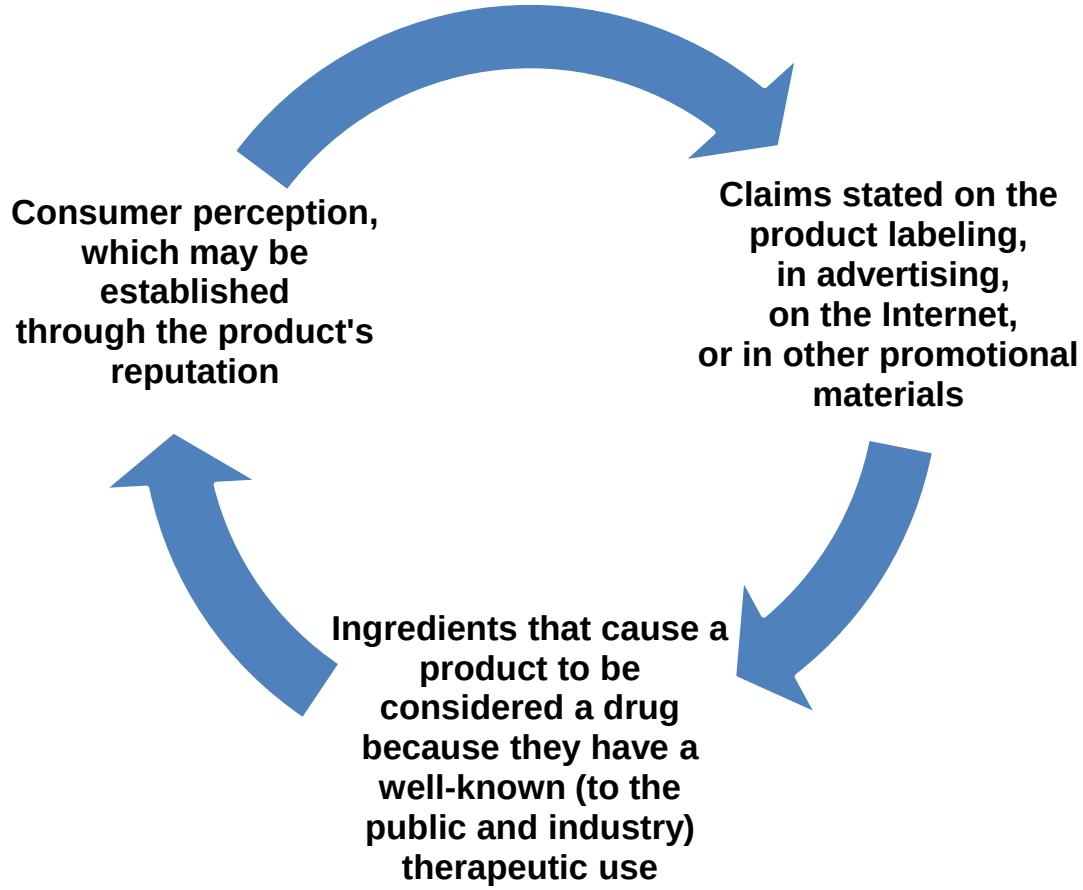
What is a Cosmetic?

- Defined in the Federal Food, Drug, and Cosmetic Act (FD&C Act), Section 201 (i)
- Articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body...
  - for cleansing
  - beautifying
  - promoting attractiveness
  - altering the appearance
- Excludes “Soap” (defined in 21 CFR 701.20)

What is a Drug?

- Defined in FD&C Act, Section 201 (g)
- Articles intended
  - For use in the diagnosis, cure, mitigation, treatment, or prevention of disease
  - To affect the structure or any function of the body of man or other animals

How is a Product's Intended Use Established?



