Cosmetic Testing, Safety and Efficacy

SCC Ontario April 6, 2016
Objectives

- Safety Testing
  - Today’s standard
  - Associated claims
- Efficacy testing
  - Industry standard methodology
  - Industry Standard instrumentation
  - Study design
- US regulatory
  - NAD
  - FTC
- What makes a good study
- Study responsibilities
Cosmetic Safety Testing Today

- In 1991 the CTFA published safety testing guidelines.
- Updated March 2007.
- Cosmetic Ingredient Review panel establishes generally recognized as safe (GRAS) ingredients.
- Testing new and existing products consisting of GRAS ingredients still needs to be performed.
- When developing a safety profile, the type of application and length of contact with the body must be considered.
Cosmetic Safety Testing

Today safety standard

• A cosmetic product shall be “generally recognized as safe”.

• There is no FDA safety standard for cosmetic products within the act.
  
  • In the Federal Register of March 3, 1975 (40 FR 8912 at 8916), FDA advised that "the safety of a product can be adequately substantiated through (a) reliance on already available toxicological test data on individual ingredients and on product formulations that are similar in composition to the particular cosmetic, and (b) performance of any additional toxicological and other tests that are appropriate in light of such existing data and information. Although satisfactory toxicological data may exist for each ingredient of a cosmetic product, it will still be necessary to conduct some toxicological testing with the complete formulation to assure adequately the safety of the finished cosmetic."

• CIR review of ingredients

• Voluntary Cosmetic Registration Program (VCRP)

• Voluntary reporting of serious adverse events (SAE)
Cosmetic Safety Testing Today

- Preclinical Testing
  - Toxicity
    - Tox Risk Assessment (TRA)
  - In-Vitro
    - Dermal irritancy
      - Skin culture techniques
        - MTT Assay
        - Biomarkers PLA2, prostaglandins and interleukins
      - Non skin vegetable based protein disassociation tests
        - IRRITECTION Skintex
Cosmetic Safety Testing Today

- Ocular irritancy
  - HET CAM assay
  - Tissue culture techniques
    - MTT Assay
    - Biomarkers PLA2, prostaglandins and interleukins
  - Non tissue vegetable based protein disassociation tests
    - IRRITECTION Eytex

- Non-animal preclinical testing
  - Mutagenicity (Ames)
  - Microbiological APE
The Human Repeated Insult Patch Test (HRIPT) is the most popular safety test used today. It consists of the following steps:

- **Induction phase** involves the repetitive application of a test material under an adhesive patch unit, for at least 9, over a period of consecutive weeks. The patches are applied to the same skin site on 50, 100, 200 or more subjects defined as “normal” individuals.

- **Rest or incubation phase.** During this phase no further patches are applied, for a period of approximately two weeks.

- **Challenge phase** is the application of one patch, usually to a previously unpatched “virgin” site.

- **The strength of this test** is its ability to predict irritation and allergic response.
Cosmetic Safety Testing Today

• In-Use Studies: The product would be tested in use or exaggerated use conditions. Evaluation conducted by physician, trained evaluator or by the test subject.

• Products containing known irritants

• Regime product groups

• Hygiene products

• Pediatric products
Cosmetic Safety Testing Today

- Products to be used around the eye need special consideration.
  - An ophthalmology in-use study should be considered.
- Children’s products need additional testing
  - An in-use study monitored by a pediatrician should be considered.
- If any the ingredients are not GRAS, additional testing needs to be considered.
  - A larger HRIPT Panel
  - Multiple *In-Vitro* studies
Claims are made to:

- Persuade the consumer
- Stay competitive
Cosmetic Efficacy Claims Support

• A cosmetic claim is not a structure/function claim

• Efficacy Studies are used to validate claims

• Advertising is regulated by the Federal Trade Commission

• Efficacy claim on cosmetics labels must be supported by valid (Industry Standards) studies

• Validation studies must comply with industry standards

• Labeling is regulated by the FDA
  • Mandatory statements: ingredients, warnings, etcetera
Cosmetic Efficacy Claims Support

• Formulation Claims
  • Contains Aloe
  • Contains Honey “A natural humectant”
  • Oil Free

• Performance claims
  • Hypoallergenic
  • Dermatologist Tested
  • Ophthalmologist Tested
  • Suitable for contact lens wearers
  • Instantly boosts hydration levels by over X%
  • In 2 weeks, consumers perceive a 74% decrease in fine lines and wrinkles

• Under most circumstances only performance claims need to be validated
Cosmetic Efficacy Claims Support
Performance Claims

- Anti-aging
- Fine line and wrinkles (appearance)
- Skin elasticity
- Skin firmness
- Age spots
- Skin texture
- Moisturization
- Humectantcy
- Barrier function
- Flaky skin
- Skin tone
- Oil control
- Comedone control

