
Microbiologics
BIOMATERIAL
DESIGN
SERVICES
WE CREATE CONFIDENCE IN SCIENCE

www.microbiologics.com

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INTRODUCTION

TRUSTED EXPERTISE IN BIOMATERIAL DESIGN AND TESTING SERVICES

Microbiologics has a proven track record of partnering with diagnostic and biopharmaceutical companies to successfully bring new diagnostic instrumentation, assays and therapeutics to market.

We are the world's leading experts and go-to collaborators in designing biomaterials of all types that are critical for assay development, drug development, vaccine screening, quality control testing and beyond. With each engagement, we apply our inventive spirit, deep expertise, vast resources and unparalleled support to create the best products and services for our fellow scientists. Because we never lose sight of our shared mission to protect the health and safety of people around the world through continuous scientific innovation.

CONNECT WITH OUR TEAM

Our knowledgeable team is ready to answer your questions and get started with designing a customized program to fit your unique project needs. As a trusted industry partner with more than 5 decades of experience, we can provide valuable insights and guidance to improve outcomes and accelerate commercialization.

Contact Business Development

Phone	1.320.253.7400
US Toll Free	1.800.599.2847
Email	businessdevelopment@microbiologics.com

ANTI-INFECTIVE TESTING:

ANTIBACTERIAL AND ANTIFUNGAL

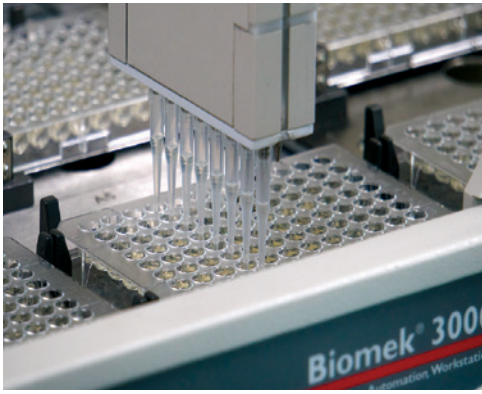
DELIVERING STANDARD AND CUSTOM ASSAYS

We provide quality antibacterial and antifungal testing services integral to the discovery, development, and registration of new antimicrobial agents.

Our testing services include screening/susceptibility testing, lead characterization studies, test method development, and characterization/ID. Our scientists have a broad range of technical expertise in antimicrobial research and development, from discovery all the way through the regulatory submission and review process. Contact us for standard and custom assays to meet your unique needs.

Screening/Susceptibility Testing

We offer high throughput screening, primary and secondary profiling, and a repository of clinical isolates.



Repository of Clinical Isolates

Recent clinical isolates of prevalent Gram-positive and negative pathogens, including anaerobic pathogens along with fungi available for screening. Isolates with genetically characterized resistance mechanisms (e.g. KPC, NDM-1, OXA) also available.

High Throughput Screening

Microbiologics has conducted a variety of high throughput screens of compound collections using the Biomek 3000/Biomek FX platforms. We offer whole cell screens of bacteria, yeast, and fungi utilizing compound collections arrayed in 96-well plates. In addition, we offer end points of whole cell screens which can include either MIC values, absorbance of culture readings using a Spectramax, or Alamar Blue readings, as well as enzymatic screens using compound collections.

Primary Profiling (Spectrum of Activity) and Secondary Profiling (MIC50/MIC90)

To characterize the spectrum of activity of the lead compound or further differentiate between lead compounds based on MIC, primary profiling is offered by performing susceptibility testing on a diverse group of clinically relevant Gram-positive and Gram-negative pathogens, including anaerobes and fungi if applicable. Secondary profiling studies are then conducted to understand the activity of the lead compound against representative populations of target pathogens at volumes sufficient to understand the MIC50/MIC90.

Susceptibility Testing Methodology (CLSI M2, M7, and M100)

- **Broth Microdilution MIC Testing:** Custom panels are created using a 96-well format. Compounds can be provided as dry powders or as solutions.
- **Agar Dilution MIC Testing:** Compounds can be provided as dry powders or as solutions.
- **Disk Diffusion Testing:** Using manufactured disks for disks made in house.

LEAD CHARACTERIZATION STUDIES

Microbiologics provides lead characterization studies including mechanism of action, in vitro pharmacodynamics, and development of resistance.