Fundamental Differences Between Cosmetics and OTC Drugs

Cosmetics	OTC Drug
- No pre-market approval or clearance required	- Pre-market approval or Monograph demonstrating Safety & Efficacy needed

- GMP – voluntary
  - No mandatory records access
	- Subject to GMP by regulation
	  - Mandatory records access

- No mandatory establishment or product registration	- Establishments & products must be registered
- Adverse events reporting is not mandatory	- Serious adverse events must be reported to the FDA

Cosmetic vs. Drug

- Products can be cosmetics, drugs, or both
  - Antimicrobial cleanser
  - Antidandruff shampoo
  - Anticaries toothpaste
  - Antiperspirant-deodorant

- If it meets definition of drug, it must comply with drug requirements-even if it is also a cosmetic

- No legal definition of "**cosmeceutical**"

FDA's Authority over Cosmetics

- Cosmetics must not be adulterated or misbranded
- FDA authority is post-market – meaning FDA does NOT have the authority to approve cosmetic products or their ingredients, with the exception of color additives
- The manufacturer is responsible for making sure cosmetics are safe before they are marketed; may do testing or use available data for similar products
- Cosmetics should be labeled properly as per the Federal Food, Drug and Cosmetic Act (FD&C Act) and the Fair Packaging and Labeling Act (FPLA)

Prohibited Under FD&C Act

Adulterated Cosmetics (Sec 601)

- Harmful or injurious under labeled or customary conditions of use
  - Formulation
  - Container
  - Contamination
- Unapproved Color Additive
  - "Coal Tar Hair Dye Exemption" (Sec. 601 (a))
- Manufactured or held under "insanitary" conditions

Misbranded Cosmetics (Sec 602)

- False or misleading labeling
- Required information missing or presented improperly
- Deceptive container
- Doesn't comply with 1970 Poison Prevention Packaging Act (Child resistant)

Microbiological Safety of Cosmetics

- Cosmetic products are not expected to be aseptic and there are no widely acceptable standards for microbial numbers in cosmetics
- For cosmetic products, FDA generally follow the guidance e-BAM, Ch 23 https://www.fda.gov/Food/FoodScienceResearch/LaboratoryMethods/ucm565586.htm
    - Not more than 500 colony forming units (CFU)/g for eye-area products
    - Not more than 1000 colony forming units (CFU)/g for non-eye area products
    - How probiotics will fit is unclear

Cosmetic Ingredients Prohibited or Restricted by Regulation

- Bithionol
- Chlorofluorocarbon propellants
- Chloroform
- Halogenated salicylanilides
- Hexachlorophene
- Mercury compounds
- Methylene chloride
- Sunscreens in cosmetics
- Vinyl chloride
- Zirconium in aerosols
- Certain cattle materials

https://www.fda.gov/cosmetics/cosmetics-laws-regulations/prohibited-restricted-ingredients-cosmetics

What is a Color Additives?

1960 Color Additive Amendments to the Act (FD&C Act, Section 201 (t))

Substances that impart color to a food, drug, cosmetic, medical device, or to the human body

- Color additives are primary ingredients in cosmetics
  - to beautify the body (lipsticks, eye shadows, mascaras, blushers…)
  - to enhance the marketability of products (shampoos, bath oils…)
  - to mask the colors of other ingredients in products (lotions, creams…)

Requirements

- Must be safe and pre-approved
  - color additives must be used appropriately
  - manufacturers must submit samples to OCAC labs for every batch of certifiable color additive marketed in the U.S.
  - certifiable additive batches are NOT tested by FDA for micro

More resources: https://www.fda.gov/industry/color-additives

Labeling and Claims

What Constitutes Labeling?

