TOSOH BIOSCIENCE, INC.

G8
Variant Analysis Mode
Operator's Manual

Version 3.4.2

IVD

Supplied by

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Safety Precautions

Read these safety precautions before use and handle the analyzer properly and be sure to follow the instructions here for safe operation.
The meanings of WARNING and CAUTION are as follows:

WARNING
Indicates a hazard with a medium level of risk which, if not avoided, could result in death or serious injury.

CAUTION
Indicates a hazard with a low level of risk which, if not avoided, could result in minor or moderate injury.

During installation

WARNING

- **Connect an appropriate power source**
  - Connect to the power supply which gives sufficient power capacity and little voltage variation.
  - Fire may occur if the power capacity is insufficient or the voltage exceeds the specifications.

- **Check the grounding connection**
  - Electrical shocks may result if the grounding is incomplete.
  - Be sure to connect the system to a three-pin power socket.
  - In addition to preventing electrical shocks, the grounding also prevents loss of sensitivity because of noise and analyzer malfunctions.
  - Do not connect the grounding line to gas pipes, water pipes, lightning rods, or telephone grounding lines.
    Gas pipes: May cause explosions or fires
    Water pipes: Do not sufficiently work as grounds
    Lightning rods and telephone grounding lines:
    Dangerous when struck by lightning

CAUTION

- **Carefully select the installation location**
  - The analyzer must be placed a least 1 foot (300 mm) from any external water source.
  - Refer to **"Chapter 2, Section 2.4 Installation locations"** in this manual and select an appropriate location for installation.

- **Do not change the power cord, use an extension cord, or plug multiple cords into the same socket.**
  - The above use may cause fires or electrical shocks.
  - Make sure no dust is clinging to the plug and firmly insert the plug down to the bottom with no looseness.
  - Dust clung to the plug or looseness between plug and socket may cause fires or electrical shocks.

During use

WARNING

- **Take great care to prevent infections**
  - We strongly recommend that the operation be executed only by those persons with full knowledge about clinical tests and how to handle potentially infectious materials.
  - Blood to be tested might have been infected by pathogen. Misconduct on operation may cause infection to the operator or others working together. During operation take great care in handling test samples and use protection such as glasses, gloves, mask to prevent infection.
  - Used column, filter, sampling needle and vial may have been contaminated with infectious materials. To dispose of these units and samples, follow the instructed procedure in compliance with regulations on medical waste.

CAUTION

- **Do not operate in any other way than instructed in this manual.**
  - This may cause troubles such as disorder or injury or inaccurate result.

- **Check for eluent leakage**
  - Leakage of Elution Buffer or Hemolysis and Wash solution may cause fires, electrical shocks or corrosion.
  - When an eluent leakage is found, stop the operation and unplug the power cord then put on appropriate protection and then wipe off the eluent and take measures to stop the leakage by checking the tube connections.
  - Contact Technical Support when a leakage cannot be stopped.

- **When a problem occurs (burning smell, etc.), immediately stop operation, disconnect the power plug and contact Technical Support.**
  - Fires and electrical shocks may occur if operation continues.

- **Do not place fingers, rods, or other objects into moving or driving unit during operation.**
  - The motor is contained inside the unit. Fingers or other objects may get caught and get injured.

- **Close the cover and door during operation.**
  - Keep the cover and front door closed during operation. The operating, heated-up units and circuit with high voltage may have operator caught, wrapped up, burned, shocked, or otherwise injured.
  - Moreover not try to add any sample rack or sample during operation except for STAT port
- **Do not operate and stop the assay by plugging and unplugging the power.**
  - This may cause fires or electrical shocks.
  - Never fail to use the POWER KEY located on the front or main power switch on the left side of the analyzer.

CAUTION

- **Do not damage the power cord.**
  - If the power cord is pulled, forcefully bent or fixed, these may cause fires or electrical shocks.
  - When unplugging the power cord, be sure to pull on the plug itself.
  - Do not touch the analyzer with wet hands.
  - It may cause electrical shocks.

- **Those who are not trained with this analyzer must not perform any operation daily required to maintain the unit.**
  - It may cause infectious disease by injury or contaminated blood samples unless an operator understands what procedure is required such as putting on protection (glasses, gloves, mask) during the daily maintenance.
  - When replacing the sampling needle, it may damage the unit if moved too forcefully without unplugging the main power cord. Unplug the main power cord before
  - conducting any maintenance.
  - If you have any question about maintenance, contact Technical Support.

- **Dispose properly of wastes**
  - Wastes such as used sample vials, filter elements, columns and buffers accompanied with assay should be properly handled. When handling these, use protection like gloves and do not touch them directly. Dispose of these properly in accordance with the medical waste law not to damage the environment or health.

- **Put on protection**
  - When handling samples, waste or calibrators; put on protection such as glasses, gloves and mask to prevent infection.

- **Do not put any reagent containers outside the designated place for the unit.**
  - If the reagent leaks inside the unit, it may cause short circuit or poor electrical insulation or electrical shocks.

- **Use the designated parts mentioned in this operator's manual.**
  - For the consumables and spare parts, use the parts listed in this operator's manual.

- **For diagnostic purposes, the results obtained from this assay should be used in conjunction with other data (e.g. symptoms, results of other tests, clinical impressions, therapy, etc.)**

Removal of equipment from use for repair or disposal

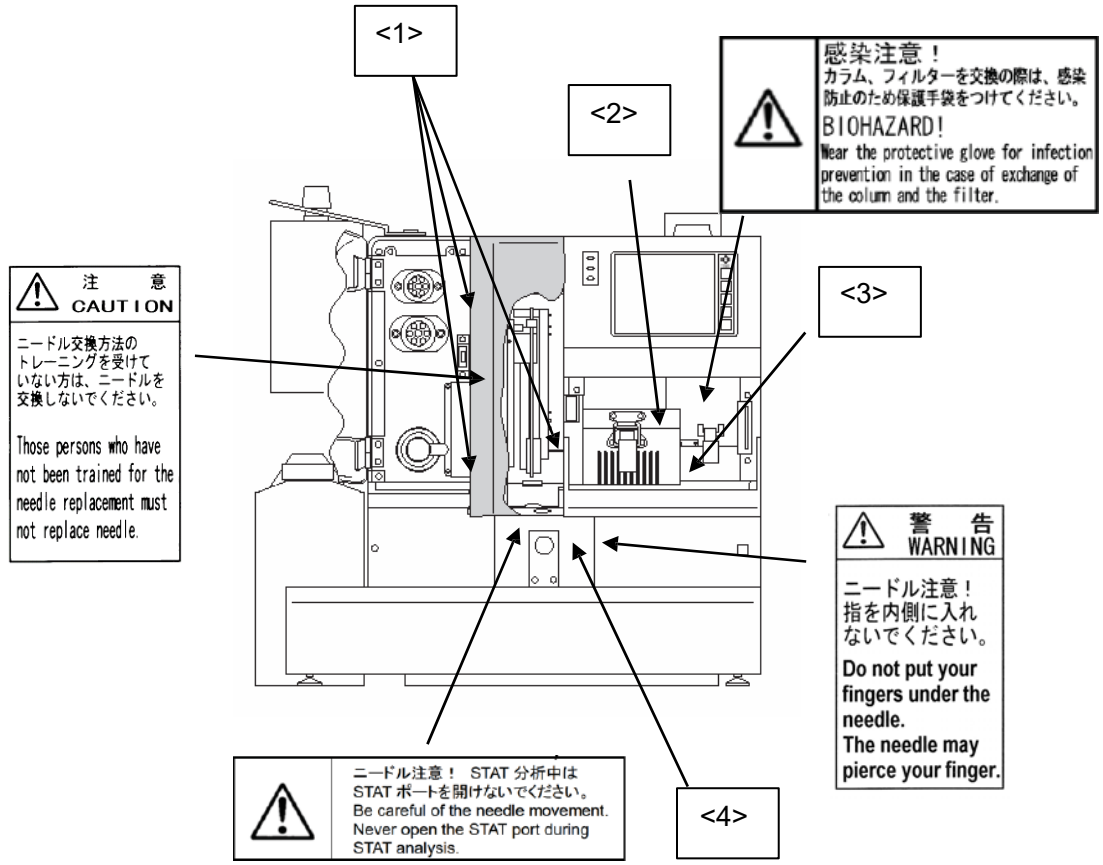
WARNING

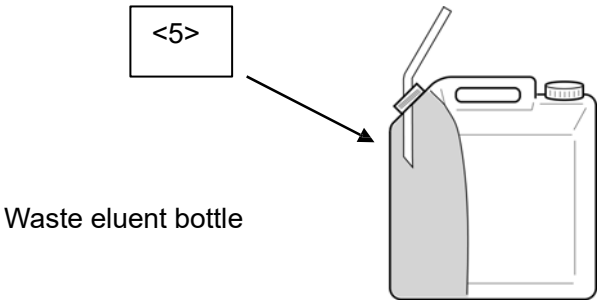
- **Contact Technical Support**
  - **Blood to be tested might have been infected by (a) pathogen(s). Misconduct on repair or disposal may bring infection to you or others working together. In the case of repairing and disposing, please contact Technical Support.**

Other precautions

- The warning labels are attached to the unit. Read the instruction thoroughly and follow.

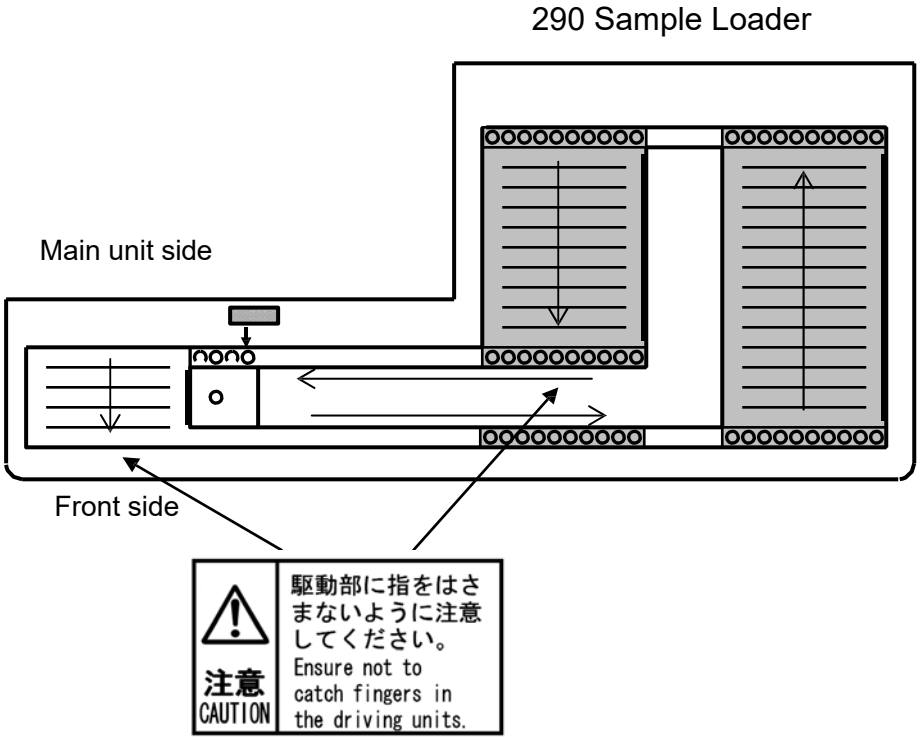
Placements of warning and caution labels





Waste eluent bottle

Placements of caution labels



<1> Needle Cover Caution Label

Sampler mechanism.
Don't open this cover except maintenance.
Turn off the main power before opening the instrument.

<2> Column Oven Biohazard Label

Be sure to wear appropriate protective clothing, such as gloves, when handling the column oven, as column has been contaminated by potentially infectious specimens.

<3> Filter Unit Biohazard Label

Be sure to wear appropriate protective clothing, such as gloves, when handling the filter unit, as filter element has been contaminated by potentially infectious specimens.

<4> STAT port Biohazard Label

Be sure to wear appropriate protective clothing, such as gloves, when handling the STAT port, as the inside of the STAT port has been contaminated by potentially infectious specimens.

<5> Waste Bottle Biohazard Label

Be sure to wear appropriate protective clothing, such as gloves, when handling the waste bottle, as waste liquid has been contaminated by potentially infectious specimens.

When the warning or caution labels have become faded, dropped off or become illegible, contact Technical Support.

- Keep this manual with the instrument so that you can read it when necessary.

Symbols on the product labels

European Conformity

Manufacturer

Authorized representative in the European Community

Catalogue number / Part number

In Vitro diagnostic medical device

Supplied by

Serial number/ Column number

— Copyrights —

- Copying or reprinting all or a part of this manual without the manufacturer's written approval is prohibited.
- The content of this manual is subject to change without notice.

For repair, contact your local authorized Tosoh representative

- Fires, electrical shocks and other problems may occur if the instrument is disassembled, repaired or remodeled by yourself.

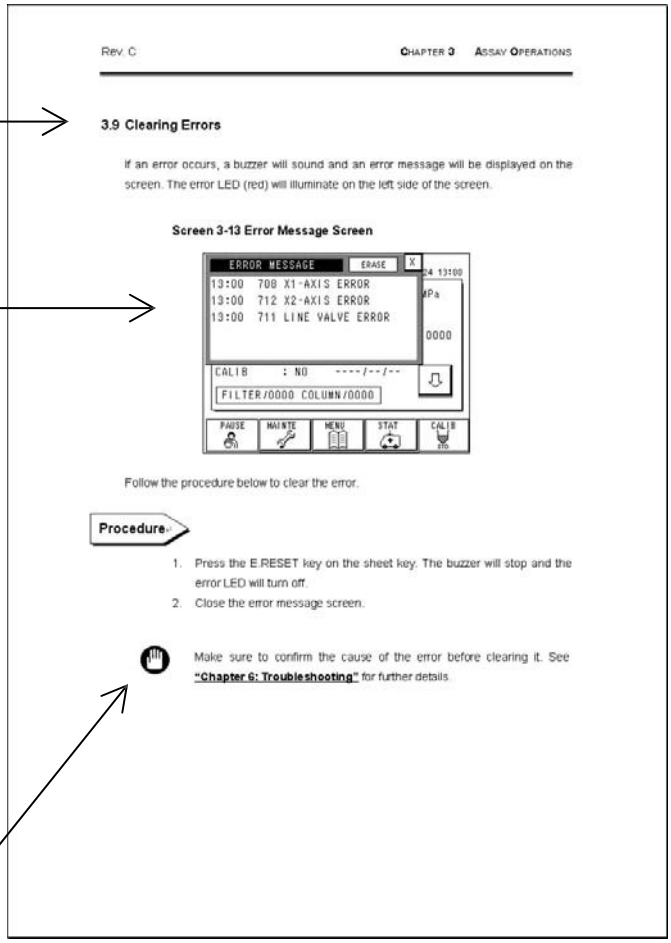
TOSOH CORPORATION

How to Use This Manual

This G8 Variant Analysis Mode Operator's Manual is designed to ensure you will have the information you need to use and operate the HLC-723G8 system safely and correctly.
This manual is organized according to the layout shown below. Use this as a reference when reading this manual.

Section Heading
Sections are divided into 3 subsections.

Illustration
Provided for your clear and precise understanding of the text.


Rev. C CHAPTER 3 ASSAY OPERATIONS

3.9 Clearing Errors

If an error occurs, a buzzer will sound and an error message will be displayed on the screen. The error LED (red) will illuminate on the left side of the screen.

Screen 3-13 Error Message Screen

Follow the procedure below to clear the error.

Procedure

1. Press the E.RESET key on the sheet key. The buzzer will stop and the error LED will turn off.
2. Close the error message screen.

Make sure to confirm the cause of the error before clearing it. See "Chapter 6: Troubleshooting" for further details.

Stop sign warns potential operational mistakes.

Point Key Point provides helpful hints for mastering system operations.

Chapter 1 Introduction and Applications

Tosoh Automated Glycohemoglobin Analyzer HLC-723G8

1.1 Overview and Intended Use

The Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 is intended for *in vitro* diagnostic use for the quantitative measurement of % hemoglobin A1c (HbA1c) (DCCT/NGSP) and mmol/mol hemoglobin A1c (IFCC) in venous whole blood specimens. This test is to be used as an aid in diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes, and for monitoring of long –term blood glucose control in individuals with diabetes mellitus.

Summary and Explanation of the Test

Diabetes causes elevated levels of glucose to circulate in the blood[1]. The American Diabetes Association (ADA) recommends a general percent hemoglobin A1c (% HbA1c) goal of <7%, with personalization determined on a case-by-case basis[2]. Maintaining normal levels of blood glucose is part of the routine clinical management of diabetes. Continuous and careful management of blood glucose levels prevents development of serious long-term complications resulting from vascular impairment such as retinopathy, nephropathy, and neuropathy[3].

Although a fasting blood glucose measurement gives the clinician information about the patient's status over the last twelve hours, the stable HbA1c offers a more accurate indication of the patient's long-term diabetic control over the last two to three months[4].

Glycohemoglobin is a general term for hemoglobin-glucose complexes in which glucose is bound to the alpha and beta chains of hemoglobin. The most quantitatively prevalent complex is called HbA1c, in which glucose binds to the N-terminus of the beta chain of HbA.

HbA1c is nonenzymatically synthesized in two steps:

The glucose aldehyde group and the free amino group on the valine in the N-terminus of the hemoglobin beta chain react to form the Schiff base, aldimine (also known as labile HbA1c or LA1c).

A stable ketoamine form of the hemoglobin complex (SA1c) is then produced by a reaction known as Amadori rearrangement.

The level of LA1c changes rapidly in response to changes in blood glucose concentration. However, the level of the SA1c does not fluctuate significantly in response to physiological factors. Consequently, the SA1c measurement provides a better indication of the average glucose level over the previous two to three months (the average red blood cell life span).

Formation of Labile and Stable Forms of A1c (LA1c and SA1c)

In the past, accurate measurement of SA1c was possible only after removing LA1c by pretreatment. The Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 can individually resolve SA1c and LA1c on the chromatogram without manual pretreatment, allowing accurate measurement of SA1c directly.

The Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 uses non-porous ion-exchange high performance liquid chromatography (HPLC) for rapid, accurate and precise separation of the stable form of HbA1c from other hemoglobin fractions. Analysis is carried out without off-line specimen pretreatment or interference from Schiff base.

The analyzer dilutes the whole blood specimen with Hemolysis & Wash Solution, and then injects a small volume of this specimen onto the TSKgel G8 Variant HSi column. Separation is achieved by utilizing differences in ionic interactions between the cation exchange group on the column resin surface and the hemoglobin components. The hemoglobin fractions (designated as A1a, A1b, F, LA1c+, SA1c, A0, and H-V0, H-V1, H-V2) are subsequently removed from the column by performing a step-wise elution using the varied salt concentrations in the Variant Elution Buffers HSi 1, 2, and 3.

The Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 analyzer aspirates the whole blood specimen and dilutes it with Hemolysis and Wash solution at a ratio of 1/200. Approximately 4 µl of the diluted and hemolyzed sample is loaded into the sample loop at the injection valve and injected onto the TSKgel G8 Variant HSi column. Inside the column, the net charges of the hemoglobin proteins interact with the negative charges on the non-porous resin. The time from injection of the sample to the time the specific peak elutes off the column is called retention time of that fraction. As each fraction elutes, it passes through the LED photometer flow cell, where the analyzer measures changes in absorbance at 415 nm. The analyzer plots a chromatogram showing the changes in absorbance versus retention time for each fraction, represented as a peak.

The Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 software has been written so that each of the expected fractions has a window of acceptable retention times. If the designated peak falls within the expected window, the chromatogram peaks will be properly identified. The software designates a hemoglobin fraction as P0X (where X is the order of the peak as it elutes from the column, starting from “0”) if it does not match a defined window of retention time. To keep the peaks within their appropriate windows, it may be necessary to modify the speed at which the buffers move through the system by changing the pump flow rate.

As the analyzer measures the absorbance of each fraction at 415 nm, it integrates and reduces the raw data, and then calculates the relative percentages of each hemoglobin fraction.

The data can be stored on the instrument or transmitted to a host computer through a bi-directional interface. A printout of the final results includes the sample ID, date, percentage and retention time of each fraction of hemoglobin, sA1c percentage and total A1 percentage (A1a+A1b+sA1c), along with a chromatogram of the elution pattern of the hemoglobin fractions. If a sample contains a hemoglobin variant, the column elutes the fraction depending upon its charge.

The Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 is certified by the National Glycohemoglobin Standardization Program (NGSP). The final reportable result is traceable to both the International Federation of Clinical Chemistry (IFCC) and the Diabetes Control and Complications Trial (DCCT).

1.2 Test Components and Materials Provided

The following components are available for the Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 Variant Analysis Mode.

Part #	Description	Packaging
0018767	Tosoh Hemoglobin A1c Calibrator Set	
	Calibrator 1 (approximately 5.5%)	5 x 4 mL
	Calibrator 2 (approximately 10.5%)	5 x 4 mL
	Buffered human red blood cells, 2 mg/mL human hemoglobin	
220232	Tosoh Hemoglobin A1c Control	
	Normal	4 x 0.25 mL
	Abnormal	4 x 0.25 mL
0021955	TSKgel G8 Variant HSi	1 each
0021956	G8 Variant Elution Buffer HSi No.1 (S)	1 x 800 mL
0021957	G8 Variant Elution Buffer HSi No.2 (S)	1 x 800 mL
0021958	G8 Variant Elution Buffer HSi No.3 (S)	1 x 800 mL
018431US	HSi Hemolysis & Wash Solution (L)	1 x 2000 mL
0021600	Filter Element	5/pkg
0018581	Sample Cups	1000/pkg
0019563	Thermal Paper	10 rolls/pkg
0018723	Supply Line Filters for Buffer Lines	1/pkg
0019500	Sampling Needle Assembly	1 each

The Tosoh Japan inventory system uses a double zero at the beginning of all part numbers in the package insert (IFU).

