MIB-100

Manual Inspection Booth

Referee Level Inspection Environment

NEW! Models Available!

MIB-100 with standard Corian® solid surface adjustable shelf / armrest and optional easy adjust multi-position side shelves

Patented Instrument Design providing a large volume of uniform illumination for the inspection of pharmaceutical products!

from PHOENIX IMAGING Ltd.

MIB-100 Background Information

Harmonization of in-process measurements, announced as a target area by the FDA, requires accurately transferable data. The high priority for this requirement stems from the USP affirmation of the manual clinical inspection at the injection site as the reference performance standard that must be matched or exceeded. This benchmark inspection is a single container inspection which uses manual manipulation to inspect the injectable dose for freedom from visible particle contamination. The USP affirmation imposes specific requirements on the validation of any alternative visible particle inspection system. The first requirement is an accurate assessment of the human inspection capability for visible contaminating particles. Following this initial determination, in accordance with cGMP, any alternative inspection method must be shown to be at least as effective in the elimination of particle contaminated containers from a batch of injectable products. Accurate measurement of the single container human inspection capability for visual contamination in parenteral products is an essential prerequisite. It supplies the benchmark performance against which any alternative inspection method or device is validated. To achieve replicable measurements from human performance, the conditions and action sequence of the inspection must be accurately defined and reproduced.

Knapp's 1980 PDA Journal Paper established the fact that the primary data describing the inspection for contaminating particles in injectable products is the probability of particle detection. This determination has, since first publication, been widely repeated and accepted. The direct use of the procedure described by Knapp requires multiple inspections of each container in a sampled set to determine the containers experimental rejection probability. Following this determination the containers are sorted into two groups. RZN, is the number of containers in the Reject Zone. The Reject Zone Effeciency is the average rejection probability of containers in the reject zone. The rejects in the Accept and Gray Zones do not contribute to product quality: they are an excess inspection cost. Visible particle rejects have been shown to be randomly distributed. No sampling assay can evaluate their effect. Any evaluation of their effect most be based on a 100% validated inspection.

A Calibration Curve relating particle size to particle detection probability is used to define the commencement of the visble contaminating particle region. Such a curve can be prepared with a set of durable NIST traceably sized microspheres. The rejection probability for each container in this set is evaluated within 95% confidence limits by trained inspectors using standard methodology in standard conditions. The particle size detected with a probability of 0.7071, approximately 95µm from initial data, defines the onset of the Reject Zone. From the data on hand a 50µm particle is detected with 10% probability and a 33µm particle is detected with 4% probability.

The Calibration Curve is determine with a single particle per container. The presence of multiple sub-visible particles can also be rejected with probability >0.7071 since each additional particle increases the rejection probablity of the container.

Conversion of this research procedure, which requires multiple inspections of a sample to determine the experimental rejection probability of each container in a sampled set, can now be converted to the measurement of the size of any contaminating particles in each container. This measurement can be approximated manually using a low power stereo microscope with a horizontal manipulator and a calibrated comparator. An alternative is the automated NIST traceable particle size measurements provided by the Phoenix Imaging ParticleScope™ Instrument.

The Phoenix Imaging Manual Inspection Booth (**MIB-100**) has been designed to provide an optimum test environment for critical visible particle inspections. Earlier standardization efforts were based on measured light intensity at a specific inspection point under a light source. The exponential variation of light intensity with distance from the light source limited the utility and replicability of such specifications. When manual inspection point variability is considered, a spatial volume in which the light intensity is maintained constant is required for practical inspection applications. A recently patented design achieves such a test environment. The variation of light intensity in a 10 liter volume was reduced to ± 5%, less than ½ the light intensity variation that is manually detectable. When inspections for contaminating particles are conducted within the controlled light intensity volume, data variability due to light intensity variation is eliminated.

The **Manual inspection Booth**, following the current recommendations of the Illumination Engineering Society, operates with 550 foot-candles in the light intensity stabilized inspection volume. NOTE: This illumination intensity is in the range recommended for critical inspections for long periods. The particular value has been selected to provide separation between sub-visible and visible contaminating particle measurements. This higher intensity also minimizes the effect of the reduction in contrast sensitivity that accompanies the aging process.

