Bayer

# INTRODUCTION

K962125

AUG - 2 1996

## INTRODUCTION

The *Technicon Immuno 1*® system is an automated clinical immunoassay analyzer. All tests can be run in random access, batch, and STAT modes at a throughput rate of up to 120 tests per hour. Up to twenty-two (22) methods can be loaded on the system at one time.

The system performs latex agglutination and magnetic-separation enzyme immunoassays on serum. Magnetic-separation enzyme immunoassays are divided into two (2) groups: sandwich assays and competitive assays.

Latex agglutination assays utilize the competition between the analyte in the sample and the hapten-Ficoll* conjugate in Reagent 1 for binding sites on antibody-coated latex particles in Reagent 2. The binding of the hapten-Ficoll conjugate to the coated latex particles results in the formation of large aggregates which increases the turbidity of the reaction solution. The analyte in the sample inhibits the formation of these aggregates. The agglutination rate is measured by monitoring the optical density (turbidity) of the reaction liquid.

Magnetic separation competitive assays utilize the competition between the analyte in the sample and the analyte attached to the alkaline phosphatase enzyme in Reagent 2 for binding sites on the fluoresceinated antibody in Reagent 1.

Magnetic particles coated with an antibody to fluorescein are added to the mixture of sample, Reagent 1 and Reagent 2. The fluorescein molecule conjugated to the analyte antibody, bound to either the analyte in serum or to the analyte conjugated to the alkaline phosphatase enzyme, binds to the magnetic particles. After removal of excess reagent and the addition of substrate, the absorbance of the reaction liquid is read to determine the analyte concentration.

In magnetic separation sandwich assays, binding occurs at two different sites on a single analyte in the sample. Reagent 1 (antibody conjugated to fluorescein) and Reagent 2 (antibody conjugated to alkaline phosphatase enzyme) are added simultaneously to the sample. An excess of the two reagents drives the reaction. Binding of the resulting immune complex to a magnetic particle allows it to be separated from excess reagents. Upon addition of the substrate, the reaction absorbance is read to determine the analyte concentration. The reaction rate is directly proportional to the sample analyte level.

## STATEMENT OF CONTENT

This Manual contains specific, assay-related information and data for Bayer methods performed on a Technicon Immuno 1 system.

The procedures necessary for the preparation, use, and storage of Technicon Immuno 1 system reagents and calibrators are provided in the applicable method sheet. Also refer to the tab titled "Reagent Information"; pages INTRO-8 through INTRO-11.

* Ficoll is a trademark of Pharmacia Fine Chemical Inc., Piscataway, NJ

Throughout this publication Bayer Corporation, Business Group Diagnostics is referred to as "Bayer."

## SAMPLE COLLECTION AND PREPARATION[1-4]

**WARNING - POTENTIAL BIOHAZARDOUS MATERIAL**
**Any samples of human blood, plasma, or serum should be handled cautiously as a biohazardous material according to good laboratory practices.**

The blood sample should be collected in a commercially available collection tube using routine venipuncture techniques. During sample collection and preparation, hemolysis of erythrocytes should be avoided. The effect of hemolysis on a method is described in the "Interferences" section of the specific method sheet when it is significant. Samples should be processed in a manner that will prevent the introduction of clots into the system.

1. After drawing the specimen from the patient, perform identification procedures consistent with your laboratory protocol. Place the collection tube in an upright vertical position and allow the specimen to stand undisturbed for a period of thirty (30) minutes prior to centrifugation.
2. Before placing the specimen in the centrifuge, carefully rim the collection tube to free the clot from the glass. Perform this procedure carefully so that the cells are not hemolyzed.
3. For optimum separation, the specimen should be centrifuged for twenty (20) minutes at a speed that produces a relative centrifugal force (RCF) of 2200 x gravity (*g*). Consult centrifuge manufacturers instructions for further information.
4. The primary collection tube can be placed directly into the sample rack (refer to the *Technicon Immuno 1 System Operator's Manual - UNIT 2* for allowable tube sizes) or carefully decant the serum from the primary collection tube into a clean Technicon Immuno 1 system sample cup or secondary tube. Make certain that no clots are decanted into the clean cup.

*The serum should be separated from cells within two (2) hours* after collection. If samples cannot be assayed immediately after separation, they should be stored in stoppered containers at 4 °C to 8 °C.

When determining the sample requirements, include the applicable dead volume: collection tubes 500 µL (maximum) and insert cups 1 mL (75 µL) or 2 mL (90 µL).

> **CAUTION!**: *To avoid having insufficient sample, carefully* dispense specimen so that no air bubbles are entrapped in bottom of cup.

Special analyte-specific storage conditions such as freezing, protection from direct exposure to light, or the addition of a preservative will be noted in the method sheets where applicable.

Additional sample collection and preparation information is available in texts by Kaplan and Pesce and Tietz. In addition, the National Committee for Clinical Laboratory Standards (NCCLS) has published two documents on sample collection.

## ALIBRATOR AND CONTROL PRODUCTS

### WARNING - POTENTIAL BIOHAZARDOUS MATERIAL

Any product prepared from human blood, plasma, or serum should be handled cautiously as a biohazardous material according to good laboratory practices.

Each donor unit used in the preparation of these products was tested by an FDA approved method for the presence of the antibody to Human Immunodeficiency Virus (HIV) as well as for hepatitis B surface antigen and found to be negative (was not repeatedly reactive).

Because no test method can offer complete assurance that HIV, hepatitis B virus, or other infectious agents are absent, these products should be handled at the Biosafety Level II as recommended for any potentially infectious human blood specimens in *Protection of Laboratory Workers From Infectious Disease Transmitted by Blood, Body Fluids, and Tissue - Second Edition; Tentative Guideline (1991)*, Document M29-T2, promulgated by the National Committee for Clinical Laboratory Standards (NCCLS).

