



# BIO SCIENCE LABORATORIES, INC.

**GLP/GCP Product Efficacy and Safety Testing**

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## GLP/GCP Product Efficacy and Safety Testing

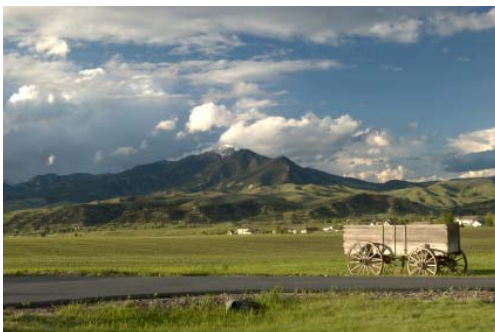
Now in our 20th year, BioScience Laboratories, Inc. has helped hundreds of product companies get their products approved and differentiated in the United States, Canada, Europe, and around the world. Our scientists have the expertise to design studies and test according to the guidelines established by the U.S. EPA and FDA, Health Canada, and the European Union. Our in-depth understanding of the market allows us to guide clients to develop testing protocols that result in unique, product-differentiating label claims.

### Company History

BioScience Laboratories was founded in Bozeman, Montana in 1991 by Dr. Daryl Paulson, Ph.D. The author of numerous texts and papers on the subject of antimicrobial testing, Dr. Paulson is known for pioneering the use of statistics in the design, execution and analysis of efficacy and safety studies. With a commitment to scientific excellence and customer satisfaction, Dr. Paulson has led BioScience Laboratories through several stages of growth while keeping the company firmly planted in the community of Bozeman, where he and his staff enjoy the high quality of life filled with beautiful scenery and nearby outdoor adventures. Planning for the next twenty years of continued commitment to the antimicrobial testing industry, their clients, and their employees, the company owners, Dr. Paulson and his wife Marsha Paulson, are building a 14,000 square foot laboratory building and a 7,000 administrative building in Bozeman near the campus of Montana State University.



Daryl Paulson, Ph.D. and Marsha Paulson



#### Bozeman, MT

|            |         |
|------------|---------|
| Population | 35,000  |
| Elevation  | 4820 ft |
| Founded    | 1883    |

Home of Montana State University Bozeman and the County Seat of Gallatin County.

# BIO SCIENCE LABORATORIES, INC.



## GLP/GCP Product Efficacy and Safety Testing

### Customer Service

The commitment to customer service is shared by the entire staff at BioScience Laboratories. Our Senior Account Executives are available 24 hours a day, 7 days a week to answer your questions about current or upcoming studies at BioScience Laboratories. Our Study Directors work together with our clients to design each study to provide definitive answers to the client's questions about the product's efficacy and safety. Our Participant Recruitment team is focused on finding the correct test population that meets the requirements of each study. Our Quality Assurance experts observe, audit, and review each study with an un-biased eye to ensure that the study was conducted with the quality to meet federal regulation and with integrity to meet our client's needs.

### Value

At BioScience Laboratories, we believe in providing our customers with added value for each and every project. This approach starts with understanding the client's market differentiation and their regulatory compliance goals. Our team of experts provides upfront advice on the study design, such that the client can use the results to create a competitive advantage and meet the applicable regulatory requirements. Throughout the life of each study, we work together with the client to ensure the study is completed on budget, on time, and with the high level of quality required for regulatory submission. Our ability to apply meaningful techniques for statistical analysis to test data provides our clients with the information necessary to make informed decisions about their product.



### BioScience Laboratories Value Chain



## GLP/GCP Product Efficacy and Safety Testing

### Quality Program

BioScience Laboratories, Inc. maintains a GLP/GCP quality program that ensures our clients' studies are performed well and in compliance with regulatory requirements. Each study undergoes a quality review prior to initiation, in-process audits, and a final quality audit upon completion. A continuous quality improvement process is in place to address any discrepancies and consistently enhance the value of our services.

Our laboratory facility is registered with the FDA. In addition, in its nearly two-decade history, our Quality Assurance program has experienced more than 200 successful audits performed by federal agencies, third-party auditing firms, and dozens of our clients. We invite you to visit and audit our facility to verify, first-hand, how our quality program assures that your study is performed accurately and in compliance.

**Partnering with a laboratory that understands the regulatory requirements and intra-industry competitive pressure can mean the difference between the success and failure in new product approval and product acceptance by end-users. BioScience Laboratories, Inc., enjoys strong, professional relationships with the CDC, EPA, FDA, USDA and Health Canada; these relationships are passed on as added value to our clients in the form of adherence to the most current regulations and approved practices.**

To ensure that you receive the most reliable, high-quality laboratory services, all studies at BioScience Laboratories, Inc., are performed in accordance with the relevant standards and methods specified by the following:

- American Association for the Advancement of Medical Instrumentation (AAMI)
- American Association for Textile Colorists and Chemists (AATCC)
- American Society for Testing and Materials (ASTM)
- Association of Official Analytical Chemists (AOAC)
- Centers for Disease Control and Prevention (CDC)
- EPA Good Laboratory Practices (GLPs)
- European Norms (EN)
- FDA Good Clinical Practices (GCPs)
- FDA Good Laboratory Practices (GLPs)
- Health Canada
- Personal Care Products Council (PCPC) Soap and Detergents Association (SDA) Healthcare Continuum Model
- United States Pharmacopeia (USP)

## GLP/GCP Product Efficacy and Safety Testing

### Scientific Expertise

The core expertise of BioScience Laboratories, Inc. is testing the efficacy and safety of antimicrobial products. We have been performing *in-vivo* and *in-vitro* studies for topical antimicrobials, hard surface disinfectants, medical devices, pharmaceuticals, cosmetics, and personal care products for twenty years.