- Skin elasticity
- Skin soothing claims
- Safe for sensitive skin
- Reduce the appearance of cellulite
- Evenness of skin tone
Cosmetic Efficacy Claims Support
Performance Claims

- Hair product claims
- Bounce
- Volume
- Manageability
- Color
- Color fade
- Frizz and split ends
- Nail product claims
- Peeling
- Cracking
- Strengthening
- Salon testing
Cosmetic Efficacy Claims Support
Performance Claims

Clinical significance versus statistical significance

- Clinical significance: readily apparent the changes made as a result of the products performance.
- Statistical significance: Does the data provide a real change, as tested by statistical methods, chi squared, t-test, ANOVA, SAS, etcetera.
- Regulators want to see both clinical and statistical significant product benefits to substantiate a claim.
- Clinical photography is often used as an integral part of proving, or documenting both statistical and clinical significance
Cosmetic Efficacy Claims Support
Performance Claims

Claims can be substantiated, or validated using one or both of the following ways

- **Subjective Support**
  - “In two weeks consumers perceived a X% decrease in fine lines and wrinkles”
  - “Long wearing”
  - Sensory Claims
  - Calibrated expert graders

- **Objective Support**
  - Bio-instrumentation
    - Instantly boost hydration level by X%
    - Reduction of wrinkles by X%
  - Calibrated expert graders
Cosmetic Efficacy Claims Support
Performance Claims

Claims that can be substantiated by subjective methods

- **Sensory Claims**
  - Odor and malodor
  - Sting
  - Feel

- **Consumer preference**
  - Product A versus B
  - Test product versus the consumers “normal” product

- **Self-perceived product benefits**
  - In-use questionnaire based studies
Cosmetic Efficacy Claims Support
Performance Claims

Claims that **MUST** be substantiated by objective methods

- Quantitative claims
  - Wrinkle and fine line reduction
  - Firmness
  - Moisturization
    - Percentage increase
  - Elasticity
  - Skin tone
  - Sebum production
  - Flaking skin
Cosmetic Efficacy Claims Support Methods

All efficacy studies for skincare products should be performed in an appropriate environmental room.
Cosmetic Efficacy Claims Support Methods

Moisturization

- Electrical conductance/capacitance
  - Corneometer ®
  - Novameter ®
  - MoistureMeter ®

- Transepidermal water loss
  - TEWL Meter ®
  - Vapometer ®
  - Servomed Evaporimeter ®
Cosmetic Efficacy Claims Support Methods

Wrinkle and fine line reduction

**PRIMOS 3D®**

- State of the art imaging system
- to quantify wrinkles and fine lines
- Competitive instrumentation,
  - Foytes ® system
  - Skin-Visiometer® SV 600
- Competitive technology
  - Image analysis of silicone replicas
  - Calibrated expert grading
Viscoelasticity

- Suction/Torsion
  - Cutometer
  - Dermflex
  - Twistometer
- Competitive instrumentation
  - Balistometer
- Competitive technology
  - Pinch/Recoil method
Skin Tone Measurements

- L*A*B* measurement instruments
  - Minolta Chromameter
  - IMS Smartprobe
  - Datacolor

- Competitive instrumentation
  - Digital photography with computer color image analysis

- Competitive Technology
  - Expert calibrated grading
Cosmetic Efficacy Claims Support Methods

Clinical Photography

• VISIA CR Photographic System
• Charmview
• Digital Microscope Systems
• Epiflash systems
Study design

• Seasonality
  • Study duration/number of visits
    • How long will the product take to reach peak efficacy plus add a bit more as a safety margin
      • To ensure most of the panel reached peak efficacy
      • Possible regression
  • Volunteer population
    • Number of subjects
      • Statistical power computation
      • Industry standard
  • Inclusion criteria
    • Gender
    • Ethnicity
    • Age
    • Any desired medical condition
      • Atopic
      • Diabetic
Study design

• Exclusion criteria
  • Interfering medication
  • Inappropriate skin type
  • Disease or medical condition
  • Inability to follow instructions

• Methodology
  • Instrumental
  • Expert graders

• Usage direction from the sponsor
• Optional questionnaire from the sponsor
Study design

Anti-ageing

- **Seasonality** (Winter is cold and dry)
  - Duration/number of visits
  - How long will the product take to reach peak efficacy plus a safety margin **Supplier data 8 weeks**
    - To ensure most of the panel reached peak efficacy
    - Possible regression 12 week study, baseline, 6 and 12 weeks

- **Volunteer population**
  - Number of subjects
    - Statistical power computation, **Two group 60 each**
    - Industry standard **30-35 subject in one or two groups?**
  - Inclusion criteria
    - Gender **Female**
    - Ethnicity **All**
    - Age range **55-69 years of age**
    - Any medical condition **Mild to moderate wrinkles**
Study design