Table 1 lists the calibrator and control products available for use with the system. Refer to the current Price List, applicable method sheet, or package insert for further information. Also refer to the tab titled "Reagent Information"; pages INTRO-8 through INTRO-11.

**Table 1: CALIBRATORS AND CONTROLS**

| PART NUMBER | DESCRIPTION | PACKAGING (mL) |
|---|---|---|
| T03-3187-01 | *Technicon SETpoint*™ AFP Calibrator 1<br>*Technicon SETpoint*™ AFP Calibrators 2-6 | 1 x 4.0<br>5 x 2.0 |
| T03-3188-01 | *Technicon SETpoint*™ CEA Calibrator 1<br>*Technicon SETpoint*™ CEA Calibrators 2-6 | 1 x 4.0<br>5 x 2.0 |
| T03-3562-01 | *Technicon SETpoint*™ CA 125 II† Calibrator 1<br>*Technicon SETpoint*™ CA 125 II Calibrators 2-6 | 1 x 4.0<br>5 x 2.0 |
| T03-3554-01 | *Technicon SETpoint*™ CA 15-3† Calibrator 1<br>*Technicon SETpoint*™ CA 15-3 Calibrators 2-6 | 1 x 4.0<br>5 x 2.0 |
| T03-3563-01 | *Technicon SETpoint*™ CA 19-9† Calibrator 1<br>*Technicon SETpoint*™ CA 19-9 Calibrators 2-6 | 1 x 4.0<br>5 x 2.0 |
| T03-3562-01 | *Technicon SETpoint*™ CK-MB Calibrators 1-6 | 6 x 2.0 |
| T03-3252-01 | *Technicon SETpoint*™ Cortisol Calibrator 1<br>*Technicon SETpoint*™ Cortisol Calibrator 2-6<br>Cortisol Calibrator Reconstitution Diluent | 1 x 4.0††<br>5 x 2.0††<br>1 x 15.0 |
| T03-3251-01 | *Technicon SETpoint*™ Ferritin Calibrator 1<br>*Technicon SETpoint*™ Ferritin Calibrators 2-6 | 1 x 4.0<br>5 x 2.0 |
| T03-3596-01 | *Technicon SETpoint*™ Folate Calibrator 1<br>*Technicon SETpoint*™ Folate Calibrators 2-6<br>Folate Calibrator Reconstitution Diluent | 1 x 4.0††<br>5 x 2.0††<br>1 x 15.0 |
| T03-3541-01 | *Technicon SETpoint*™ PSA Calibrator 1<br>*Technicon SETpoint*™ PSA Calibrators 2-6 | 1 x 4.0<br>5 x 2.0 |
| 03-3148-01 | *Technicon SETpoint*™ Reproductive Calibrators<br>Reproductive Calibrators Diluent | 6 x 2.0††<br>1 x 15.0 |

† A trademark of Centocor Inc., Malvern, PA 19355-1307
†† When reconstituted as directed.

**Table 1: CALIBRATORS AND CONTROLS** (Cont)

| PART NUMBER | DESCRIPTION | PACKAGING (mL) |
|---|---|---|
| T03-2864-01 | *Technicon SETpoint*™ TDM Calibrator 1<br>*Technicon SETpoint*™ TDM Calibrators 2-6<br>TDM Calibrator Reconstitution Diluent | 1 x 4.0††<br>5 x 2.0††<br>1 x 15.0 |
| T03-3174-01 | *Technicon SETpoint*™ $T_4$ Calibrator 1<br>*Technicon SETpoint*™ $T_4$ Calibrator 2-6 | 1 x 4.0<br>5 x 2.0 |
| T03-3568-01 | *Technicon SETpoint*™ TSH Calibrator 1<br>*Technicon SETpoint*™ TSH Calibrator 2-6 | 1 x 4.0<br>5 x 2.0 |
| T03-2872-01 | *Technicon SETpoint*™ $T_3$ Calibrator 1<br>*Technicon SETpoint*™ $T_3$ Calibrator 2-6 | 1 x 4.0<br>5 x 2.0 |
| T03-3076-01 | *Technicon SETpoint*™ T Uptake Hypothyroid Control<br>*Technicon SETpoint*™ T Uptake Euthyroid Reference<br>*Technicon SETpoint*™ T Uptake Hyperthyroid Control | 1 x 2.0<br>1 x 2.0<br>1 x 2.0 |
| T03-3393-01 | *Technicon Immuno 1 TESTpoint*™ Ligand Control | 2 x 5.0<br>(3 levels) |
| T03-3464-01 | *Technicon SETpoint*™ Vitamin B12 Calibrator 1<br>*Technicon SETpoint*™ Vitamin B12 Calibrator 2 - 6 | 1 x 4.0<br>5 x 2.0 |
| T03-3401-01 | *Technicon SETpoint*™ Free $T_4$ Calibrators | 6 x 2.0 |

†† When reconstituted as directed.

## SYSTEM SOLUTIONS

Table 2 lists the products currently available for use with Technicon Immuno 1 systems. Those system solutions that are necessary to perform this method may also require preparation. Refer to section titled "Start of the Day" in the "OPERATION" section of the *Technicon Immuno 1 System Operator's Manual* for complete instructions on the preparation and use of the system solutions or refer to tab titled "Reagent Information"; pages INTRO-8 through INTRO-11.