Presurgical Wash Procedure

Efficacy Testing of topical antimicrobials is conducted on healthy human subjects and takes place in our Clinical Trials Laboratory. Such testing includes, but is not limited to evaluation of handwashes, hand sanitizers, surgical scrubs, preinjection and precatheter insertion preparations, healthcare personnel hand antiseptics, preoperative preparations, and presurgical washes.

The BioScience Laboratories Skin Technology Center offers clinical-testing services for both personal and professional skincare products. Standard, validated protocols have been developed to substantiate a wide variety of cosmetic and personal care product claims, as well as claims for prescription and over-the-counter drug products. The Skin Technology Center also performs skin irritation studies, skin moisturization studies, photoirritation, photosensitization, phototoxicity, photoallergenicity, and SPF testing (UVA/UVB).

Scientists in our Microbiology In-Vitro Laboratory are well-trained on ASTM, AATCC, AOAC, CLSI, and EN standard methods. The efficacy testing services of this laboratory include MIC/ MBC , biofilm (prevention and removal), time-kill kinetics, clean room disinfectant validation, zone of inhibition and custom efficacy Studies for disinfectants and other products requiring EPA registrations and FDA 510(k) submissions.

Studies can also be designed and executed to differentiate existing products within the market and support our unique label claims. Additionally, the In Vitro Laboratory uses tissue models prepared by the company leading the development of alternatives to animal testing methods to perform safety testing on Cosmetics, Surfactant-based Products, Pharmaceuticals and Chemicals as well as products for Personal Care, Hair Care, and Household Cleaning . These tests include Ocular Irritation, Skin Irritation, Dermal Corrosion, Oral Irritation, and Cytotoxicity.



Time-Kill Testing

## GLP/GCP Product Efficacy and Safety Testing



Clinical Virology Studies: Application, Exposure and Recovery

The Virology Laboratory works together with the Clinical Laboratory and In-Vitro Laboratory to perform antiviral efficacy studies for topical antimicrobial products, disinfectants, and any product with antiviral efficacy claim. BioScience Laboratories. Our virology laboratory personnel are well-trained on the various ASTM and EN standard methods to assist clients with new product development, R&D projects, marketing claims, and supporting EPA, FDA, EU, and Health Canada label claims.

### Gallatin Institutional Review Board

To protect the well-being and health of the subject volunteers, BioScience Laboratories, contracts the services of the Gallatin Institutional Review Board (GIRB), which comprises seven members – two physicians, three nurses, one member of the clergy, and a member from the general public. The GIRB operates in accordance with guidelines specified in 21 CFR Parts 50 and 56 and is registered with the OHRP and the FDA. Prior to recruitment of subjects, the GIRB reviews and approves study protocols for safety and ethical propriety. The GIRB also ensures that unexpected and/or untoward physical reaction of any kind experienced by a subject during the course of a clinical study, termed an Adverse Event (AE), is addressed, treated, and resolved appropriately and in a timely way.

***Institutional Review Board (IRB) – “An independent body constituted of medical, scientific, and nonscientific members, whose responsibility it is to ensure the protection of the rights, safety, and well-being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trials, of protocols and amendments, and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects.”***

**Guidance for Industry, E6 Good Clinical Practice: Consolidated Guidance International Conference on Harmonisation, April 1996**

## GLP/GCP Product Efficacy and Safety Testing

### Clinical Trials

BioScience Laboratories has twenty years of experience performing clinical studies testing a wide variety of products.

#### Antimicrobial Persistence Evaluations

- Agar Patch
- Cup-Scrub Retrieval Past-Exposure
- Extended-Use Claims

#### Consumer Product Evaluations

- Cade and Modified Cade Handwashes
- Non-Water-Aided Hand Sanitizers
- General-Use Antimicrobials Soaps
- Food-Handler Handwashes

#### Generic Pharmaceuticals

- Bioavailability Studies
- Bioequivalence Studies

#### Healthcare Evaluations

- Surgical Scrub Formulations
- Preinjection and Precatheter Insertion Preparations
- Healthcare Personnel Hand Antiseptics
- Preoperative Preparations
- Catheter Maintenance
- Presurgical Washes
- Full Body Shower Washes
- Protective Barrier Preparations

#### Skin Technology

- Skin Irritation Studies
- Skin Moisturization Studies
- Bioinstrumentation Testing
- Claims Substantiation
- Photoxicity
- Photoallergenicity
- SPF Testing (UVA/UVB)

#### Virology

- Handrub Antiviral Efficacy
- Handwash Antiviral Efficacy
- Product-Specific Antiviral Efficacy



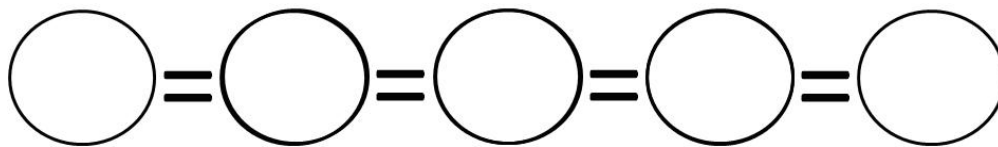


## GLP/GCP Product Efficacy and Safety Testing

### Product Differentiation

Selling your product can be more profitable, when we show you how to differentiate it from competitors' products. Most handwash product, wound product, and medical device product manufacturers have their products approved by meeting the standards of the Food and Drug Administration (FDA) or the Environmental Protection Agency (EPA) and then simply look for avenues to sell those products. Unfortunately, many of those products are indistinguishable from the other products within the same market. Manufacturers and distributors have appropriate product claims, but the products lack any differentiation, or specific characteristics that could create a niche market opportunity for those products.