FD&C Act Section 201 (k) and (m)

Labeling Requirements

Principal Display Panel (PDP)

- Identity statement
- Net quantity of contents

Information Panels

- Name and place of business
- Distributor statement
- Ingredient declaration
  - Ingredients declared in descending order of predominance (>1%)
- Direction for safe use
- Warning, caution statements

Cosmetic Labeling Guide
http://www.fda.gov/Cosmetics/Labeling/Regulations/ucm126444.htm

Cosmetic Claims

- FDA does not approve cosmetic labeling
- FDA does not require pre-market clearance of cosmetic product claims
- FDA does not have a specific list of “acceptable” vs. “non-acceptable” claims
- FDA evaluates cosmetic label claims in total context of all wording and images present in labels and collateral promotional literature (including print advertising and websites)

Examples of Cosmetic vs. Drug Claims

Cosmetic Claims	Drug Claims
• Cleansing • Moisturizing • Softening • Freshening • Smoothing • Soothing • “Helps”… • “Improves appearance of”…	• Anti-inflammatory • Acne • Eczema • Psoriasis • Scars/Wounds • Anti-septic/Anti-bacterial Anti-microbial • Blood/Muscle Circulation

Compliance and Enforcement

Tools for Compliance and Enforcement

- Targeted establishment inspections
- Routine inspections
- Post-Market surveillance / Sampling programs
- Detention/refusal (Imports)
- Warning Letters
- Recalls and Alerts
  - Recalls, Market Withdrawals, and Safety Alerts
  - Import Alerts
- Seizures
- Injunctions
- Criminal prosecution

More information can be found at https://www.fda.gov/cosmetics/cosmetics-compliance-enforcement

FDA Surveillance of Cosmetics

- Post-Market surveillance is the most important tool to monitor safety of cosmetic products
  - Use of publicly available source of data
  - New products and ingredients
  - New technologies

- Sampling assignments is another mechanism to monitor
  - Microbiological contaminations
  - Heavy metals
  - Chemical contaminants and degradants
  - Allergens
  - Ingredients with known toxicological profiles

- Adverse events analysis
  - CAERS
  - MedWatch

CAERS - CFSAN Adverse Event Reporting System

- CAERS stores adverse events (AEs) reported through MedWatch
- Cosmetic-related AE can be filed by a consumer, manufacturer, or health care professional (via phone, online, or by paper)
- AE reporting is voluntary, the quality & quantity of reports may vary
- FDA AE data is available for download or by submitting a Freedom of Information Act Request
- CAERS is a source of information on cosmetics-related safety signals. FDA reviews AE data and may use it to promote public health and/or communicate safety information related to cosmetic products or ingredients to the public

https://www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program

Types of Adverse Reactions Reported to FDA

Allergy/Sensitization/Irritation Keywords	Disfigurement Keywords
Swollen	Hair Loss
Allergy/Allergic Reaction	Hair Breakage
Hives/Rash	Balding
Itchy	Bald Spots
Redness	Scarring
Swelling	Discoloration

Microbiome and Cosmetics

- Microbiome and Skin Microbiome
- Cosmetics: Spotlight on the Microbiome
- Why are Probiotics in Cosmetics?
- Regulatory Landscape of Probiotics
- International Cooperation on Cosmetics Regulation (ICCR)
- Market Analysis

The Human Microbiome

Microbiome Definition

"The collective genomes of the microbes (composed of bacteria, bacteriophage, fungi, protozoa and viruses) that live inside and on the human body" - The Human Microbiome Project - National Human Genome Research Institute[1]

- The microbiome varies greatly among different body sites [1]

Skin Microbiome Key Messages

- Skin is the largest external organ of the body and just like the human gut, it houses bacteria, fungi, yeast, and viruses, known as skin microbiome [2]
- Most of these skin microbes are harmless or commensal organisms that play essential roles in inhibiting colonization by pathogenic microbes or modulating innate and adaptive immune systems[3]
- Humans display a high intra- and interindividual variation in skin microbial composition where each individual has a "virtually unique microbiota" [2,3]
- When damaged or diseased, skin harbors a reduced diversity of microbial species compared to healthy or normal skin[2,3]

[1] The Human Microbiome Project. https://www.genome.gov/27549400/the-human-microbiome-project-extending-the-definition-of-what-constitutes-a-human/

[**2**] Grice EA and Segre JA. 2011. 'The skin microbiome', *Nature Reviews Microbiology*, 9: 244–253. https://www.nature.com/articles/nrmicro2537

