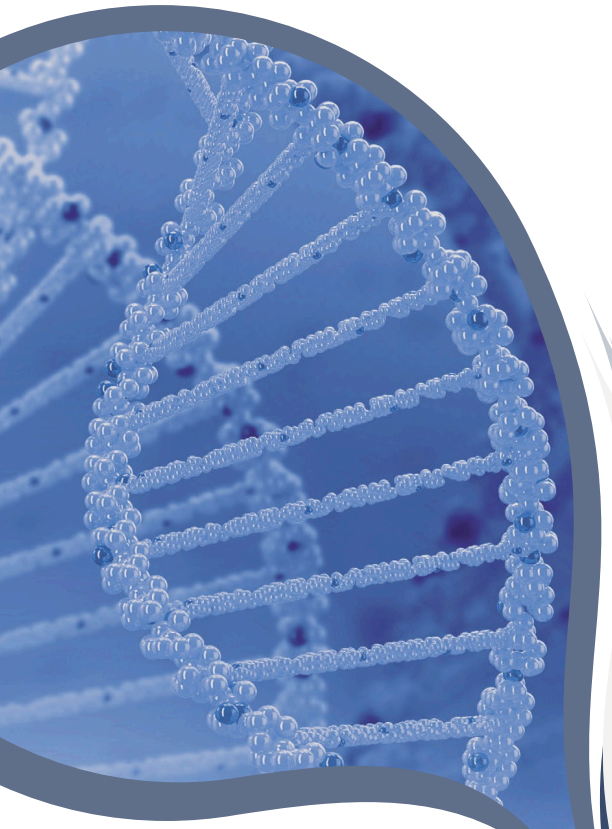

hylabs®

Service laboratories division - Tests Portfolio

2025

Services are applied to all sectors including: Cell therapy, pharma, biotechnology, medical devices, medical cannabis, Agtech, seeds and plants, hospitals, academia & research institutes.

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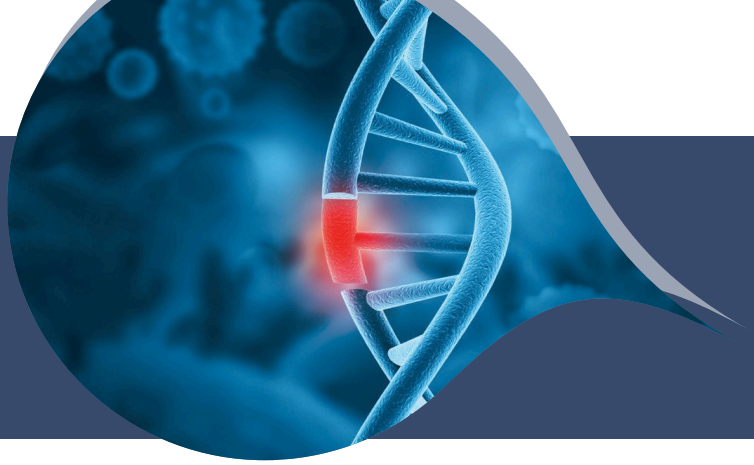


Molecular Biology Lab

Sanger sequencing - As a leading provider of genomic services, we offer our customers a full range of sequencing services using high-throughput and custom strategies. Projects are treated with the highest level of quality, integrity, and confidentiality. GMP certified.

NGS Sequence - The Next Generation Sequencing (NGS) lab, ISO9001 accredited, provides complete NGS solutions for any project. Whether it's your first NGS project or your hundredth, we will help you find the right NGS solution for your research. From planning the experiment to DNA/ RNA extraction, library prep, sequencing, and analysis we are here to help you.

Crispr analysis (guide SEQ, multiplex PCR, on-target) Amplicon design, sequencing, and analysis for on-target and off-target gene editing events. Validated protocols designed by Hylabs with increased sensitivity and detection compared to current methods.

Microbiome – 16S/ITS/18s/customized profiling - Processing a broad and diverse range of samples (environmental, tissue, fecal…) allows for the identification and relative quantification of the microbial community of a sample. Services include DNA extraction, library preparation, sequencing, and bioinformatic analysis of the data. We specialize in customized protocols for low biomass / hard to amplify samples.