Figure 1. Product Claims are the Same  
(Must Sell at the Same General Price)



Because products lack differentiation, consumers consider them to be the same. Products are marketed and sold based on their distribution channels or competitive cost. Is there a better way to differentiate your product to increase your market share and profit margin? Definitely, yes.

### What Does Your Product Do Better?

The question is this: How does your product compare with competitors' products? What makes your product more appealing to the consumer?

For example, current surgical scrubs in your marketplace include:

- Ø CHG – your product
- Ø Alcohol + CHG
- Ø Alcohol

With a CHG product, you have already met the FDA standards through a surgical scrub claim. You discover that alcohol + CHG products are faster-acting than your CHG, and those products are rendering your product nearly obsolete.



## GLP/GCP Product Efficacy and Safety Testing

Example:

| Product       | Speed | Long-Acting |
|---------------|-------|-------------|
| CHG           | O     | X           |
| Alcohol       | X     | O           |
| Alcohol + CHG | X     | X           |

where:

O = none present

X = Present

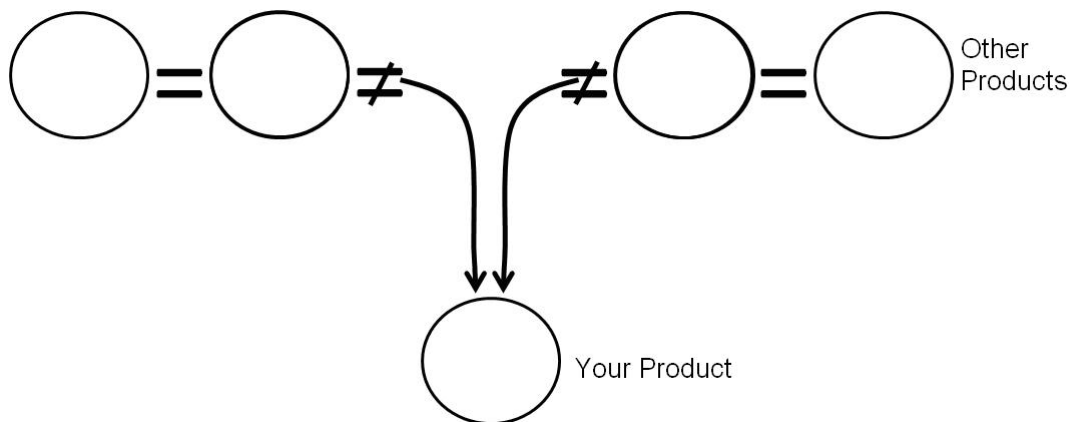
What options do you have? You might be forced to drop the price to secure sales, and seemingly lowering your price every year.

But BioScience Laboratories, Inc. offers ways of designing a variety of studies that can determine your products' strengths and others products' weaknesses, which will help you differentiate your product, giving you a competitive edge and allowing you to sell your product based on its positive attributes. This aids you in increasing sales and profitability.

At BioScience Laboratories, we looked at a number of variables and found that CHG does not sting and burn the skin when applied to an open cut on your hands. Also, upon repeated use, it was found to prevent dryness on the hands. If applicable, you could begin your marketing program with specific product attributes in mind.

We design studies in such a way that you clearly see your product's differentiation.

Figure 2. Your Product is Differentiated





## GLP/GCP Product Efficacy and Safety Testing

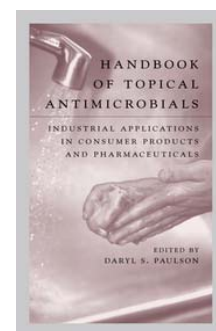
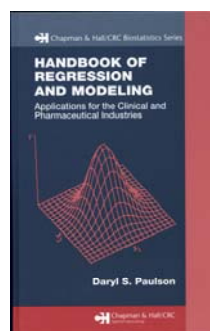
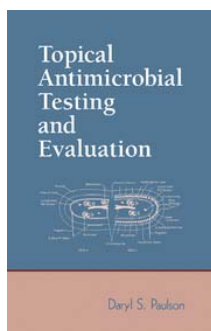
Now, you are able to sell your product for more money and increase your market share.

Please note that these are not claims you must support with FDA/EPA testing; however, they are mechanisms to enable you to show, scientifically, that differences do exist between your product and others on the market. This product differentiation may be the competitive edge you are seeking.

Contact [Daryl Paulson](#) at BioScience Laboratories, Inc., and I will work together with you to design a study to differentiate your product in the current competitive market.