[**3**] Rosenthal et al., (2011). Skin microbiota: Microbial community structure and its potential association with health and disease. Infect Genet Evol. 2011 Jul; 11(5): 839–848. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3833721/pdf/nihms437148.pdf

Cosmetics: Spotlight on the Microbiome

Key Messages from the literature

- In line with consumer demand and market trends, beauty formulators are rethinking cosmetic products[4,5]
- Each cosmetic ingredient has an effect on the biodiversity of the skin ecosystem[4]
- Microbiome-friendly products are meant to remove bad bacteria while promoting the good ones[4,5]
- Data from Mintel* show huge advances in the utilization of the skin microbiome in the cosmetics market, with growth estimated at a global CAGR of 6% between 2016 and 2021

[**4**] Lee et al., (2018). Effects of cosmetics on the skin microbiome of facial cheeks with different hydration levels. Microbiologyopen. 2018 Apr; 7(2): e00557. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5911989/pdf/MBO3-7-na.pdf

[**5**] Huang and Tang. Probiotics in personal care products. Microbiol Discov. 2015; ISSN 2052-6180, Vol 3, Article 5 https://pdfs.semanticscholar.org/ecfd/da47c84eecf6d4a48e4ab2774a01ade23234.pdf

[**6**] On-the-go formats make a splash with female skincare users. Mintel Press Office https://www.mintel.com/press-centre/beauty-and-personal-care/on-the-go-formats-make-a-splash-with-female-skincare-users

***, Mintel** Group Ltd, London-based market research firm. Mintel Global New Products Database (GNPD) is an online, publicly available database (non-FDA database). The GNPD has products from ~50 countries, provides product ingredients lists, packaging, distribution and pricing information.

Distinct Approaches Targeting the Skin Microbiome: Market Analysis

Cosmetic product may contain one or more of the following based on ingredient declaration:

1. Probiotics	"Live microorganisms which when administered in adequate amounts confers a health benefit on the host"[6]
2. Prebiotics	Prebiotics act as food sources for the good bacteria, promoting their growth**
3. Postbiotics	Soluble factors (products or metabolic by-products), secreted by live bacteria, or released after bacterial lysis**

Source: Global New Products Database (GNPD)-Mintel.

[6] Food and Agriculture Organization and World Health Organization Expert Consultation. Evaluation of health and nutritional properties of powder milk and live lactic acid bacteria. Córdoba, Argentina: Food and Agriculture Organization of the United Nations and World Health Organization; 2001. http://www.fao.org/3/a-a0512e.pdf

** Not FDA's definition.

Examples of Product Claims & Description in Labeling

to		on
Balance / Rebalance / Restore Aid / Support /Maintain Optimize / Encourage / Promote Nourish / Soothe Purify / Shield /Target	→	Skin's microbiome Skin's microflora Skin's delicate ecosystem Enrichment of good bacteria Healthy microbiome Skin's natural microbiome

or Microbiome-friendly formula

Source: Global New Products Database (GNPD)-Mintel.

Cosmetics Targeting Skin Microbiome

Probiotic, Probiotics are live microorganisms that are intended to have health benefits**

Postbiotic, Soluble factors (products or metabolic by-products), secreted by live bacteria, or released after bacterial lysis**

Key Messages

- Cosmetic products targeting the skin's microbiome mostly have "probiotic" claims and/or descriptions in their labeling, but some labels have "prebiotic" or both "probiotic and prebiotic"
- However, majority of cosmetic products carrying the "probiotic" labels have **postbiotics** (90%)
- Analysis of the ingredients list shows that the form in which "probiotics" or postbiotics added to formulations are either ferment, extract, filtrate or lysate

Source: Global New Products Database (GNPD) by Mintel – non FDA database
** Not FDA's definition

Why are Probiotics in Cosmetics?