**Table 2: SYSTEM SOLUTIONS**

| PART NUMBER | DESCRIPTION | PACKAGING |
|---|---|---|
| T01-3130-01 | Substrate Reagents | Reagent: 2 x 386.0 mg<br>Diluent: 2 x 62.0 mL<br>2 empty, labeled cassettes |
| T01-3543-01 | *mIMP*™ Reagents | mIMP Reagent<br>1 x 23.5 mL<br>IMP Buffer<br>1 x 23.5 mL |
| T01-3601-01 | *IMP*® Buffer Reagent | 2 x 23.5 mL |
| T01-2879-52 | *IMP*® Wash Solution | 2 x 4.0 L |
| T01-3060-52 | Cuvette Wash Solution 1 | 2 x 4.0 L |
| T01-3570-52 | Cuvette Wash Solution 2 | 2 x 4.0 L |
| T01-3061-01 | Sample Probe Fluid | 6 x 30.0 mL |
| T01-3062-01 | Reagent Probe Fluid | 6 x 100.0 mL |
| T03-3574-01 | Sample Diluent-B | Reagent: 6 x 50 mL†<br>Diluent: 6 x 50 mL |

† - When reconstituted as directed.

**Table 2: SYSTEM SOLUTIONS** (Cont)

| PART NUMBER | DESCRIPTION | PACKAGING |
|---|---|---|
| T01-3367-01 | System Troubleshooting Reagents | Native ALP Reagent: 1 x 10 mL<br>Native ALP Buffer: 1 x 15.0 mL<br>Buffer Cassette: 2 x 15.0 mL<br>(5X) ALP Reagent: 1 x 10.0 mL<br>*Enzyme* Cassette: 1 x 15.0 mL<br>Enzyme Cassette: 1 x 30.0 mL<br>3 Empty, labeled cassettes |

## OPERATION

All information pertaining to the operation of the analyzer is included in the applicable *Technicon Immuno 1* System Reference or Operator's Manual provided with your system.

**NOTICE**

**Any modification of computer disks and/or the programs contained on such disks can adversely affect the control of instrument performance and thereby invalidate the results obtained and the claims that have been made regarding system performance.**

**Bayer cannot be responsible for errors that are introduced by, or result from, any modification or alteration of the computer disks and/or the programs contained on such disks by the user, or for any direct or indirect consequences resulting from such modification or alteration.**

## CALCULATION OF RESULTS

The system automatically performs all calculations that are necessary for obtaining final results. The system prints out the results for each sample in concentration units. The derivation of results from raw absorbance data is explained in the "Calculation of Results" section of the applicable Technicon Immuno 1 System Reference or Operator's Manual.

## INTERPRETATION OF RESULTS

System operators and laboratory supervisors are responsible for operating and maintaining Bayer products in accordance with the procedures described in the applicable Product Labeling (Operator Manuals, Package Inserts, Reference Manuals, Bulletins, etc.) and for determining that these products conform to the applicable performance claims.

If, under these prescribed conditions of operation and maintenance, an aberrant or abnormal result, as defined by the laboratory protocol, occurs, laboratory personnel should first make certain that the system is performing and is being operated in accordance with the Product Labeling; then follow the laboratory protocol for advising the clinician of a result that appears to have deviated from the norms established by the laboratory.

Bayer products do not make diagnoses on patients. Bayer intends its diagnostic products (systems, reagents, software, hardware, etc) to be used to collect data reflecting the patient's chemical, hematological, or immunological status at a certain point in time. Such data must be used in conjunction with other diagnostic information and with the attending physician's evaluation of the patient's condition to arrive at a diagnosis and a clinical course of treatment.

Any malfunction of a Bayer diagnostic product (i.e., failure to meet a performance specification or to perform as intended) should be appropriately addressed by laboratory personnel. Various sections of the Product Labeling previously noted address malfunctions and their possible effect on results.

### Automatic Reagent Cassette Switching

The system provides the capability of allowing the user to routinely place multiple reagent cassettes of the same reagent with the same or different lot number in the reagent tray. When the reagent inventory for the lead cassette counts down to zero, the system software will automatically switch to the subsequent cassette(s) to complete the remaining tests in the worklist for that method.

The lead cassette identification and the sequencing of subsequent cassettes follow these resident software rules:

1. The cassette having the earliest installed date is the designated lead.
2. If two (2) cassettes are installed on the same day, the cassette having the fewest number of remaining tests is the designated lead.
3. If two (2) or more cassettes are installed on the same day and the number of tests remaining is equal, then the cassettes are sequenced in accordance with their ascending numerical reagent tray position.

In the event multiple cassettes of differing lot numbers are installed, the system will roll over to a cassette with a different lot number. If the different lot has a stored and accepted calibration, then test results will be printed using the lot specific calibration data. If a within lot calibration has not been accepted on the different lot then rate data will be obtained, but held internally. Results for the different lot number will be calculated and released when a within-lot calibration is performed and accepted. Until then, the results for that test remains suppressed and "WA" flags are printed in their place.

### Automatic Substrate Cassette Switching

Up to five (5) substrate cassettes can be installed on the system. When the substrate cassette in use reaches "0 Tests Left," the system will automatically roll over and begin to use the next available substrate cassette.

The system has resident software rules to select which cassettes to roll over to or to use first:

1. The substrate cassette with the earliest installation date and lowest number of tests remaining.
2. If the installation date and number of tests remaining are equal, the substrate cassette in the lowest numerical position will be used first.

### Recommendations for Use

To determine if multiple reagent cassettes are installed on the system, check the "REAGENT INVENTORY SCREEN." If the number of tests ordered is larger than the number of tests left in the primary cassette, then cassette roll over will occur.

**NOTES**

1. *Quality Control*: As described in the analyte specific Method Sheets, control samples should be assayed at the beginning of each shift or at some other interval chosen by the laboratory; whenever a new reagent is used (same or different lot) prior to reporting patient results; following maintenance or cleaning of any detection system component. Refer to the "Quality Control" section of the analyte specific Method Sheet.