### Daryl S. Paulson, Ph.D. - President and CEO

Dr. Paulson has extensive experience in skincare research designs, clinical trials, and biostatistics. He is the author of the standard texts of the industry -- *Topical Antimicrobial Testing and Evaluation*, *Applied Statistical Designs for the Researcher*, and *Handbook of Regression and Modeling: Applications for the Clinical and Pharmaceutical Industries*. -- as well as the editor of the *Handbook of Topical Antimicrobials: Industrial Applications in Consumer Products and Pharmaceuticals (Manufacturing Engineering and Materials Processing)*. Dr. Paulson has designed the procedures used at BioScience Laboratories, Inc., for evaluation of skin care and cosmetic products, as well as the statistical models applied to assess the data. These include factorial designs, Analysis of Variance designs, regression analysis, exploratory data analysis, and integrative and statistical design for both parametric and nonparametric forms of data.



### Antimicrobial Product Evaluations

BioScience Laboratories has twenty years of experience in conducting clinical studies on antimicrobial products used in food service, healthcare, and janitorial sanitation settings, as well as antimicrobial products used by the general consumer.

#### Health Care Personnel Handwash

BioScience Laboratories has performed more than 100 healthcare personnel handwash studies per the Tentative Final Monograph (TFM), pp. 31448-31450. Formally, the studies involve 18 subjects per product tested, which, at a minimum, will be two – a test product and a reference product required for internal validity of studies performed for FDA approval. The general concept of the test is to determine how effectively handwash products or products designed for application without water can eliminate transient, contaminative bacteria from the hands.

BioScience Laboratories frequently designs relatively inexpensive, proof-of-concept studies of healthcare personnel handwash products, which require fewer subjects per product and relax certain other of the requirements mandated by the TFM, but which are well-designed statistically. Data from these studies are not intended for submission the FDA, but to indicate whether products are worth funding in a full clinical study.

#### Surgical Scrub

BioScience Laboratories performs surgical scrub studies per the Tentative Final Monograph (TFM), pp. 31445-31448.

These studies typically involve 30 subjects. BioScience Laboratories often will design relatively inexpensive pilot studies of surgical scrub products that use fewer subjects per product and ease some of the other requirements mandated by the TFM. Data from these studies will not be submitted to the FDA, but will serve as the basis for designing the much more extensive clinical study to follow.



Cylinder Sampling Method



### Antimicrobial Product Evaluations

#### Preoperative Preparation

BioScience Laboratories performs preoperative preparation studies per the Tentative Final Monograph, pp. 31450-31452 and the ASTM's Standard Method E 1173. Following the sampling for baseline, test sites are treated with a product according to procedures and for a period of time specified by protocol. After times of exposure specified by protocol, cylinder-sampling is performed. As a general rule, all sites of product application are assessed visually for signs of skin irritation at each sampling time, and if present, it is documented.

#### Agar Patch

The results of this test are used to make a claim of substantive persistence of bactericidal/bacteristatic activity. This is a very desirable attribute for an antimicrobial product intended for use by healthcare personnel and by the general public. BioScience Laboratories performs Agar Patch testing per ASTM Standard Method E 1882 using the forearms of human subjects as the sites of product application. The difference in bacterial populations between the control plate exposed to untreated skin and a test plate exposed to treated skin constitutes the result of testing.

#### Foodhandlers Handwash

With a lack of an FDA defined method for demonstrating efficacy of food-handler handwash products, BioScience Laboratories has developed a method and submitted it to ASTM Subcommittee E235-15 for review and approval as a standard method. Since this method is not appropriate for alcohol-based handrubs, BioScience Laboratories has also designed studies to test the efficacy of these products.

#### General-Use Handwash

For general-use handwash studies, BioScience Laboratories follows the ASTM Standard, E1174, which includes a method for testing of general-use handwash products. This corresponds well to the method proposed by the Soap and Detergent Association (SDA) and Personal Care Products Council (PCPC).



### Skin Technology Testing

The BioScience Laboratories Skin Technology Center offers a wide variety of clinical-testing services for both personal and professional skincare products. Standard, validated protocols have been developed to substantiate a wide variety of cosmetic and personal care product claims, as well as claims for prescription and over-the-counter drug products. Protocols are custom-designed to support specific needs and test requirements. The high elevation and year-round low humidity of Bozeman, Montana provide an excellent environment for specialized skin studies.

#### Moisturization

Studies of this kind assess variables such as dryness and moisturization. For evaluating these skin qualities, BioScience Laboratories uses the latest scientific instrumentation:

- Tewameter -- measures rate of transepidermal water loss, an indicator of damaged skin
- Corneometer -- measures epidermal water content, an indicator of dryness and damaged skin
- Visioscan -- measures several qualities of the skin, such as scaliness and wrinkling, by means of digital scanning and computer analysis of the resulting image
- Digital Photography -- provides visual display of the skin for subjective pre-/post-application comparisons
- Dsquake® tab – provides an indicator of dryness, harvests and preserves for enumeration epidermal squames by adhesively lifting them from the skin.

BioScience Laboratories scientific personnel are trained extensively for visual evaluation of skin condition, and we can provide board-certified dermatologists for studies of products requiring dermatologically tested claims.

#### Irritation

The Skin Technology Center performs studies of the irritancy potential of topical antimicrobial products by means of multiple applications (15 or more) of a product beyond those necessary to demonstrate the antimicrobial efficacy of a healthcare personnel hand cleanser per the FDA Tentative Final Monograph [FR 43:4, 06 Jan 78, p. 1244]. The additional applications are not preceded by applications of the challenge bacterial suspension. The evaluations are performed visually and, in some studies, by means of the instrumentation described above.