Note: Volumetric pipettes are required but not supplied by Tosoh Bioscience, Inc.

1.3 Warnings and Precautions

The calibrators, column, and reagents are intended for in vitro diagnostic use only on the Tosoh Automated Glycohemoglobin Analyzer HLC-723G8. Do not use these test components on other systems.

℞ only. US Federal law restricts this device to sale by or on the order of a licensed healthcare practitioner.

The Elution Buffers and Hemolysis & Wash Solution contain sodium azide that may react with lead or copper plumbing to form potentially explosive metal azides. When disposing of such reagents, always flush with large volumes of water to prevent azide build-up.

Do not use reagents and columns past the expiration date.

Human blood products used in the preparation of the Tosoh Hemoglobin A1c calibrators and controls have been tested by standard, approved methods and found to be negative for the presence of Hepatitis B surface antigen and for antibodies to HCV and HIV.

Because no testing method can offer complete assurance that products derived from human blood will not transmit infectious agents, always handle these materials with the same precautions used for patient specimens.

1.4 Storage and Stability

Unopened and stored at 2-8°C, the Tosoh Hemoglobin A1c calibrator and control sets are stable until the expiration date printed on the label. After reconstitution, calibrators are stable for one week when stored at 2-8°C. Refer to the control package insert for stability data.

Unopened G8 Variant Elution Buffers HSi (S) 1, 2, and 3 are stable until the expiration date printed on the label. After opening, Elution Buffers are stable for three months. Store at 4-30°C.

Unopened Hemolysis & Wash Solution is stable until the expiration date printed on the label. After opening, Hemolysis & Wash Solution is stable for three months. Store at 4-30°C.

The unopened TSKgel G8 Variant HSi column should be stored at 4-15°C in a cool location away from direct sunlight. The column is stable until the expiration date printed on the label. Columns are warranted for 2500 injections.

1.5 Specimen Collection and Handling

Collect venous whole blood specimens in vacuum collection tubes containing K2- EDTA or K3-EDTA and mix thoroughly. Specimens may be stored up to fourteen days at 2-8°C before analysis. Specimens may be stored up to twenty-four hours at room temperature (10-25ºC) before analysis. The minimum volume required for analysis directly from collection tubes is 1 mL of whole blood. Venous Whole blood samples as small as 50 µL may be used when appropriate sample cup and software options are selected.

1.6 Procedures

A. Reagent and Column Preparation and Installation

The TSKgel G8 Variant HSi column, Elution Buffers, and Hemolysis & Wash Solution are provided ready to use.

Note: The instrument warranty does not cover service visits or parts required due to reagent spillage. Please replace liquid reagents using the appropriate procedure as outlined below.

Installing G8 Variant Elution Buffer HSi

Press the **STOP** key to put system in STAND-BY status.

Remove buffer containers to be replaced.

Break the seal on the storage caps of the new buffer containers, leaving the caps in place.

Carefully place the capped buffer bags on the rack on the instrument. Verify that the buffer bag is supported on the rack by the octagonal shaped lip at the base of the threads.

For each reagent, remove the cap, carefully squeeze the buffer bag by hand to minimize air pockets, and then place the appropriate color-coded tubing into the corresponding bag. Ensure that the end of the tubing is touching the bottom of the container.

Securely tighten reagent caps.

From the MAIN screen, select **MAINTE**, then **REAGENT CHANGE**. Once the buffers have been correctly installed, select the appropriate buffer, then press **CHANGE**.

Installing Hemolysis & Wash Solution

Press the **STOP** key to put the system in STAND-BY status.

Remove the empty container.

Break the seal on the storage cap of the new container, leaving the cap in place.

Place the Hemolysis & Wash Solution bottle on the bench at the left side of the instrument, beside the H/W Solution port.

Remove the cap, then place the Hemolysis & Wash Solution tubing into the container. Ensure that the end of the tubing is touching the bottom of the container.

Securely tighten reagent cap.

From the MAIN screen, select **MAINTE**, then **REAGENT CHANGE**. Once the Hemolysis & Wash Solution has been correctly installed, press **H/W**, then press **CHANGE**.

Installing TSKgel G8 Column

Press the **STOP** key to put the system in STAND-BY status.

Unscrew column fittings and remove used column.

Remove protective plugs from new column. Do not discard the plugs, as they are needed for storage. Verify that the column master lot matches the Elution buffer lot.

Check flow direction - the arrow on the column should point to the left as it is placed on the instrument.

Slide the inlet tubing until it extends ¼ inch past each end fitting. Connect the tubing to the inlet (right) side of the column.

Take special care that buffer coming from the tube does not spill onto the analyzer unit by holding absorbent paper or gauze at the outlet end of the column when priming.

From the second page of the MAIN screen, press **PUMP FLOW** to start pumping the buffer. When buffer solution flows from the outlet (left) side of the column, press **PUMP FLOW** again to stop the pump.

Connect the tubing to the outlet side of the column.

Press **PUMP FLOW** to start pumping and check for leaks. The pressure should rise to the pressure level that is indicated on the column inspection report + 4 MPa. If leaks occur, tighten fittings.

When the pressure reaches a steady state, press **PUMP FLOW** again to stop pumping.

From the MAIN screen, select **MAINTE**, then **REAGENT CHANGE**. Press **COLUMN RESET** to set column count back to zero.

Before calibrating the newly installed column, run at least three whole blood samples to prime the column. Calibrate the system and run controls.

Calibrator Preparation

Remove caps from the calibrator vials.

Reconstitute calibrators 1 and 2 using a volumetric pipette to add 4.0 mL Type I Reagent Grade water to each vial.

Replace respective caps and mix thoroughly by inversion.

Store reconstituted calibrators upright at 2-8°C for up to seven days.

B. Calibration Procedure

The analyzer has a two-point automatic calibration function. Each laboratory must

monitor QC results according to good laboratory practices to determine when to recalibrate. Calibration frequency should be based upon QC results and chromatogram quality. Calibration is stable for at least seven days if the system is calibrated and maintained according to the procedures provided in the Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 Operator's Manual.

Verify that there is sufficient volume of G8 Variant Elution Buffers HSi and HSi Hemolysis & Wash Solution. Replace if necessary.

Check analyzer status.

If the analyzer is OFF, press the POWER key at the bottom of the display. The analyzer begins WARM UP.

After WARM UP is complete, the instrument will enter STAND-BY status.
Select **CALIB** from the MAIN screen. Once selected, it will be reverse highlighted. A pop up menu will appear to remind the operator to enter the calibration values. Press **CALIB-1** and enter the assigned value for Calibrator 1 from the calibrator vial label.

Press **CALIB-2** and enter the assigned value for Calibrator 2. The assigned values differ from lot-to-lot. Calibrator 1 is approximately 5.5% and Calibrator 2 is approximately 10.5%.

Pipette at least 400 µL of each calibrator into sample cups. Place the sample cups in the rack with Calibrator 1 in position 1 (on the left) and Calibrator 2 next to it in position 2. Place an empty rack on the loader to signal the end of the run. Press the **START** key to begin the calibration.
The analyzer samples Calibrator 1 three times and Calibrator 2 two times. The analyzer discards the first measurement of Calibrator 1, and uses the remaining four measurements to calculate factors A and B. Following a successful calibration, patient and control samples will be calculated using the new factors.

Calibration Acceptability Criteria

When the calibration procedure is completed, the analyzer automatically accepts or rejects the calibration results. If the calibration is unsuccessful, recalibration will be required. A Calibration Error message appears and the run aborts if:

The two SA1c% results for Calibrator 1 differ by 0.3% or more.
The two SA1c% results for Calibrator 2 differ by 0.3% or more.

Any of the four calibrator results differ from its assigned value by ± 30% or more.

C. Assay Procedure

Verify that there is sufficient volume of G8 Variant Elution Buffers HSi and HSi Hemolysis & Wash Solution. Replace if necessary.

Check analyzer status.

If the analyzer is OFF, press the POWER key to the right of the display. The analyzer begins WARM UP. If the analyzer is ON and calibrators or controls or sample testing is in progress, another rack can be added at any time.

Mix each specimen by gentle inversion.

Place specimen tubes in the rack.

Place an empty rack on the loader to signal the end of the run.

If starting from STAND-BY or WARM UP status, press the START key to begin the procedure.

Quality Control

In order to monitor and evaluate the accuracy and precision of the analytical performance, controls should be assayed daily and after column replacement. Tosoh suggests running at least two levels of quality control material. The mean of one should be in the non-diabetic range (4-7% HbA1c) with the second in the range of 9-12% HbA1c.

If the value of one or more control specimens is out of the acceptable range, recalibrate the system and rerun the controls before testing patient samples.

QC materials should be used in accordance with local, state, federal and accredited organizations.

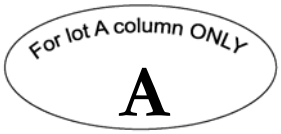
Controls should be diluted with HSi Hemolysis & Wash Solution to obtain an optimal Total Area (TA) in the range of 700-3000. However a TA in the range of 500-4000 is acceptable and reportable for whole blood specimens.
Laboratory policy for this particular assay designates the following:

Control Material: _____
Frequency: _____

1.7 Procedural Notes

To avoid an error condition during calibration, place calibrators 1 and 2 in the first sample rack in positions 1 and 2 respectively.

Always use the G8 Variant Elution Buffer(s) HSi in combination with a TSKgel G8 Variant HSi column of the identical lot number. The column lot number is indicated by a single uppercase alphabetical character (A, B, etc.) on the label of the column box. The elution buffer label displays an alphabetic character corresponding to column lot number, as shown below.



HSi Hemolysis & Wash Solution may be used with any master lot of column/buffers since it is not lot matched to the other components.

The reagents must be at room temperature (15-25°C) prior to use.

Never pour or transfer reagent from one bag or container to another; results may be compromised.

When replacing the column, run at least three whole blood samples to prime the column then recalibrate the system before running quality control materials.

Replace the filter element if pressure is greater than the pressure level that is indicated on the column inspection report +4 MPa or after 400 injections.

If the column is not to be used for more than one week, remove it from the analyzer and seal the ends with the protective plugs and store in cool place at 4-15°C. Avoid direct sunlight.

At least once a day check the waste container to ensure that there is enough space remaining to accommodate a run. If necessary, empty container and add about one liter of fresh 5% sodium hypochlorite solution (household bleach).

1.8 Limitations of the Procedure

Total Area

Dilution studies demonstrate that the assay is linear from a Total Area of 500 to 4000. However, the optimum Total Area is 700 to 3000.

Abnormal Red Cell Survival

The life span of red blood cells is shortened in patients with hemolytic anemias, and the actual life span depends upon the severity of the anemia. As a consequence, specimens from such patients may exhibit decreased glycohemoglobin levels compared to patients with normal red cell life span. The life span of red blood cells is lengthened in polycythemia or post-splenectomy patients. Specimens from such patients may exhibit increased glycohemoglobin levels.

Hemoglobinopathies

The most commonly observed hemoglobin variants are HbS, HbC, HbD and HbE. These variants in their heterozygous state elute after the HbA0 peak in their designated windows: HbS (H-V1 peak), HbD (H-V0 peak) and HbC (H-V2 peak). The HbE (P-HV3 peak) appears between SA1c and HbA0 peaks. In all these cases, the SA1c% is reportable when these hemoglobin variants are present in the heterozygous state.

When either of these hemoglobin variants is identified, the SA1c% is calculated in a proprietary way, depending on the type of hemoglobin variant, based on the area of SA1c, the area of identified hemoglobin variant and other peaks. When a P-HV3 peak is detected, a Flag 43 is also reported.

Glycemic monitoring for any patients displaying any homozygous hemoglobin (other than HbAA) such as HbSS, HbCC or the double heterozygous SC, cannot be performed using SA1c because there is no hemoglobin A present. Alternative testing is mandatory for these types of patients.

Warning
This device is for prescription use only.

Hemoglobin A1c should not be used to diagnose Diabetes Mellitus in patients with iron deficiency and hemolytic anemia, various hemoglobinopathies, thalassemias, hereditary spherocytosis, malignancies and severe chronic hepatic and renal disease.

Hemoglobin A1c should not be used in pregnant patients, patients with heterozygous sickle cell trait, hemolytic diseases and recent significant or chronic blood loss.

Hemoglobin A1c should not be used in the diagnosis of gestational diabetes.

In cases of rapidly evolving type 1 diabetes the increase of HbA1c values might be delayed compared to the acute increase in glucose concentrations. In these conditions diabetes mellitus must be diagnosed based on plasma glucose concentration and/or the typical clinical symptoms.

Only the percent HbA1c values measured by this device should be reported to the health care provider. The test report displays %HbF and other detected hemoglobin variants; however, the performance characteristics of the hemoglobin variants detected by this device have not been reviewed or cleared by the FDA and therefore should not be reported to the healthcare provider. The hemoglobin variants detected by this device are only to ensure the validity of the HbA1c results because increased levels of hemoglobin variants may interfere with the percent HbA1c measurement. If a hemoglobinopathy is suspected, an FDA cleared test system for their measurement should be used Hemoglobin A1c testing should not replace glucose testing for type 1 diabetes, in pediatric patients and pregnant women

Interpretation of Results

The SA1c measuring range is 4.0 – 16.9%.

The ideal retention time for SA1c is 0.59 minutes.
The ideal retention time for A0 is 0.90 minutes.

Results will not be reported if the Total Area (TA) is <500 which can be seen in severe anemia. Results will not be reported if the TA is >4000 which can be seen in polycythemia. (See "abnormal red cell survival in previous section). The optimal goal for Total Area is between 700-3000. However, a TA in the range of 500-4000 is acceptable and reportable for whole blood specimens.

The chromatogram must be examined for any unidentifiable peaks (i.e., P00, P01,) before the A0 peak. Do not report the result if these peaks exist.

When there is a question concerning the chromatography, repeat the sample.
If the repeated sample also displays unusual characteristics, it is appropriate to evaluate whether the unusual result is due to an abnormal sample, a procedural error, an instrument malfunction or a sample-handling problem. For further information, see the Troubleshooting Section in this Operator's Manual.

1.9 Expected Reference Values

Reference Ranges (non-diabetic): HbA1c 4.0-6.0 % (mean 5.0 %, SD 0.5 %)

Ref: American Diabetes Association. 2. Classification and diagnosis of diabetes: *Standardsof Medical Care in Diabetes—2020*. Diabetes Care 2020;43(Suppl. 1):S14–S31

146 apparently healthy adults were tested and fell within the range of 4.4-6.1%. These were representative of the US population.

Each laboratory should determine a reference interval that corresponds to the characteristics of the population being tested.

The values referred to in this document have been determined with a National Glycohemoglobin Standardization Program (NGSP) certified method. It is known that the relationship between HbA1c results from the NGSP network and the IFCC network is expressed by using the following equation:

$$\text{NGSP (\%)} = 0.09148 \times \text{IFCC (mmol/mol)} + 2.152$$

The diagnosis of diabetes and identification of persons at increased risk of developing diabetes follows the ADA Guideline of 6.5% for the cut-off and values between 5.7% and 6.4% as being at increased risk.

1.10 Performance Characteristics

Dilution-Total Area / Linearity

Packed red blood cells from a normal specimen collected in EDTA were diluted with Hemolysis & Wash Solution and assayed. The study demonstrates that the assay is linear in samples with Total Area values from 500 to 4000.

Total Area	Hb A1c%
505	10.6
658	10.6
1144	10.6
1620	10.6
2164	10.7
2846	10.6
3328	10.7
3545	10.7
4047	10.7

Recovery / Linearity

Two studies were conducted on the Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 to demonstrate recovery and linearity. In the first study, two whole blood specimens were collected in EDTA. The observed values of the neat specimens were established by HPLC measurement. The theoretical value was a calculated % based upon mixing two samples at different ratios and dividing by the dilution factor. The diluted specimens were run in triplicate, and the average value is listed as the observed % in the table below. The acceptance criteria were 100 ± 5%. The recovery study demonstrates that the results between 2.2% and 16.9% were accurate and are listed on the table below.

High sample (ratio)	Low sample (ratio)	Observed %HbA1c	Theoretical %HbA1c	Recovery %
0	10	2.2	2.2	100.0
1	9	3.6	3.6	100.0
2	8	5.1	5.1	100.0
3	7	6.6	6.6	100.0
4	6	8.0	8.1	98.8
5	5	9.4	9.6	97.9
6	4	11.2	11.0	101.8
7	3	12.4	12.5	99.2
8	2	14.0	14.0	100.0
9	1	15.5	15.5	100.0
10	0	16.9	16.9	100.0

In the second study, linearity was established using a commercially available linearity material. The manufacturer's instructions were followed, and linearity was shown between 3.2% and 18.4%. These observed values are within ± 5% of the assigned values.

Level	Assigned Value	Mean	% Recovery
1	3.1	3.2	103.2
2	5.8	5.9	101.7
3	10.2	10.37	101.9
4	18.6	18.43	99.1

Correlation

To identify and effectively treat people with diabetes it is critical to have accurate and timely diagnostic testing and methods that are aligned to the NGSP standard[5].

The methods comparison study was conducted in accordance with CLSI EP09c: Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Third Edition.

This was a two-site study, designed to determine the analytical performance of the Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 with Version 5.24 software (G8 v5.24) analyzer when compared with the Trinity Premier Hb9210™ (Premier) NGSP SRL method. The analytical instruments were physically located in two independent laboratories, one an NGSP SRL (DDL) and the second at the Tosoh QA lab (TBQAL).

The accuracy was measured by comparing HbA1c values obtained with the G8 v5.24 against HbA1c values assigned to the same matching samples using an NGSP SRL method (Premier).

Regression analysis was conducted to determine if any changes across the measuring interval (4.0-16.9%) were significant between the two methods. Results described below conclude that there is no significant difference between the methods.

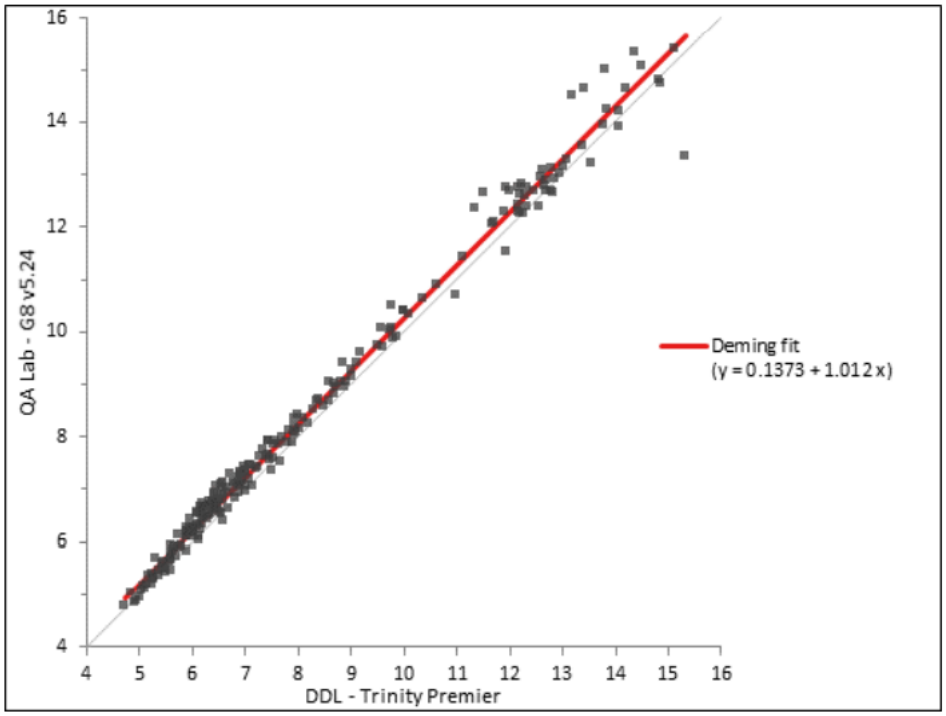
	y-intercept	95% CI	Slope	95% CI
Deming	0.1332	-0.0339 to 0.3002	1.013	0.9894 to 1.036
Passing-Bablok	0.0702	-0.0484 to -0.1864	1.021	1.006 to 1.036

The method comparison using the Passing- Bablok and Deming regression analysis concluded that the two methods are well within the allowable bias of ± 6 %.

% HbA1c	% Bias (Deming)	% Bias (Passing-Bablok)
5.0	4.0	3.5
6.5	3.3	3.2
8.0	3.0	3.0
12.0	2.4	2.7

*The maximum of Deming and Passing Bablok related bias estimates were used in the calculation of the 'Total Error [%]' estimation.

Method Comparison Deming Regression Analysis of G8 v5.24 vs NGSP SRL (Trinity Premier)



Precision:

Total Error [%]					
	Passing Bablok		Deming		
HbA1c Level	`%TE´	%Bias	`%TE´	%Bias	$\%CV_{Total}$
Sample1 [5%]	5.48	3.5	5.99	4.0	0.974054
Sample2 [6.5%]	5.31	3.2	5.41	3.3	1.042108
Sample3 [8%]	5.59	3.0	5.59	3.0	1.281173
Sample4 [12%]	4.45	2.7	4.15	2.4	0.870450
*: Calculated as: `|%Bias| + 1.96 x $\%CV_{Total}$ x (1+ %Bias/100)´					

The study is designed in accordance with CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline - Third Edition. It was conducted at two separate sites using three different G8 v5.24 analyzers (two analyzers at TBQAL, and one at DDL). Results were generated with three separate reagent lots (including columns), over 20 non-consecutive days per reagent lot, for a minimum of 60 days. Venous whole blood samples collected from 4 donors at four different concentrations of HbA1c; 5.0%, 6.5%, 8.0% and 12.0%, were tested at each run.