Other drawbacks associated with earlier generations of fluorescent lights used for inspection purposes have also been eliminated. These drawbacks include light intensity variation as the lamps aged and as the line voltage varied. The current sources employ phosphors with improved color rendering capability. The variation of light intensity as the line voltage varied has also been eliminated. The lamps are feedback stabilized to maintain set point light intensity until end-of-life. Predicted end-of-life is now 5 times longer than any available in 1980. Also eliminated was the inspector fatigue resulting from the stroboscopic images that result for any movement in a volume illuminated with fluorescent lamps excited with 60 cycle line voltage. [This effect is increased in regions in which 50 cycle line voltage is standard. The specially designed negative feedback stabilized 50 kHz fluorescent excitation source reduces the flicker intensity of the fluorescent light sources below human detection limits].

Inspector fatigue has been shown to adversely affect the accuracy of the inspection for visible contaminating particles by as much as 30%. The Phoenix Imaging Manual Inspection Booth has been designed so that the sequence of motions required from an inspector during the inspection are smoothly continuous and are adjustable to the body dimensions of the inspector. These adjustments are made tool-free.

This adjustment concept normalizes the onset of fatigue for all inspectors. It departs in an important way from the design concept of commercially available test booths in which inspectors of all physical dimensions are required to perform a sequence of motions between spatially identical positions. In presently available manual inspection stations the movements required during the inspection are the same for all inspectors. A consequence of this arbitrary requirement is that shorter inspectors must stretch between the required movement points and tall inspectors are cramped in performing the required movements. Both extremes impose additional fatigue elements.

An alternative to this one-size-fits-all approach is to provide the flexible adjustment capability of the Phoenix Imaging MIB-100 and a smooth optimized inspection sequence.

In the Phoenix Imaging Manual inspection Booth all adjustments to conform inspection motions to individual physical dimensions are performed at most once per shift. The required adjustment sequence starts with the adjustment of the vertical eye position of the inspector to the marked vertical center-line between the two light sources. The primary adjustment brings the eyes of the inspector to the center-point between the two vertically disposed inspection light sources. This adjustment places the nominal inspection point position at the center of the stabilized light volume. The illumination path is folded to bring the inspection volume closer to the inspector as illustrated by light yellow shaded area in Figure 1 below.

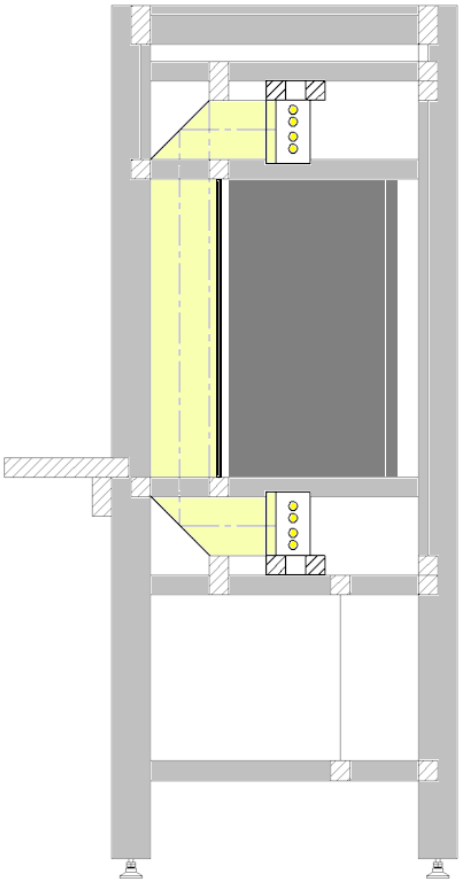


Figure 1 - MIB-100™ Illumination Path

This adjustment places the nominal inspection position at the center of the stabilized light volume. This adjustment can be made with the vertical height adjustment of the adjustable arm rest and inspectors chair height or the movement of the top and bottom light sources.

Patent No. 5,940176 granted and others patents pending.

The position of the light source can be adjusted by simply loosening the lock handles and sliding the lighting support panels either backward or forward as illustrated in Figure 2. Movement of the panels should be in opposite directions in order to insure that the light output inside the inspection volume remains constant.