### Skin Technology Testing

#### Sensitization

The BioScience Laboratories Skin Technology Center provides sensitization testing (potential for induction of Type IV allergy) per the Modified Draize Test, as required by the FDA.

The method requires that the product and its vehicle (product without active principle) be tested. During the Induction Phase of testing, test materials are applied to skin sites on the upper backs of 200 subjects and patched three times per week for three weeks, the same sites of application each time, for a total of nine applications. Patches remain in place 48 hours at a time on weekdays and 72 hours on weekends. Evaluation and scoring of skin reactions are performed and recorded at the time of each patch removal. The Induction Phase is followed by a Rest Phase of two weeks duration, during which no product applications are performed. Then, during the Challenge Phase, materials are applied to new skin sites on the back and patched for a 48-hour period of exposure, at the end of which patches are removed. The challenge sites are evaluated 30 minutes and 24, 48, and 72 hours after patch removal for evidence of allergic reaction.

#### Cumulative Irritation (RIPT)

The Skin Technology Center performs the Repeat Insult Patch Test (RIPT) for cumulative skin irritation, as required by the FDA.<sup>1</sup>

The method requires that the product and its vehicle (product without active principle) be tested, along with a high-irritancy control material (generally, sodium lauryl sulfate, or SLS; also known as sodium dodecyl sulfate, or SDS), and a low-irritancy control material (e.g., 0.9% saline), by applying small quantities of the materials to single sites on the skin of the upper back of 30 or more subjects each day for 21 days and occlusively patching each site while the material is wet. The degree of irritation at the sites is scored by a trained evaluator (BioScience Laboratories personnel and/or a licensed dermatologist) for degree of erythema/vesiculation/peripheral extension each day prior to reapplication of the materials.

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<sup>1</sup> FDA/CDER Guidance for Industry, *Skin Irritation and Sensitization Testing of Generic Transdermal Drug Products*, December 1999.

### Virology Testing

BioScience Laboratories assists clients with new product development, R&D projects, marketing claims, and supporting EPA, FDA, EU, and Health Canada label claims. Our virology laboratory personnel are well-trained on the various ASTM and EN standard methods and provide clinical and in vitro services including:

|                            |                                    |
|----------------------------|------------------------------------|
| Disinfectant Studies       | Time-kill Kinetic Studies          |
| Fingerpad Method (in-vivo) | Studies using in-vitro skin models |
| Handrub Method (in-vivo)   |                                    |

### Virology Disinfectant Studies

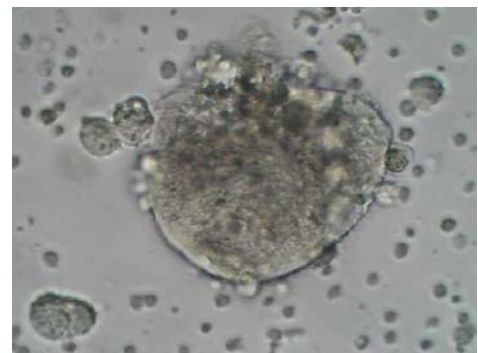
These studies are designed to provide virucidal efficacy data for disinfectant products challenged with various viruses. Testing is performed based on a modification of the AOAC Official Method 961.02, Germicidal Spray Products as Disinfectants (17th Edition, 2000), as specified by the U.S. Environmental Protection Agency requirements set forth in the Pesticide Assessment Guidelines, Subdivision G: Product Performance.

### Virology Time-Kill Kinetics

The virucidal suspension test (in vitro time-kill method) is based on the ASTM Standard Method E 1052 for evaluating the antiviral properties of test formulations when challenged with virus strains of interest. BioScience Laboratories has developed methods designed for high-throughput screening evaluations of virucidal compounds based on the suspension test method. These evaluations will allow our customers to screen multiple concentrations of products to determine which formulation is the most effective before conducting the testing required for regulatory approval.

### Virology Library

The BioScience Laboratories Virology Laboratory maintains over thirty virus strains including Hepatitis A, Human Immunodeficiency Virus (HIV-1), Poliovirus, Rotavirus, and six strains of Influenza. All Viruses have been validated internally according to Good Laboratory Practice Standards (GLPs), as required by the FDA and EPA.



HIV-1 MN Syncytia C8166

## GLP/GCP Product Efficacy and Safety Testing

### In-Vitro Microbiology Testing

The BioScience Laboratories personnel are well-trained on ASTM, AATCC, AOAC, CLSI, and EN standard methods. In vitro services include:

|                         |                                       |
|-------------------------|---------------------------------------|
| MIC/MBC                 | Preservative Efficacy Test            |
| Time-Kill Kinetics      | Biofilm Prevention and Removal        |
| Zone of Inhibition      | Clean Room Disinfectant Validation    |
| Custom Efficacy Studies | Medical Device Antimicrobial Efficacy |