The results demonstrate that the HLC-723®G8 With Software v5.24 shows an acceptable % bias ranging from 2.7-4.0% and an overall %CV ranging from 0.87 to 1.28%. In combining the data from the Precision and Method studies, the % Total Error was calculated at each % HbA1c level and summarized below:

Summary of Precision Analysis per Concentration Level (% CV)

Mean HgbA1c	Repeatability	Between Run	Between Day	Between Lot	Between Analyzer	Total
5 %	0.35	0.24	0.49	0.53	0.50	0.97
6.5%	0.33	0.13	0.45	0.44	0.75	1.04
8 %	0.26	0.19	0.51	0.58	0.97	1.28
12 %	0.23	0.14	0.56	0.57	0.20	0.87

Matrix study for K2 EDTA and K3 EDTA:

A matrix comparison study with the Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 (G8) was performed to evaluate the effects of two different EDTA anticoagulants, K2-EDTA and K3-EDTA, on the %HbA1c measurement using version 5.24 software.

Fifty (50) venous whole blood matching samples, collected in K2 EDTA and K3 EDTA tubes with approximately ten specimens per concentration range (>4.7 – 6.0%, >6.0 - 6.5%, >6.5 – 7.0%, >7.0 - >9.0% and 10.0 - 16.9%), were tested by the clinical testing laboratory investigational site.

All analysis was done in accordance with CLSI EP09-A3 Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Third Edition. The statistical methods demonstrate that K2-EDTA and K3-EDTA show no clinical or statistical difference and thus may be used interchangeably for testing HbA1c on the G8 HPLC Analyzer.

Comparison of various regression analysis methods (N=47)

Regression Analysis	Regression Equation
Least-Squares	y=-0.02021+1.004x
Deming	y=0.02062+1.004x
Passing-Bablok	y=0.01676+1.004x

1.11 Interference:

This interference study was developed according to the CLSI guideline Interference Testing in Clinical Chemistry (EP7-A2).

- Interference studies were conducted on known concentrations of %HbA1c. Specimens were spiked with increasing amounts of the interferent[6,7,8]. Interference was determined as a variance greater than the measured value ± 5%.

Potential Interferent	Range tested	%A1c Concentrations	Concentration in which no significant interference was observed
Acetylated Hb	10 - 50 mg/dL	6.5 and 9.5	50 mg/dL
Albumin	500 - 5000 mg/dL	6.6 and 14.7	5000 mg/dL
Aldehyde Hb	5.0 - 25 mg/dL	6.3 and 12.6	25 mg/dL
Ascorbic Acid	3.0 - 25 mg/dL	6.4 and 10.8	25 mg/dL
Carbamylated Hb	5.0 - 25 mg/dL	6.5 and 9.8	25 mg/dL
Bilrubin C	2.0 - 21 mg/dL	6.5 and 14.3	21 mg/dL
Labile Hb	200 – 1000 mg/dL	6.4 and 10.3	1000 mg/dL
Lipemia	100 - 1000 mg/dL	6.4 and 14.1	1000 mg/dL
Rheumatoid Factor	110 - 550 IU/mL	6.3 and 12.6	550 IU/mL
Bilirubin F	2.0 - 18 mg/dL	6.5 and 14.3	18 mg/dL

Hemoglobin Variant Interference Study:

Possible interference when measuring HbA1c in clinical specimens due to variant hemoglobins is well known and documented. Common hemoglobin variants have been shown to interfere with HbA1c results with some assay methods[8,9]. The prevalence of hemoglobinopathies varies among populations[10].The most common of the beta chain variants are hemoglobins S, C, D and E.

The study conducted at NGSP SRL site was designed in accordance with CLSI EP07 Interference Testing in Clinical Chemistry; Approved Guideline – Third Edition [5] and CLSI EP09-A3 Measurement Procedure and Bias Estimation 2013. Venous whole blood specimens containing varying levels of the variant were tested in triplicate on both the Tosoh Automated Analyzer HLC-723G8 with software version 5.24 (G8 5.24) and the comparator. The percent of the variant in question was ascertained from the Sebia Capillarys 2 instrument using the Hemoglobin method.

Interference studies were conducted on known concentrations of %HbA1c and the specified variant in venous whole blood. Non-clinically significant interference was defined as </=6% relative difference in the results from the comparator at 6% or 9% HbA1c. Based on the results, the G8 5.24 does not demonstrate any clinical interference on the HbA1c levels at the % levels of variant for each hemoglobin variant as listed below.

Percent Relative Bias from Reference Method at Low and High Concentration of HbA1c Samples

Hemoglobin Variant/ Hemoglobinopathy	Percent Relative Bias from Reference Method at Low and High Concentrations of HbA1c Samples			
	~6.5 % HbA1c		~8.0 % HbA1c	
	Calibrated Relative % Difference	Range	Calibrated Relative % Difference	Range
HbAD	-0.5	0.08 to 0.30	-1.7	-0.04 to 0.36
HbAS	-2.7	-0.04 to 0.13	-3.2	-0.14 to 0.21
HbAC	-1.9	0.03 to 0.17	-1.1	0.06 to 0.34
HbAE	-1.3	0.001 to 0.27	-1.2	-0.10 to 0.49
HbA2	-4.2	-0.17 to 0.06	-5.1	-0.37 to 0.12
HbF	-0.7	0.10 to 0.25	-1.6	-0.01 to 0.34

Variant Samples Used in Hemoglobin Variant Study

Hemoglobin Variant/Hemoglobinopathy	n	Range in % Abnormal Variant/Hemoglobinopathy	Range in % HbA1c Concentration
HbC	26	30.8 to 37.8	4.8 to 9.8
HbD	24	22.6 to 40.7	5.3 to 9.347
HbE	26	20.0 to 30.9	4.763 to 9.7
HbS	29	28.2 to 38.9	4.9 to 10.5
HbA2*	20	2.7 to 5.5	5.85 to 10.1
HbF*	21	0.4 to 43.35	4.36 to 8.9

*Hemoglobinopathies

Fetal Hemoglobin and interference:

Elevated levels of Fetal Hemoglobin (HbF) seen with Hereditary Persistence of Fetal Hemoglobin (HbFH) may interfere with the A1c result.

Samples spiked with various concentrations of umbilical cord blood were measured by the G8 v5.24 and a cleared diagnostic HbA1c device (Bio-Rad Variant II Turbo 2.0) to compare results at 6% and 8% HbA1c levels. At up to 25% Fetal Hgb the G8 v5.24 device did not interfere at clinically relevant levels of HbA1c.

In the homozygous and double-heterozygous forms of variant hemoglobins (e.g. HbSS, HbCC or HbSC), there is no HbA present; therefore, no HbA1c value can be determined. Other abnormal hemoglobin variants have not been evaluated on the Tosoh HLC-723G8 assay.

An erroneous result including misidentification of hemoglobin variant may be obtained with a deteriorated specimen, therefore it is important to use a fresh specimen.

The Tosoh Automated Analyzer HLC-723G8 TSKgel column is warranted to 2500 injections. Column deterioration is suspected if the chromatogram resolution decreases.

1.12 References

1.12.1 American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes--2020. Diabetes Care, 2020. 43 (Suppl. 1): S14 - S31.

1.12.2 American Diabetes Association, Diagnosis and classification of diabetes mellitus. Diabetes Care, 2014. 37 Suppl 1: p. S81-90.

1.12.3 DeFronzo, R.A., et al., Type 2 diabetes mellitus. Nat Rev Dis Primers, 2015. 1: p. 15019.

1.12.4 Goldstein, D.E., et al., Tests of glycemia in diabetes. Diabetes Care, 2003. 26 Suppl 1: p. S106-8.

1.12.5 National Glycohemoglobin Standardization Program. 2020; Available from http://www.ngsp.org/network.asp.

1.12.6 Coriello A, Giugliano D, Dello Russo P, Sgambato S, D'Onotrio F. Increased glycosylated hemoglobin A1 in opiate addicts. Evidence for hyperglycemic effect of morphine. Diabetologia 1962;22:379.

1.12.7 Nathan DM, Francis TB, Palmer JL. Effect of aspirin on determinations of glycosylated hemoglobin. Clin Chem 1983;29:466-9.

1.12.8 Fluckiger R, Harmon W, Meier W, Loo S, Gabbay KH. Hemoglobin carbamylation in uremia. N Eng J Med 1981;304:823-7.

1.12.9 Rohlfing,C., Hanson, S., Wykamp, C. ; Effects of hemoglobin C, D, E, and S traits on measurements of hemoglobin A1c by twelve methods; Clinica Chemica Acta 455 (2016) p 80-83

1.12.10 Little,R., Rohlfing, C., Sacks, D.; The National Glycohemoglobin Standardization Program: Over 20 years of Improving Hemoglobin A1c Measurement. Clin Chem 65:7 (2019) p 839-848

1.12.11 A.G., Motulsky, Frequency of Sickling Disorders in U.S. Blacks, N. Engl. J. Med. 288 (1973) p 31-33

Chapter 2 Preinstallation

A Tosoh Bioscience representative with sufficient training will install the analyzer.

This chapter provides specific preinstallation information that has been reviewed with you by a Tosoh representative prior to shipment of your Tosoh Automated Glycohemoglobin Analyzer HLC-723G8.

If questions arise or further information is required, please contact Tosoh Bioscience, Inc. Technical Support at 800-248-6764.

A Tosoh Bioscience representative will remove the panel of the main unit during installation, uncovering high-voltage assemblies. These are dangerous to touch. Never attempt to install or unpack the device yourself. Save all packing lists. The Tosoh Clinical Support Specialist or Field Service Engineer will check and inspect all items.

The analyzer will be uncrated and placed on the counter by the shipping company. Unpacking by unauthorized persons may void the warranty.

If the analyzer must be moved from one place to another, please contact Tosoh Bioscience, Inc. Technical Support at 800-248-6764 for assistance.

2.1 Parts Inspection

The analyzer components are packaged separately and consist of: the main unit, accessories, and the sample loader. Two sample loaders (SL) are available, 90SL with 9 racks and 290SL with 30 racks. Each component comes with the accessories indicated below.

1. Main Unit (HLC-723G8)

- Warranty Card 1
- Inspection Certificate 1
- Power Cord for the Main Unit 2 m 1
- Waste Bottle 10 L 1
- Waste Tube Silicon 9 mm × 12 mm × 1.6 m 1
- Tie Wrap CV-150 5
- Wrench 1/4" × 5/16" 1
- Wrench 8 × 10 mm 1
- Screw Driver (+) 100 mm 1
- Hex Wrench 9/64" 1
- Hex Wrench 3 mm 1
- Hex Wrench 2.5 mm 1
- Sample Cup 20
- Printer Paper (Thermal paper roll) 1
- System external device storage (Smart Media Card or USB stick) 1
- Holder for reagent pack 1
- Accessory box 1
- Fingertight connector 1
- 13mm diameter adapter for SYSMEX® sample rack 1

2. 90 Sample Loader (G8-90SL)

- Warranty Card 1
- Inspection Certificate 1
- Vial Adapter 10
- End Marker for 90SL 2
- Mounting Screw 4

3. 290 Sample Loader (G8-290SL)

- Warranty Card 1
- Inspection Certificate 1
- Vial Adapter 10
- End Marker for 290SL 2
- Mounting Screw 4

4. Main Products, Consumables and Optional Products

Main Products/ Column, Reagents, Calibrators, Controls

Part Number	Part Name	Description	Unit
0021955	TSKgel G8 Variant HSi	1 column	1 box
0021956	G8 Variant Elution Buffer HSi No. 1	800 mL × 10 packs	1 box
0021957	G8 Variant Elution Buffer HSi No. 2	800 mL × 10 packs	1 box
0021958	G8 Variant Elution Buffer HSi No. 3	800 mL × 10 packs	1 box
018431US	HSi Hemolysis & Wash Solution (L)	2000 mL x 2 bottles	1 box
0018767	Hemoglobin A1c Calibrator Set	Level 1, 2 (4 mL) × 5 each	1 box
220232 or 0021974	Hemoglobin A1c Control	Low, High (0.25 mL) × 4 each or Level 1, 2 (0.5 mL) × 4 each	1 box

- The expiration dates for the column and reagents are noted on their product labels.

Consumables

Part Number	Part Name	Description	Unit
0021600	Filter Element	5 pieces	1 bag
0018581	Sample Cup	1000 cups	1 bag
0019563	Printer Paper	10 rolls	1 box
0017092	Needle Wash Block O-ring	5 pieces	1 bag
0018517	Plunger Seal	1 piece	1 bag
0018723	Suction Filter	1 piece	1 bag
0019500	Sample Needle Assembly	1 piece	1 box
0005952	Injection Valve Rotor Seal	1 piece	1 bag
0018718	Teflon® Tip (for 250 µL syringe)	2 pieces	1 bag
0019515	Teflon® Tip (for 5 mL syringe)	2 pieces	1 bag
0019495	AS Valve Rotor Seal	1 piece	1 bag
0021601	Sample Loop	1 piece	1 bag

Optional Products

Part Number	Part Name	Description	Unit
0016320	Waste Buffer Bottle	10 L	1 bottle
0021641	Silicon Tube	15 m for waste fluid	1 piece
0018432	Sample Rack (without adapter)	1 piece	1 bag
0018433	13mm Adapter for SYSMEX® sample rack	10 pieces	1 bag
0018496	12mm Adapter for SYSMEX® sample rack	10 pieces	1 bag
0018497	14mm Adapter for SYSMEX® sample rack	10 pieces	1 bag
0018808	Adapter (rotation prevention)	50 pieces	1 bag
0018806	Elution Buffer Cap O-ring	5 pieces	1 bag
0019509	Vial adapter for SYSMEX sample rack	10 pieces	1 bag

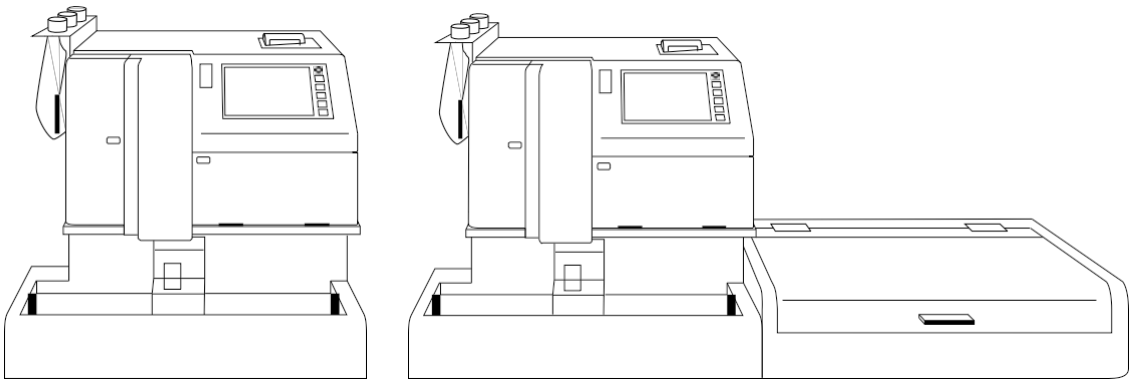
Ordering Consumables

Any consumable part or reagent that is required for use is only to be purchased from Tosoh for use on Tosoh equipment. Only Tosoh parts or reagents can be used with a Tosoh Analyzer.
The consumable parts can be ordered from Tosoh Bioscience, Inc. in any of the following ways:

- Via telephone by calling Tosoh Bioscience, Inc. Customer Service at 866-527-3587, 8:30 a.m. to 8:30 p.m. EST Mon-Fri
- Via FAX at 800-685-7595
- Via mail by sending an order to: Tosoh Bioscience, Inc, Customer Service Department, 3600 Gantz Road, Grove City, OH 43123-1895
- Via email by sending an order to: bioscienceorders@tosoh.com

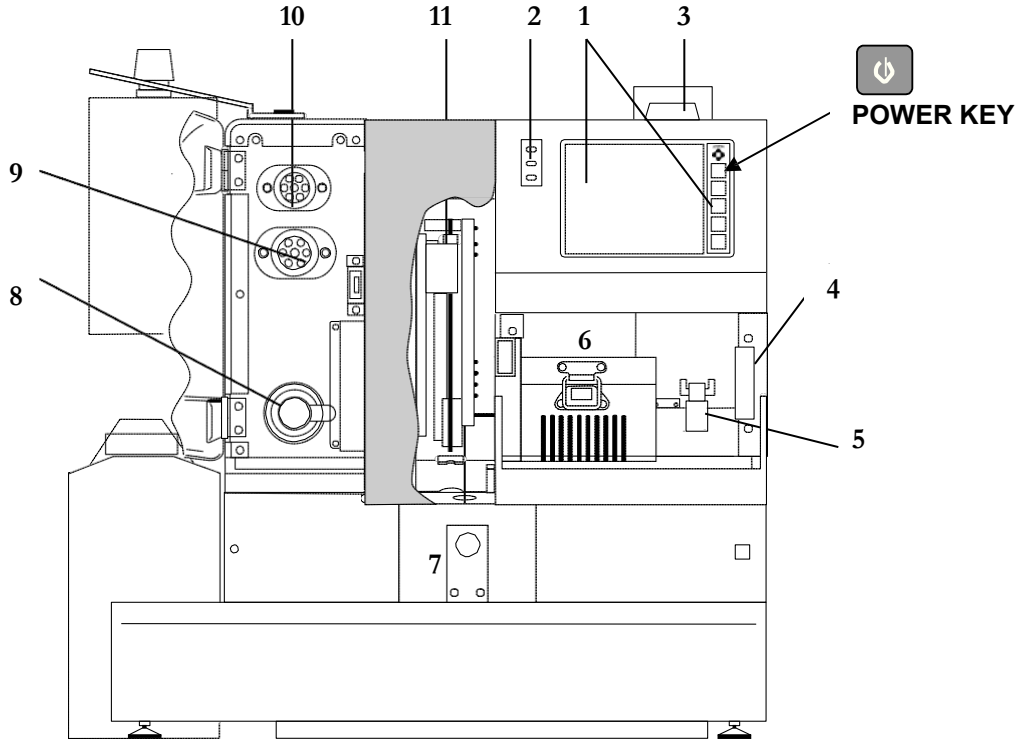
2.2 Analyzer Configuration

Fig. 2-1 G8-90SL **Fig 2-2 External Appearance (G8-290SL model)**



2.3 Units and Functional Parts

Fig. 2-3 Front View



1. Operation panel

The operation panel is a monochrome LCD with touch keys. The operation is controlled through the touch keys on the screen. All settings may be made from the screen.
Individual basic function keys such as POWER, START, STOP, HOME and ERROR RESET are provided on the right side of the display. Routine operations are performed with these keys.

2. LED panel

Three kinds of Light Emitting Diodes (LEDs) indicate the analyzer status: Power, Run, and ERROR.

3. Printer

The printer paper roll is thermal-sensitive. It prints out assay results, error messages and parameter status. The assay results can be printed out in three different formats. The paper roll can print about 350 sample results depending upon the format.

4. Storage device

The analyzer is equipped with an internal Smart Media socket or an internal USB socket. Use an external storage device corresponding to each socket. It is used to store assay results, update and backup program versions.
When a USB stick is used, the format usable in the analyzer is FAT32.
The number of sets of assay results that can be stored in the formatted external storage device is as follows:

- Smart Media card (32MB, FAT): A maximum of 12,000 sets of assay results (but up to 500 days, even though less than 12,000 assay results)
- USB stick (1GB, FAT32): a maximum of 240,000 sets of assay results (but up to 500 days, even though less than 240,000 assay results)

The last 800 sets of assay results are also automatically saved to the analyzer's internal memory.

1. Only insert an external storage device corresponding to the internal Smart Media socket or the internal USB socket.
2. The capacity of a Smart Media card that can be used is 128 MB or less.
3. A USB stick that has a security function cannot be used.
   The number of assay results that can be saved differs depending on the formatting method and the type of files saved together.
4. The format of data used by other applications or the format of a brand new external storage device may differ, thus reducing the number of assay results that can be saved. Prior to use, it is recommended to format the external storage device with the analyzer or a Windows-based PC. External storage devices formatted by the analyzer can also be used on a PC.

5. Line filter

The line filter prevents impurities such as dust from a broken valve seal from entering the assay line. The filter element is easily replaced by hand.

6. Column oven

The column oven contains the column.
The column must be kept at a constant temperature at all times to prevent temperature fluctuations that affect the test results. The column oven maintains a constant temperature so that no wait time is required prior to starting an assay, unless the main power switch (side circuit breaker) is turned off. The column is easily replaced by hand without using any special tools.

7. STAT port position

This position can be used for any type of specimen, i.e., whole blood in a tube, whole blood in a sample cup, or diluted sample in a sample cup. This position will also prioritize the sampling.

100 mm primary tubes cannot be used in STAT port position.

8. Drain valve

If an air bubble enters the pump ensuing in low pressure errors, open this valve to expel the bubble with a drain flush. Do not open this valve during an assay.

9. Injection valve

This valve is used to inject a sample into the assay line after sample dilution. The sample loop volume is 4 µL.