The normal mode of operation is to use the lamps in matched positions. Each MIB-100 is provided with lamp positions labeled as seen in Figure 2, Pos. 1, Pos. 2, and Pos. 3. The system power supplies are adjusted with the lamps at Position2 so that the upper and lower lamp outputs are nearly equivalent (±5 ft-cd).

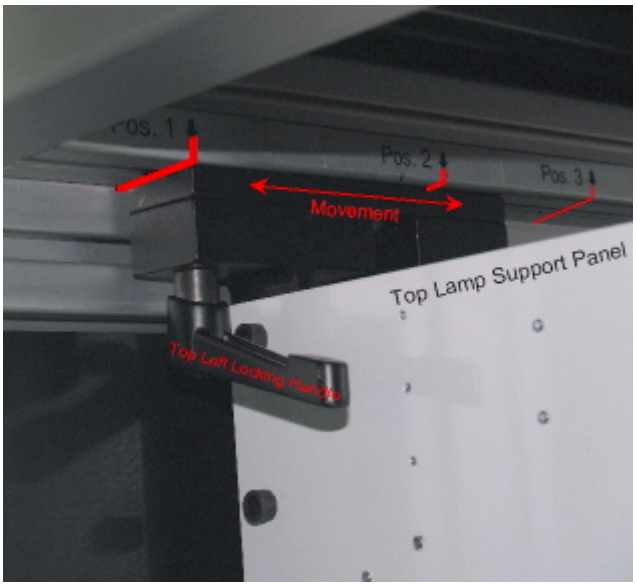


Figure 2 - MIB-100™ Lamp Support Panel Adjustment Blocks with Locking Handles

The Phoenix Imaging MIB series are provided with a pair of precision power supplies that incorporate active-loop feed back curcuits that monitor the output of the lamps. A photo-sensitive device is positioned to accurately measure the luminous flux produced by the lamps.

A precision potentiometer with a dial indicator is used to adjust the output of the lamps to the desired level. The standard configuration system allows the output at the center of the inspection volume to be adjusted between ~2000 to 8600 Lux with a potentiometer adjustment and/or lamp position settings. Each system is provided with charts at the three lamp support panel settings for the Potentiometer Setting vs. Output at the center point (Lux).

The lighting system used in the MIB-100 (& MIB-200) is a special design that provides optimum illumination over extended periods of time. The lamps selected for MIB-100 provide approximately 5,000 - 10,000* hours of life in which the intensity maintains at an acceptable output level. The standard operating procedure requires that the lamps be changed at least once a year. The life of the lamps are dependent on the intensity at which that are operated, high intensity will shorten the time at which the system can maintain the stabilized output. Normally the lamps are changed during a scheduled shutdown.

The illumination system is designed with a closed-loop active feedback that maintains a constant luminous flux of the lamps over their lifetime. The upper and lower lamps are balanced to provide uniform illumination volume in the inspection zone. The control circuitry will provide a signal to the inspector panel when the lamps are no longer able to regulate and maintain the preset illumination intensity.

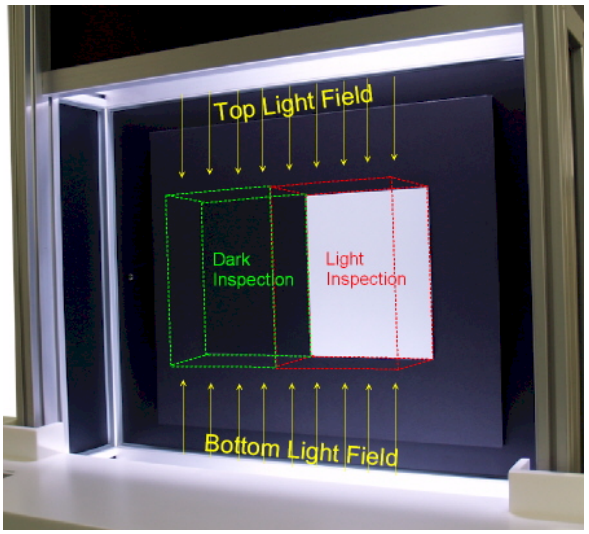


Figure 3 - Inspection Volume

The MIB-100 stabilized inspection volume is approximately 11 liters with the following dimensions, 250mm (H) x 400mm (W) x 120mm (D). The inspector normally does not require the use of the entire volume during the inspection process. The inspectors are trained to target the center point vertically and horizontally at which the movement sequence of the inspection commences. The movement between the Light inspection and Dark inspection location is usually less than 200mm in which the luminous flux will vary less than 5%.