Mechanism of Action Studies

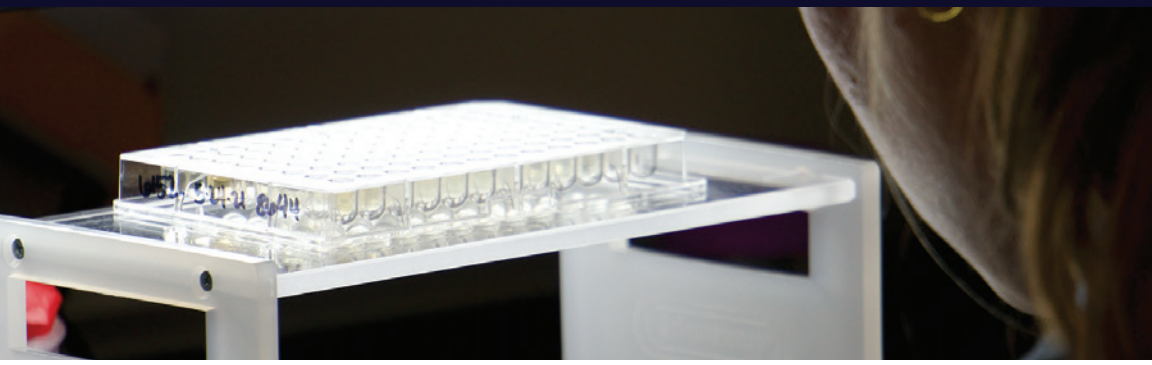
Determining the mechanism of action (MOA) of new agents is essential to the discovery process and is also a required component of the Investigational New Drug (IND) filing. Microbiologics utilizes a variety of whole cell, molecular, and biochemical techniques to determine the MOA. We provide macromolecular synthesis inhibition, transcription/translation assay (cell-free), cell-lysis assay (ATP leakage, RBC lysis), and enzyme assays (IC50 studies).

In Vitro Pharmacodynamic Studies

Following CLSI protocols, Microbiologics conducts an assessment of an antimicrobial agent's ability to kill or suppress growth of target organisms using the following assays (assays conducted in accordance with CLSI M26, where applicable): time-kill MBC/MFC, serum bactericidal titer, and post-antibiotic effect.

Development of Resistance Studies

An assessment of the ability of bacteria to develop resistance to new agents is an important early consideration in the discovery phase. Microbiologics provides spontaneous mutation frequency (SMF) assays and serial passage assays.



TEST METHOD DEVELOPMENT

We provide tier 1 quality control and parameter studies, tier 2 broth/agar MIC and disk quality control studies, disk diffusion development, and method correlation studies.

TIER 1

Quality Control and Parameter Studies (CLSI M23)

Evaluation of testing parameters on in vitro activity (pH, inoculum size, cation concentration, protein binding/activity and serum, etc.).

Development of preliminary Tier 1 Quality Control Ranges at a single test laboratory in accordance with CLSI M23.

TIER 2

Broth/Agar MIC and Disk CLSI M23 Quality Control Studies

Multi-laboratory study to establish QC ranges of new agents in accordance with CLSI M23 and including presentation to the QC working group.

Disk Diffusion/Alternate Test Methods Development and/or Evaluation

Method Correlation Studies

(broth vs. disk, agar vs broth, etc.)

CHARACTERIZATION/ISOLATION/ID

We provide bacterial and fungal culture identification, isolation and molecular biology services.

Culture

Isolation of a variety of organisms from a given test sample across a variety of matrices such as skin swab, fecal, urine, tissue, etc.

Bacterial/Fungal ID

- Bruker MALDI Biotyperv
- 16S rRNA gene sequencing
- DuPont Riboprinter
- Crystal ID (BBL Crystal ID)

Molecular (PFGE, PCR, Sequencing)

Our team is highly experienced in the application of a variety of molecular biology techniques that aid the discovery and development process:

- PCR of genes involved in resistance and/or target identification
- DNA sequencing for mutational analysis or for 16S rRNA identification
- Bioinformatics to align sequences and provide a comparison of reference genes
- Pulsed field gel electrophoresis for analysis of patient isolates (treatment failures) and epidemiological typing (e.g. USA typing of S. aureus)

ANTI-INFECTIVE TESTING:

ANTIVIRAL TESTING

TESTING VACCINES AND THERAPEUTICS AGAINST VIRUSES

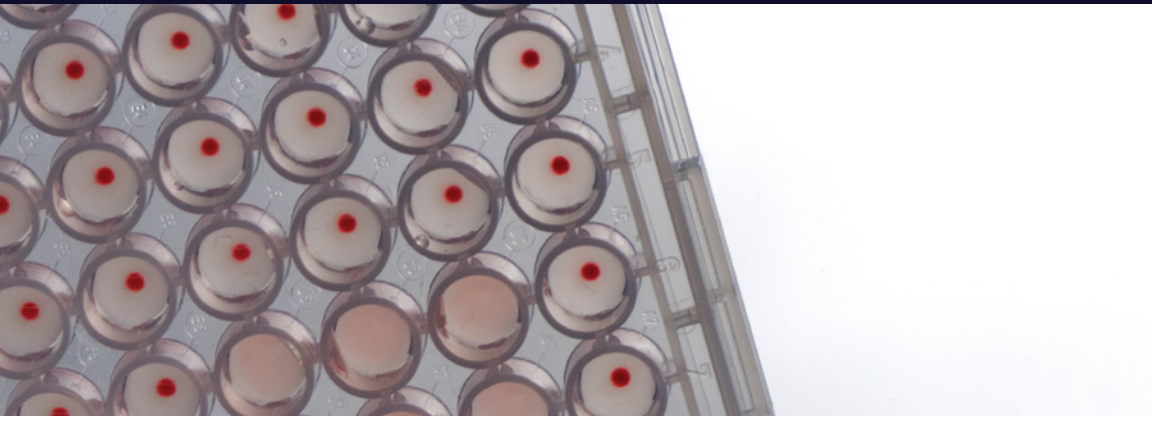
With deep expertise and experience in the field of virology, we offer a comprehensive menu of testing services to support antiviral drug and vaccine development for biopharma companies worldwide.

As a leading Contract Research Organization, we have developed a proven process for in-vitro testing of these compounds to determine their potential efficacy and inform optimal dosing regimen.

Select Assays Performed:

- Inhibition of infection
- Titer reduction assay
- Plaque assay
- Plaque inhibition assay
- Inhibition of specific viral enzymes such as influenza neuraminidase
- Neutralization of infectivity by antibody or antibody like molecules
- TCID50 assay
- IC50 assay
- Fluorometric neuraminidase assay
- Hemagglutination assay
- Hemagglutination inhibition assay
- Microneutralization assay
- EID50 assay
- SRID assay
- Textiles and plastics assay (AATP)

VIRAL ASSAY DEVELOPMENT SERVICES



DEVELOPING ASSAYS FOR PRODUCT RELEASE TESTING

Our team of approachable experts will work with you to develop assays for your product release testing. With your virus, we will develop the assay for detecting replication competent virus.

Plaque Assay – Determines infectious virus particles in a sample. Virus is sequentially diluted and dilutions are plated on susceptible cells. Cultures are overlaid with nutrient agarose and plaques or pocks formed by cytopathic viruses can be quantitated.

Plaque Inhibition Assay – This assay is requested frequently to test the efficacy of antiviral drug candidates. Drug is included in the agarose overlay and if effective will reduce the size and/or number of plaques observed.

TCID50 Assay – Quantitates infectious virus particles in a sample. Virus is sequentially diluted and dilutions are plated in replicate wells of susceptible cells. The TCID50 (50% Tissue Culture Infectious Dose) is the dilution of virus which will produce pathological change in fifty percent of cell cultures inoculated at a particular dilution. TCID50 values are normally very close to the Plaque Assay values for most cytopathic viruses.

IC50 Assay – This assay is requested frequently to test the efficacy of antiviral drug candidates. The drug is included in the agarose overlay and if effective will reduce the size and/or number of plaques observed.

Fluorometric Neuraminidase Assay – This assay measures a fluorogenic substance released by the active influenza neuraminidase enzyme. It is used to screen for antiviral drug activity against neuraminidase and determine the 50% Drug Inhibitory Dose.

SRID Assay – The SRID Assay is used to quantitate the amount of antigen in a sample. Antigen concentration is determined by the degree of antigen/antibody precipitate around a well into which detergent solubilized virus is placed. A standardized antigen preparation and a specific polyclonal antibody are required.

Hemagglutination Assay – Detects the presence of certain viruses that agglutinate red blood cells. This assay can be used to quantitate or type many virus strains. For example, influenza virus possesses the capacity to agglutinate red blood cells of specific animal species. It does this by cross linking sialic acid residues on the surface of red blood cells. In some labs, the hemagglutination assay is preferred for detecting influenza virus growth. The hemagglutination titer of an influenza virus sample can be determined when dilutions of virus are mixed with human or turkey red blood cells. The presence of virus will hold the red cells in a diffuse matrix and prevent them from settling out to the bottom of the well.

Hemagglutination Inhibition Assay – This test is based on the inhibition of vial agglutination by a specific antibody and can be used for virus identification or for assay of antibodies. This assay is still used as a standard for measuring the efficacy of influenza vaccines and potency of neutralizing antibodies.

Microneutralization Assay – An excellent test to determine if an antibody may have therapeutic effects. This assay measures the ability of an antiserum to inhibit cytopathogenic effect of about 100 virus infectious units. The antibody/virus mixture is plated on susceptible cells and inhibition is tracked.

EID50 Assay – The 50% Egg Infectious Dose assay is carried out in the same manner as a TCID50 where every well is represented by a unique egg. Each virus dilution is injected into replicate eggs which are tested after a period of incubation for signs of virus growth. With influenza, we use the hemagglutination (HA) assay. We utilize other immunological tools for the detection of other viruses.