Metagenomics – Whole genome sequencing of DNA extracted from various mixed/diverse population samples (environmental, tissue, cultured..) allows for the complete identification and relative quantification of the microbial community of a sample using de novo assembly of genomes and customized metagenomics analyses. Services also includes pathogen detection and identification.

Whole Genome and Exome Sequencing - Sequencing of whole genomes both small (virus, plasmid, bacteria, yeast, parasites…) and large (human, plant, mouse…) are performed by preparing libraries from the sample, sequencing, and analysis. Services include: DNA extraction, exome selection, library preparation, sequencing and customized Bioinformatic analysis. Services include: plasmid assembly, cell line contamination, snp/indel/CNV/SV analysis, mapping to reference genome, AMR resistance, serotyping, viral detection, and more.

Amplicon sequencing - For amplicon sequencing we utilize a two-step PCR protocol, to amplify your region of interest and add the adaptor and index sequences required for Illumina sequencing. Service includes primer design, first and second step PCR, sample QC, sequencing, and analysis. Samples can be sent at any stage of preparation and we will continue with them. Analyses include SNP/indel, consensus sequence, mapping to reference sequence, and on-target analysis of editing.

Transcriptome sequencing - RNAseq studies are performed to compare differential gene expression levels between different treatments, or to study splicing patterns or post-transcriptional modifications. Services include RNA extraction, poly-A selection, rRNA depletion, directional RNA library prep, sequencing, and analysis.

Targeted DNA/RNA sequencing /MLST - This procedure is used to amplify selected sequences and targets, such as multiplex pcr, or customized kits to measure in parallel multiple targets per sample. We utilize a special pipeline for customized primer design that allows all targets to be amplified in a single multiplex 2 step PCR. Steps include target design, DNA extraction, library preparation, sequencing and customized analysis. Targeted sequencing is a good alternative to whole genome sequencing, and focuses on amplifying only your targets of interest, for reduced cost and increased sequencing depth for improved detection.

Small RNA sequencing - This procedure sequences miRNA, piRNA and snoRNA using specialized protocols for RNA extraction and library preparation, including enrichment of small RNAs from total RNA. Sequencing and analysis to identify and quantify miRNA population and other small RNAs.

Residual DNA using real time PCR (GMP certified) - The procedure for detection of host cell

residual DNA in a tested sample by qPCR includes DNA purification from the tested sample, qPCR detection of residual DNA using TaqMan or SYBR green assays, and primers/probe designed for the tested host cell DNA.

Gene Copy Number using real time PCR (GMP certified) - Determination of a transgene copy

number in the genome is one of the major tests required as part of genetic stability testing. The qPCR method for Gene Copy Number (GCN) determination is based on normalization of the qPCR values obtained for the tested gene to those of a known single copy gene of the relevant organism.

Gene expression using Real Time PCR (GMP certified) - Gene expression performed by reverse

transcription-qPCR (RT-PCR) consider the gold standard for accurate, sensitive and fast test. The RT-qPCR method for gene expression determination is based on relative or absolute quantification using TaqMan or SYBR green assays.

Nucleic acids extraction and manipulation - Nucleic acid extraction is one of the basics and at the same time critical steps in the assays. As a leading lab with highly skilled analysts, we provide this service and working with wide range of kits, reagents and techniques for optimal results.

qPCR Release tests - qPCR has been shown to be a great tool for microorganism (including viruses) presence test and quantitation due to its speed, accuracy, and its enormous dynamic range. The microorganism amounts can be quantitated in either a relative or an absolute manner, using a standard curve.

Tissue Culture unit - Tissue culture unit provide a wide range of services including cell viability assays , cytotoxicity testing (according to ISO 10993), transfection, overexpression and gene silencing, complete cell signaling solutions and custom assay development.

Virology lab (COVID-19 POCs & Others) - We perform tests and design unique projects, based on ASTM and ISO standards, for our variety of customers ranging from pharma, cell therapy and startup companies to academic researchers. Our laboratory is ISO 9001 and ISO 17025 accredited, cGMP-compliant and operates at a BSL-2+ facility.