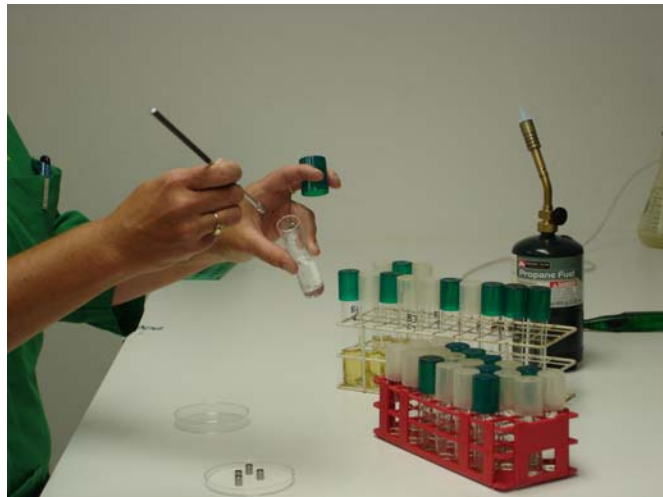
BioScience Laboratories has been approved by the Center for Disease Control and Prevention (CDC) to test strains of Vancomycin-resistant *Staphylococcus aureus* (VRSa), in addition to many strains of methicillin-resistant staph (MRSa) and other drug-resistant species of bacteria and yeasts that are important nosocomial pathogens.

#### MIC/MBC

These types of studies define a test material's potency in terms of the concentration at which it will inhibit growth of (Minimum Inhibitory Concentration, or MIC) or kill (Minimum Bactericidal Concentration, or MBC)  $5 \times 10^5$  (500,000) challenge microorganisms during a 18 to 20 hour period of incubated ( $35^\circ \pm 2^\circ \text{C}$ ) exposure.

#### Time-Kill Kinetics

These types of studies are referred to as "suspension tests" because a measured volume of the suspension of challenge bacteria or fungi is transferred into a liquid test material, dilute or "neat," to determine how rapidly the challenge species are killed. The microorganisms are exposed to the test material for exact times specified by the protocol, after which a measured quantity of the test material/species suspension is transferred to a neutralizing fluid that is non-toxic to the challenge species and proven effective for stopping the antimicrobial activity of the test material. These same procedures are applied, in principle, to testing surface-active antimicrobials per ASTM and AATCC methods.



Disinfectant Time-Kill Testing



### In-Vitro Microbiology Testing

#### Preservative Efficacy Test

The majority of cosmetic products include as part of the formulation one or more ingredients intended to function as preservatives intended to prevent growth of microbial contaminants. BioScience Laboratories tests the effectiveness of the preservatives according to the specifications of the *U.S. Pharmacopeia Method 51, Antimicrobial Effectiveness Testing* and ASTM Standard Method E 640.

#### Biofilm Prevention and Removal

BioScience Laboratories tests formulations for their ability to prevent biofilm formation and/or treat preexisting biofilms using the CDC Reactor, the Drip Flow Model, or the MBEC™ P & G assay. Qualitative and quantitative analysis of biofilms is available, including the application of confocal scanning laser microscopy (CSLM) and scanning electron microscopy (SEM).

#### Zone-of-Inhibition

This diffusion test is used to evaluate the –static/-cidal activity of water-soluble, leachable antimicrobial formulations that will diffuse into a nutrient agar medium. Selected challenge species are inoculated onto the surface of agar plates, and the test materials are laid on top or pipetted into wells cut into the agar. Following incubation, the “zones” of “no growth” are measured.

#### Clean Room Disinfectant Validation

BioScience Laboratories performs cleaning validation studies for which AOAC-like methods are designed to appraise the ability of disinfectant products used in specific cleaning routines to eliminate bacteria and/or fungi from surfaces of interest to the Sponsor. Each study is custom-designed to meet the Sponsor's needs.

#### Medical Device Antimicrobial Efficacy

The in-vitro microbiology laboratory performs Quantitative and Qualitative assays to measure the antimicrobial activities of medical devices, components, and surface-active materials treated with antimicrobial agents.

#### Custom Efficacy Studies

BioScience Laboratories specializes in designing the right efficacy study to meet the product's unique label claims. Custom studies can be designed for disinfectants, cleaning products, medical device materials, disinfectant processes, and more.



## GLP/GCP Product Efficacy and Safety Testing

### Wound Care

BioScience Laboratories now offers a program for product differentiation of wound dressings that provides the data to increase your market share. The results of our services -- **Antibacterial Evaluation, Absorbency Studies** and determination of **Moisture Levels (Normal and Increased)** -- will provide you with the data to definitively show your wound dressing is the best in its class.

With the support of clinical and in-vitro data, you will be able to show your customers that your product:

- is comfortable
- holds moisture
- adheres to the skin
- can be worn for days
- has antimicrobial efficacy
- does not cause irritation
- does not stick to the wound
- does not hurt to remove



**"You have completed your 510K and received approval to market your product. Now how can you say your product is better than the competition? The answer is to complete a product differentiation study with BioScience Laboratories." -- Daryl Paulson, Ph.D, CEO of BioScience Laboratories**

Contact [Dr. Paulson](mailto:experts@biosciencelabs.com) to learn about product differentiation studies for wound dressings.

## GLP/GCP Product Efficacy and Safety Testing

### Safety Testing

BioScience Laboratories' Skin Technology Center offers a broad spectrum of clinical testing services for evaluating in-use safety of products by means of standard, validated protocols. The clinical laboratory is equipped with a multi-port Solar Light Simulator with adjustable wavelengths for use in Phototoxicity and SPF studies.