Textiles and Plastics Assay (AATP) – The antiviral activity of textiles and plastics (AATP) test measures antiviral activity of plastics and other non-porous surfaces treated with antiviral agents. This assay will determine the log reduction of virus compared to the customer supplied untreated control.

CONTRACT RESEARCH AND MANUFACTURING ORGANIZATION (CRMO) SERVICES

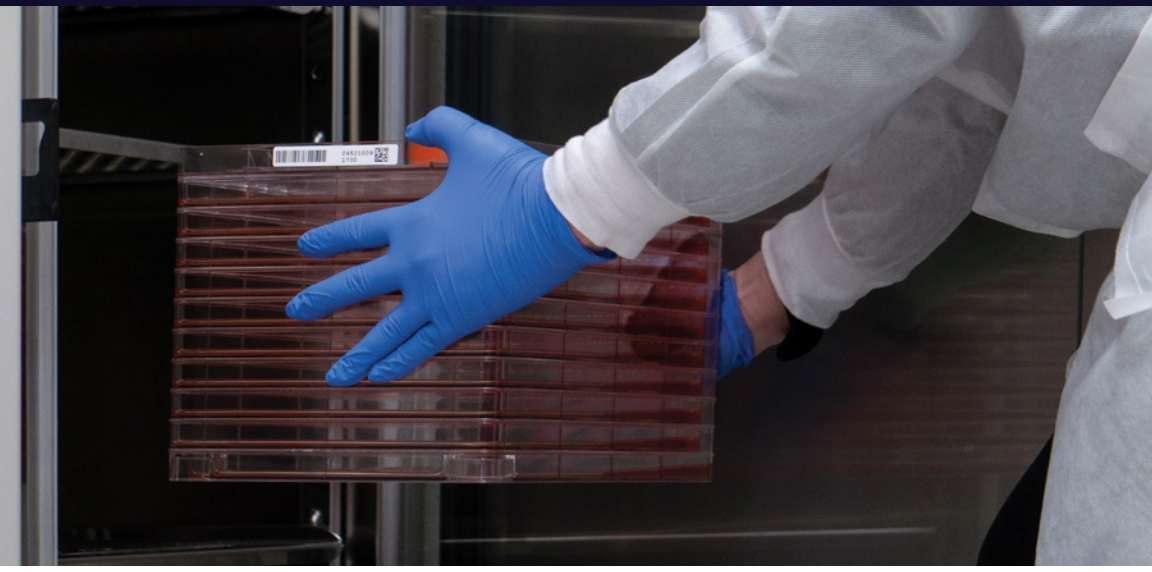
DRUG DEVELOPMENT TESTING PROGRAMS DESIGNED WITH YOUR GOALS IN MIND

Microbiologics offers a full array of services for biopharmaceutical organizations to develop and bring new anti-infective drugs, therapeutics and vaccines to market safely and efficiently.

Our approachable team of experts will work with you to develop a custom program around your research goals.

- Post market surveillance studies
- Efficacy immunogenicity studies
- Immunoassay development within ELISA platforms
- Testing with viral and bacterial neutralization assays across multiple platforms
- Biomaterials and testing for a broad range of therapeutics and assay development
- Support of influenza and coronavirus vaccine trials
- Biosafety Level 1, 2, and 3 laboratories
- Expertise in biomaterial growth and characterization with highly specific concentrations
- Developing targeted biomaterials as whole genetic sequences, inactivated strains for synthetic nucleic acids
- Consulting services throughout the development process
- Services support Good Laboratory Practices (GLP) and Good Manufacturing Practices (GMP)
- Global Virology Center holds ISO 13485:2016 certification

VIRAL STOCK PRODUCTION



HIGH TITER VIRUS PRODUCTION AND REVERSE GENETICS

We are the go-to collaborators for growing, titering, and purifying viruses from a variety of species.

We are classified to handle BSL-2 and BSL-3 pathogens in our certified biocontaminent laboratories. We are skilled in making both wild type and recombinant viruses and can grow viruses from small to large scale.

Virus Products:

- Crude infected cell extracts
- Infectious virus preparations
- Highly purified infection virus preparation
- Quantitated virus samples for use in device validation
- Engineered virus containing your gene of interest
- Quantitated viral proteins and nucleic acids
- Viral RNA and DNA
- Viral protein extracts
- Inactivated virus

HIGH-TITER VIRUS PRODUCTION

Our highly specialized team has extensive knowledge and skill in growing both wild type and recombinant viruses.

Below are just a few examples of the viruses we have in our vast library of biomaterials. We can also help source additional virus species of interest, or if you have your own strain, we can help you securely send it to us.