. Calibration: As described in the analyte specific Method Sheets, calibration should be performed when a method is implemented on the system. Recalibration is required after replacement of major components, a change in the lot number of reagents, mIMP Reagents, Substrate Reagents, or as indicated by quality control results. Refer to the "Calibration" section of the analyte specific Method Sheet for details.

3. If desired, cassette roll over may be disabled by not placing secondary cassettes in the reagent tray.

## WASTE DISPOSAL REQUIREMENTS

! ; and regulations enacted to protect the environment and to encourage resource conservation, require the disposal of hazardous and biohazardous wastes in a specified manner.

Some of the wastes from Technicon Immuno 1 system can be classified as hazardous or biohazardous wastes. It is essential that the laboratory take appropriate steps to determine the laws and regulations applicable to their disposal and to effect compliance.

It is necessary for you to sample instrument effluent in order to evaluate compliance with applicable regulations. The laboratory should contact a local licensed biohazardous waste disposal firm for assistance.

The principal wastes associated with the use of the Technicon Immuno 1 system are reagent cassettes, reaction trays, reagent containers, sample containers, and system waste.

**CAUTION: Do not incinerate the reaction trays.**

Sample containers with human specimens, control materials, and all reagents, also should be handled and disposed of in accordance with the prevailing regulations and guidelines of ncies holding jurisdiction over the laboratory.

. er to the product label and to *Material Safety Data Sheets* letails concerning any special precautions related to the handling of reagents.

## SYSTEM METHOD SHEETS

Each Method Sheet provides information relevant to an individual analyte. The Method Sheets are alphabetized within the manual and contain information and data described in NCCLS** Publication GP2-A and by the FDA in 21 CFR. A laboratory procedure manual is mandatory for good laboratory practice and regulatory compliance. To aid in the preparation of a laboratory procedure manual, refer to Table 3 (pages INTRO-12 and INTRO-13) for a cross-reference of the information contained in our Method Sheets with the guidelines for Clinical Laboratory Procedure Manuals published by the National Committee on Clinical Laboratory Standards (NCCLS Approved Guideline GP2-A).

***Bayer Method Sheets are presented in a consistent format with the headings listed below. The following is a brief description of the information included under each section heading:***

## TECH-CHECK™ TABLE

This table contains information which can be used to reference assay specific information, i.e. method principle, CLIA complexity, range of reportable results, specimen type, sample test volume, minimum sensitivity, standardization, and units used in the assay.

## INTENDED USE

This section contains a brief statement of intended use for the method as a *in vitro* diagnostic procedure for quantitating analytes in human serum.

## SUMMARY AND EXPLANATION

This section contains a short history of the method with pertinent references to previous related methods.

## PRINCIPLES OF THE PROCEDURE

This section provides a physical, chemical, and biological explanation of the method and a description of the chemical reactions, where applicable.

## REAGENTS

This section describes the reagents required to perform the method including reagent packaging information, product descriptions, materials required but not provided, and reagent preparation instructions. Analyte specific calibrator information also may be included.

Throughout this Section three words are used to signal the presence of hazards associated with the use and handling of reagents. These words are — in descending order of severity — **DANGER!**, **WARNING!**, and **CAUTION!**

The following briefly explains the significance of each of these headings:

**DANGER!**
Signals the presence of a hazard that is life threatening. This hazard can result from the presence of, the handling of, or the use of substances that are highly toxic, extremely corrosive, or extremely flammable.

**WARNING!**
Signals the presence of a hazard that is injurious but not life threatening under ordinary circumstances. This hazard can result from the presence of, the handling of, or the use of substances such as toxic liquids or gases, irritants, or flammable materials.

**CAUTION!**
Signals the presence of a hazard that could cause illness, burns, skin reactions, etc. This hazard could result from the presence of, the handling of, or the use of substances such as toxic liquids or gases, irritants, or flammable materials.

The customer must maintain a constant awareness of the hazards and warnings associated with all reagents. Where necessary, appropriate safety equipment should be used (e.g., eye protection, gloves, lab coats). Users should follow the handling and safety precautions specified in the *Material Safety Data Sheets* provided by Bayer.

### Reagent and Calibrator Preparation

This section describes the preparation and use instructions for the reagents and calibrators that are unique to each method. The system solutions that are necessary to perform each method also require preparation. Refer to the section titled "Start of the Day" in the "OPERATION" section of the *Technicon Immuno 1 System Operation Manual* for complete instructions on the preparation and use of the system solutions or the tab titled "Reagent Information"; pages INTRO-8 through INTRO-11.

** ailable from National Committee for Clinical Laboratory Standards, East Lancaster Avenue, Villanova, PA 19085

## STORAGE AND STABILITY

Reagent and calibrator storage and expiration dates are printed on the product label. When stored unopened these products are stable through the last day of the month stated in the expiration date.

The on-system stability stated in the method sheet represents the *minimum* stable period for the working reagent. On-system reagent performance was established by monitoring control recovery means within ±2 total standard deviations after activation. The total standard deviation is obtained from the imprecision claims of the method. The user may elect to use reagents for a longer period if results from the recommended Quality Control Protocol indicate acceptable performance. Bayer assumes no responsibility for the performance of any reagents which are used beyond their expiration dates.

Method sheet minimum stability claims apply to all situations where the relative humidity is equal to or above 25%. At lower relative humidities between 15% and 25%, results from the recommended Quality Control Protocol may indicate that more frequent calibration may be required.

The system solutions when stored as indicated (unopened at appropriate temperature) are stable through the last day of the month stated in the expiration date.

The system solutions listed below are stable on-system after reconstitution or opening for the period indicated in Table 4.