* - Effective lamp hours depend on operational lamp intensity.

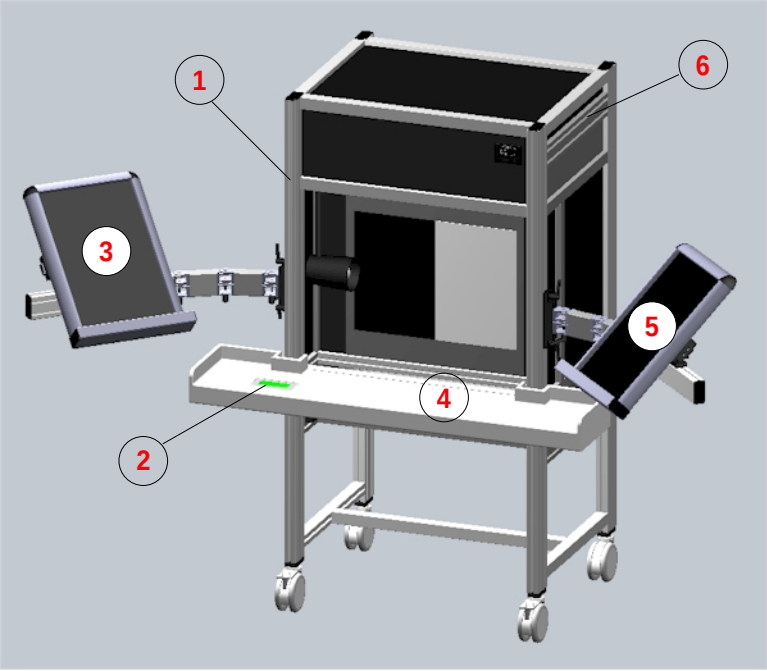


Figure 4 - MIB-100™ V2.3.6 Shown with the Optional Production Side Shelves and adjustable padded vinyl armrest.

The MIB-100 with Optional Side Shelves is shown in Figure 4 above. In the interest of clarity only selected elements have been shown. The framework is designed so that the shelves and armrests can be adjusted for height of the operator. The Figure legends are 1) Central structure fabricated from extruded aluminum sections that accommodate movements of the optional inspector interface elements, numbers 3, 4 and 5. The height of the inspectors eyes are adjusted to be at the vertical center point of the top and bottom lights which are not visible in the illustration. The armrest (item 4) is adjustable up/down to center the inspector's hand position at the center of the inspection volume. The design intent is to make the position and posture of the inspector as comfortable as possible. The operator interface panel for version 2.3.4 with padded vinyl armrest is mounted flush with the armrest surface. Item 2 in Figure 4 illustrates a remote operator interface panel. A pair of LED indicator lamps are incorporated into the back wall to provide visual signals for inspection operations. The optional side shelves with inclined tray support (3) holds containers to be inspected. The tray holder is inclined to position particles in the heel of the container before inspection to avoid the random positioning of particles at or near the containers rotation axis. The input and disposition tray supports can be modified to fit the exact size of the trays used by your organization.

For example, some customer may prefer a single tray on the shelves; others prefer two trays on the shelves. No. 5 is the optional accepted container tray; a cage for rejected containers is positioned across the top of No. 5 or separate "reject box" in mounted below. After function identification has been entered and checked, the color displayed on the face of the TFT flat panel monitor is used to time and control the inspection sequence. The external housing for the operator monitor is labeled (2). The shelf labeled (6) supports a local printer on the MIB-200 model.

When using the optional side shelves (trays) the operating position of the inspector can be placed within the tactile center of the inspection position. The vertical position of the inspectors elbow is measured and recorded. The center points of both trays are adjusted to this height above the floor (z axis of system). The trays are then adjusted to provide full access with forearm and wrist motions. The side shelves can be raised or lowered on each side of the MIB-100 framework. The horizontal support rail of the side shelves can be pivoted at the point where they attach to the MIB-100 vertical support either toward or away from the inspector. The side shelves can also be moved along the horizontal support rail toward or away from the pivot point.