Commonly Requested Viruses Include:

- Adenovirus
- Influenza A & B
- Herpes
- Minute Virus of Mice
- Polio
- Respiratory Syncytial Virus
- Rhinovirus
- SARS CoV-2
- Varicella-Zoster Virus
- And Many More

Reverse Genetics

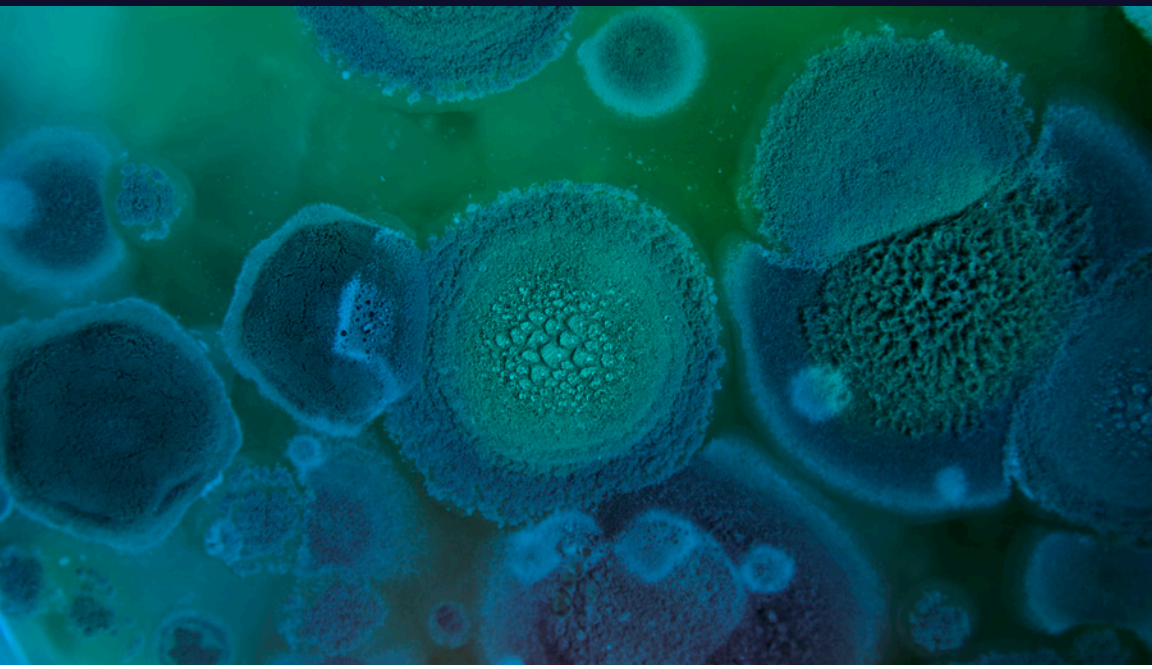
For drug discovery projects where mutations in viral polymerases or other viral genes are required for study, Microbiologics offers reverse genetics services. Using molecular biology techniques, reverse genetics enables production of viruses with intentional changes to existing genes, such as desired mutations. It also enables deletion of all or part of a viral gene, or addition of genes not normally found in the viruses. For example, a BSL-2 virus can be engineered to express glycoproteins from other viruses, including BSL-3 and BSL-4 viruses. Our team has experience developing reverse genetics systems for Influenza A and B, Vesicular stomatitis virus (VSV) and SARS-CoV-2.

MICROBIAL GROWTH AND PRESERVATION

CUSTOM MANUFACTURING BACTERIA/FUNGI, PARASITES, PHAGE, AND NUCLEIC ACID

We custom manufacture bacteria, fungi, parasites, phage, and nucleic acid.

Our versatile manufacturing capabilities allow us to design and produce customized solutions that alleviate your unique challenges. Whether you need a specific preservation method for bacteria and fungi, custom slides for parasites, ultra-filtrate high-grade purity for phage or multiple target copy numbers for nucleic acid, we've got you covered. Contact us with your needs, and we'll design a solution in the easy-to-use format you desire.



BACTERIA AND FUNGI

Microbiologics provides a variety of preservation methods for bacteria and fungi including lyophilization, liquids, spores and antigens, delivered in easy-to-use formats. Whether you need qualitative or quantitative material, genome copy numbers, inactivated material, microbiome, single strains or a combination of strains, we are ready to help you develop what you need for your custom project or IVD research program.