Key Messages from the literature

- The composition of the human microbiome at each body site is distinct[7]
- The composition and function of the microbiome can be changed by exogenously added probiotics[8]
- GNPD-Mintel reports that the use of Lactobacillus-based probiotic skincare products increased by 98% in the US from 2013 to 2017[6]
- Probiotics has been proposed to be used as a strategy for microbial supplementation and/or promotion of microbial diversity[8]

[**6**] On-the-go formats make a splash with female skincare users. Mintel Press Office https://www.mintel.com/press-centre/beauty-and-personal-care/on-the-go-formats-make-a-splash-with-female-skincare-users

[**7**] Versalovic J. The Human Microbiome and Probiotics: Ann Nutr Metab 2013;63(suppl 2):42-52. https://doi.org/10.1159/000354899

[**8**] Dreno et al., 2016. MB in healthy skin, update for dermatologists. J Eur Acad Dermatol Venereol, 30: 2038-47. https://onlinelibrary.wiley.com/doi/epdf/10.1111/jdv.13965

Regulatory Landscape of Probiotics World Scenario

	Food, Functional food, Novel food	Natural health product	Dietetic food	Dietary supplement	Biotherapeutic Pharmaceuticals	Cosmetics
Australia	yes					
Austria					yes	
Belgium					yes	
Brazil	yes					
Canada		yes			yes	
China	yes				yes	
Denmark	yes					
Finland	yes					
France					yes	
Germany					yes	
India	yes					
Italy			yes		yes	
Japan	yes					
Malaysia	yes					
New Zealand	yes					
Sweden	yes					
USA	yes			yes	yes	

- **No current policy regarding probiotics in cosmetics in the US**
- **There are currently no international guidelines on the regulation of probiotics in cosmetics**
- **Probiotic categorization, standards, and regulations differ among different countries for other product categories**
- **No harmonization of standards among EU countries, US, and Canada**

Degnan, F. H. 2008. 'The US Food and Drug Administration and probiotics: regulatory categorization', *Clin Infect Dis*, 46 Suppl 2: S133-6; discussion S44-51. https://academic.oup.com/cid/article/46/Supplement_2/S133/277296

International Cooperation on Cosmetics Regulation (ICCR)

- Established in 2007, ICCR is a voluntary international group of cosmetics regulatory authorities and relevant cosmetics industry trade associations
- The group meets on an annual basis to discuss common issues on cosmetics safety and regulation
- The topics addressed: allergens, alternatives to animal testing, cosmetics safety assessments, nanotechnology/nanomaterials, unwanted trace elements, and microbiome-cosmetics
- The work products: white papers, overviews of general principles, and recommendations on specific regulatory and safety issues (may include definitions, acceptable levels, methodologies, endorsement of other international standards)
- These work products can be adopted, endorsed, implemented, etc. by individual jurisdictions
- The ICCR work products can also provide an international “guidance”, “reference” or “standard” for use by ICCR and other regulatory authorities worldwide

The ICCRs "Microbiome and Cosmetics" Joint Working Group

- At the ICCR's 12th annual meeting (Tokyo, Japan in July 2018), the Steering Committee agreed to create the "Microbiome and Cosmetics" JWG
- At present JWG has ~45 members

ICCR Voting Members

	Regulators	***Industry***
Brazil	ANVISA	ABIHPEC
Canada	HC	CAC
European Union	EC	CE & EfFCI
Japan	NIHS & MHLW	JCIA
United States	FDA	PCPC & ICMAD

Observers

	Regulators	***Industry***
Israel	MOH	IACM
South Korea	MFDS	KCA
South Africa	DOH	CTFASF
Thailand	FDA	TCMA
Taiwan	FDA	TWCIA