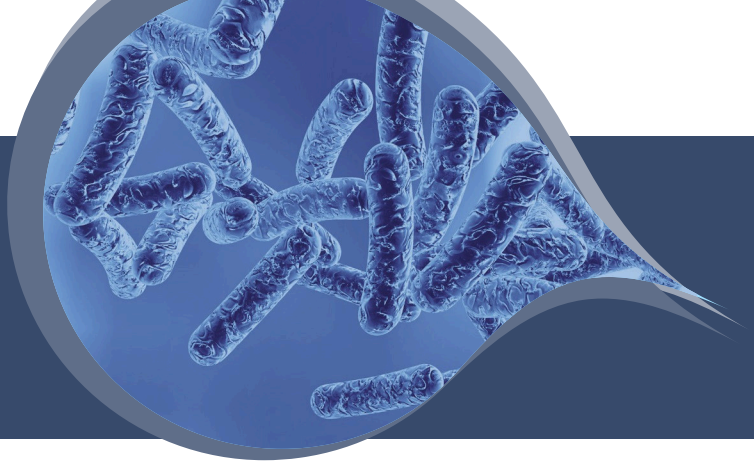
Elisa and biochemical analysis - The enzyme-linked immunosorbent assay (ELISA) is an immunological assay commonly used to measure antibodies, glycoproteins, antigens and proteins in biological samples. Our project managers will help you to choose the most suitable kit according to the need of the test and perform the assay.

Bacterial & Fungal Identification (MALDI-TOF-MS, rRNA-Sequence) - Our molecular methods
provide fast and the most accurate results for Bacterial and Fungal identification. Bacterial identification by this method based on sequencing of 16s rRNA and Fungal- on sequencing ITS and D1/D2 genes.

Mycoplasma test (Culture, 28 days / Nested PCR 2-3 Days qPCR (24H))- Mycoplasma, a smallest free-living microorganism, has adverse effects on the characteristics of a contaminated cell line including changes in growth, morphology, metabolism and more. Testing for mycoplasma is a necessary quality control requirement to assure the safety of biotechnological products and related materials introduced during the manufacturing process. As a leading service lab in Israel, we offer both microbial and molecular testing methods: mycoplasma culture method (28 days), nested PCR method (1-3 days) and the latest innovative Real-time PCR (8-24 hours). Our standard operation procedure relies on USP<63> and EP<2.6.7> and GMP approved.

PBRT - The assay designed and validated to provide product safety testing for retroviruses. The test is extremely sensitive and is the first choice for detection of RT in live viral-vaccines and gene therapy preparations. GMP certificated.

Protein purity by SDS-PAGE - SDS-PAGE is a basic and accessible method of separating proteins based on their molecular mass. The method commonly used for protein purification analysis of manufactured and purified samples.



Microbiology Lab

Sterility test - We considered to be the most critical lab in Israel for sterility test products release. That specialty testing is due to our vast experience in adopting rapid methods such as BacT/ALERT and HB&L (see below) and by the fact that we test and support the critical companies in Israel from the Cell therapy, Biopharma and medical devices sectors. Sterility testing is performed in order to establish the presence or absence of viable microorganisms, and is carried out in a clean room, under aseptic conditions with highly trained technicians. The test may be carried out using a Membrane Filtration technique or by Direct Inoculation of the culture medium with the product to be examined. Samples are incubated for 14 days in two types of media, which allow the detection of both aerobic and anaerobic microorganisms. Hy Laboratories provides sterility test in a Clean Room Class 1000 (ISO 6/Grade B) and under laminar air flow hood Class 100 (ISO 5/GradeA) conditions, and serves the healthcare, pharmaceutical, medical device, and cell therapy industries.