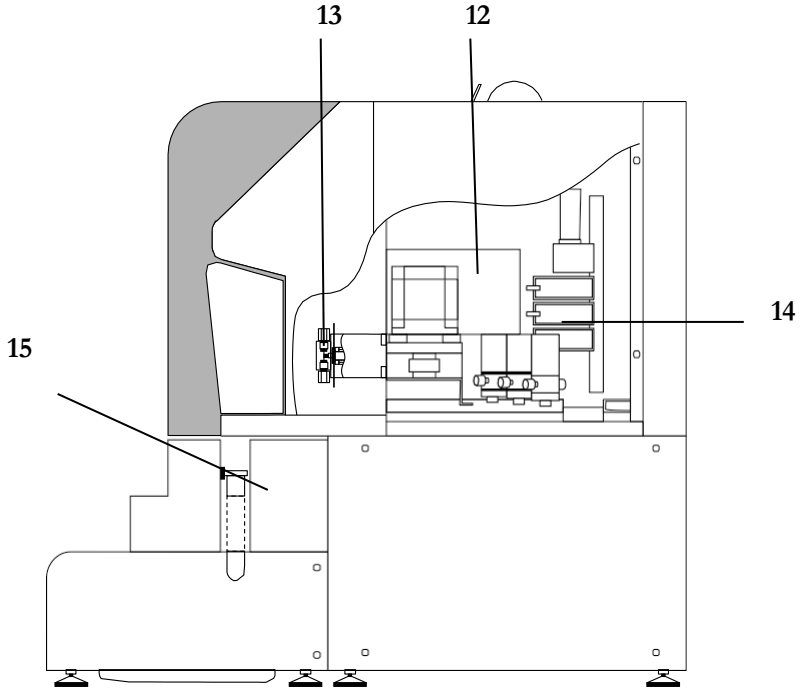
10. Rotary valve

The rotary valve is used to switch flow paths during sampling and elution buffer priming.

11. Sampling mechanism

The analyzer automatically senses the sample tube using micro switches and aspirates 4 µL of whole blood. The whole blood sample is automatically diluted approximately 1:200 and introduced into the assay line. When the assay begins, the sample rack is transferred and continuous sampling starts and continues until an empty rack on the loader is detected.
When a query is requested from the host computer, (hereinafter, "host"), only the samples for which a query has been requested can be assayed, skipping the others.

Fig. 2-4 Right Side View



12. Detector

The detector is used to detect changes in the absorbance level of hemoglobin in the sample separated with the column. The light source is a blue LED. The detector and column temperatures are both controlled by the column oven.

13. Pump

The pump uses the plunger method to deliver the elution buffer required for the assay. The pump operates continuously to deliver the elution buffer during the assay and feeds three different concentration elution buffers in 1.6 minute cycles by switching the solenoid valves. It also forms a gradient and the hemoglobin fractions are separated by the column.

14. Degassing unit

The degassing unit removes air bubbles in the pumped elution buffer. The vacuum pump runs intermittently to keep a constant vacuum pressure in the chamber.

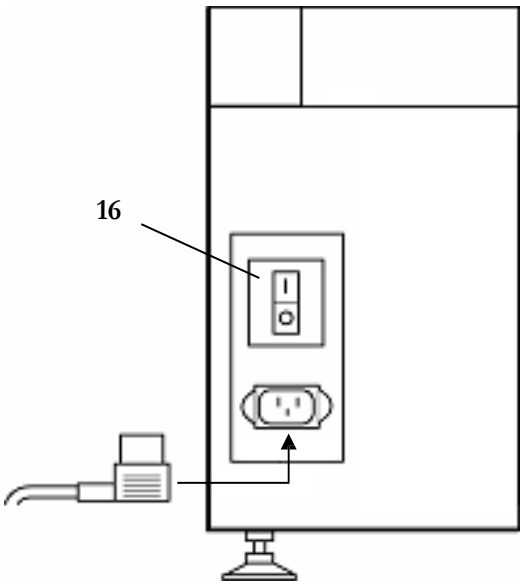
15. Bar code reader

The bar code reader reads the bar code label on the primary tube and the analyzer prints it on the report in the ID field. Assay information can be requested from the host using the bar code. If a sample cup is used, attach a bar code label on a vial adapter, set the adapter in the rack, and place the sample cup in the adapter.

16. Main power switch

The main power switch is located above the AC inlet, on the left side rear of the main unit. Always keep the main power switch in the ON position. Using the POWER key on the right side of the display, the instrument can be switched on and off.

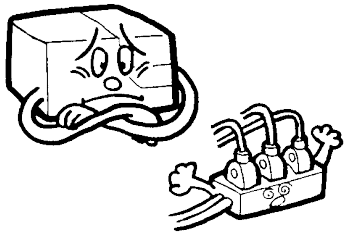
Fig. 2-5 Left Side Rear



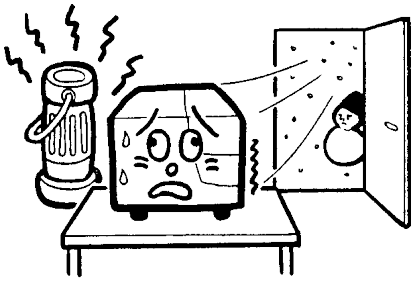
2.4 Installation Locations

DO NOT install the unit in the following locations:

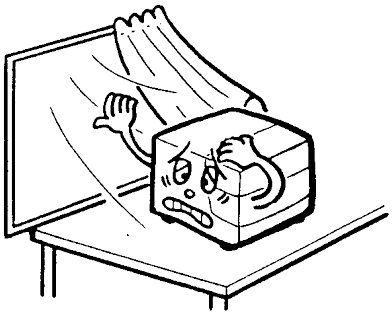
- **Locations with large fluctuations in the power source**



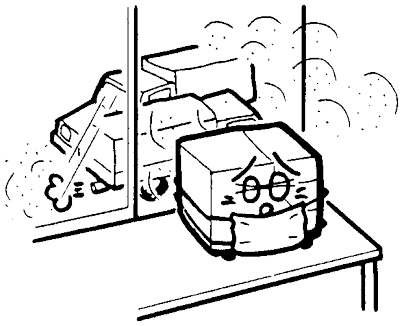
- **Locations with rapid temperature changes.**



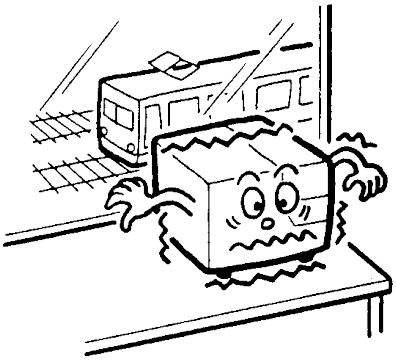
- **Locations in the path of direct air currents**



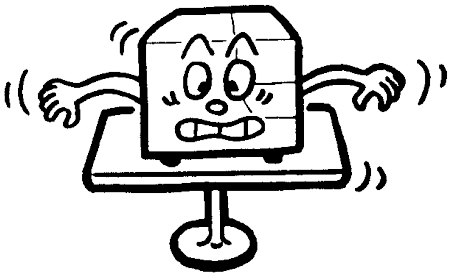
- **Locations with large amounts of dust or dirt**



- **Locations with excessive vibration**



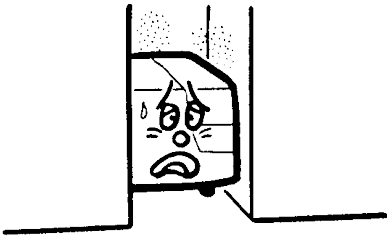
- **Unstable locations**



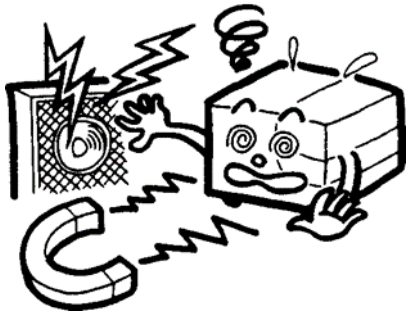
- **Locations with high humidity (>80%)**
- **Locations near water sources, such as a sink**

- **Locations with a flame nearby**

- **Locations with poor ventilation**



- **Locations where strong magnetic fields or high frequencies may be generated.**



Installation Environment

Install the unit on an even tabletop with no direct sunlight, air currents, dust or vibrations.
Operate the unit under the conditions indicated below.

Environmental conditions

Temperature:	15°C ~ 30°C
Humidity:	20% ~ 80% (no condensation)
Dust:	~ the quality in an office
Altitude:	6,600 ft.

CAUTION

Do not use in an environment with drastic temperature fluctuations. Such an environment can cause condensation to form, resulting in short circuits or improper functioning.

Electrical Requirements

Electrical Specifications appear on the nameplate located on the back of the instrument. In the US the Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 should be connected to a standard dedicated AC outlet rated at 100-240 VAC (auto-switching), 15 amp, 60 cycle. Outside of the US, the instrument should be configured according to the electrical requirements of the institution.

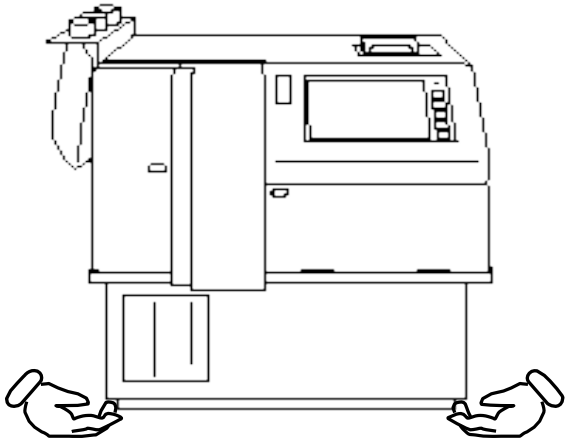
Environment of Transportation and Storage

Transport and store under the following conditions.

Temperature:	5°C ~ 50°C
Humidity:	80% or less (no condensation)
Other:	Keep dry and store indoors

The analyzer should only be moved by two or more people using both hands to grasp the bottom section of the main unit (Fig. 2-6).

Fig. 2-6 Where to grasp the analyzer when moving it



Required Installation Space

Refer to the figures below and be sure to secure sufficient space around the analyzer to prevent the fan located in the rear of the instrument from being blocked. Also, provide a height of about 36 inches, equal to 16 inches plus the height of the main unit (20 inches). In addition, avoid direct ventilation from other instruments. 50 mm is ~ 2 inches
100 mm is ~ 4 inches
530 mm is ~ 21 inches

Fig. 2-7 Installation Space (Main unit + 90SL)

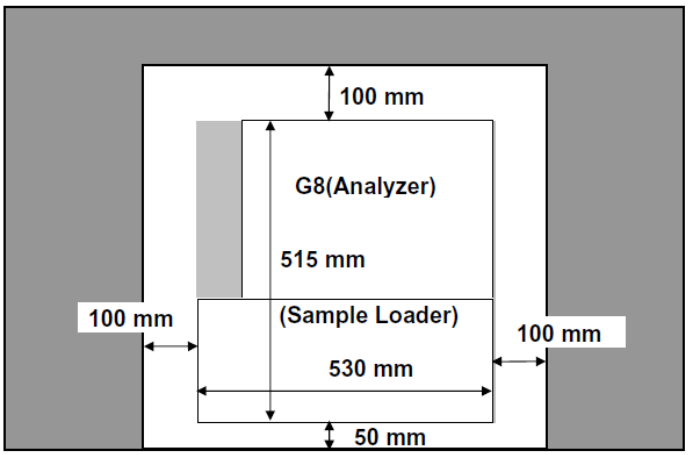
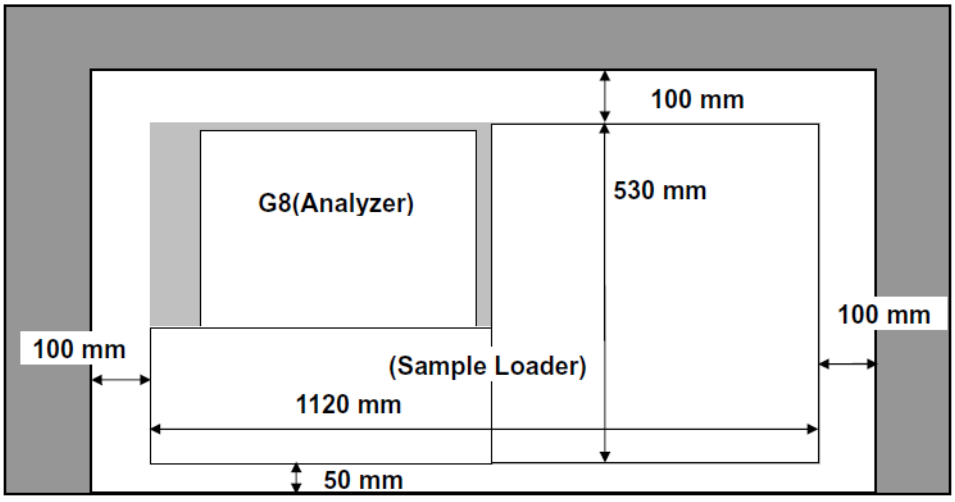


Fig. 2-8 Installation Space (Main unit + 290SL)
1120 mm is ~ 44 inches



2.5 Connections

Waste Tube

Insert the waste tube firmly into the waste port located on the bottom of the main unit. (Refer to Fig. 2-9). Securely tighten the waste tube with the tie wrap provided in the accessory box.
Insert the other end of the tube into the waste bottle. (Refer to Fig. 2-10)
Note: if the waste tube is bent, the waste liquid may not drain out smoothly. Adjust (cut) the tube length to keep the tube end above the waste liquid level.

Fig. 2-9 Waste Tube Connection

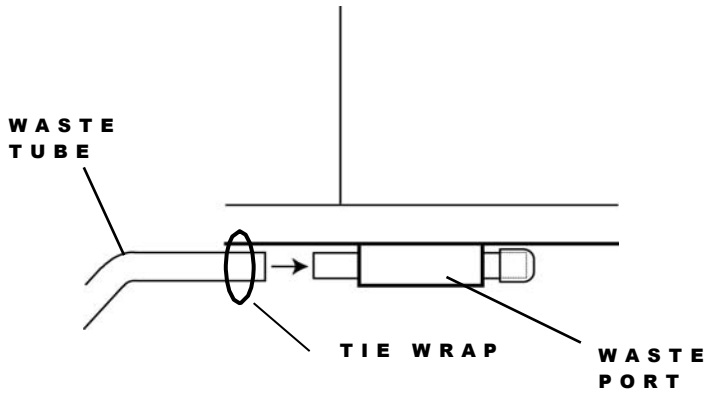
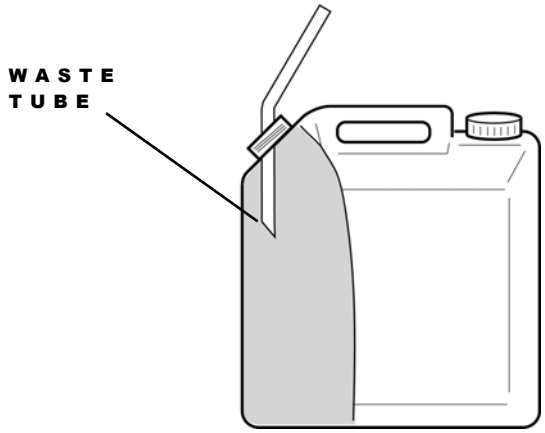


Fig. 2-10 Tube Insertion into Waste Buffer Bottle



When changing the analyzer location, make sure that the tube is not loose, broken or bent and that the waste liquid drains unobstructed.
The sample loader must also be temporarily disconnected when changing the analyzer location. Please contact the authorized representatives.

1. If the waste tube is bent and waste liquid cannot drain, the sample dilution may not be accurately performed during the assay.
2. Keep the waste tube end above the top of the waste liquid.

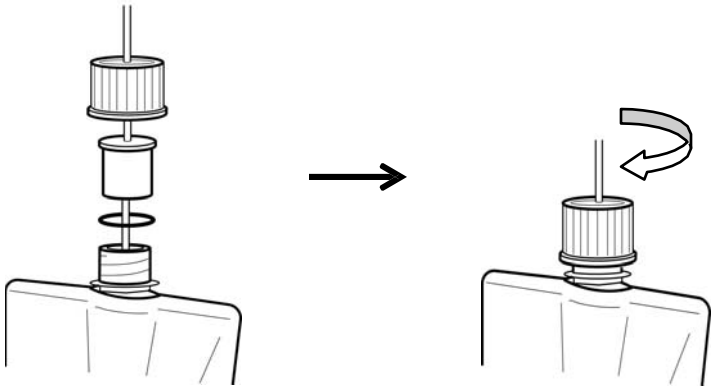
Elution Buffer Tubing (Suction Tube)

Match the color marks of the elution buffer tube with the same color on elution buffer pack No. 1, 2, and 3, and then insert the tube into the aluminum pack and seal by closing the bottle cap squeezing all air out of the pack.

Elution Buffer No. 1: **green**
Elution Buffer No. 2: **red**
Elution Buffer No. 3: **yellow**

The suction filter is attached to the end of each elution buffer tube. If the tube is bent, straighten it out before connecting it and make sure it reaches the bottom of the aluminum pack.

Fig. 2-11 Suction Tube Connection (Aluminum Pack)

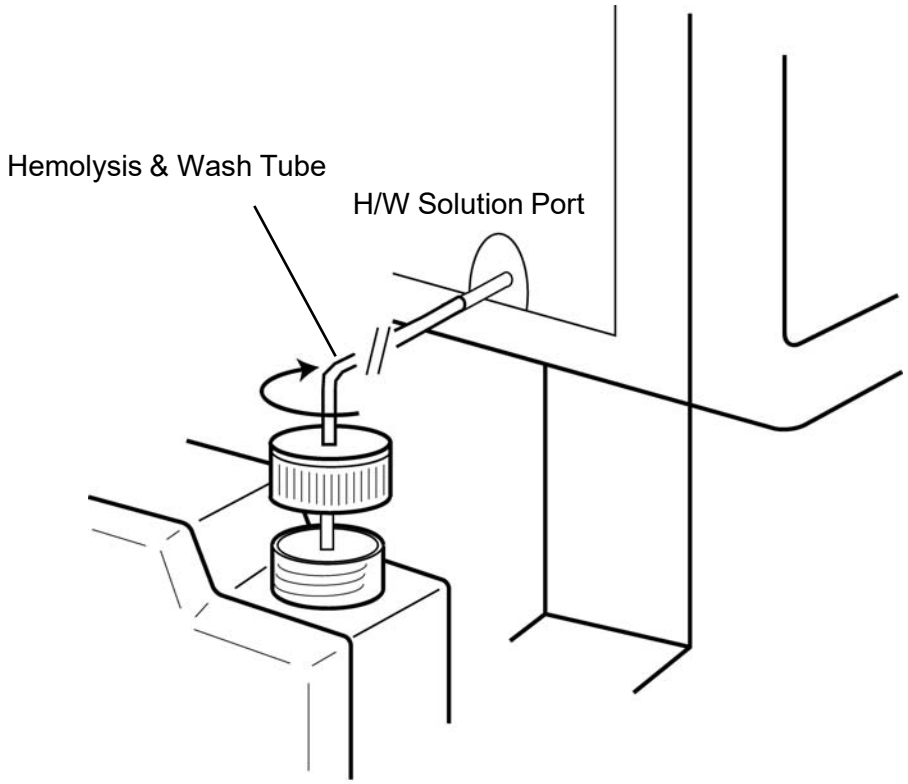


For aluminum pack reagents, squeeze the pack manually to remove as much air space as possible, and then firmly close the bottle cap. If the cap is loose, the elution buffer may deteriorate. It will also become difficult to check the remaining volume visually.

Hemolysis & Wash Solution Tube

Open the Hemolysis & Wash (H/W) solution cap and insert the Hemolysis & Wash solution tube (with anchor and bottle cap) into it and tighten the bottle cap. The H/W tube is sticking out of the H/W Solution port on the left side of the main unit. Make sure that the weight has reached the bottom of the bottle.

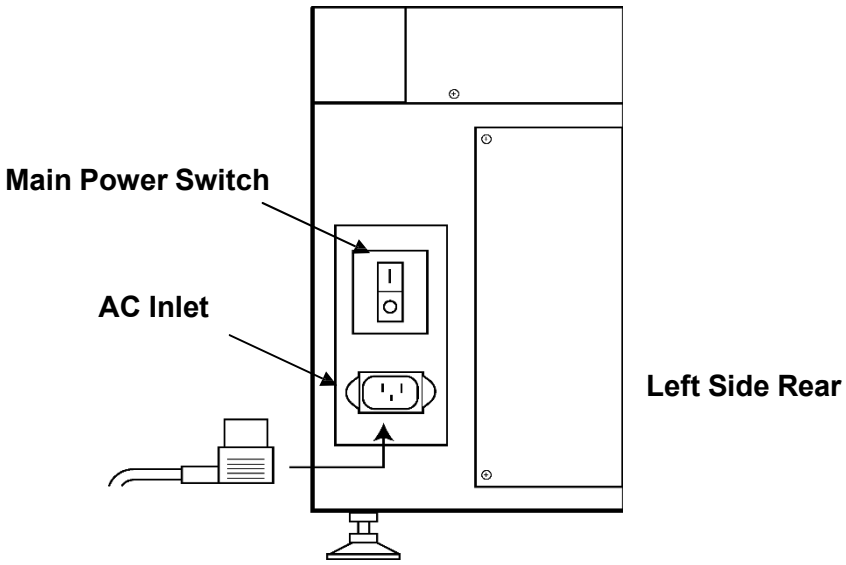
Fig. 2-12 Hemolysis & Wash Solution Tube Connection (main unit and bottle connections)



Power Source

Securely connect the power cord to the AC inlet of the main unit.
Make sure that the unit's main power is off (O) before inserting the plug into the socket.
The socket's power capacity must be 10 A or above. Be sure to connect the unit to three-pin power socket.