**Table 4: SYSTEM SOLUTIONS STABILTY**

| DESCRIPTION | STABILITY (DAYS) |
|---|---|
| Substrate Reagent | 30 |
| mIMP Reagent | 60 |
| IMP Wash Solution | 30 |
| Cuvette Wash Solution 1 | 30 |
| Cuvette Wash Solution 2 | 30 |
| Sample Probe Fluid | 30 |
| Reagent Probe Fluid | 30 |
| Sample Diluent-B | 30 |

If substrate cassettes are to be removed from the system, and temporarily stored in a 2 °C to 8 °C refrigerator, protect the contents from light. Evaporation covers provide adequate dust and evaporation protection for refrigerator storage.

## SAMPLE HANDLING

For a detailed explanation of sample handling, refer to page INTRO-1 of this manual under the heading "Sample Collection and Preparation."

Refer to the specific Technicon Immuno 1 system, method sheets for details about special analyte specific sample handling requirements or dilutions.

## MATERIALS REQUIRED BUT NOT PROVIDED

This section lists the additional materials other than the reagents and calibrators that are required to perform the methods.

## PROCEDURE

This section refers the user to the "OPERATION" section of the Reference or Operation Manual for general operating instructions.

## QUALITY CONTROL

This section specifies recommended quality control material and quality control frequency for the individual method. In general, Bayer recommends that Technicon Immuno 1 systems be monitored daily using the Technicon TESTpoint Ligand Controls (Prod. No. T03-3393-01) or, at least two (2) levels of commercially prepared control materials. Controls should be run at the beginning of each shift, or at some interval chosen by the laboratory whenever a new reagent is used, and following the performance of any detection system maintenance or cleaning. The laboratory must evaluate all control results prior to reporting patient results. If control results fail to meet the laboratory's established criteria for acceptability, all patient test results obtained in the unacceptable test run must be evaluated to determine if patient test results were adversely affected. The laboratory should take and document appropriate corrective actions, which may include recalibration, before reporting patient results.

If commercially prepared controls are used, the laboratory must verify that they respond properly on the system.

## CALIBRATION

This section specifies the calibration type, frequency and procedure, for each method and identifies the calibration material to be used, where appropriate.

### Calibration Procedure

This section refers the user to the "OPERATION" section of the Technicon Immuno 1 System Reference or Operation Manual for specific calibration instructions.

### Calibration Schedule

This section lists the minimum duration of calibration stability with the use of multiple reagent cassettes within a single lot of reagent. By monitoring control recovery of newly activated cassettes within a single reagent lot, Bayer has determined that the results remain within ±2 total standard deviations. The total standard deviation is obtained from the imprecision claims of the method. The user may elect to use a calibration for a longer period of time if results from the recommended Quality Control Protocol continue to indicate acceptable performance.

## RESULTS

This section describes the numeric printout, expected flags or messages, and specific conditions or cautions that apply to the method.

## ITATIONS OF THE PROCEDURE

The section describes substances, conditions, and patient states that have been reported to cause actual or apparent physiological changes in the analyte concentration.

Bayer makes every effort to identify in the Troubleshooting, Maintenance, and Bibliography sections of the Product Labeling, the potential effects caused by instruments, reagents, or endogenous substances, including known interferences on ent results. However, it is impossible to provide information that would be applicable to every clinical situation. This information is provided in lieu of attempting to define the need for additional testing which involves medical judgement in individual cases. The decision whether or not to report a diagnostic result rests with the laboratory.

## EXPECTED VALUES

Expected values were determined from sera of asymptomatic donors. Approximately one-hundred (100) adult donor specimens were assayed and the central 95% range was calculated by one of two procedures:

- Nonparametric (2.5 and 97.5 percentiles)
- Parametric (mean ± 2 standard deviations)

Any deviations from these procedures are noted in the method sheets.

Ranges of expected values can vary depending on age, diet, location, etc; therefore, users should evaluate their usual population to determine their own laboratory specific ranges.

### erapeutic Drug Assays

therapeutic ranges were taken from the literature cited in ach method sheet.

## PERFORMANCE CHARACTERISTICS

This section provides technical information related to method performance characteristics, including imprecision, correlation, linearity, and sensitivity.

A description of each statistical parameter and the protocol followed to compute that parameter are contained in the paragraphs that follow.

### Imprecision

Imprecision is defined as the degree of variability among repeated independent measurements of the same sample using external evaluation data.

Within-run imprecision refers to the reproducibility of the method when samples are assayed within a single run.

Total imprecision extends the within-run estimates to include between run and between day components of variation.

Imprecision estimates were computed at specified analyte levels using human serum pools and control materials in a protocol similar to that recommended in the NCCLS document EP5-T2, *Precision Performance of Clinical Chemistry Devices – Second Edition; Tentative Guideline (1992).*

All imprecision data were obtained over a single calibration period using a single lot of individual reagents and calibrator. Unless otherwise noted, imprecision was evaluated using two (2) systems per method, twenty (20) days per system, one to two (1 - 2) runs per day, and two (2) or more samples per run.

The imprecision values for each method, described on each of their respective Method Sheets, are point estimates of *average* imprecision that can be expected on the system. Since this is a point estimate, any single system tested with a similar protocol could yield a different estimate of imprecision and yet not be significantly different from the published average imprecision.

The NCCLS document, EP5-T2, describes a statistical test (Chi Square) for comparing an instrument's performance and the expected performance. A user should be able to obtain imprecision data which pass the Chi Square test at the 95% confidence level.

### Correlation Data

Correlation data were determined using human serum samples from external evaluation sites by comparing the performance of Technicon Immuno 1 system with the performance of a reference method or a comparative system, where applicable.

Regression statistics were computed using a protocol similar to that recommended in the NCCLS document EP9-T, *Method Comparison and Bias Estimation Using Patient Samples; Tentative Guideline (1993).*

Regression data in each method indicate the linear least squares fit between the Technicon Immuno 1 system (**y**) and the comparative system/method (**x**), unless noted otherwise.