The JWG's Deliverables

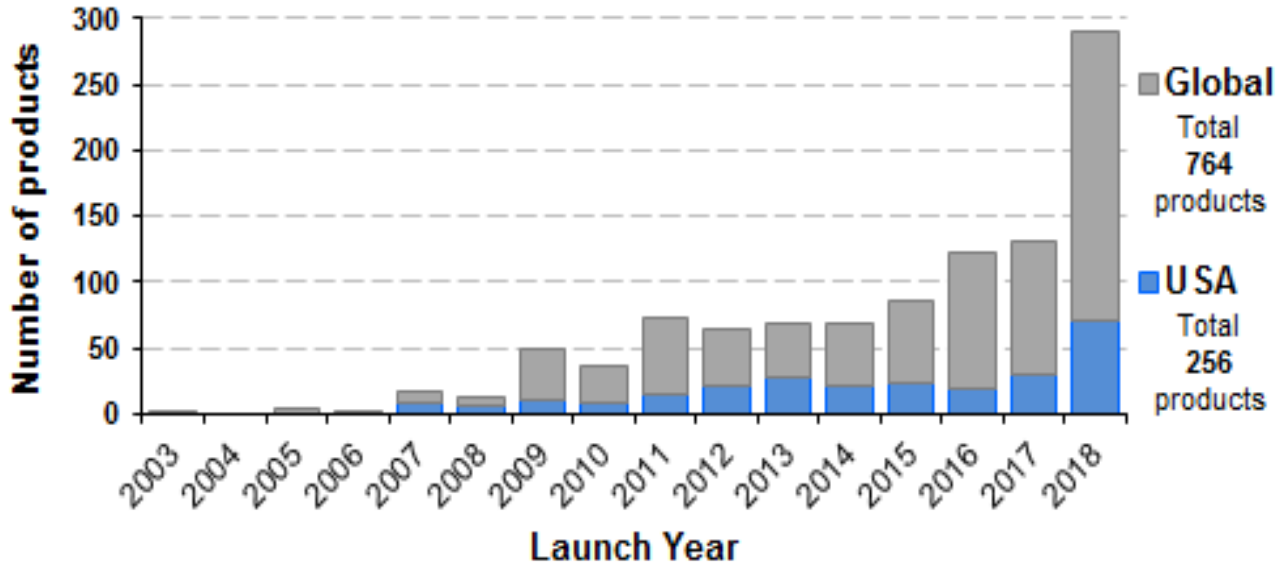
I. Survey and describe the terminology currently used for cosmetic products that work with the skin's microbiome to achieve a cosmetic function (i.e., probiotics, prebiotics, postbiotics, etc.)

II. Provide a summary of what products and approaches are being advanced within the ICCR jurisdictions that work with the skins microbiome to achieve a cosmetic function

III. Provide an overview of regulatory approaches in each jurisdiction governing cosmetic products that work with the skins microbiome to achieve a cosmetic function

The deliverable from this effort will be a high-level report that would then serve as the groundwork for further recommendations in this area.

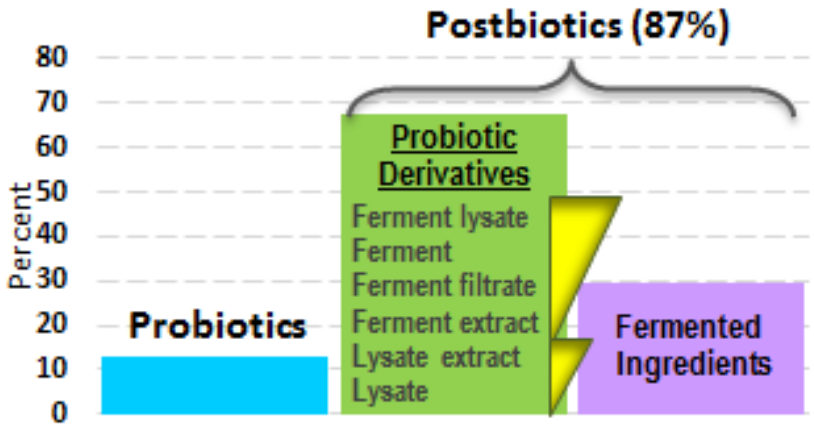
Probiotic Cosmetics are on the Rise



Result:

- Source: Global New Products Database (GNPD)-Mintel.
- Keywords used for screening: Probiotic
- Total products screened: 1,530,000
- Found: Globally 764 products (0.05%) and in the US 256 products (0.017%)
- The 91% of the US “probiotic” cosmetics are skincare products