Fig. 2-13 Power Cord Connection



Caution

1. Do not use the same power source as that used for high capacity equipment such as a refrigerator or a compressor.
2. Do not touch the power source with wet hands. This may cause electrical shocks.
3. Be sure to ground the unit.
4. Do not place anything in front of the switch.
5. Leave enough space to allow the power cord connector to be unplugged from the AC inlet.
6. Never insert too many power cords into the same socket. Never use with an extension cord.

2.6 Column Connection

The dedicated column for the Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 is the TSKgel G8 Variant HSi.
Never use the G8 column with any other instrument.

Refer to the instruction manual included with the column, and to “Chapter 5, Section 5.6 Column Replacement” of this manual for information on how to connect the column.
Be sure to check for any damage to the package or packaging components before use. If any damage is observed, contact your local representative.
Next, confirm that the following inserts are included with the column.

- Instructions For Use 1
- Inspection Report 1

Column Connection Procedure

1) Take the column out of the box and remove the protective plugs on both ends. Do not throw away these plugs as they are needed for storage.
2) Be sure that buffer delivery has been completely stopped (the status "STAND-BY" is displayed on the MAIN screen). Open the column oven and disconnect the flow line and remove the used column.
3) Press the arrow key located on the lower right side of the screen. The key for manual buffer delivery is displayed. Use the key to run the pump and confirm that buffer is being delivered from the column flow line end. Use the key to stop the pump. Be careful not to spill the buffer draining from the flow line onto the unit. Wipe with paper if necessary.
4) Verify the proper column flow direction, which is drawn on the label, by an arrow and connect the flow line to the inlet side of the column. Use the screen key to run the pump and verify that buffer is draining from the outlet side of the column. Stop the pump and connect the outlet side of the column to the flow line.
5) Use the screen key to start the pump again, verify that the pressure is rising quickly and that there is no leakage at the flow line connection. After that, stop the pump and close the column oven.
6) Select the REAGENT key from the MAINTE screen, press the COL.RESET key, and reset the column counter to zero.

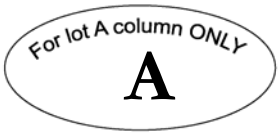
Column Use Cautions

1) Be sure to carefully read the instructions contained in this manual and related instructions provided in the G8 Variant Elution Buffer HSi and HSi Hemolysis & Wash Solution package inserts.

2) The TSKgel G8 Variant HSi column is designed exclusively for use in combination with the analyzer system, elution buffers and Hemolysis & Wash solution listed below, never in any other combinations.
   - Tosoh Automated Glycohemoglobin Analyzer HLC-723G8
   - G8 Variant Elution Buffers HSi No. 1, 2 and 3
   - HSi Hemolysis & Wash Solution

3) When changing a column, be sure to prime a sample several times and always check the chromatographic quality.

4) Always use the TSKgel G8 Variant HSi column in combination with the G8 Variant Elution Buffer HSi of the identical lot number. The column lot number is indicated by a single uppercase alphabetical character (A, B, etc.) on the label of column box.
   The elution buffer label displays an alphabetic character corresponding to column lot number, as shown below.



5) Care must be taken to ensure that the solutions are delivered only in the direction indicated by the arrow on the name plate on the column being used.
6) When the column is not used for more than one week, remove the column from the analyzer unit, reattach its protective plugs to protect it from drying out and store in cool dark place at 4 to 15 °C.
7) Do not bump or shake the column.
8) If the pressure is more than the pressure (which is indicated on the column inspection report) +4 MPa, first replace the line filter. If the pressure still does not drop, replace the column.

NOTES

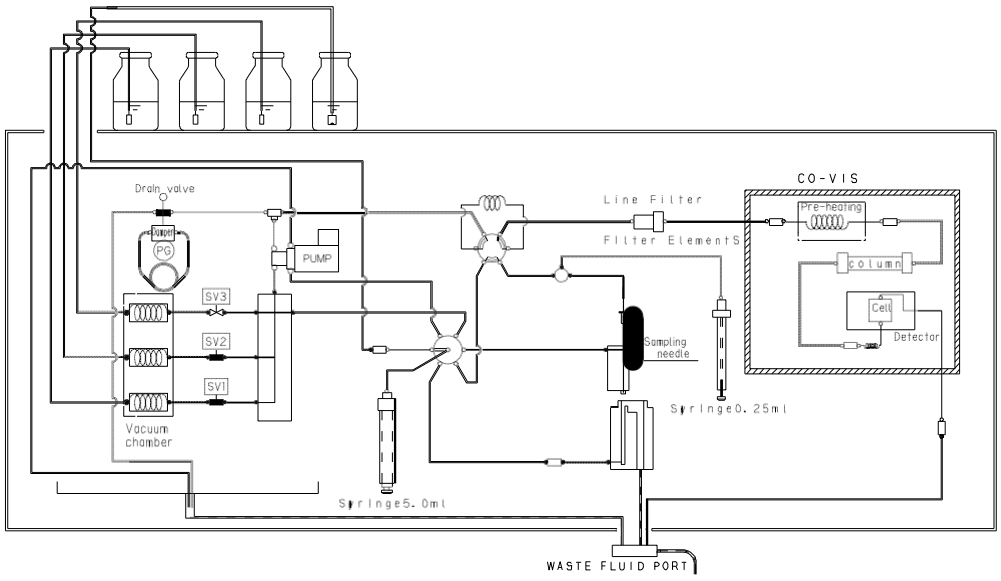
Chapter 3 Assay Operations

3.1 Assay Principles

Based on the principle of high performance liquid chromatography (HPLC), the analyzer uses a cation exchange column to separate hemoglobin components by different ionic charge. The various components of hemoglobin, including hemoglobin A1c, are separated into 6 fractions and assayed. The results are available every 1.6 minutes. Separation is performed with Elution Buffers with three different salt concentrations.
Fig. 3-1 shows the flow path of the main unit. Each Elution Buffer is degassed by the on-line degassers and switched by the solenoid valves as programmed, then delivered by the pump to the column after passing through an injection valve and filter. Approximately 3 µL of the whole blood sample from the primary tube is aspirated by the sampling needle and diluted by the HSi Hemolysis & Wash Solution in the dilution port. Next, the diluted sample is aspirated into the nozzle and injected into the assay line then delivered to the column.

The absorbances of the hemoglobin components are separated in the column and are then continuously monitored by the detector. After the assay is complete, results for the various hemoglobin fractions are output to the printer as percentages along with the chromatogram.

Figure 3-1 Flow Path Diagram

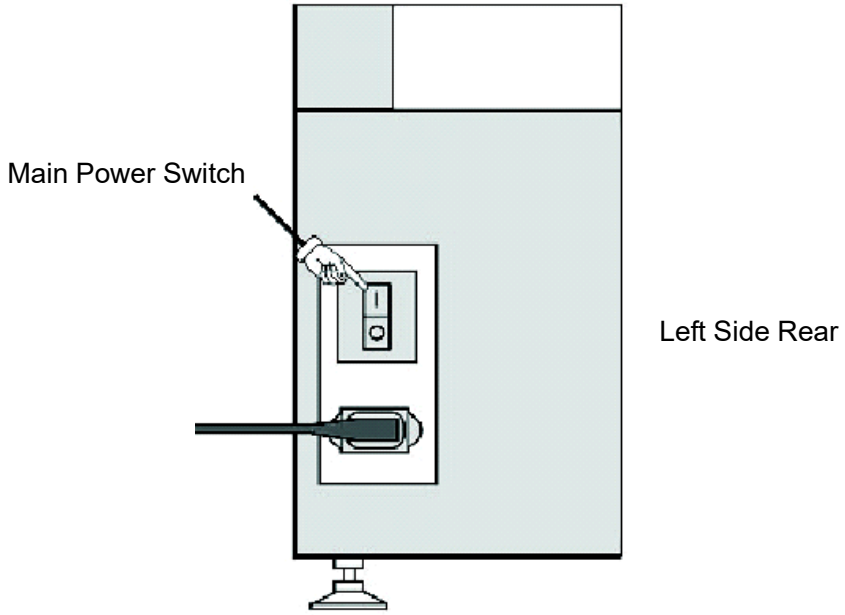


3.2 Power On

Turning Main Power On

The main power switch of the analyzer is located at the back of the left side, just above the AC inlet.
The side marked "**I**" indicates power on, and the side marked "**O**" indicates power off.

Figure 3.2 Turning Main Power On



The main power switch also acts as a breaker. If the main power switch is turned off immediately after the power is turned on, the analyzer may short-circuit. If this should occur, be careful not to touch any metal parts of the analyzer. Immediately turn the main power off, unplug the power cord from the power socket and contact a service representative.

CAUTION

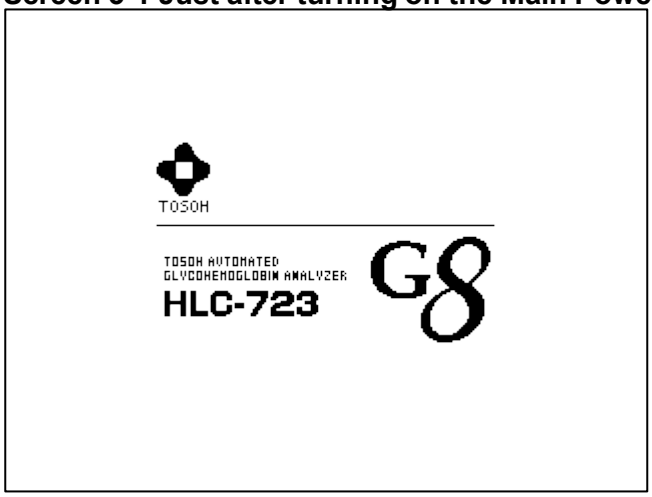
Do not touch the power source, sheet key, or screen with wet hands. You could receive an electric shock.

The memory is cleared when the analyzer is shipped. When you start the analyzer for the first time, insert the system external storage device in advance in order to read the system program. If the system has been already installed, please make sure that there is no external storage device in the storage device socket or a s for saving the results is installed in the socket before startup.

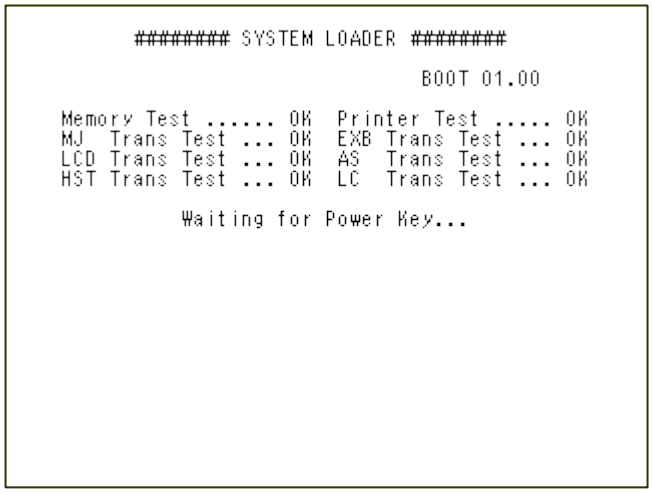
Procedure for Powering ON

1. Turn on the main power.
   The analyzer beeps at startup and Screen 3-1 is displayed.
   Then the analyzer automatically performs a check of its internal circuits. The messages on Screen 3-2 will appear, and the backlight on the screen will temporarily dim.

Screen 3-1 Just after turning on the Main Power

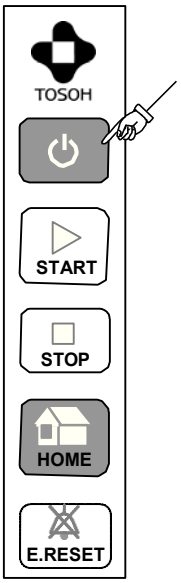


Screen 3-2 Display after main power is turned on, before the Power Key is pressed (normal operation) External Storage Device is not needed for normal operation



2. Make sure that there is no external storage device in the storage device socket or a storage device for saving the results may be installed in the slot before startup. If a system external storage device is in the slot, it will be read during startup, and the internal memory will be overwritten.
3. Press the POWER key located at the top of the key sheet on the right side of the control panel.
   The POWER LED on the left side of the control panel will illuminate when the key is pressed.

Fig. 3.3 Power Key On



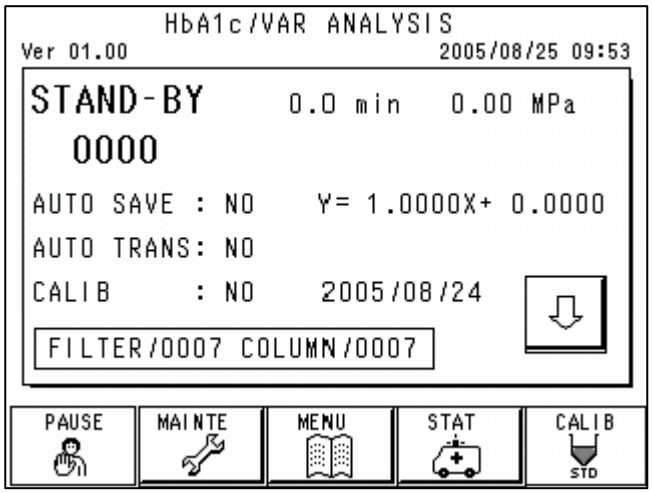
4. The system program, AS (auto-sampler) program, and backup parameters will all be automatically checked. This is the normal operating status when the system external storage device is not read.

Screen 3-3 Display after Power Key On and Before System Startup
(Normal operating status when system external storage device is not read)

```
        ######## SYSTEM LOADER ########

                                  BOOT 01.00

Memory Test ..... OK  Printer Test ..... OK
MJ  Trans Test ... OK  EXB Trans Test ... OK
LCD Trans Test ... OK  AS  Trans Test ... OK
HST Trans Test ... OK  LC  Trans Test ... OK

      Sampler(AS) ........ 01.00
      Searching AS ....... Not Found


      Searching System ... Not Found

      Checking Data ...... Alive


           Launching System...
```

5. If there are no problems with the backup program or other parameters, the analyzer automatically starts and the main screen appears.

Screen 3-4 Main Screen (first screen)



6. The startup sequence continues. The sampling mechanism is checked, the pump is washed, the elution buffers are primed, the sampling and dilution flow lines are initially washed, and WARMING UP starts.

If the main power switch is turned on and the screen does not display, or if an error is displayed, or some other event prevents the analyzer from activating the WARMING UP sequence, turn off the main power switch and then follow the procedures from Step 1. If the analyzer still doesn't start, contact Technical Support.

Battery Backup

The analyzer uses an internal battery to store the following information. If the main power switch is turned off, the analyzer has in its memory the following:

- System Program
  (program for operating the entire instrument)
- AS Program
  (program for operating the sampling and the loading unit)
- Assay Parameters
  (parameter files related to analyzer operating conditions)
- Assay results (result data)
  (assay results stored in the main unit memory)

Therefore, there is no need to load system information from the system external storage device, except when upgrading the system program. The internal battery has a life span of approximately 5 years. If battery power fails, the information indicated above will not be backed up when the main power is turned off. A message indicating that no system program was loaded may appear when the analyzer is started under these circumstances. If this happens, you must install the system program using the storage device socket.

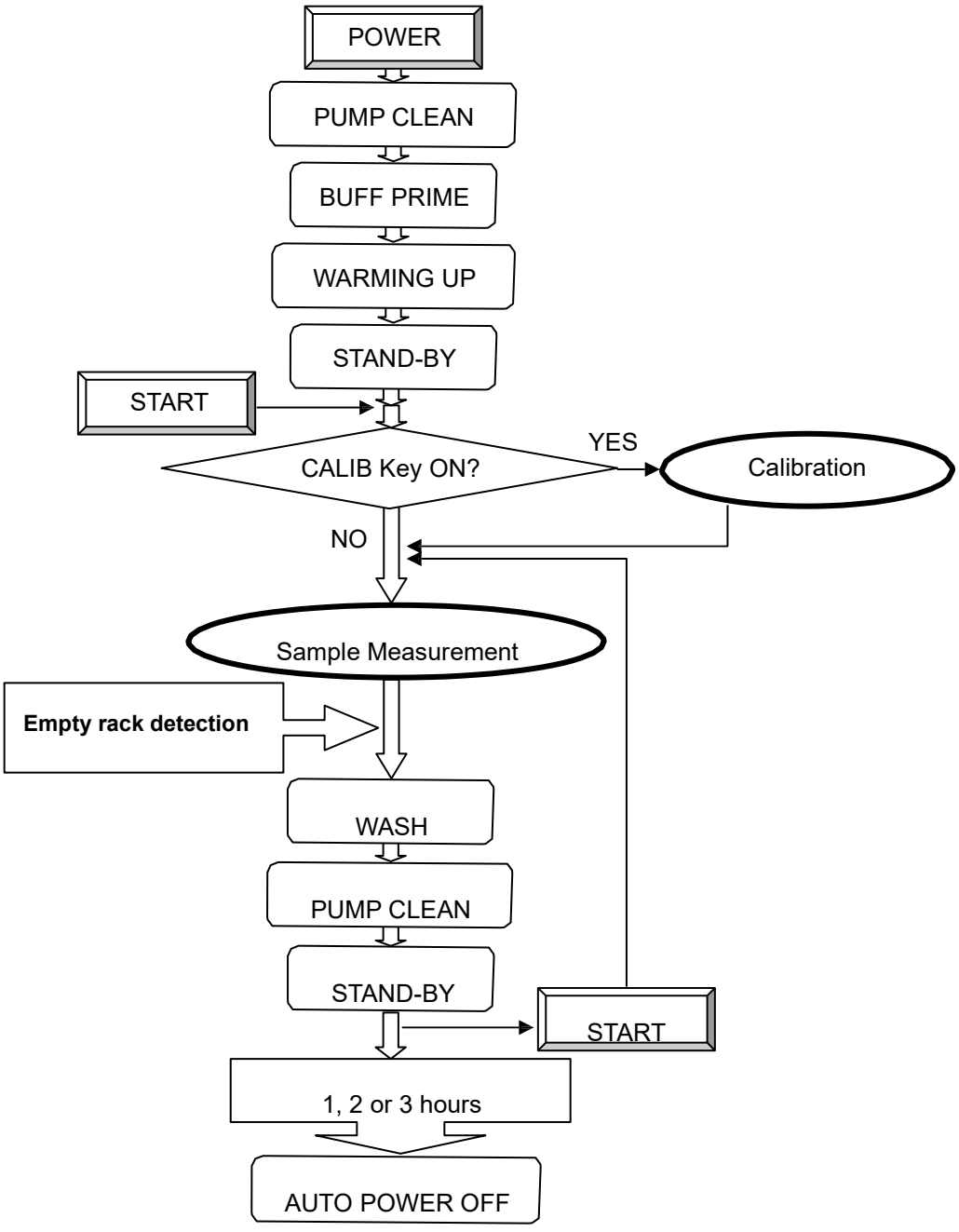
Refer to Chapter 7 for details regarding how to download programs and data from the external storage device. Even if the batteries are no longer functional, as long as the main power switch is on, the information indicated above is backed up and operation can be performed normally.

To return the backup parameters to their default factory values, input "CLR" in the password screen. Turn the main power switch off and then on again to restart the analyzer. All parameters are returned to their default factory settings.
See Chapter 4, Section 4.7: Card (External storage device) and Chapter 4, Section 4.14: Password Input for further details.

3.3 Assay Flow

The flow of standard assay operations is shown below.

Figure 3.4 Assay Flow Chart



The current condition of the analyzer and the current operation in progress are shown in the status of the **MAIN** screen.

Assay operations are stopped and the instrument enters STAND-BY state when the STOP key is pressed once during operation. Press the STOP key twice in succession to perform an EMERGENCY STOP.

1. When the STOP key is pressed during an assay, the results of the sample currently being assayed are printed and the wash operation is performed.
   When the STOP key is pressed twice in succession during an analysis, an emergency stop is performed, and the wash operation is immediately started. The assay is cancelled and results of the current assay are not printed.
   If the STOP key is pressed twice in succession during the wash operation, the analyzer will enter STAND-BY status and buffer delivery will stop.
2. In the same way, the PUMP CLEAN, BUFF PRIME, and WARMING UP operations, which are performed automatically after the power is turned on, can also be cancelled by pressing the STOP key. However, when the warming up cycle is interrupted, unreliable assay results can be obtained. When an operation has been cancelled, switch the POWER OFF then ON to automatically perform the operations again.

The BUFF PRIME and WARMING UP operations need to be completed prior to the first assay of the day (do not stop these operations).

3.4 Operation Status

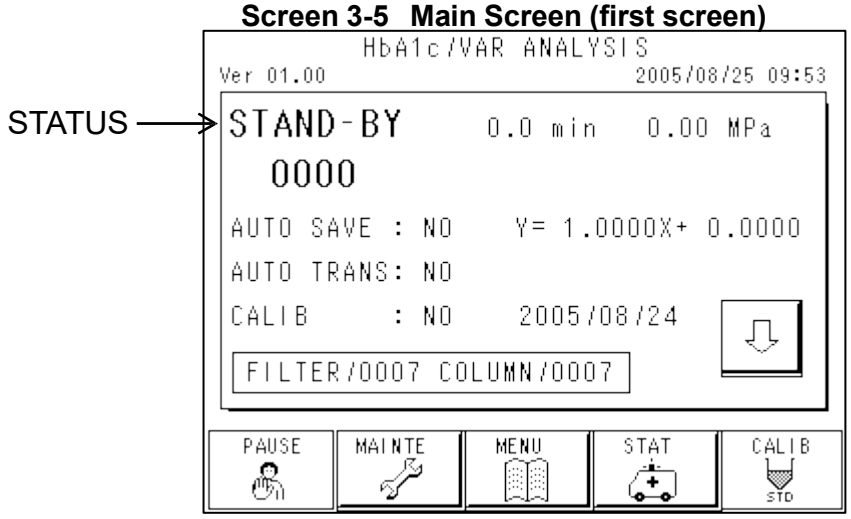
After the POWER key is pressed, the first screen displayed is the main screen (first screen). HbA1c/VAR ANALYSIS is displayed at the top of the screen. During analysis, the main screen should remain displayed. The current operation status is displayed in the upper left of the screen. The following status indications are displayed.