### Sensitivity

This section lists the smallest concentration that can be detected within a run. It is equivalent to two (2) within-run standard deviations of the Level 1 (0.0) calibrator. The 0.0 calibrator is run twenty (20) times on three (3) systems.

### Specificity

This section lists the highest concentration of common interfering substances evaluated and found not to have a significant affect on results. Substances that could affect results are shown by a listing of the percent (%) observed cross-reactivity.

### Analytical Range

This section describes the concentration range across which acceptable results can be obtained from the method.

Some specimens may exceed the range of the method and produce error flags or messages. The details of these flags and messages are available in the Reference Manual for the Technicon Immuno 1 system. Specimens that produce these errors should be diluted using a Class A volumetric pipette or equivalent and reassayed according to directions available in the specific method sheets.

### Revision Bar

A vertical black bar appearing in the margin of the page indicating change(s) in the text and/or in the contents of a table in the document. The revision bar allows the reader to identify quickly and easily the revised material within the document.

## BIBLIOGRAPHY


1 Kaplan LA and Pesce AG: *Clinical Chemistry — Theory, Analysis, and Correlation*, St. Louis, CV Mosby (1984) pp 43-50

2 Tietz NW: *Textbook of Clinical Chemistry*, Philadelphia, PA, WB Saunders Company, pp 478-518 (1986)

3 *Standard Procedure for the Collection of Diagnostic Blood Specimens by Venipuncture*. NCCLS Standard ASH—3. Villanova, PA, National Committee for Clinical Laboratory Standard (1977)

4 *Approved Standard Procedures for the Collection of Diagnostic Blood Specimens by Skin Puncture*, NCCLS Standard H4—A. Villanova, PA, National Committee for Clinical Laboratory Standard (1982)




Bayer Corporation
Business Group Diagnostics
Tarrytown, NY 10591-5097 USA

REVISED: September 1995

## REAGENT INFORMATION: A USER'S GUIDE TO REPLACING AND PREPARING *TECHNICON IMMUNO 1* SYSTEM REAGENTS, CALIBRATOR, AND CONTROLS

The *mIMP*™ (monoclonal Immuno Magnetic Particle) Reagents and IMP Buffer that are used on the Technicon Immuno 1 system are listed in Table A.

**Table A: mIMP REAGENT AND IMP BUFFER**

| PRODUCT NAME | COMPONENT | PRODUCT NUMBER | TOTAL NUMBER OF UNITS* | QUANTITY | REAGENT PREPARATION REQUIRED |
|---|---|---|---|---|---|
| mIMP Reagents | mIMP Reagent | T01-3543-01 | 4000 | 1 | Ready-to-use |
| | IMP Buffer | | 2000 | 1 | Ready-to-use |
| IMP Buffer Reagent* | IMP Buffer | T01-3601-01 | 4000 | 2 | Ready-to-use |

* For mIMP Reagent 1 unit = 5 µL; for IMP Buffer 1 unit = 10 µL.

**WARNING!** Contains 0.1% sodium azide. See Technical Bulletin TT6-0319-11. Harmful if swallowed. After contact with skin wash immediately with plenty of water.

### Instructions to Replace mIMP Reagent / IMP Buffer

1. Remove IMP compartment cover.
2. Mix new cup by inversion and remove gray stopper.
3. Replace desired cups. It is important to note the position of the cups.
4. Replace IMP compartment cover (directional arrow must face forward).
5. Reset number of tests on REAGENT INVENTORY screen.

The Substrate Reagents that are used on the Technicon Immuno 1 system are listed in Table B.

**Table B: SUBSTRATE REAGENTS**

| PRODUCT NAME | PRODUCT NUMBER | QUANTITY | REAGENT PREPARATION REQUIRED |
|---|---|---|---|
| Substrate Reagents | T01-3130-01 | 2 Substrate<br>2 Diluent<br>2 Empty Labeled Cassettes | Reconstitution;<br>Lyophilized Material |

**CAUTION!** Avoid contact with eyes, skin, or clothing. Wash thoroughly after handling. Avoid ingestion.

### Instructions to Replace Substrate Reagent

1. Pour entire contents of one (1) Diluent into one (1) Substrate reagent bottle.
2. Gently swirl and allow to stand for five (5) minutes.
3. Gently mix reagent. *Do not* allow the reagent to foam.
4. Remove gray stopper from the fill port at the top of the cassette tower.
5. Slowly pour the contents of the Substrate Bottle into the cassette.
6. Reinsert the gray stopper into the fill port.
7. Remove and discard the gray stopper from the aspiration port.
8. Open the substrate compartment cover; system *must not* be processing samples.
9. Remove empty cassettes and install the full cassette(s). It is important to note the position of the cassette(s).
10. Up to five (5) substrate cassettes can be positioned on the system. For additional information, refer to page INTRO-3 in the section titled "Automatic Substrate Cassette Switching."
11. Reset the number of tests on the REAGENT INVENTORY screen.

The Wash Solutions that are used on the Technicon Immuno 1 system are listed in Table C.

**Table C: WASH SOLUTIONS**

| PRODUCT NAME | PRODUCT NUMBER | TOTAL VOLUME | QUANTITY | REAGENT PREPARATION REQUIRED |
|---|---|---|---|---|
| Cuvette Wash 1 | T01-3060-52 | 4 Liters | 2 | Ready-to-use |
| Cuvette Wash 2 | T01-3570-52 | 4 Liters | 2 | Ready-to-use |
| IMP Wash | T01-2879-52 | 4 Liters | 2 | Ready-to-use |

**CAUTION!** Avoid contact with eyes, skin, or clothing. Wash thoroughly after handling. Avoid ingestion.

### Instructions to Replace Wash Solutions

1. Open center door of analytical console.
2. Replace empty wash solutions.
3. Install new wash bottle onto shelf.
4. Using a single edge razor blade, cut off the end of the straw allowing 0.25 inch to protrude from cap.
5. Using a sharp point object, puncture the vent hole.
6. Attach appropriate colored tubing onto the end of straw.
7. Close access door.
8. Reset the number of tests for each wash solution replenished on REAGENT INVENTORY screen.
9. Perform FDT to prime lines. Refer to the *Technicon Immuno 1 Maintenance / Troubleshooting Manual, UNIT 3*, for instructions.