The side shelves on which the customer product trays rest can also be tilted either up or down with respect to the horizontal plane. In addition, a provision is made so that the position of the customer tray can be adjusted either +/- displacement in the tilt plane. The adjustments place the center of an inclined tray of vials to be inspected in a position accessible with the left forearm and wrist motions (this assumes a right handed person). A similar inclined tray receives the accepted and rejected containers in 2 compartments that are accessible with right forearm and wrist motions. (All dimensional adjustments are standardized to tighten with clockwise motions and release with counter-clockwise motions.)

The inspection is performed in a smooth, continuous sequence. The sequence of right hand inspection movements commences with pickup from the container transfer position using peripheral vision and tactile sensory. The container is transferred to the nominal inspection point and then rotated 1-¼ turns to an abrupt stop, which transfers velocity to the contaminating particle. Inspection commences as soon as the container agitation sequence is finished. A programmable delay is set between start trigger, agitation and inspection.

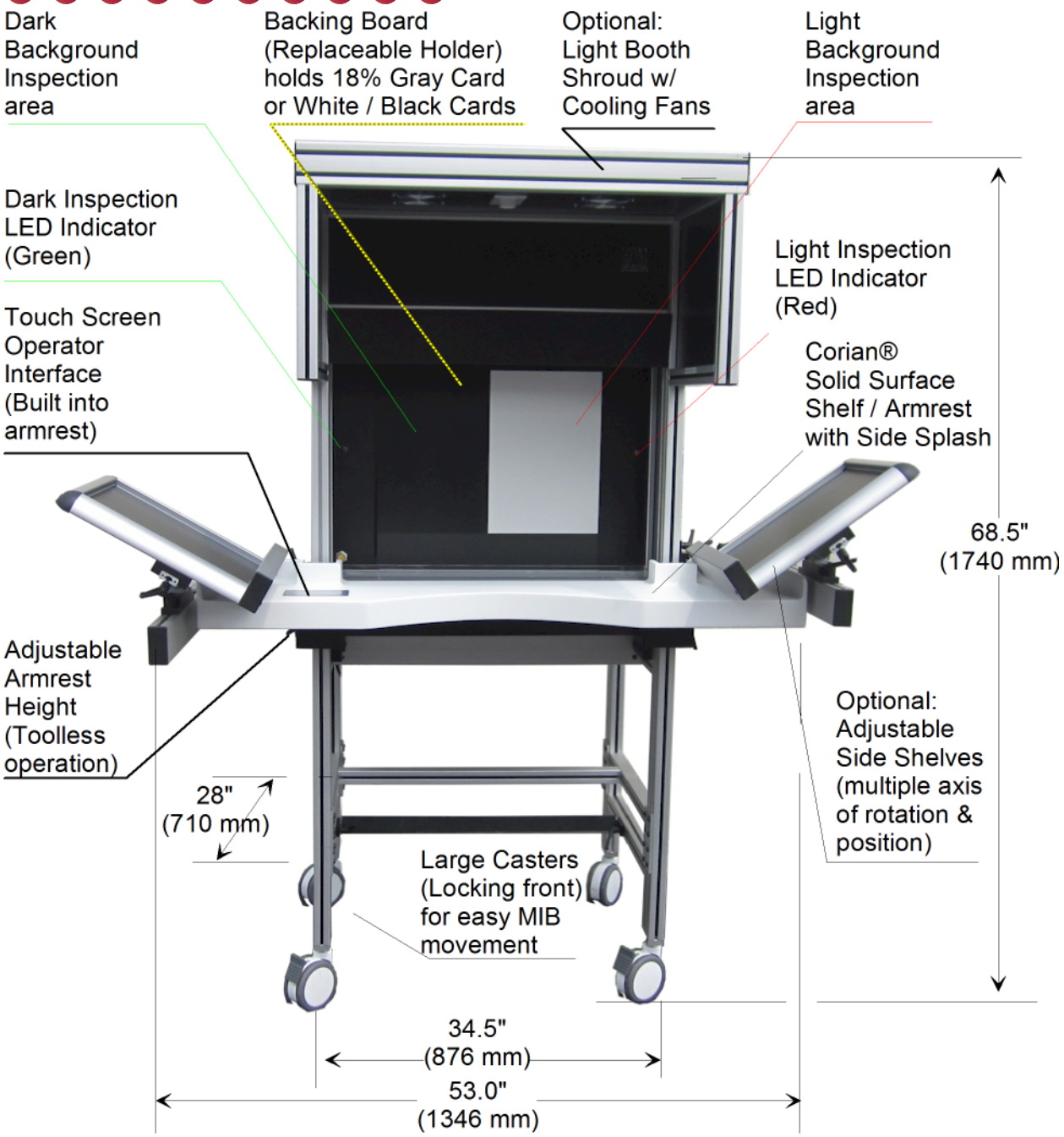


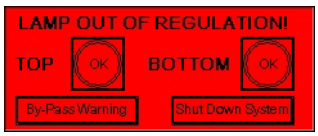
Figure 5 - MIB-100™ V2.3.6 Configuration shown with Shroud, Side Shelves and Curved Armrest

The MIB-100 is designed for the greatest stability and maximum functionality. The design incorporates a replaceable Backing Board so that either White/Black backgrounds or the new 18% Gray Card backgrounds may be used for the inspection process. The Backing Board is secured to the back of the inspection chamber using industrial grade Velcro® strips. The panel is removed by grasping the upper corners of the Backing Board and pulling forward. This also provides an easy method for replacement of damaged or soiled backgrounds. Replacement units are centered vertically and horizontally between LED indicator lamps.