Status

- WARMING UP
- STAND-BY
- ANALYSIS
- WASH
- BUFF PRIME
- PUMP CLEAN

See the following pages for further details.

Screen 3-5 Main Screen (first screen)

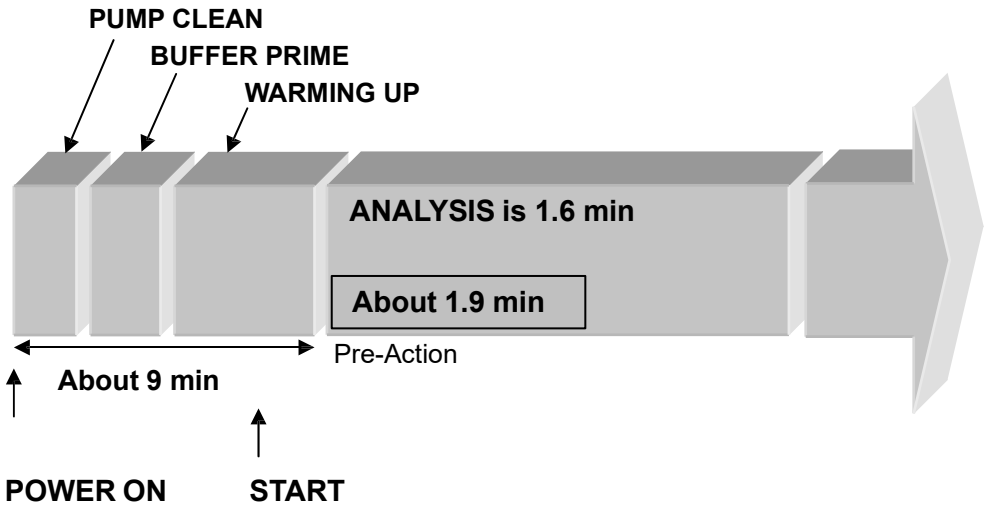


Status Types

WARMING UP

Press the POWER key  . After PUMP CLEAN and BUFF PRIME, the pump will run the reagent and automatically equilibrate the assay lines and column. After pumping each Elution Buffer sequentially for 9 minutes, the analyzer will enter the STAND-BY status and stop the flow. During this process, the sampling line will be washed twice. Although the WARMING UP operation can be aborted by pressing the STOP key, always make sure to complete the WARMING UP operation before the first assay of the day to ensure accurate results. During the WARMING UP operation, set the samples and calibrators to be assayed and press the START key. The system will go into the ANALYSIS state automatically and start the assays after completing the WARMING UP operation.

Figure 3-5 Start Command during the WARMING UP Operation



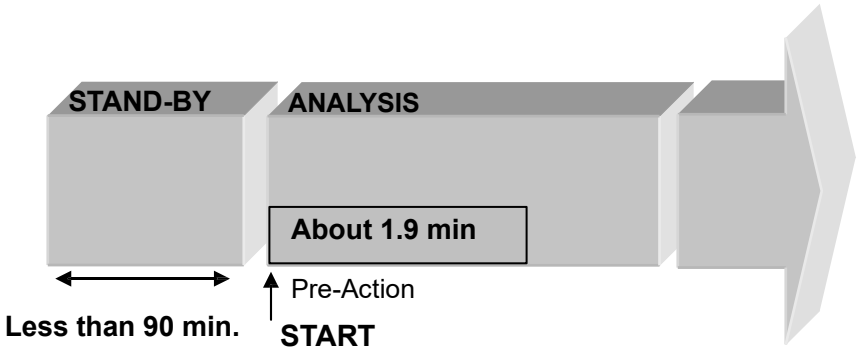
The first result prints out in 3.5 minutes after Warming Up has completed. Subsequent results print every 1.6 minutes.

STAND-BY

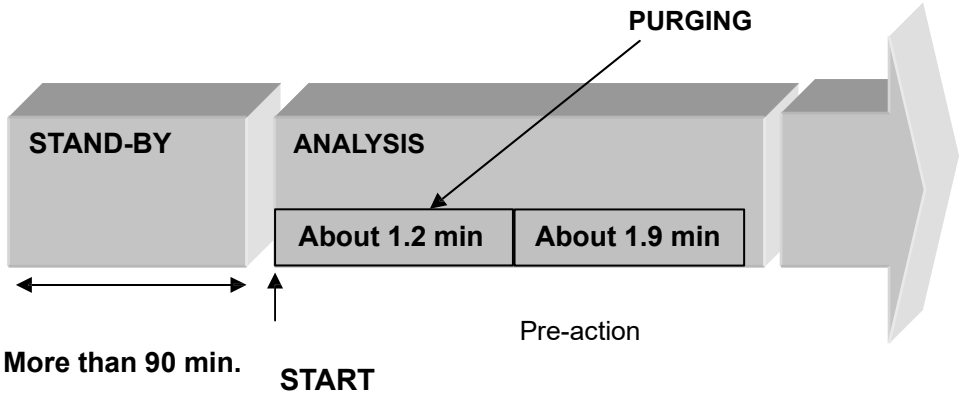
When the WARMING UP or WASH operations are complete, the analyzer enters the STAND-BY. In this state, the pump stops flow and elution buffer is not consumed. If two hours elapse without pressing any key or touch panel, the power will automatically be turned off. The waiting time before power-off can be changed with the OFF TIMER setting on the PARAMETER screen.

Fig. 3-6 Start Command during STAND-BY

a) If STAND-BY time is less than 90 minutes



b) If STAND-BY time continues for 90 minutes



ANALYSIS

Place the calibrators, controls and samples on the sample rack and press the START key. The assay will start and the analyzer will enter the ANALYSIS state. When the system starts from the STAND-BY state, the analyzer transfers the rack and begins sampling as soon as the sample cups are detected. If the sample is whole blood, it is diluted with the HSi Hemolysis & Wash Solution before injection. The diluted sample is then injected into the sample loop. At the same time, pre-action (preliminary reagent flow) in the assay line is run (for a total of 1.9 minutes) and the assay of the first sample then begins (sample injection).

Next, subsequent samples are processed in a 1.6-minute cycle and the result (HbA1c % or mmol/mol) is printed. It takes approximately 3.5 minutes until the assay result is printed from the time the first sample is detected. However, if the analyzer has been in the STAND-BY state for 90 minutes or more, a PURGING operation is done to replace all Elution Buffers and to clean the line. Pump transport starts after that. Since the PURGING operation takes about 1.2 minutes and it will take a total of approximately 4.7 minutes until the first assay result is printed.

The STOP key can be pressed at any time during ANALYSIS to abort the assay. If this is done, the sample currently being assayed is completed, the results for that assay are printed, and the WASH operation is performed. If the STOP key is pressed twice, an emergency stop is performed, the assay is immediately aborted, and the WASH operation performed. If the STOP key is again pressed twice, the WASH process is cancelled; the analyzer enters STAND-BY state, and the flow is stopped.

When the sensor detects an empty rack passing through the sampling position, the system recognizes the end of the assay, prints the last results and performs the WASH operation.

CAUTION

Make sure to place an empty rack at the end of the samples to stop the assay process. If this is not done, the assayed samples will be assayed again due to the rotating structure of the sample loader. Primary tubes could also stay pulled up due to the piercing action after assay. If the tube is assayed again in this state, the analyzer's needle could be damaged.

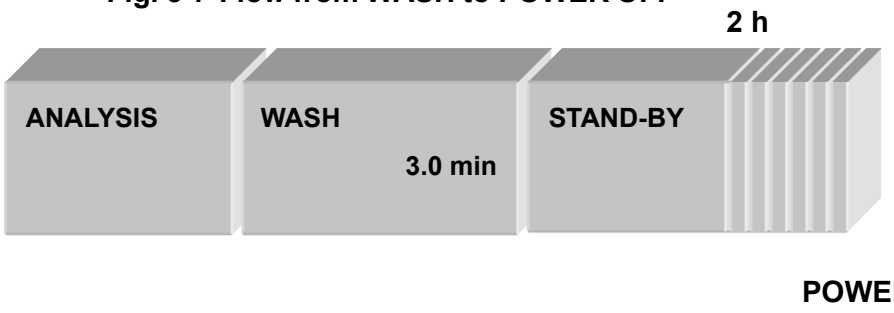
Point

1. 1. The time that elapses from when the START Key is pressed until the sample is detected depends on the location of the sample. To speed up detection, place the sample in position 1 of the rack if possible. However, the rack placement position is limited to the range indicated in Fig. 3-16 and Fig. 3-17.
2. The assay ends by placing an empty rack at the end or pressing the STOP key.

WASH

The analyzer enters the WASH status when the assay is complete. In this state, Buffer No. 3 is automatically pumped for 1.0 minute, and then Buffer No. 1 is pumped for 2.0 minutes to wash the column. Once this is complete the analyzer enters the STAND-BY state.
The WASH operation can be cancelled by pressing the STOP key twice; then the analyzer enters the STAND-BY state and stops flow.
Always perform a WASH operation when an assay is complete. If the WASH operations are insufficient, the column life is reduced and results for the next sample to be assayed may be affected. In addition, when an emergency stop is performed during analysis and flow is stopped (the STOP key is pressed 4 times), the sample currently under assay will remain in the column. This can shorten the column life. For executing a WASH operation, please assay a dummy sample and perform a Wash operation completely.

Fig. 3-7 Flow from WASH to POWER OFF



If the sample's ID is queried to the host computer (query mode), release the query mode and assay a dummy sample. Please make sure that the WASH operation has been executed.

BUFFER PRIME

When the power is initially switched on, the analyzer automatically delivers 5 mL of each Elution Buffer in order to replace the buffer in the flow line with fresh liquid (this is called a PRIME operation).
In addition, when a buffer PRIME or CHANGE is performed on the MAINTE - REAGENT CHANGE screen, the BUFF PRIME status will also be displayed during execution.

PUMP CLEAN

In order to clean contamination or salt precipitation from the pump plunger,
the back surface of the plunger seal is automatically washed with 5 mL Hemolysis & Wash Solution after the power is turned on and the WASH is complete.

PURGING (does not display as a status on the screen)

If the analyzer has been in the STAND-BY state for 90 minutes or more, all elution buffers in the flow line are automatically replaced with a new buffer (1 mL, each) just before starting assays. At the same time, the sample line is automatically washed with 5 mL of the HSi Hemolysis & Wash Solution. This process takes about 1.2 minutes. The ANALYSIS status is displayed during this time. Once the PURGING operation is complete, pump delivery and sampling automatically starts.

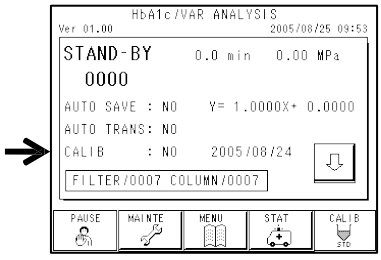
3.5 Daily Check

Be sure to check the following items before starting an assay (START command).

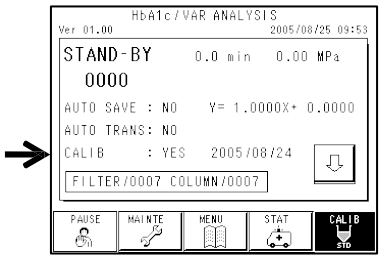
1. Check the calibration setting

On the main screen (first screen), check the status of the calibration and the CALIB key display.

Perform a calibration before actual sample testing. Use the Tosoh Hemoglobin A1c Calibrator Set to calibrate the analyzer. Other calibrators cannot be used. The assigned values for the calibrators differ for each lot. Input the new assigned value when you change lots. The assigned values in NGSP units are printed in the Instructions for Use and on the vial; the assigned values in IFCC units are printed only in the Instructions for Use. The lot number is printed on the calibrator box, Instructions for Use and vials. See “Chapter 3 Section 3.6: Calibration” for information concerning input of calibration values.



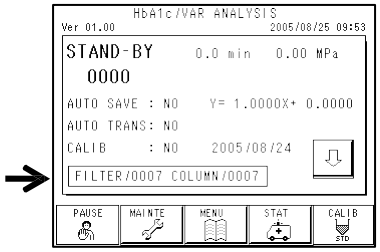
Main Screen - Not Highlighted



Main Screen - Highlighted

2. Check the column and filter count numbers

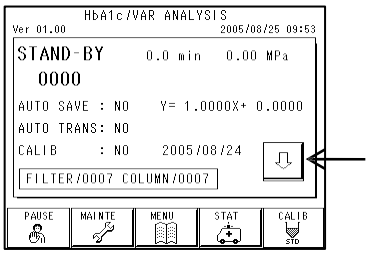
Column
The number shown on the main screen is the number of injections since the last column replacement.
Replacement period: as needed
Refer to Chapter 5, Section 5.6: Column Replacement for instruction for replacement of the column.



Filter
The number shown on the main screen is the number of injections since the last replacement.
Replacement period: 400 injections
Refer to “Chapter 5 Section 5.7: Filter Replacement” for situations requiring filter replacement.

3. Check the remaining volumes of Elution Buffers and Hemolysis & Wash Solution

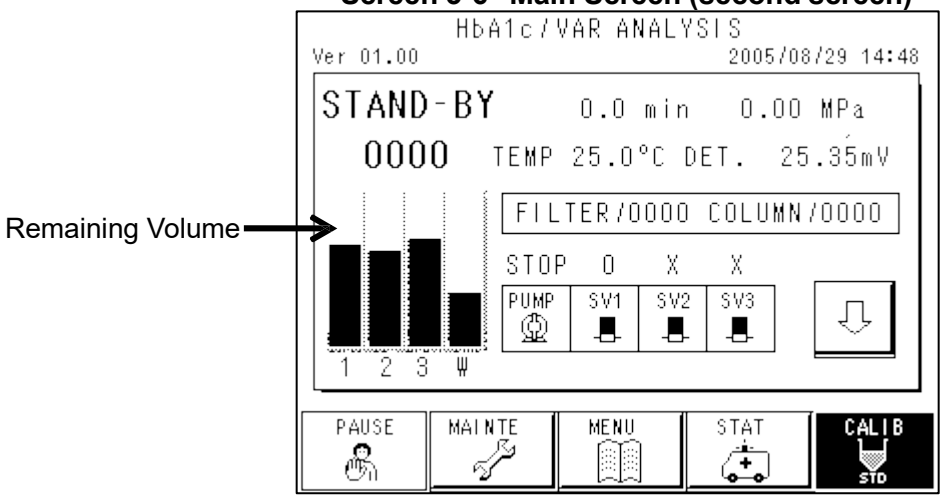
Press the ⇩ key on the right bottom of the main screen (first screen). The second main screen will appear and a bar graphs will display the remaining volumes of each buffer.
Approximate consumption volumes are shown below for each buffer.
In addition, be aware that some reagents are used in the PUMP CLEAN, BUFF PRIME, WARMING UP, and WASH operations. Confirm that the remaining volumes are sufficient.



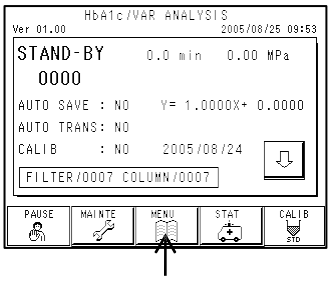
Main Screen

Elution Buffer 1: 0.80 mL/test
Elution Buffer 2: 0.88 mL/test
Elution Buffer 3: 0.72 mL/test
Hemolysis & Wash Solution: 3.95 mL/test

Screen 3-6 Main Screen (second screen)



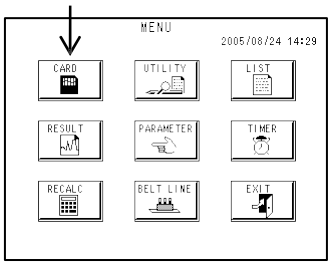
4. Check external storage device space for assay result storage



Main Screen

Insert an external storage device into the socket and select CARD key from the MENU screen. A list of assay result folders stored in the external storage device will appear and the percentage of used storage device will be displayed on the upper left hand side of the screen. The number of sets of assay results that can be stored differs depending upon the type of the external storage device. Refer to “Chapter 2, Section 2.3: Units and Functions, 4. Storage device”.
If the list data is stored together, this number will be reduced.

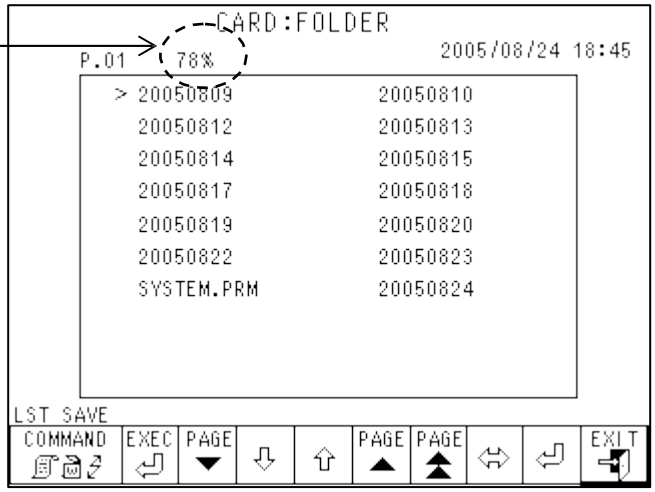
Use the PARAMETER screen to set the type of data to be stored. Since assay results are also stored in the RESULT memory in the main unit, saving the results on an external storage device is not absolutely necessary. Up to 800 assay results can be stored in the RESULT memory. When this number is exceeded, existing data is overwritten, starting with the oldest results.



MENU Screen

Screen 3-7 CARD: FOLDER Screen

External storage device space in use



Point

1. If data other than RAW data assay results are stored in the external storage device (system files, etc.), the space available for storing results is reduced. In addition, the storage device cannot be formatted during an assay. Check the remaining volume prior to giving the start command and load a formatted external storage device prior to starting the assay.
2. The number of results which can be stored in an external storage device may depend on how the storage device is formatted. Prior to use, we recommend formatting the storage device on the G8 Analyzer or a Windows-based PC. External storage devices formatted by the analyzer can also be used on a PC.

5. Check the remaining volume of thermal printer paper.

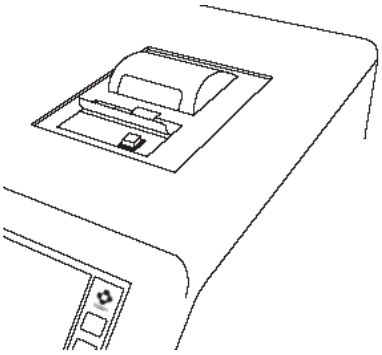
A red bar indicates a small volume of paper remaining. Replace the roll with a new roll when this red bar appears.

If the paper looks like it will run out during an assay, press the PAUSE key in the main screen to temporarily pause the analysis. Wait until the results of the sample currently being processed are printed, and then replace the paper. After replacement, press the PAUSE key to restart the assay. The assay will restart automatically once the PAUSE key is pressed or if no further input is received for approximately 16 minutes.

If the printer paper runs out during an assay, since the results are stored in the RESULT memory in the main unit, the result can be printed using the RECALC screen (recalculation) after all sample assays are complete. Transmissions to the host will continue regardless of the printer paper status.

When using Format 0, about 350 results can be printed with one roll.
See Chapter 3, Section 3.12: Interpretation of Results.

Fig. 3-8 Printer Unit



6. Check Waste Buffer Bottle

Be sure to empty the waste buffer bottle before starting an assay.

CAUTION

The waste fluid includes blood components. Never handle the waste buffer bottle or waste tube with your bare hands. Always wear protective clothing (goggles, gloves, mask, etc.) to prevent infection during handling. Dispose of the waste buffer in accordance with your facility's standard procedures.

7. Other Items to Check

Check the flow line connections, particularly the filter and the column inlet and outlet for leaks during WARMING UP operations. Tighten the connection if a leak is found.

The Elution Buffers, Hemolysis & Wash Solution, column, and filter cannot be replaced during an assay. When replacement is required, press the STOP key to make a temporary stop and wait for the analyzer to enter the STAND-BY state. Make the replacement while in the STAND-BY state.

3.6 Calibration

The Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 has a two-point automatic calibration function for stable HbA1c (SA1c). When the analyzer processes calibrators, it calculates the slope and intercept from a linear regression equation to determine quantitative results for patient samples and controls. Use only the Tosoh Hemoglobin A1c Calibrator Set (P/N: 0018767) for calibration of the Tosoh Automated Glycohemoglobin Analyzer HLC-723G8. Other calibrators cannot be used and may give erroneous results.

The Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 has been certified by the National Glycohemoglobin Standardization Program (NGSP) to give results traceable to the Diabetes Complications and Control Trial (DCCT) as well as by the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) to give results traceable to the IFCC reference method.

The analyzer accepts assigned values of calibrator both in NGSP units (%) and IFCC units (mmol/mol). Assigned values in each unit are printed on the Instructions for Use of "Hemoglobin A1c Calibrator Set".

Each laboratory must monitor QC results according to good laboratory practices to determine when to recalibrate. Calibration frequency should be based upon QC results and chromatogram quality.