- Cumulative Irritation
- Skin Sensitization
- In-Use Evaluations
- Photosensitization
- Photoirritation
- Phototoxicity
- Photoallergenicity



Solar Light Simulator

The elimination of testing using animals, with all of its labor, expense, and social issues, is just one of the many benefits that BioScience Laboratories can provide. BioScience Laboratories uses an in-vitro methodology to evaluate Cosmetics, Surfactant-based Products, Pharmaceuticals, and Chemicals as well as products for Personal Care, Hair Care, and Household Cleaning. The In-Vitro Laboratory uses the ET-50 method and the EpiDerm and EpiOcular tissue models prepared by the MatTek Corporation, a company leading the development of alternatives to animal testing methods. These models, derived from normal human cells, will not have the test results compromised by the species extrapolation error inherent in all animal studies.

- Ocular Irritation
- Dermal Irritation
- Dermal Corrosion
- Oral Irritation
- Cytotoxicity



In-Vitro Safety Testing



## GLP/GCP Product Efficacy and Safety Testing

### **Cumulative Irritation (In-vivo)**

We perform the Human Repeat Insult Patch Test (RIPT) for cumulative skin irritation in accordance with the *FDA/CDER Guidance for Industry, Skin Irritation and Sensitization Testing of Generic Transdermal Drug Products, December 1999*. The method requires that the product and its vehicle be tested, along with a high-irritancy control material and a low-irritancy control material by applying small quantities of the materials to single sites on the skin of the upper back of 30 or more subjects each day for 21 days and occlusively patching each site while the material is wet. The degree of irritation at the sites is scored by a trained evaluator for degree of erythema/vesiculation/peripheral extension each day prior to reapplication of the materials.

### **Sensitization (In-vivo)**

Sensitization testing is conducted using the Modified Draize Test in accordance with the *FDA/CDER Guidance for Industry, Skin Irritation and Sensitization Testing of Generic Transdermal Drug Products, December 1999*. During the Induction Phase of testing, test materials are applied to skin sites on the upper backs of 200 subjects and patched three times per week for three weeks, the same sites of application each time, for a total of nine applications. Patches remain in place 48 hours at a time on weekdays and 72 hours on weekends. Evaluation and scoring of skin reactions are performed and recorded at the time of each patch removal. The Induction Phase is followed by a Rest Phase of two weeks duration, during which no product applications are performed. Then, during the Challenge Phase, materials are applied to new skin sites on the back and patched for a 48-hour period of exposure, at the end of which patches are removed. The challenge sites are evaluated 30 minutes and 24, 48, and 72 hours after patch removal for evidence of allergic reaction.

### **Ocular Irritation (In-Vitro)**

BioScience Laboratories uses MatTek's EpiOcular tissue and the MTT ET-50 testing method to predict the irritating effects of test articles, as an in-vitro alternative to the Draize (rabbit eye) test. The EpiOcular evaluation is 3-10 times more sensitive than the Draize in accurately predicting ocular irritation, making it a great option for testing your product.

### **Dermal Irritation/Corrosion (In-Vitro)**

BioScience Laboratories employs MatTek's EpiDerm model for this testing. EpiDerm is mitotically and metabolically active and closely approximates the responses to products exposure exhibited by its in-vivo counterpart, the Human Repeat-Insult Patch Test.



## GLP/GCP Product Efficacy and Safety Testing

### Statistics

At BioScience Laboratories, we believe the accurate interpretation of study results is critically important to a study's value. Hence, the results from studies that include a statistical design are more accurate than are those studies with no statistical approach. Hence, we promote a statistical design at the study's beginning. Just as a single type of microbiological evaluation is not valid for every product, statistical analysis, too, must be specifically designed in order to allow for smaller sample sizes, unambiguous results, and lower overall cost.

BioScience Laboratories, Inc. uses Analysis of Variance (ANOVA), factorial designs, regression analysis, including logistic regression, nonparametric statistics, *t*-tests, proportions, factorial designs, response surface methodology, and meta-analysis. However, the primary statistical model used at BioScience Laboratories is Analysis of Variance (ANOVA). For our clients without extensive experience in statistical application, we can also assist. Your data can be presented with a simplified approach using the Analysis of Means (ANOM). ANOM sets 95% decision levels and uses the mean values only. If any values exceed the decision levels, those factors are different. Download the BioScience Laboratories, Inc. poster "[Should you perform statistical analysis?](#)" for a complete discussion.)

**Analysis of Variance (ANOVA)** – For example, suppose you want to compare two-factor components, 1) three products and 2) four sample times. Then, the two-factor ANOVA is:

$$\hat{y} = A + B + (A \times B) + e$$

where:

$\hat{y}$  = Colony Counts (Log<sub>10</sub> scale)