The MIB-100 white background is constructed of white powder coat painted aluminum sheeting free of imperfections pre-cut to a 11" x 16" size. The matte black background is a black painted aluminum sheet attached to backing board also pre-cut to 11" x 16" size. Both backgrounds are permanently attached to the Backing Board edge to edge with no visible shadow line between them. The 18% Gray Card is 16" x 22" in size and is attached to the center of the Backing Board. The PLC software is pre-configured to perform either Light/Dark inspection or Gray Card inspection selectable at the beginning of an inspection session.

MIB-100 INSPECTION CONTROL SEQUENCE

There is a long list of features built into the MIB-100 PLC Pacer Softwre that allows the user to control the inspection sequence and data recording. The MIB-100's primary function is to provide a consistent inspection environment. The system insures that the lighting is volume is uniform and that all of the components are functional. If the lighting fails to meet the set level of intensity, a signal is generated that informs the user of the fault. The normal procedure when a lighting abnormality is incountered is to shut down the system and replace the lamp. The system will indicate the position of the defective lamp, top or bottom. The continuous monitoring of the lamps insures consistent inspection environment. There are several inspection methods built into the MIB-100 PLC Pacer Software. The methods include the industry standard Light / Dark Background inspection and the newer 18% Gray Card inspection. Either inspection method can be performed in a Indexed or Continuous Operating Mode. The system also provides the option to "collect" or "not to collect" data after each inspection cycle. The MIB-100 PLC Pacer Software allows all of the options to be selected using the operator interface built into the Corian® armrest / shelf. System setup is easy using the the simple to follow set up screens.

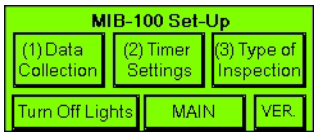


STEP 1: TURN-ON THE SYSTEM

Power up the system and alow it to stabilize, this takes about 5 minutes after which the system will indicate that it is ready.

STEP 2: MAIN SCREEN

This menu allows the operator to alter the settings, initialize inspections and obtain results from those inspections.

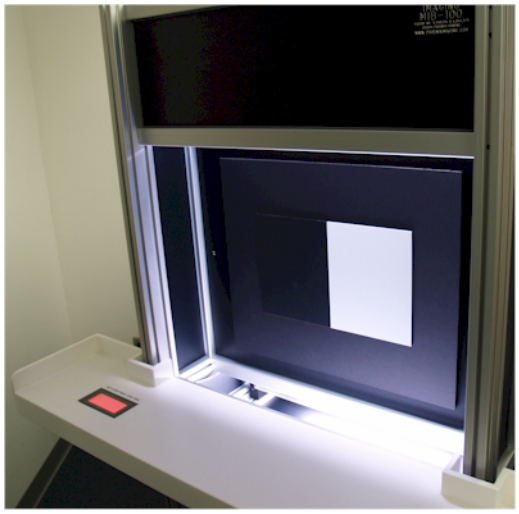


STEP 3: SET-UP MENU

The user selects whether to use data collection after each insepction cycle, adjust the duration of the timers and the type of inspection to perform.