Rapid Sterility test before transplantation (HB&L, Gram, BacT/ALERT) - Hy Laboratories offers

Rapid Sterility Testing by the BacT/ALERT or HB&L Instruments. The BacT/ALERT is FDA and GMP approved automated system for rapid sterility testing. Based on CO2 emissions and a colorimetric sensor, the BacT/ALERT is able to detect the presence of microbial growth in 7 days sterility test. The presence of resin in the BacT/ALERT bottles enables the detection of microorganisms also in inhibitory substances and samples. The method is suitable for blood, biopharmaceutical, cell therapy and turbid samples. The HB&L is a highly sensitive instrument that utilizes light scattering technology to detect the presence of microorganisms' growth in few hours. The principle of the method is kinetic detection on two detectors at 30º and 90º with Laser Light Scattering at 650 nm colimated and focalized on liquid culture media maintained mixed and thermostated at 37ºC. The Sterility test result in such short time is critical for the release of final products mostly in the cell therapy field, but may be adopted to other products, based om specific method development

Endotoxin tests - BET (bacterial endotoxin test) also known as LAL (Limulus Amebocyte Lysate), is an assay for the detection and quantification of bacterial endotoxins, a component of the cell walls of gram-negative bacteria, in drugs and biological products. Endotoxins are fever-inducing substances that can be harmful or fatal if administered to humans above certain concentrations. The assay is derived from the fact that the horseshoe crab (limulus Polyphemus) blood cells (amebocytes) react with bacterial endotoxins.

We provide services in 3 BET assays:

LAL Gel-Clot assay – a qualitative assay, considered as the "Gold Standard" in pharmacopeial monographs. The test involves mixing the sample and the LAL in a test tube and incubating, a positive result is indicated by the formation of a clot at the bottom of the tube. Suitable for all sample types. Kinetic Turbidimetric assay – a quantitative photometric assay, utilizing the clot formation as a parameter. The test involves mixing the sample and the LAL and placing the test tube for incubation inside a 96 tube spectrophotometer, which tracks the change in absorbance as the clot is forming compared to a standard curve. Suitable for drug, medical devices and water testing. Kinetic Chromogenic assay – a quantitative colorimetric assay, quite similar to the turbidimetric assay. Tracks the change in color of the sample-LAL mix compared to a standard curve. suitable for medical devices and water testing. *Both turbidimetric and chromogenic assays involve a use of a 21 CFR part 11 compliant software. The chromogenic assay also available using PTS equipment by Charles River.

Media Fill - Media fill is designed to evaluate and validate aseptic performance either by qualified personnel or of assembly lines producing sterile products. Using a sterile microbiological growth medium in place of the actual articles, the test assess whether the aseptic procedures are adequate to prevent contamination during real time production.

Cleaning & Disinfection validations – The manufacturing of reusable medical device must accompany detailed instructions on how to reprocess the device between patient uses in the hospitals. Cleaning of the device is a critical step in reprocessing of any device after it has been used on a patient. Failure to remove foreign material from the device can interfere with the effectiveness of subsequent disinfection and/or sterilization. Residues of protein and TOC are being tested as part of Cleaning Validation, after performing a shortened cleaning procedure according to TIR30. Log reduction of chosen microorganisms is being tested as part of Disinfection Validation, after performing a shortened disinfection procedure according to TIR12.

Sterilization Validation (ETO, Gamma, Autoclave, Chemical, VHP) - Sterilization validation is a

crucial part of the development of medical device in order to assure the SAL (sterility assurance level) needed for a medical device. At Hy Laboratories we perform sterilization validation for products going through Radiation sterilization (Gamma/Beta), Ethylene Oxide sterilization, Autoclave, STERRAD sterilization and Dry Heat. We have vast experience in setting those validations with complexed and combined medical devices including submission to the CE and FDA.

GPT - A growth promotion test (GPT) ensures that the medium is capable of supporting or inhibiting the growth of indicator microorganisms, both ATCC strains and customers' wild strains. Our lab provides GPT for culture solid media and broths using various methods such as: Direct Inoculation, Pour Plate, Spreading on Surface and Membrane Filtration. In case of broths media, the medium is inoculated with a small number of microorganisms and the result is qualitative, either "growth" or "no growth". For GPT on solid media, the test is quantitative and the recovery of the spiked microorganisms should be 50-200 % from spiked control plates.