The analyzer is calibrated using CAL(1) and CAL(2) calibrators with different HbA1c assigned values. Use the "Hemoglobin A1c Calibrator Set" or "G8 HbA1c Calibrator Set (S)" for calibration (P/N: 0018767 or 0023528).

We recommend calibrating the analyzer once a week. Be sure to calibrate in the following situations.

When control values assayed are out of range
Calibrate when the control assay value falls outside the QC range. Measure the control sample again to confirm that it falls within the QC range before assaying a patient sample.

- **After column replacement**
  Calibrate after a new column has been installed.
- **After analyzer maintenance**
  Calibrate after periodic maintenance or repair.
- **When an assay condition is being modified**
  Calibrate when a parameter value (such as the flow factor) is being changed on the analyzer.

Use the Tosoh Hemoglobin A1c Control (P/N: 0021974 or 220232) or other quality control material after the calibration.

CAUTION

Each laboratory must carry out the daily test result control and check the results for good laboratory practices.

1. Automatic Calibration

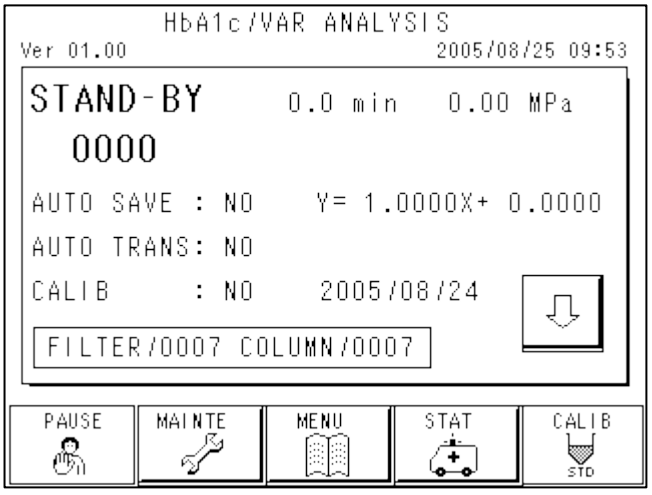
Check the CALIB message on the main screen (first screen). The following messages can be displayed.

- **CALIB: YES**
  Automatic calibration will be performed before the samples are assayed.

- **CALIB: COMPLETED**
  This indicates that calibration is complete. Subsequently, automatic calibration will not be performed even if the START key is pressed. Set the calibrator samples to start the assay. They will be tested in accordance with the factors displayed on the screen. When the CALIB key is pressed on the main screen, the display message will change to YES and calibration will be done again. The display will change to NO when the power is turned off with the power key or by the timer.

- **CALIB: NO**
  The CALIB key is not selected. Calibration will not be performed. The test result will be calculated by the factors displayed on the screen.

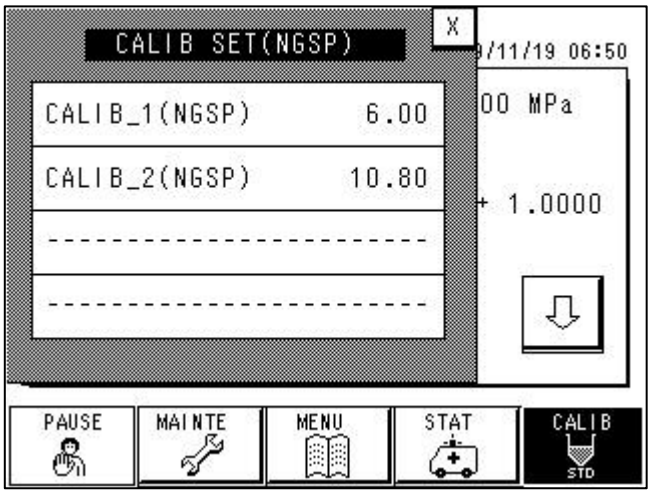
Screen 3-8 Screen is CALIB.: NO



Calibration Procedure

1. Press the CALIB key located at the bottom right of the main screen.
   The key is highlighted and the calibrator's assigned value input screen is displayed. Confirm the assigned value. If the calibrator lot has changed or if the assigned value is incorrect input the correct value. Press the X mark at the top right of the screen to close the screen.

Screen 3-9 Assigned Value Input Screen (for NGSP units)



The analyzer accepts assigned values of calibrator both in NGSP (National Glycohemoglobin Standardization Program) units (%) and IFCC (International Federation of Clinical Chemistry and Laboratory Medicine) units (mmol/mol). Assigned values in each unit are printed on the Instructions for Use of "Hemoglobin A1c Calibrator Set".

The title line of the Assigned Value Input Screen displays the unit of assigned values which should be entered.

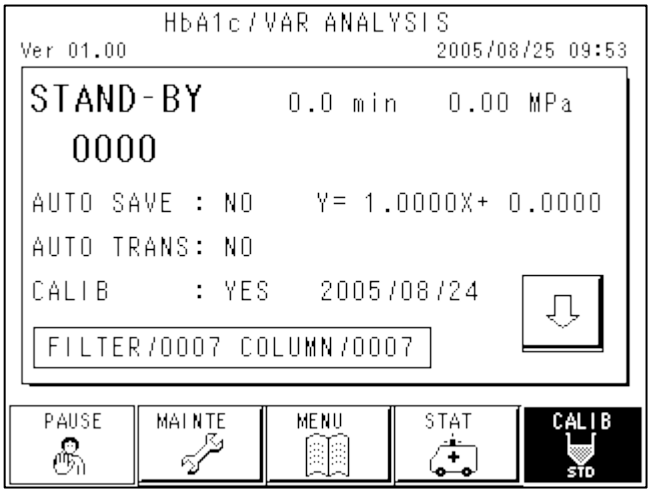
For entering in NGSP units:

For entering in IFCC units:

To switch the units in which assay results are reported, change the Printout format on the PARAMETER screen (page 2 of 4). Refer to "Chapter 4 Section 4.6: Parameter Setting" for specific procedures.

After entering assigned values, close the Assigned Value Input Screen by pressing the X mark at the top right of the Screen. Verify that the CALIB key on the main screen is highlighted and that the CALIB message is YES.

Screen 3-10 Screen is CALIB.: YES

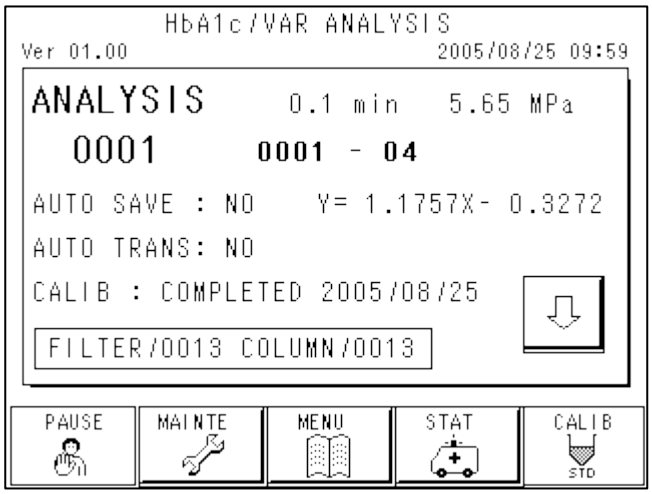


First set the LEVEL 1 and LEVEL 2 calibrators in the sample vials at the No.1 and No.2 positions of the first rack. Press the START key. The calibration will be processed automatically before real samples are assayed.

Once the automatic calibration is complete, the CALIB message will change to COMPLETED and the CALIB key will no longer be highlighted.

In addition, the calibration factors determined will be displayed on the screen. Behind the calibrators in the rack, place patient samples that will be assayed and their values will be corrected using the newly calculated calibration factors.

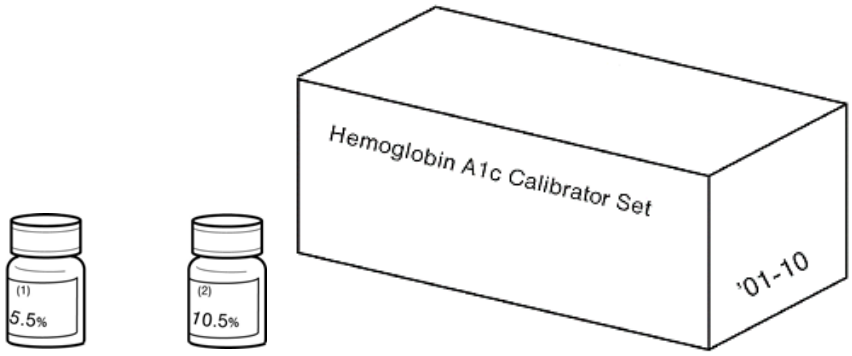
Screen 3-11 Screen is CALIB.: COMPLETED



2. Calibrator Reconstitution

Read the calibrator Instructions for Use for details regarding the proper handling of the Tosoh Hemoglobin A1c Calibrator Set. Use only Tosoh Hemoglobin A1c Calibrator Set for the calibration of the Tosoh Automated Glycohemoglobin Analyzer HLC-723G8. Performance characteristics of other calibrators cannot be guaranteed, and may give erroneous results.

Fig. 3-9 Calibrator Set



3. Calculation of calibration factors

The following instructions are for entering assigned values in NGSP units. However, the same applies for entering assigned values in IFCC units.

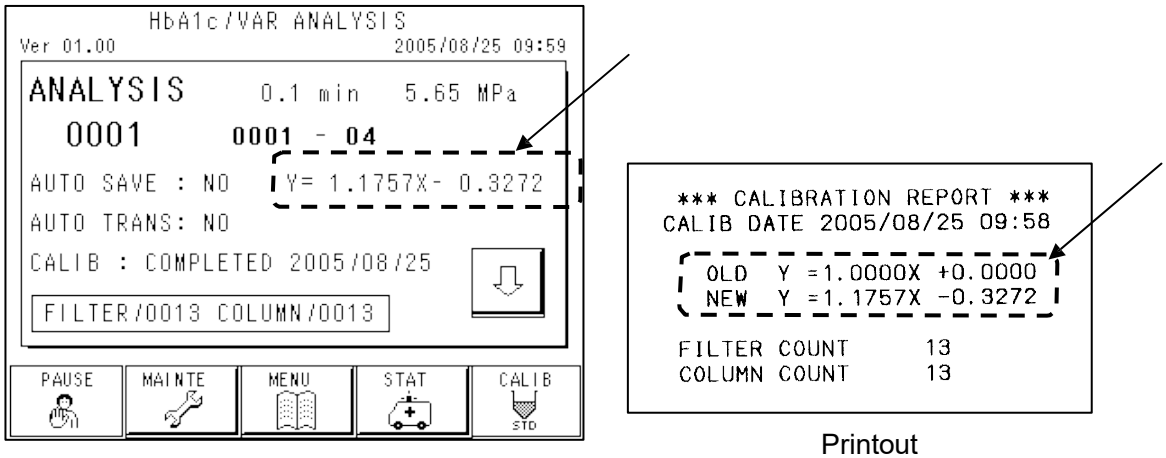
The No. 1 and No. 2 samples on the first sample rack are treated as CALIB-1 and CALIB-2. CALIB-1 is the low value calibrator (approximately 6.0%) and CALIB-2 is the high value calibrator (approximately 10.8%). The low value calibrator is assayed 3 times and the high value calibrator is assayed 2 times for a total of 5 times.
The first assay result for CALIB-1 is discarded and the average HbA1c% of the 2nd and 3rd assay is calculated as the result for CALIB-1. The average HbA1c% of the 4th and 5th assay is calculated as the result for CALIB-2. Based on the assay results and the assigned values, the following linear equation is used to calculate the calibration factors.

Object of correction: HbA1c%
Correction formula: (HbA1c% after correction) = A x (HbA1c% before correction) + B

A = (CALIB-2 assigned value - CALIB-1 assigned value) / (CALIB-2 assayed value - CALIB-1 assayed value)
B = CALIB-2 assigned value - (CALIB-2 assayed value x A)

The calculated calibration factors are automatically input in the PARAMETER screen and displayed on the main screen along with the calibration date in the form: Y = AX+B.

Fig. 3-10 Screen and Printout Examples



Screen

Printout

After the FORMAT set value is entered in the PARAMETER screen (refer to “Chapter 4 Section 4.6: Parameter setting”), the indication for the calibration factors to be printed on assay results will be printed as “CAL(IN) = AX + B” or “CAL(N) = AX + B”, to show the units used for calibration and currently applied. If the FORMAT set value is changed, the indication for the calibration factors will be changed accordingly.

4. Calibration error

A calibration error occurs when the calibrator assay results meet the following conditions. When an error occurs, the assay automatically stops, and after washing, the analyzer enters the STAND-BY state. If a calibration error occurs, samples placed behind the calibrator will not be assayed. The main screen display changes to NO and the CALIB key is not highlighted. When the operation is again started, calibration is performed again because it has not been completed.

-Error conditions

2. The difference in the SA1c% value between the 2nd and 3rd assay result is 0.3% or more.
3. The difference in the SA1c% value between the 4th and 5th assay result is 0.3% or more.
4. One or more of the SA1c% of the 2nd through the 5th assay results differs more than 30% from the assigned value.

When assigned values in IFCC units (mmol/mol) are entered, the calibration error will be checked after automatically converting the entered values into NGSP units (%) using the Master eq.: NGSP (%) = 0.09148 x IFCC (mmol/mol) + 2.152.

Calibration errors could be caused by the following:

1. The calibrator has been left for more than 1 week after dilution or has been left at room temperature for a long period of time.
2. The filter or column is clogged and the pressure is high.
3. There is a leak.
4. Samples other than the calibrator were assayed.

Perform calibration again after replacing the filter and column, preparing a new calibrator and tightening the tubing line fittings.

Use 500 µL or more of both CALIB-1 and CALIB-2 (low and high). An assay may not start with an insufficient volume of less than 500 µL. While in the automatic calibration mode, if a sample other than the calibrator sample is placed in the first and second positions and assayed, a calibration error will occur or the calibration factors may be calculated based on the values obtained with the samples.

3.7 Samples

Types of Sample Containers

Primary tubes and special sample cups can be assayed by the analyzer. They can be placed in random order in the sample racks. Load samples as shown in Fig. 3-12.

PRIMARY TUBE
Tubes with rubber caps can be directly placed in the sample rack. The sizes of tubes that can be directly placed are 12-15 mm diameter × 75mm and 12-15 mm diameter × 100mm.

For safety, a finger guard for 75mm primary tubes is attached to the analyzer. Remove the finger guard when using primary tubes greater than 75 mm in height.

CAUTION

Do not put your finger under the needle. The needle may pierce your finger.

The minimum required sample volume is approximately 1 mL for whole blood.
If the volume of the sample is insufficient, dilute 5 uL of the sample with 1 mL of the Hemolysis & Wash Solution in a sample vial. This dilution rate is just a guideline. Please see “SAMPLE VIALS” on next page for specific procedures.

For samples with a low hematocrit blood cells may not be sampled. It is advisable to collect a sample of a sufficient quantity (1 mL or more) and mix by turning the primary tubes upside down prior to placing the primary tubes in the sample rack. If the volume is < 1 mL, the blood can be put into the alternative/STAT position and programmed appropriately. See next section “SAMPLE CUPS”.

When using a SYSMEX® Rack
If you are using a SYSMEX® rack, attach a rack adapter to the sample rack for 12-14 mm diameter primary tubes. The following tube adapters are available: 12 mm diameter adapter (P/N 0018496), 13 mm diameter adapter (P/N 0018433), 14 mm diameter adapter (P/N 0018497). The adapter for 13 mm diameter tube is included as a standard accessory.

CAUTION

If the primary tube adapter is too loose, the tube may tilt during sampling and the sampling needle may not pierce at the proper location. The needle may be bent or broken. Be sure to use an adapter size that is appropriate for the primary tube diameter.

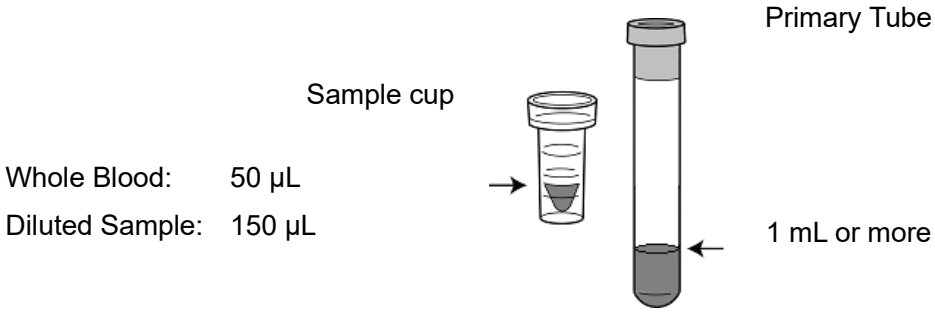
SAMPLE CUPS

Use a sample cup when processing diluted samples, calibrators, control, or small volumes of whole blood.
When you use a sample cup, you can use a vial adapter (P/N: 0020101).

If you are using a SYSMEX® rack, make sure to put on a rack adapter or attach a vial adapter (P/N: 0019509) before placing the sample cup in the adapter.

After dissolving the calibrator, dispense the necessary volume into the sample cup. A minimum of 500 µL of each calibrator is required.
If the sample volume is low (below 1 mL) and cannot be aspirated from the primary tube, or the TOTAL AREA of the assay results are below 500, test results may be unreliable. Assay the sample again using the following procedure.

Fig. 3-11 Minimum Sample Volume



Procedure for using whole blood in a sample cup

1. Dispense 50 µL or more of the whole blood (refer to Fig. 3-11) into a sample cup. Confirm that the LOADER SMP MODE in the PARAMETER screen (refer to “Chapter 4 Section 4.6: Parameter Setting”) is set to 1 (default value is set at 0).
2. Place the cup in the sample rack and run the assay.
   If you only have one or two samples then leave the LOADER SAMPLE MODE in the default of 0 and while the analyzer status is in ANALYSIS, set a sample in the Alternative/STAT position, select CUP, and perform a STAT sample assay.

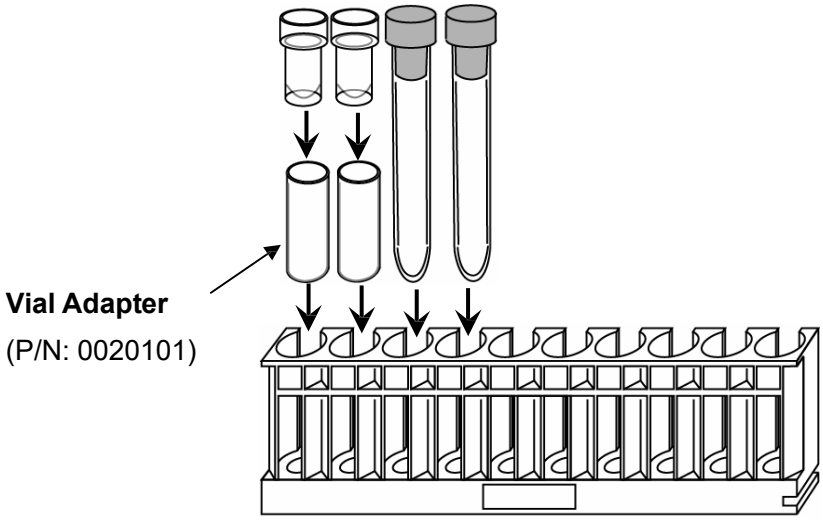
Please refer to the Instructions for Use for the buffers regarding usable types of primary tubes.

CAUTION

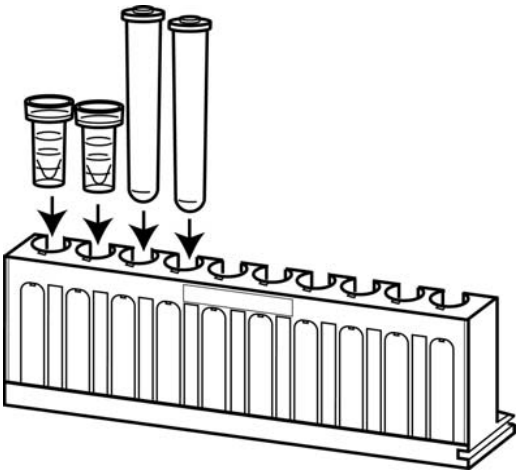
1. **If the primary tubes are loose on the Tosoh rack, adjust the rack’s holder to tightly hold the primary tubes. The sampling needle could be bent if the tubes are loose.**
2. **Insert the primary tubes straight into the racks. If the primary tube is not set straight or its bottom is not fit to the rack, the sampling needle could be bent.**
3. **If you are using 12mm-14mm diameter primary tubes on a SYSMEX® rack, make sure to attach a rack adapter to avoid the tubes from being too loose in the rack otherwise the sampling needle could be bent.**
   If primary tubes with labels and those without labels are mixed together on the same rack, or when different types of primary tubes from different manufacturers are mixed on the same rack, make sure all the tubes are firmly held in place. If the tubes are excessively loose, prepare racks with different adapter diameters for each primary tube type.