• Exclusion criteria
  • Interfering medication
  • Inappropriate skin type
  • Disease skin or medical condition
  • Inability to follow instructions
• Methodology
  • Instrumental
    • Moisturemeter (hydration)
    • Elastometer (firmness/elasticity)
    • PRIMOS 3D (fine lines and wrinkles)
    • VISIA photos (documentation)
  • Expert graders Yes (clinical relevance)
• Usage direction from the sponsor Yes
• Optional questionnaire from sponsor Yes
Study design

- Visits
- Recruiting
  - Sign informed consent
  - Qualification
  - Soap pickup for conditioning
- Baseline
  - Requalification/Acceptance
  - Product/instruction/diary
  - Questionnaire
  - Moisturemeter (hydration)
  - Elastometer (firmness/elasticity)
  - PRIMOS 3D (fine lines and wrinkles)
  - VISIA photos (documentation)
- 6 weeks
  - Questionnaire
  - Moisturemeter (hydration)
  - Elastometer (firmness/elasticity)
  - PRIMOS 3D (fine lines and wrinkles)
  - VISIA photos (documentation)
  - Expert grading
- 12 week
  - Questionnaire
  - Moisturemeter (hydration)
  - Elastometer (firmness/elasticity)
  - PRIMOS 3D (fine lines and wrinkles)
  - VISIA CR photos (documentation)
  - Expert grading
Contents of a “Good” Study

- Good Designed Preapproved Protocol by
  - Primary Investigator (PI)
  - Sub-investigators
  - Study Sponsor
  - Institutional Review Board
  - Amendments if necessary
- Appropriate Subject Selection
  - Number as based on biostatistical power computations
  - Type as defined in the inclusion/exclusion criteria in the protocol
- Compliant Subjects
  - Study direction in the protocol
  - Compliant with the clinics requirements
    - Visits
    - Medical history
- Informed Consent that is HIPAA compliant
Contents of a “Good” Study

• Appropriate Test Environment
  • Temperature and Humidity controlled
  • Proper lighting for visual grading
• Well written usage instruction
• Adequate amount of supplies/test material
• Industry standard equipment for objective support
• Well trained qualified graders for
  • Objective support
  • Subjective Support
• A designed questionnaire (when used)
  • Validated if used a sole support for a claim
• A Quality assurance statement
• A Well Written Easy to Understand Report
  • Including any deviations, amendments, adverse from protocol and impact statement form PI
Testing Organizations Responsibilities

- Fair and unbiased results
- Confidentiality
- Access to YOUR study
  - The ability to audit at anytime, including during the biophase of YOUR study, announced or more importantly unannounced
  - When appropriate interim or “top line” results
- Good and timely advice
- Industry standard methodologies
Study Sponsor’s Responsibilities

• Give clear directions to the testing facility

• To audit the study at the testing facility

• Read, understand and sign the protocol

• Bring the testing facility into the planning stage
  • This will decrease your time to market and costly mistakes

• Understand that all claims made are your responsibility
Cosmetic Efficacy Claims

- Federal Trade Commission  FTC
- National Advertising Division of Better Business Bureau (NAD)
- FDA labeling only
- National Advertising Division and ERST of the Better Business Bureau
- International regulatory bodies have similar organizations
NAD and FTC require that you are responsible for testing your own product.

Issue that arises frequently in NAD cases involves whether testing must be performed on the Advertised Product.

NAD does not have enforcement authority.
Label Review
Label Review

• “Made with botanical oils and herbs”
  • Formulation claim

• Possible noncompliant claims
  • Protective (OTC monograph claim)
  • Penetration (Drug claim)
Label Review

- 24h Cellular energizer cream
  - Not sure if this is a claim that can be substantiated

- Improves Firmness
  - Viscoelasticity study

- Cellular renewal
  - Dansyl chloride cellular renewal study
Label Review

- “Anti-wrinkle”
  - Claim may not be allowable by some regulators

- “Results in minutes”
  - Wrinkle evaluation would need to be conducted within minutes

- 3 powerful anti-aging technologies, GABA, Matrixyl 3000 and Hyaluronic Acid
  - Claim cannot be based on the addition of raw materials on multiple ingredients and without appropriate footnote
Label Review

- “Detoxify”
  - I am not sure if this is a supportable claim

- “Draws out impurities”
  - I am not sure if this is a supportable claim

- “Restores lost minerals”
  - Could be a drug or supplement claim
Label Review

- “Renews skin”
  - Dansyl chloride cellular renewal study
- Possible drug claim, drug claim, drug claim, etcetera, etcetera and etcetera
Contact Information

Craig R. Weiss
Consumer Product Testing Company, Inc.
70 New Dutch Lane
Fairfield, NJ 07004

Phone  (973) 808-7111
Facsimile  (973) 244-7503
E-mail  crweiss@cptclabs.com