Environmental monitoring – Even in the most advanced and secured clean room environment, microbial contamination is unavoidable. Environmental monitoring review of microbial controlled environments such as clean rooms and Laminar air flow hoods, is required in order to assure control is being maintained. Sampling methods rely on growth of microorganisms on media such as Soyabean Casein Digest Agar (TSA) and Sabouraud dextrose agar (SDA) which supports the growth of a wide range of bacteria, yeast, molds and fungi. Hy Laboratories offer the service of our skilled and certified samplers. Our samplers will come to your facility and perform the entire sampling process. We provide the plates and an Active Air Sampler and all other needed equipment according to the costumers needs. As well as routine sampling, a PQ validation of clean rooms is also offered including planning and advising, writing of protocol, performing the sampling and issuing a final PQ report. After the sampling process our sampling team delivers all plates and information to the Laboratory for the incubation step. Incubation time and temperature varies between different growth media. At the end of the incubation period, colony forming units are being counted and reported. Following the incubation and count, an identification of bacterial growth may be provided

Incubation & count - Even in the most advanced and secured clean room environment, microbial contamination is unavoidable. Environmental monitoring review of microbial controlled environments such as clean rooms and Laminar air flow hoods, is regulatory required in order to assure control is being maintained. Sampling methods rely on growth of microorganisms on media such as Soyabean Casein Digest Agar (TSA) and Sabouraud dextrose agar (SDA) which supports the growth of a wide range of bacteria, yeast, molds and fungi. Samples which arrive at our lab are incubated in controlled and calibrated incubators. Incubation time and temperature varies between different growth media. At the end of the incubation period, colony forming units (CFU) are being counted and reported. Following the incubation and count, an identification of bacterial growth can be provided

Storing of frozen stock culture - Creating a frozen bacterial culture for future analysis. Following Environmental monitoring, Bioburden, MLT or BID tests there is an option to prepare a stock culture of the contaminant for an analysis at a later date, stored at -800C.

Disinfectant efficacy - The purpose of this study is to determine the efficacy of the disinfectant reagents used for the sanitization of surfaces in controlled manufacturing facilities and performed according to USP ‹1072›. The disinfectants efficacy is evaluated by the determination of survival rate of selected microorganisms spiked on coupons (such as PVC, stainless steel, glass etc.) or test tubes after being exposed to selected disinfectants for a pre-defined contact time. The study can be performed with ATCC challenge microorganisms and with Sponsor environmental isolates (Wild Strains).

Bacterial Identification (By MALDI-TOF-MS) - As a leading service lab in Israel we offer both methods – MALDI-TOF-MS and the molecular biology sequence. Matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) is a powerful analytical mass spectrometry technique that is used in our lab for the identification of cultured bacteria. By identifying the unique chemical signature of each sample, bacteria can be identified down to the species level using the MALDI-TOF-MS. Samples are isolated on growth media and incubated until significant growth occurs (usually between 24-48 hours). Only when growth is observed in the isolated sample, identification procedures can take place. The MALDI-TOF-MS pulls bacterial particles mixed with ions from the matrix into a vacuum and measures each particle's mass according to its time of flight, giving a unique signature to each sample. The information gathered is then compared to our existing database to identify the specific species of the bacteria. In case the isolate is not found in the MALDI library, it can be identified by the r-RNA sequence and that isolate can be added to the MALDI library. Also, in case the isolate is mold/fungi/yeast - molecular identification is recommended.

Morphology & Ecology - Morphology – In addition to the identification of microorganisms we offer characterizing of microorganism's morphology on an agar plate. This method is used to help distinguish between groups of microorganisms. Ecology – In addition to the identification of microorganisms we offer ecology description of the identified microorganism based on known databases.

Bacterial subculture - a subculture is a new microbiological culture made by transferring a colony of microorganism from a previous culture to fresh growth medium. A subculture is needed in order to isolate a specific microorganism from a mixture or prior to identification process.

Recovery of biological indicators (Bis) – An important aspect of the sterilization validation program involves the use of biological indicators when appropriate. A biological indicator (BI) is a well-characterized preparation of a specific microorganism with a known resistance to a specific sterilization process. Sterilization alternatives: steam, dry heat, gas, radiation, vapor, chemical, or filtration. After completion of the sterilization procedure, the BIs is removed and transferred to the lab within a noted time (NMT 4 h), then added to a suitable medium and incubated for 7 days. Sterilization indicators respond to sterilization process parameters in a non-quantitative fashion; i.e., they show passing or failing results.