A = Products

1, if Product 1

2, if Product 2

3, if Product 3

B = Time

1, if Baseline

2, if 30 seconds

3, if 5 minutes

4, if 8 hours

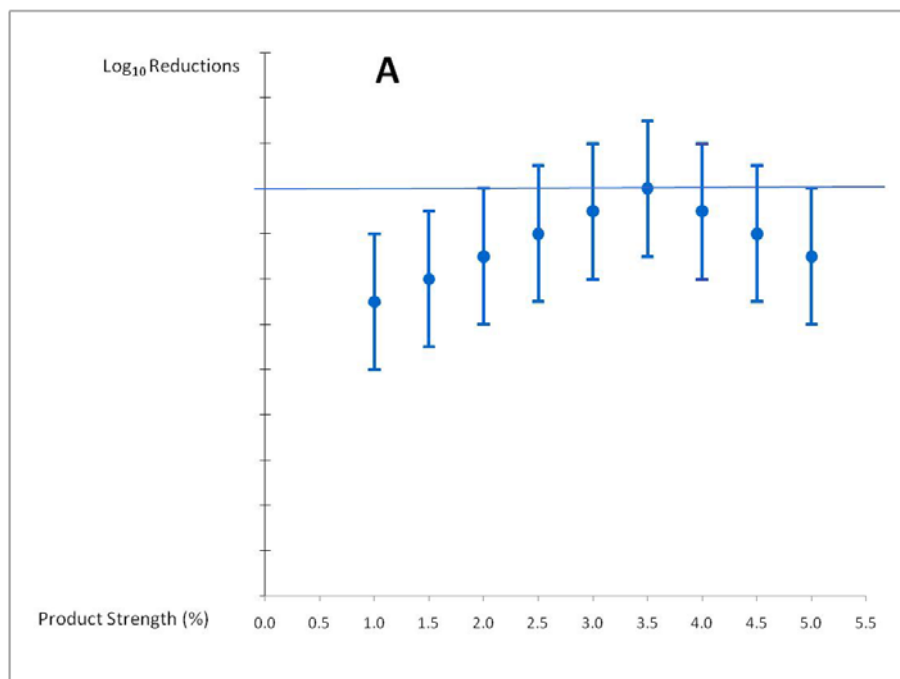
A x B = Interaction Term

e = Error Term

## GLP/GCP Product Efficacy and Safety Testing

**Analysis of Means (ANOM)** – Many people experience fear, which leads to a misunderstanding of statistics. They simply do not know what it entails. If that is a problem you face, let us know. We will also compute the ANOMs to address this problem. Once you read the ANOM section, you will be better able to understand the ANOVA.

**Response Surface Methodology (RSM)** – This methodology may be useful to graphically display the results of your pilot studies. RSM is particularly valuable when you collect only a small number of samples and cannot otherwise detect any differences. Many times, a customer wants to evaluate different concentrations, applications, etc. of a product to see if the kill rates are different. The problem is that they only use a few replicates. Using a statistic like the Analysis of Variance (ANOVA), no difference would be detected, because the error term is so large, due to the small sample size (Figure A).

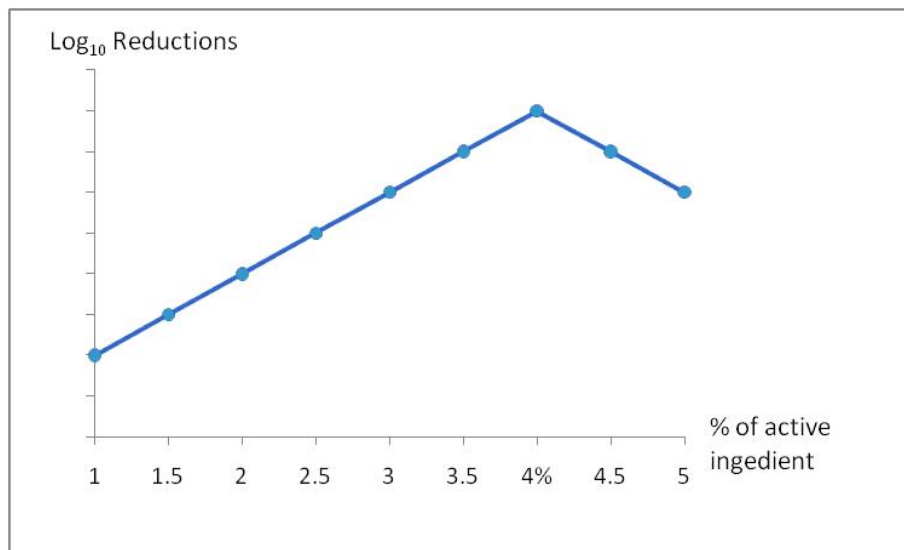


**Figure A - Compared Confidence Intervals**

All product strengths are the same, because the 95% confidence intervals overlap. The way around this is to look specifically at the mean (average) values and use Response Surface Methodology (Figure B). For instance, you can see in this example, the kill rates increase until 4.0% is reached, but then they decrease. Using the response surface methodology, we would choose the 4% concentration and test to verify that it is, in fact, the best with the 3.5% and the 4.5% concentrations.



## GLP/GCP Product Efficacy and Safety Testing



**Figure B - Response Surface Methodology**

**Meta-Analysis** – BioScience Laboratories, Inc. has always been capable in the realm of biostatistics, and now we offer a new service: meta-analysis. Meta-analysis is the process of integrating the data from multiple individual studies performed by different technicians at different times at different laboratories into one unified study.

By using meta-analysis, you can have the various non-FDA studies performed on your product integrated into one study to make sense of the results. This is important, for example, when one researcher finds your product to be very good, and another finds it to be not acceptable. Instead of favoring one researcher and discounting the other, meta-analysis integrates all the studies' results into one final result.

For FDA studies, you likely will have performed more than one study on your product. Perhaps two studies were done, one pivotal and the other, confirmatory. Meta-analysis can integrate the results from these for inclusion in your FDA submission packet.

To learn more about Meta-Analysis, download a copy of Dr. Paulson's whitepaper entitled [Some Basic Points Concerning Meta-Analysis and Clinical Trials](#).

The models are usually more difficult to make sense of, but that is why BioScience Laboratories is here to help you. For more information on Statistical Analysis, contact BioScience Laboratories, Inc. [CEO Daryl Paulson, Ph.D.](#) at 877-858-2754.