Formats

- Lyophilized pellet
- Lyophilized powder
- Liquid controls
- Spores
- Purified fungal antigens

Concentrations/Activity

- Qualitative or quantitative
- Total cell count
- CFU determination
- Genome copy# (inactivated or active)
- Single strain to combinatorial

Applications

- Custom
- IVD
- Research
- Microbiome

PARASITE

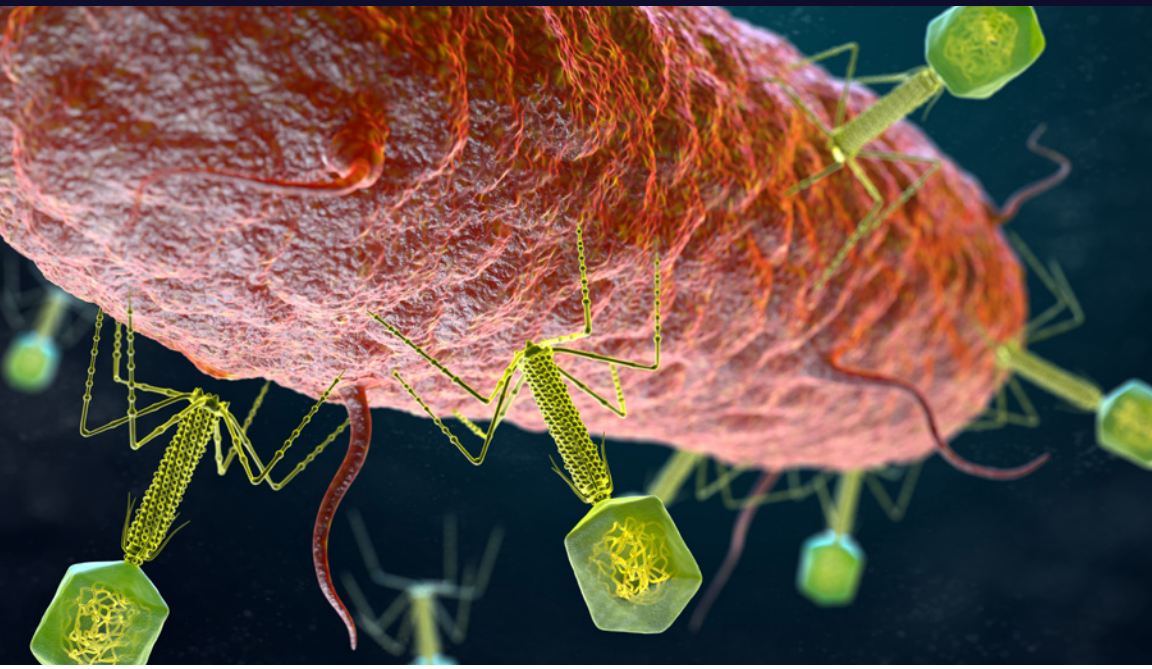
We develop custom slides and forms of suspension materials including genomic DNA and synthetic standards. We source material from other companies, create proficiencies, and develop complete product lines. We provide live and inactivated parasitic material and DNA nucleic acid solutions. Each solution is custom designed to meet our customers' unique requirements.

Formats

- gDNA
- Synthetic Standards
- Suspension Material
- Slides

Applications

- Custom
- Quality Control
- Research
- Proficiency



PHAGE

We provide MS-2, T4, T7, Q Beta, and Fr Coliphage in all forms of bacterial phage grown to your specified concentration. Whether you need a phage virus quickly in a crude format or in an ultra-filtrate high-grade purity, we will custom develop a solution that meets your needs. Contact us to learn more about how we can replicate a control virus for your testing requirements.

Species

- MS-2
- T4
- T7
- QBeta (Qβ)
- Fr Coliphage

Concentrations

- Qualitative
- Quantitative

Applications

- Custom
- IVD
- Research
- NGS

Purity

- Crude
- Ultrafiltrate
- PEG-NaCl
- Other Gradient Purified Phage Virus

NUCLEIC ACID

We partner with companies for their initial development studies. Our formats are designed for diagnostic and pathogen detection platform testing, and we develop concentrations in any desired target copy number. We work with gDNA, plasmid/synthetic DNA, and total RNA (bacteria, fungi, and parasites). Contact us with your list of strains.