Spore verifications - The aim of the test is to evaluate the total count of viable spores in biological indicators (standardized inoculated carriers) pre-sterilization.
The correct use of biological indicators (BIs) in the development, validation, and control of sterilization processes requires that their population and resistance be accurately known.
When evaluating vendor-supplied BIs, the viable spore count shall be between 50% and 300% of the manufacturer's stated value.

Water test - Water is widely used as a raw material, inactive ingredient, active pharmaceutical ingredients (APIs) as well as in cleaning applications. The testing of water samples from a water system is critical to the ongoing control of the system and assessment of the quality of the water being used. Control of the microbiological quality of water is important for many of its uses. At Hy laboratories we offer testing of the water system which includes bacteriological tests and endotoxin test. The bacteriological test is performed using mostly membrane filtration method, after that the filter is placed on suitable agar medium for detection of total count, coliforms, Pseudomonas aeruginosa, Enterococcus etc. Some grades of pharmaceutical waters, such as those used in parenteral applications (e.g., Water for Injection, Water for Hemodialysis, and the sterilized packaged waters made from Water for Injection) strictly limit the amount of endotoxins. BET (bacterial endotoxin test) is done using any of the methods suitable for water : Gel clot, turbidimetric or chromogenic. Hy Laboratories also offer the service of our skilled and certified samplers. Our samplers will come to your facility and perform sampling of the water system, then delivers it to the lab, in a timely manner, to perform the analysis.

Antimicrobial effectiveness testing (AET) - Antimicrobial preservatives are substances added to aqueous pharmaceutical products. Nonsterile dosage forms may have preservatives added to protect them from growth of microorganisms inadvertently introduced during or subsequent to the manufacturing process. In the case of sterile articles packaged in multiple-dose containers, antimicrobial preservatives are added to inhibit the growth of microorganisms that may be introduced from repeatedly withdrawing individual doses. The aim of the test is to demonstrate the effectiveness of added antimicrobial preservatives by inoculating the product with appropriate number of microorganisms. The products are divided into categories, the test procedure and specifications are determined according to the product category and pharmacopoeia. Our standard operation procedure relies on USP<51> & EP<5.1.3>.

Antibiotic potency - The activity (potency) of antibiotics can be demonstrated either by chemical methods or by microbial methods. A reduction in antimicrobial activity may not be adequately demonstrated by chemical methods thus the microbiological assay is the standard analytical method. The cylinder-plate assay depends on diffusion of the antibiotic from a vertical cylinder through a solidified agar layer in a Petri dish. The growth of the specific microorganisms inoculated into the agar is prevented in a circular area or “zone” around the cylinder containing the solution of the antibiotic. The activity of antibiotics is calculated by measuring the inhibition zone in comparison to a standard curve. Antibiotic Potency is tested according to USP <81>

Bioburden tests - Materials and products that are to be sterilized should be examined to determine the level of bioburden (microbial load/count) in the article, prior to its final sterilization.
Monitoring of in-process bioburden of pharmaceutical components and products is an essential element of the overall contamination-control program for appropriate sterilization process control.
Bioburden monitoring should be designed for the recovery of a broad range of microorganisms that are likely to be present in the material being processed.
Pre-sterilization bioburden analysis should be conducted on samples that are representative of materials produced during routine preparation and processing

Medical cannabis MLT – This test is intended for quantitative enumeration of bacteria and fungi that may grow under aerobic conditions of non-sterile products/raw materials (according to USP ‹61›) and to test for the absence of specified microorganism (according to USP ‹62›). The products/raw materials to be tested are diverse: solutions, creams, powders, tablets, inhalers, medical cannabis and more. This test is intended for samples that are classified as non-sterile. Before routine testing on a product, a validation is recommend to assure the suitability of the method to the product.

Microbial projects:
Using all the knowledge and experience we accumulated at Hy Laboratories, at our GMP laboratory, we can provide an array of microbiological services. We can tailor our services and methods to match most microbiological questions. From a proof of concept for a new product to preparing for a submission to any regulatory body.

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