The Review of 256 U.S. Cosmetics Carrying the "Probiotic" Labels

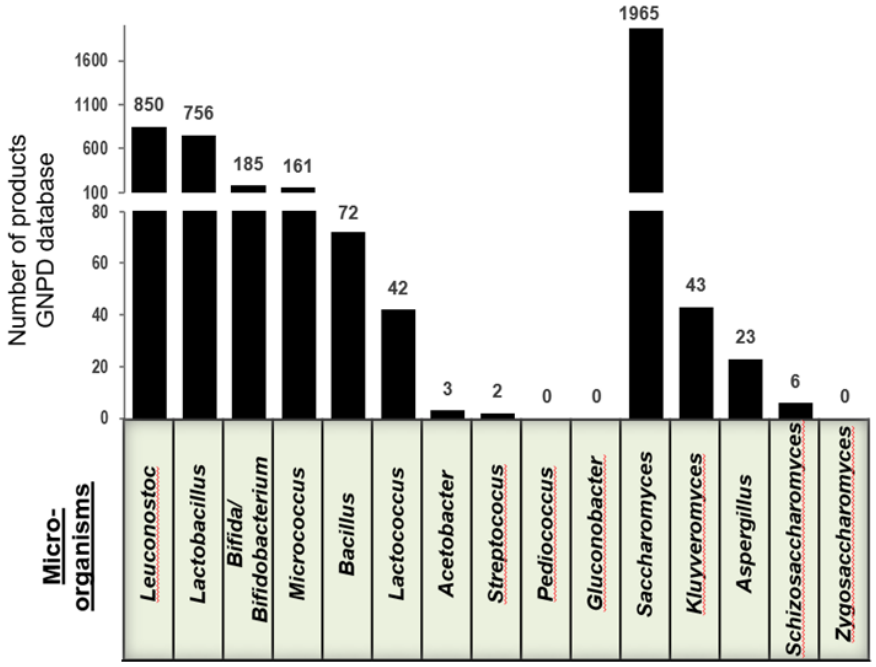


Result:

- Only 13% of the products claim to contain "probiotics" (blue bar) and Lactobacillus is the leading genus (77%)
- The other 87% of the products claiming to contain "probiotics" on the label actually have postbiotics (probiotic derivatives/green bar or fermented ingredients/purple bar)
- The most common derivatives come from the genus Lactobacillus, Bifida, Lactococcus, and Saccharomyces
- Probiotic derivatives added to formulations can be added in the form of ferments, lysates, filtrates or extracts

Source: GNPD-Mintel

Product Search Focusing on Genus Rather than Claim



Results of product search:

- Total number of U.S. products screened: 212,490
- Launch year for the product range from 2003-2018
- ~2,500-3500 products were found with one or more probiotic derivatives
- Saccharomyces, Leuconostos, and Lactobacillus are the most commonly used microorganisms for the formulation of probiotic derivatives in cosmetics

Source: GNPD-Mintel

Take Home Messages

- Cosmetics in the US are not regulated pre-market
- It is the cosmetic manufacturer's responsibility to ensure the safety of the cosmetics that they intend to market
- Safety data is not reviewed by the FDA before the products go on the market
- FDA closely monitors cosmetic product labeling. FDA can take actions against products found to be misbranded or adulterated
- FDA monitors submitted adverse events and makes the non-proprietary or confidential information in the adverse events reports available to the public
- The cosmetics market is continuously growing and innovating
- Trend, as determined from non-FDA databases, of including probiotics or postbiotics in personal care products has reportedly been progressively increasing
- The cosmetics industry is a global industry with differing international regulatory authorities which can be challenging for both regulators and the industry
- FDA has no official policy on probiotics in cosmetics
- The ICCR's "Microbiome and Cosmetics" JWG hopes to bring increased understanding and awareness to cosmetic products that target the skin microbiome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