The Reagent and Sample Probe Fluids that are used on the Technicon Immuno 1 system are listed in Table D.

**Table D: REAGENT AND SAMPLE PROBE FLUIDS**

| PRODUCT NAME | PRODUCT NUMBER | TOTAL VOLUME | QUANTITY | REAGENT PREPARATION REQUIRED |
|---|---|---|---|---|
| Sample Probe Fluid | T01-3061-56 | 30.0 mL / Bottle | 6 | Ready-to-use |
| Reagent Probe Fluid | T01-3062-56 | 100.0 mL / Bottle | 6 | Ready-to-use |

**CAUTION!** Avoid contact with eyes, skin, or clothing. Wash thoroughly after handling. Avoid ingestion.

### Instructions to Replace Reagent and Sample Probe Fluids

1. Replace as required.
2. Prime probes and lines by initializing the pumps through the maintenance menu. Refer to the *Technicon Immuno 1 Maintenance / Troubleshooting Manual, UNIT 3*, for instructions.

The Sample Diluent-B reagent that is used with the Technicon Immuno 1 system is listed in Table E.

**Table E: SAMPLE DILUENT - B**

| PRODUCT NAME | PRODUCT NUMBER | TOTAL VOLUME | QUANTITY | REAGENT PREPARATION REQUIRED |
|---|---|---|---|---|
| Sample Diluent - B | T03-3574-01 | 50.0 mL / Bottle | Lyophilized Bottle: 6 x 50 mL<br>Diluent Bottle: 6 x 50 mL | Reconstitution; Lyophilized Material |

**CAUTION!** Avoid contact with eyes, skin, or clothing. Wash thoroughly after handling. Avoid ingestion.

### .ructions to Reconstitute Sample Diluent – B

1. Remove vial closure.
2. Transfer entire contents of one (1) Reconstitution Diluent into one (1) Sample Diluent – B bottle.
3. Swirl gently and let stand for fifteen (15) minutes.
4. Mix by inversion at least five (5) times.
5. Refrigerate any unused material. Prior to reuse, mix contents thoroughly.

## Reagent Preparation Instructions

**CAUTION!** Avoid contact with eyes, skin, or clothing. Wash thoroughly after handling. Avoid ingestion.

### Ready-to-use Liquid Reagent Cassettes

1. Remove the outer shrink wrap layer.
2. Swing evaporation covers to the side.
3. Remove inner shrink wrap.
4. Remove and discard gray shipping stoppers.
5. Position evaporation covers over aspiration ports and press down to "snap" into place.

**IMPORTANT**
**Exercise covers gently to ensure proper attachment. Do not force the covers through the full length of travel.**

Do not tip the cassette. When properly installed on the system, the base portion of the tower will fill automatically. Store reagent(s) on Technicon Immuno 1 system or in refrigerator. Avoid overexposure to light.

### Latex Liquid Reagents

1. Handle per the "Ready-to-use" liquid instructions as described above.
2. Mix prior to use and remix weekly during use.
3. Slowly lay the cassette on its side with the base pointing up and allow all the liquid to drain to the tower.
4. Maintaining the cassette position (on its side), shake back and forth along the long axis about 25 times in 10 seconds.
5. Return the cassette to the upright position. Do not over rotate. When properly installed on the system, the base portion of the tower will fill automatically.
6. Store reagent(s) on Technicon Immuno 1 system or in refrigerator. Avoid overexposure to light.
7. If stored in refrigerator, mix prior to reuse.

### Lyophilized Reagents

1. Using a volumetric pipette, Class A or equivalent, pipette the specified volume of diluent into the bottle of lyophilized material.
2. Allow to stand for fifteen (15) minutes, then gently mix by inversion.
3. Remove the gray stopper at the top of the cassette tower.
4. Transfer all of the reagent into the cassette.
5. Replace the cassette tower gray stopper.
6. Prepare and handle the cassette as indicated above in the "Ready-to-use" instructions.

## Calibrator and Control Preparation Instructions

For detailed application information refer to the Clinical Method Sheet and / or product inserts for product numbers and specifications.

**WARNING - POTENTIAL BIOHAZARDOUS MATERIAL**

Any product prepared from human blood, plasma, or serum should be handled cautiously as a biohazardous material according to good laboratory practices.

Each donor unit used in the preparation of these products was tested by an FDA approved method for the presence of the antibody to Human Immunodeficiency Virus (HIV) as well as for hepatitis B surface antigen and found to be negative (was not repeatedly reactive).

Because no test method can offer complete assurance that HIV, hepatitis B virus, or other infectious agents are absent, these products should be handled at the Biosafety Level II as recommended for any potentially infectious human blood specimens in *Protection of Laboratory Workers From Infectious Disease Transmitted by Blood, Body Fluids, and Tissue - Second Edition; Tentative Guideline (1991)*, Document M29-T2, promulgated by the National Committee for Clinical Laboratory Standards (NCCLS).

### Ready-to-use Calibrator or Control

1. Remove vial closure.
2. Mix by inversion at least five (5) times.
3. Refrigerate any unused liquid. Gently mix prior to reuse.

**NOTE**

**Several calibrators are supplied with an excess volume of the Level 1 Calibrator. This excess can be used to dilute any out-of-range samples.**

### Lyophilized Calibrator or Control

1. Remove vial closure.
2. Using a volumetric pipette, Class A or equivalent, pipette specified volume of calibrator reconstitution diluent.