Species

- Designed for diagnostic and pathogen detection platforms

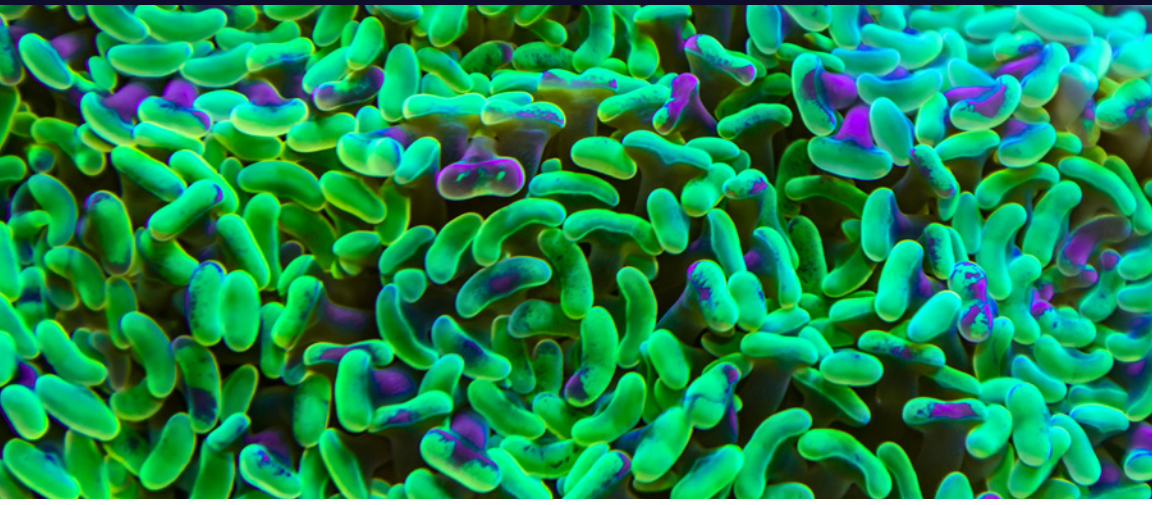
Concentrations

- Qualitative
- Quantitative (molar concentration, copy number)

Types

- gDNA
- Plasmid/Synthetic DNA
- Total RNA (bacteria, fungi, and parasites)

MICROBIOME



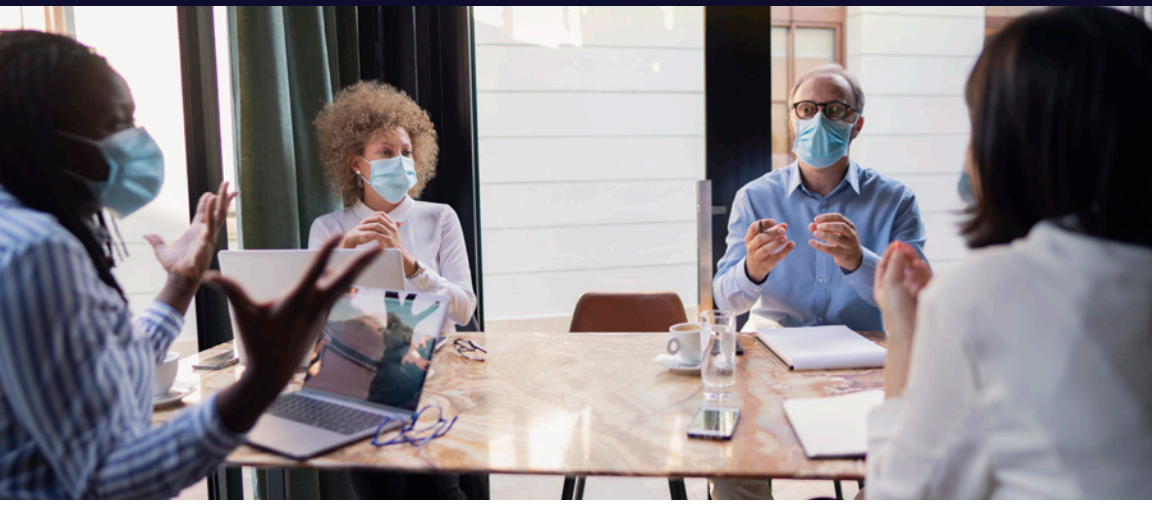
ISOLATION, EVALUATION, CHARACTERIZATION AND ENUMERATION

Researchers are just beginning to understand the complex world of the gut microbiome and how it affects human health.

We are proud to support this field of research and the opportunity it presents for improving healthcare. With more than 50 years of experience in propagating, manipulating, preserving and manufacturing biological materials, we offer a comprehensive menu of microbiome services.

- Isolation and testing of microorganisms that are constituents of the microflora (intestinal, fecal, skin, etc.)
- Evaluation of prebiotic impact on organisms in co-culture
- Characterization of probiotic or live bacterial product (LBP) strains
- Evaluating the effect of probiotics/anti-infectives on the levels of important members of the intestinal microflora
- Enumeration of viable bacteria from probiotic or LBP formulations

DIAGNOSTIC PARTNERSHIPS



CONTROLS DESIGNED FOR YOUR UNIQUE INSTRUMENT AND ASSAY

We partner with diagnostic manufacturers to create the highest quality controls for infectious diseases.

Each biological control is specifically designed for your instruments and assays, solving your unique challenges and meeting your customers' needs. We combine our extensive expertise, molecular biology technologies and world-class support services to produce the highest quality controls tailored to your specifications.