STEP 4: MODE of OPERATION

The system can be setup to require inspector input after each step in the inspection cycle, after the complete inspection cycle or to cycle continuously without inspector input. The system uses a number of timers to control the delay between each of the individual step in the inspection cycle. In a production environment the LED indicators are used to insure that inspection durations are consistent.



STEP 5a: Data Collection or No Data Collection

The system can be set to ask the operator for judgements after inspection or simply use the systems pacer functions. user selects "START" to begin the inspection.

STEP 5b: Timer Functions and Audible Alarm

The system has independent timers for "Light", "Dark" and "Gray" inspections. It also has timers for the delays before and during the inspection operations. Each can be set to 1/10 second intervals. There is a separate button to turn on or off the audible alarms.

STEP 5c: Type of Inspection, Light/Dark, 18% GRAY (or MONOCHROME) BACKGROUND

The system allow the user to select settings for Light/Dark or Monochrome background inspection. The Light/Dark can be Indexed (operator intervention is required after each inspection phase using touch screen or footswitch) or Continuous (judgement is required after the final inspection).

The system uses **Red** and **Green** LEDs that are located along the horizontal centerline of the insepction booth. They are illuminated in a sequence to aid the pace of the inspection cycle. The operator can also slect the use of audible alarms in addition to the visual pacers.

STEP 6: Perform the Desired Inspection,

The MIB-100 is designed to provide the inspector with an ergonomically friendly environment to perform a very dificult task. The system monitors the lighting to provide uniform and consistent light over long periods of time. The operator interface is designed to provide maximum flexibility with ease of operation.

RLPS™

Standard Calibration Set

A **Referee Level Particle Standard** Set is available for the training of inspectors and determination of the human visual inspector baseline using the MIB product. The Standard set provides samples seeded with a single particle of a specific size in stainless steel, glass, polystyrene, glass sards,nylon fiber. The samples are produced using customer specified containers, stoppers, seals and fill level. The standard particle sizes range from 50µm to 900µm in diameter. This sample set is designed to train and evaluate the detection capability of individual inspectors. Following the training mode, the Standard Calibration Set is used to generate a calibration curve. The calibration curve relates particle size to particle rejection probability. The use of the calibration curve provides an economically effective alternative to the re-determination of the rejection probability of each particle in the sampled container set. Without the calibration curve the rejection probability of each container in the sampled container set must be independently generated. This would entail multiple inspection of each container in the sample set to achieve 0.95% confidence results.

The RLPS™ can be extended to include fibers, floaters, metal shards and other materials found in the manufacturing process. The test solution is WFI with or without a preservative and is clear in appearance. The RLPS™ samples may also be prepared with color, turbidity or a specific viscosity to meet customer requirements. All particles are of known sizes and are NIST traceable.

Referee Level Particle Standards (RLPS™) with NIST Traceable Single Seed Particle per Container

MIB-100™ Specifications

Patent No. 5,940176 granted and others patents pending.

- Power supply: 115 VAC (60 Hz) NA or 200-230 VAC (50 Hz) EU (+/-10%), must specify voltage at time of order.
- Power Consumption: ~500 Watts
- Operating Humidity: 35-85% RH
- Operating Temperature: 0 to 40 degrees C (32 to 105 degrees F)
- Dimension & Weight: (Main Unit) 34.5" W x 28" D x 68.5" H, 175 lbs.
- Dimension & Weight: Armrest Unit 53" W x 10.75" D x 4" H, 40 lbs.
- Options available: Footswitch, Curved Armrest, -JP (Incandescent lamp), Audible Alarm, Booth Height Extension Kit, Moveable Foot Rest.

MIB-80 Standard Configuration with curved front Corian® Armrest.

MIB-90 Standard Configuration with optional hydraulic leg lift kit and extended stainless steel work surface with shrouds.

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