**NOTE**

**Several calibrators are supplied with an excess volume of the Level 1 Calibrator. This excess can be used to dilute any out-of-range samples.**

3. Swirl gently and let stand for fifteen (15) minutes.
4. Mix by inversion at least five (5) times.
5. Refrigerate any unused liquid. Gently mix prior to reuse.

Table 3: NCCLS GUIDELINE (GP2-A) AND BAYER METHOD SHEET HEADINGS CROSS-REFERENCE

| | NCCLS Approved Guideline GP2-A | Bayer Method Sheet Headings |
|---|---|---|
| ***5.1.2*** | ***Title*** | |
| 5.1.2.1 | Title | Title |
| 5.1.2.2 | Type of Specimen | Intended Use |
| 5.1.2.3 | Method or instrumentation in subtitle. | Intended Use |
| ***5.1.3*** | ***Principle*** | |
| 5.1.3.1 | Type of reaction(s) involved. | Principles of the Procedure |
| 5.1.3.2 | Clinical reasons for performing the test. | Intended Use |
| ***5.1.4*** | ***Specimen*** | |
| 5.1.4.1 | State the conditions for patient preparation. | Sample Handling / Limitations |
| 5.1.4.2 | Type of specimen | Intended Use / Sample Handling |
| 5.1.4.3 | Special handling conditions | Sample Handling |
| ***5.1.5*** | ***Reagents*** | |
| 5.1.5.1 | List reagents, supplies, and equipment | Reagents |
| 5.1.5.2 | Directions for preparation | Reagent Preparation |
| 5.1.5.3 | Parameters used to determine acceptable reagent performance | Storage and Stability |
| 5.1.5.4 | Storage requirements | Storage and Stability |
| ***5.1.6*** | ***Calibration*** | |
| 5.1.6.1 | Standard preparation | Calibration / Calibrator Package Insert |
| 5.1.6.2 | Calibration procedure | Calibration |
| ***5.1.7*** | ***Quality Control*** | |
| 5.1.7.1 | Identify control materials to be used | Quality Control |
| 5.1.7.2 | Instructions for preparing and handling control materials | Control Package Insert |
| 5.1.7.3 | Control frequency | Quality Control |
| 5.1.7.4 | Description of control tolerance limits | Control Package Insert |
| 5.1.7.5 | Corrective actions to be taken when limits are exceeded | *According to Individual Laboratory Practice* |
| 5.1.7.6 | How QC data are recorded and stored | Reference or Operator's Manual / *According to Individual Laboratory Practice* |
| 5.1.7.7 | If no controls are available, list alternatives | Not applicable |
| ***5.1.8*** | ***Procedure - Stepwise*** | |
| 5.1.8.1 | Detailed stepwise instructions | Procedure |
| 5.1.8.2 | Centrifugation requirements | Sample Handling (Intro-1) |
| 5.1.8.3 | Specify special glassware | Not applicable |

**Table 3: NCCLS GUIDELINE (GP2-A) AND BAYER METHOD SHEET HEADINGS CROSS-REFERENCE** (Cont)

| | NCCLS Approved Guideline GP2-A | Bayer Method Sheet Headings |
|---|---|---|
| 5.1.8.4 | Specify the following for photometric measurements:<br>Type of instrument<br>Wavelength<br>Cuvette size<br>Solution used as a blank<br>Linearity<br>How the raw data are used<br>Allowable time intervals<br>Stability of final solution | <br>*Reference or Operator's Manual / Description and Specifications*<br>Chemistry Program Data Sheet<br>Chemistry Program Data Sheet<br>Reagents / Procedure<br>*Linearity*<br>Reference or Operator's Manual / Theory of Operation<br>Reference or Operator's Manual / Theory of Operation<br>Not applicable |
| ***5.1.9*** | ***Calculations*** | |
| 5.1.9.1 | Give stepwise instructions | Results |
| 5.1.9.2 | Give the equation | Reference or Operator's Manual / Theory of Operation |
| 5.1.9.3 | Give an example | Reference or Operator's Manual / Theory of Operation |
| ***5.1.10*** | ***Reporting results*** | |
| 5.1.10.1 | State reference ranges | Expected or Therapeutic Values |
| 5.1.10.2 | Identify procedures to be used in reporting results to the physician | *According to Individual Laboratory Practice* |
| 5.1.10.3 | Guidelines on acceptable reporting format | Results / *According to Individual Laboratory Practice* |
| ***5.1.11*** | ***Procedure Notes*** | |
| 5.1.11.1 | Explain reasons for special precautions | Sample Handling |
| 5.1.11.2 | List possible sources of error | Sample Handling / Limitations of the Procedure / Results |
| 5.1.11.3 | Include helpful hints | Procedure |
| 5.1.11.4 | Clinical situations that may influence test validity | Limitations of the Procedure |
| 5.1.11.5 | Acceptable alternative procedures, expected differences | Correlation |
| 5.1.11.6 | Enlarge upon clinical applications | *According to Individual Laboratory Practice* |
| ***5.1.12*** | ***Limitation of Procedure*** | |
| 5.1.12.1 | State linearity and / or detection limits | Analytical Range / Minimum Detectable Concentration |
| 5.1.12.2 | State known interfering substances | Interfering Substances / Cross Reactivity |
| ***5.1.13*** | ***Bibliography*** | |
| 5.1.13.1 | Literature references | Bibliography |
| 5.1.13.2 | Manufacturer product literature | Each Method Sheet contains a method number and revision date on each page |
| 5.1.13.3 | Textbooks | |
| 5.1.13.4 | Standard Publications | |
| 5.1.13.5 | Written personal communications | |
| 5.1.13.6 | Research including supporting data for validation of methods | |