We develop easy-to-use products that accelerate commercialization and increase the adoption of your diagnostic assay in the market. We analyze your approach in the market and design a qualification program and ongoing control strategy tailored to your platform and assays. When you are ready to submit your 510(k), you will have a realized product that has been tested and developed, and have a guided path for launch.

DIAGNOSTIC PARTNERSHIPS

HOW IT WORKS

Design

We start each project by gaining a deep understanding of your business, your technology, and your customers' needs. Our R&D teams partner with you to design customized ready-to-use formats with a range of targets such as inactivated cultures, synthetic, or nucleic acid extracts.

Develop

We put our expertise to work, developing prototypes, making revisions, and creating final products to meet the unique needs of your customers. We offer an extensive menu of options in terms of targets, formats, and preservation techniques, allowing us to formulate the optimal solution for you.

Deliver

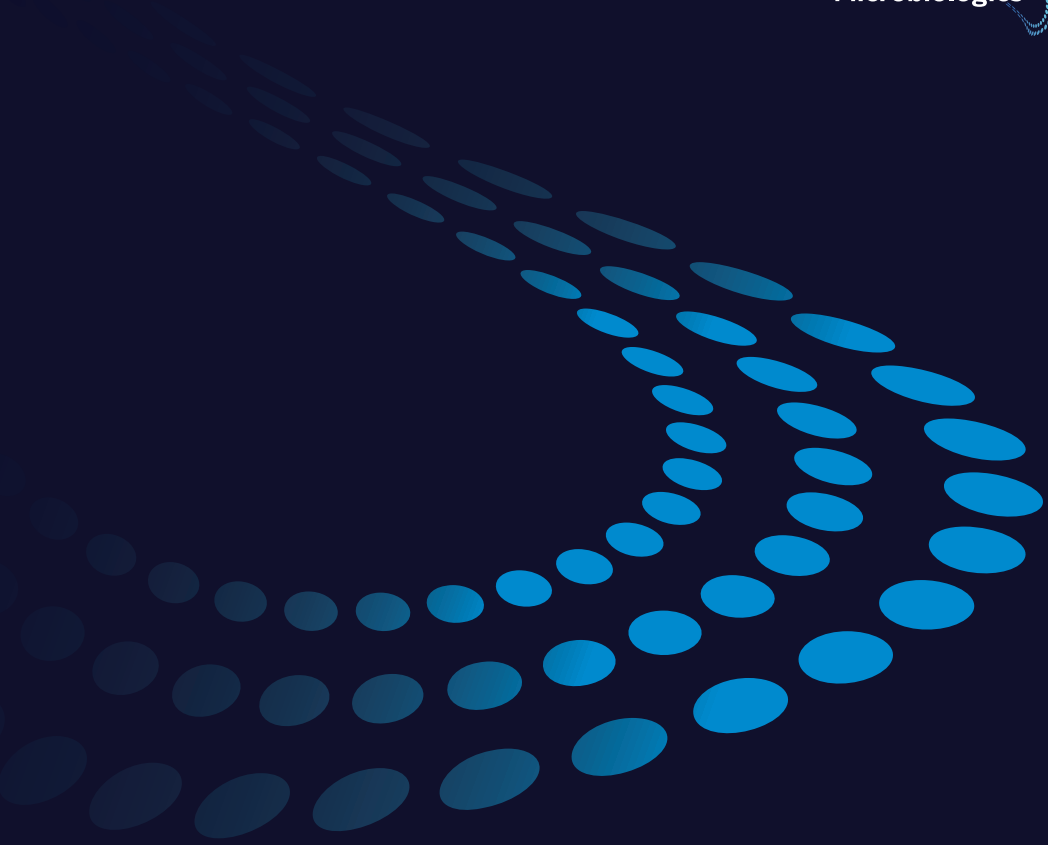
Supporting your strategy and business model for consumables, you and your customers receive the industry's best solutions for validation and quality control; which are promoted, sold and supported across the globe by the world's leading experts. We customize everything from product branding, labeling, instructions for use and packaging.

Why Microbiologics?

We are your experienced quality controls partners. We take a consultative approach to proactively guide customers down the right path. By leveraging our extensive expertise, state-of-the-art manufacturing capabilities, and a powerful distribution network, you can reduce your time to market and increase customer adoption.

- Access our extensive collection of biomaterials or provide your own isolate.
- Biomaterials are authenticated using polyphasic methods including AST, nucleotide sequencing, PCR, and MALDI-TOF MS.
- Our diverse control formats provide optimal efficiency in workflow and customer experience.
- Easy-to-use solutions that do not require refrigeration.
- An industry leading quality system reflects our ability to consistently design, develop and deliver biological controls of the highest quality.

Microbiologics®



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