Fig. 3-12 Loading Method for Primary Tubes and Sample Cups

(For Tosoh rack)



(For SYSMEX® rack with Rack Adapter)

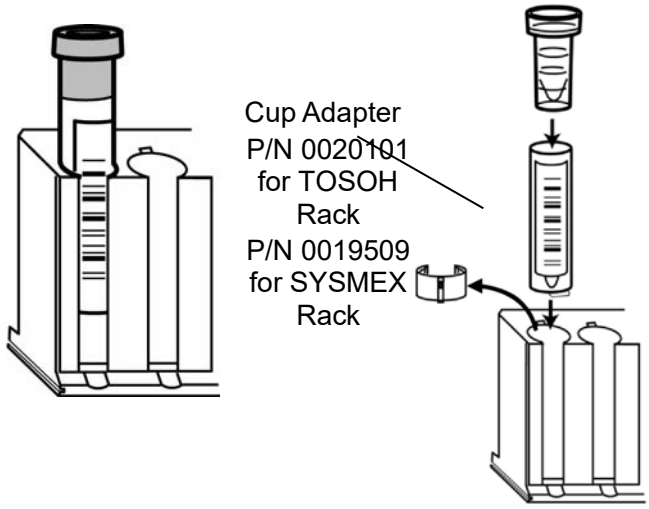


Bar Code Label Confirmation

The analyzer reads the bar code ID on the labels affixed to primary tubes and can transfer test information inquiries and assay results with IDs to the host. ID information can also be printed on the test report from the internal printer of the main unit. If a sample container with no bar code is processed, the rack number and position number will be sent or printed with the test results instead of the sample ID.

When processing primary tubes on the sample rack, the bar code label must be oriented toward the slit (the bar code will therefore face the main unit when the rack is placed in the analyzer). When attaching bar code labels to sample cups, use the optional cup adapter (P/N 0019509).

Fig. 3-13 Label Direction and Cup Adapter Setting Position in a Rack



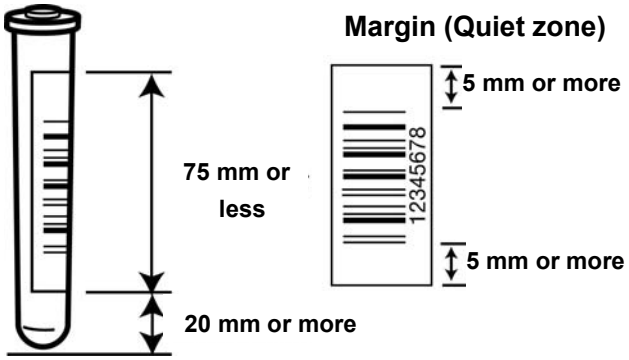
A 5mm margin (blank space) is required on the top and bottom of the printed bar code.

If a bar code cannot be read or a sample container has no bar code, the rack number and the position on the rack (1-10) will automatically be assigned instead. The rack of the first sample from the START is recognized as number 0001 (0001-03, 0008-01, etc.).

Affix the labels vertically as shown in Fig. 3-14. A reading error will occur if the label is set at an angle or if it is wrinkled.

The bar code label should not be angled more than 5°. You should also leave a margin (quiet zone) of 5 mm or more on the top and bottom of the bar code, as indicated in Fig. 3-14. There must be at least 20 mm of blank space below the end of the printed bar code sheet.

Fig. 3-14 Barcode Label Attachment Position and Size



There are strict printing specifications for each standard code used in bar-coding. Labels that do not conform to specifications (lines that are too thin, etc.) will result in a poor reading rate or may be completely unreadable. Contact your label printer manufacturer for information regarding these specifications.
Although the analyzer is compatible with most bar-coding standards, some bar code specifications do not specify an initial setting, and a reset may be required.
Refer to Chapter 7, Section 7.3: Specifications for code specifications.
Refer to Chapter 4, Section 4.19: Bar Code Reader Setting and Reading Check for details on how to change the settings.

End Marker Attachment (Optional)

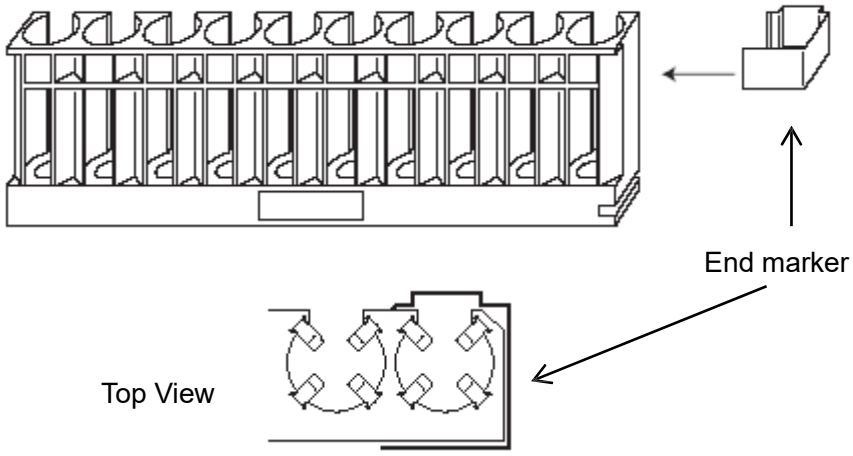
When the end marker is attached to the last rack, the assay automatically ends when the assaying of all samples set in the rack is complete.

Procedure for End Marker

1. Squeeze the end marker with fingers until the opening is 6-8 mm wide.
2. Set the end marker in the position shown in Fig. 3-15.

   Orientation: Set the flat surface on the front edge (the side with no slit) and the bending surface on the rear edge (the side with a slit).
   Position: Top of No.10 position on the final rack.

Fig. 3-15 End Marker Attachment



There are two types of end markers: for the 90SL (P/N: 0021640) and for the 290SL (P/N: 0021668). These two markers have different shapes. Verify which sample loader you are using and select the correct end marker accordingly. Selection of an improper end marker could result in improper operation and damage to the machine and its components.

Sample Rack Loading

CAUTION

Take care not to catch your fingers in the driving units when placing the racks, manually changing positions, or when adding samples during an assay.

Procedure

1. Sample racks can be loaded in the rack positions (shaded) shown in Fig. 3-16 and Fig. 3-17. A loader chuck is provided at the slit at the right bottom of the rack to prevent overturning.
2. With the 90 sample loader, the first rack is placed at A assuring that the groove of the rack fits into the ledge on the sample loader. Subsequent racks are placed in sequence from the inside out.
   Up to 9 racks can be set and 1 rack space must remain empty.
3. With the 290 sample loader, the first rack is set at B and subsequent racks are set thereafter. Up to 29 racks can be set.
4. When barcodes are to be read from primary tubes, check that the labels face the rack slit side (main unit side).
5. Attach an end marker to the last rack. An empty rack with no samples should be set as the last rack.
6. Recheck the rack direction and setting.

Fig. 3-16 Top View of 90 Sample Loader

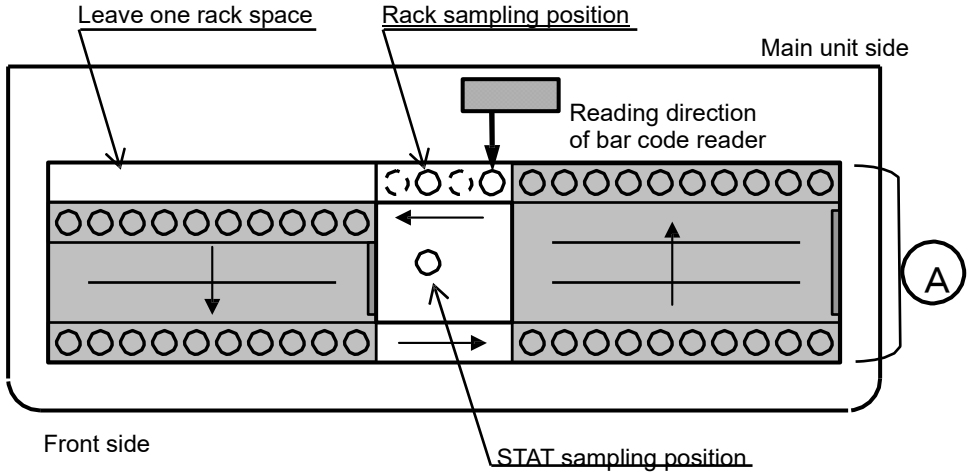
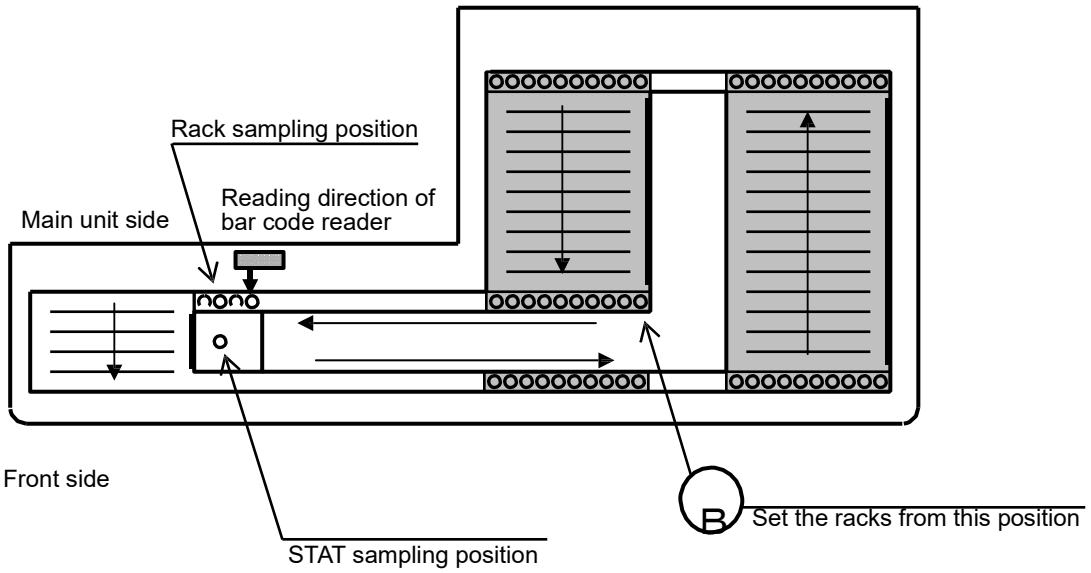


Fig. 3-17 Top View of 290 Sample Loader



1. Load the rack when the analyzer is in WARMING UP or STAND-BY state. During ANALYSIS, if the sensor is activated, a RACK POS ERROR occurs and the assay will be aborted. Never load racks or add or remove samples during an analysis. Make sure to first load all samples and sample racks before pressing START.
   If you are using the 90 sample loader, the racks can be loaded into any position as long as one rack is left empty. However, there must be 1 rack in the A position, as indicated in Fig. 3-16.
   If you are using the 290 sample loader, the assay will not be processed if the racks are loaded anywhere other than the gray area indicated in Fig. 3-17.

2. When loading racks on the sample loader, place the rack on the right side of the loader so that the groove of the rack fits into the ledge on the sample loader. Push the racks completely to the right and left ends of the sample loader. If racks are placed in an inappropriate position, a RACK POS ERROR will result, and the assay will be aborted.

Units for reporting and calibration

Assay results are calibrated and reported using the calibration factors determined with the entered assigned calibrator values and units. If the units in which assay results are reported differ from those in which the calibration factors were determined (refer to “Chapter 4 Section 4.6: Parameter Setting”), correct results will not be reported.

When the units for reporting assay results are changed by the FORMAT on the PARAMETER screen, therefore, calibration should be re-performed before assaying.

See “Chapter 3 Section 3.6: Calibration” for calibration procedures.
See “Chapter 4 Section 4.6: Parameter Setting” for setting of Printout format.

CAUTION

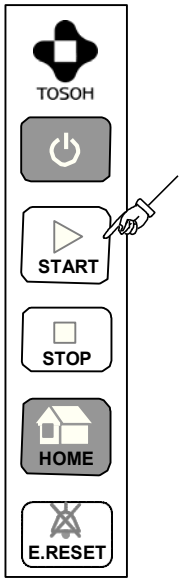
Assuming the current calibration factors were determined in NGSP units, if assays are performed under a setting to report in IFCC units, a calibration error will occur, and vice versa.

3.8 Assay Start and End

Starting an Assay

After placing sample racks on the loader correctly, press the START key on the operation panel to start the assay. The RUN LED (green) on the left side of the screen will light up and the status display will change from STAND-BY to ANALYSIS.

Fig. 3-18 START Command



If the START command is pressed during WARMING UP, the assay will start immediately after WARMING UP is complete.
Confirm the pressure displayed on the main screen and verify the flow status.
If the pressure displayed on the main screen is:
(a) greater than the pressure on the column inspection report + 4 MPa, then replace the filter.
(b) less than the pressure on the column inspection report, then proceed with priming the column.

CAUTION

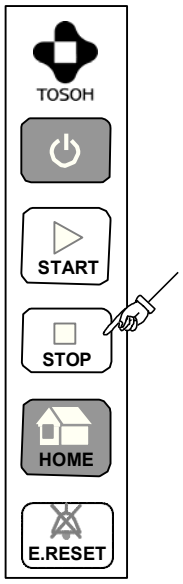
Take care not to catch your fingers in the driving units when placing the racks, manually changing sample positions, or when adding samples during an assay.

Load the racks before pressing the START key to start the assay. If you add or remove racks after the assay starts, the sensor may detect a RACK POS ERROR and abort the assay. Press the START key only after loading all samples and racks.

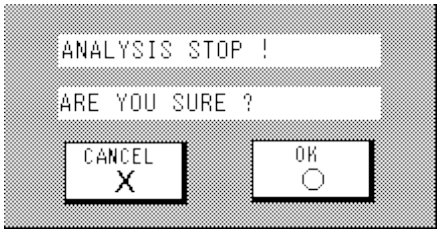
Ending an Assay

Assay results of samples will be printed and the assay will automatically end when an empty rack is detected. Thereafter, a WASH will be performed and the analyzer will enter the STAND-BY state.
To stop the assays while the assays are in process, press the STOP key. The message below (Screen 3-12) will be displayed. Press the OK key on the screen or press the STOP key again to confirm the stop process. Press the CANCEL key to cancel the stop process.
After the assay has been completed, the result will be printed, and the analyzer will enter the WASH state.

Fig. 3-19 STOP Command



Screen 3-12 The message to stop an assay



If the STOP key is pressed again after initially being pressed, operation will immediately stop and a WASH operation will be performed. Assay results of the sample currently being processed will not be reported. If the STOP key is pressed during the WASH process, the PUMP CLEAN process will be performed. If the STOP key is pressed again, the analyzer will enter the STAND-BY state.

Be sure to perform WASH when the assay is complete. If the WASH operation is insufficiently performed, some sample may remain in the column, the column lifespan may be shortened, and the next sample results may be affected.

CAUTION

Always perform a WASH operation after assaying samples. If WASH operations are performed insufficiently, sample may remain in the column, which may shorten column short life and cause sample carry-over.

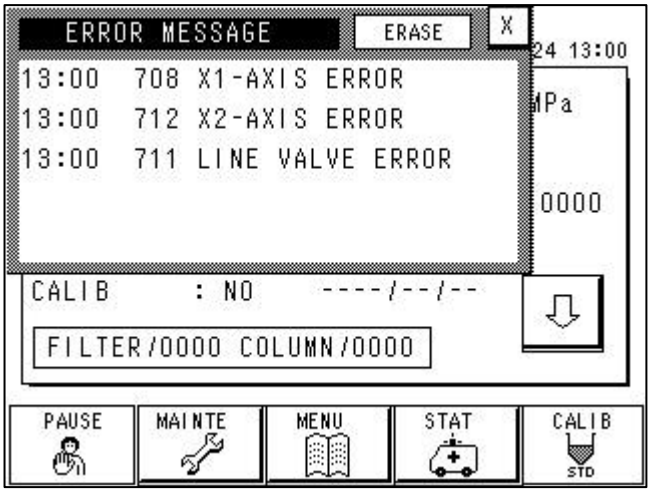
If you terminate an assay by pressing the STOP key, do not immediately remove the samples and racks. The final sample may still be in the assay after the STOP key has been pressed. If the rack or samples are immediately removed, the sensor will be activated and a RACK POS ERROR will occur, and the assay results for that sample will not be reported.

Check that all the assay results have been printed out and that the analyzer has entered into the WASH state. Once it has, remove the samples and racks.

3.9 Clearing Errors

If an error occurs, a buzzer will sound and an error message will be displayed on the screen. The error LED (red) will light up on the left side of the screen.

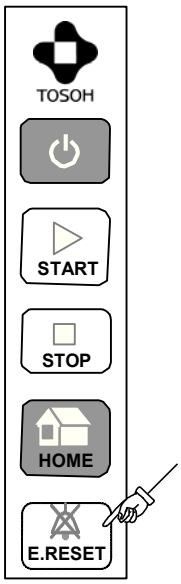
Screen 3-13 Error Message Screen



1. Press the E.RESET key on the sheet key. The buzzer will stop and the error LED will turn off.
2. Press the X key to close the error message screen.

Confirm the cause of the error before clearing it. See Chapter 6: Troubleshooting for further details.

Fig. 3-20 E.RESET Command



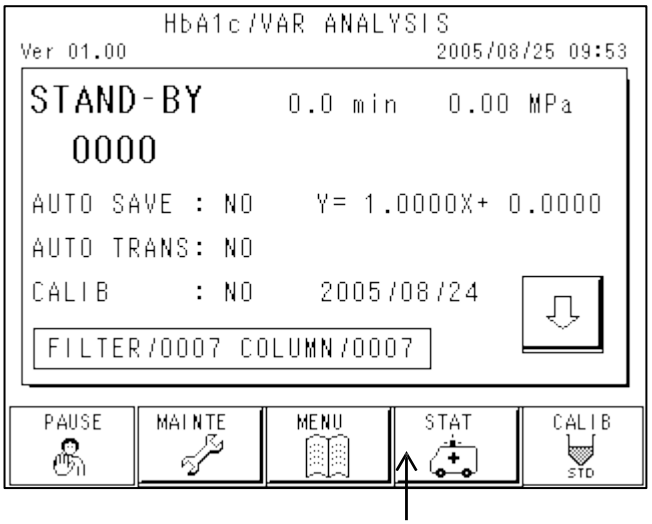
3.10 Alternative Sampling Mode (STAT)

If a priority sample needs to be assayed, set the sample in the Alternative/STAT port located in the middle of the sample loader. The sample can be processed either with a primary tube or a sample cup. Both diluted and whole blood samples can be processed.

Procedure

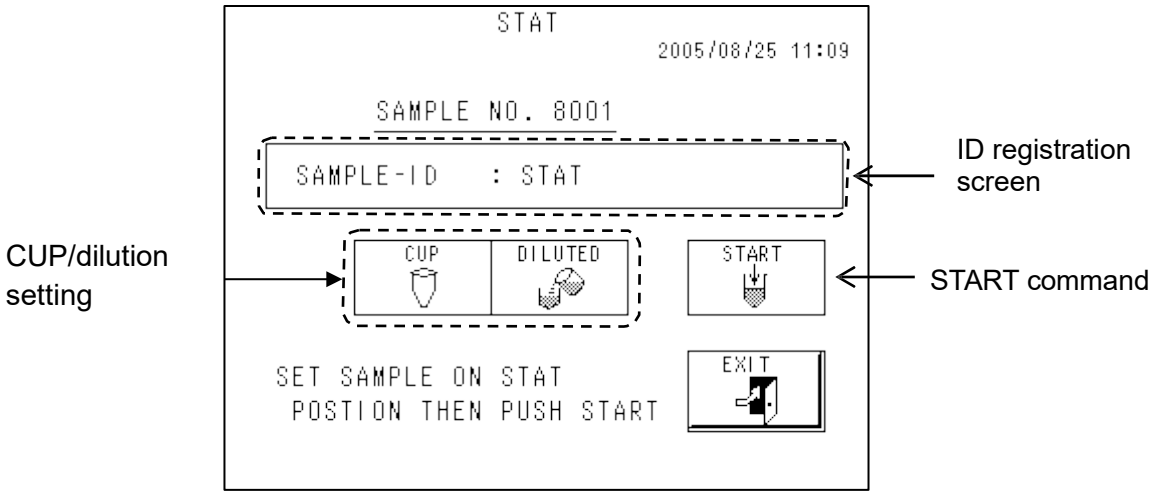
2. Verify that the STAT key on the main screen is not highlighted (i.e. STAT is not scheduled or in analysis) and manually open the STAT port.Remove any sample container already in the port and set in the sample to be assayed.
3. Press the STAT key on the main screen.

Screen 3-14 Main Screen (first screen)



4. The STAT screen will be displayed.
   Register a sample ID as required. Select the type of container (highlighted specifies cup) and dilution (highlighted indicates diluted sample) then securely close the STAT port.

Screen 3-15 STAT Screen

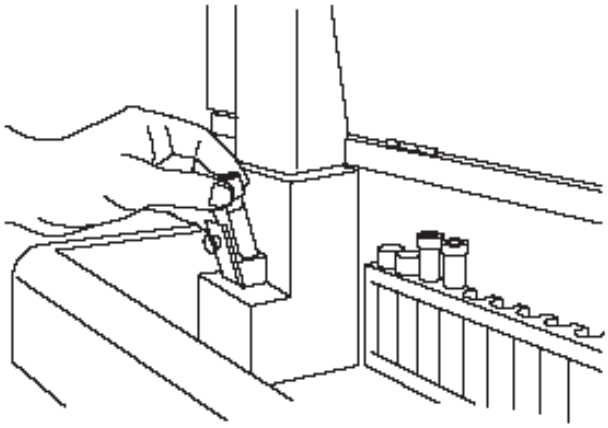


5. Press SAMPLE-ID and enter a sample ID on the ID registration screen.
   Select container/dilution type by pressing the appropriate keys:

   If whole blood in a sample cup-Press CUP key
   If prediluted blood in a sample cup – Press both CUP and DILUTED keys
   If whole blood in a tube – No keys should be highlighted

6. Remove any sample container already in the port and set in the sample to be assayed.
   Close the STAT port.

Fig. 3-21 Priority Sample Loading



7. Press the START key.
   Registration is complete when SCHEDULED is displayed at the bottom of the STAT screen.

8. Press the EXIT key. The STAT key will be highlighted when the main screen is displayed.

When the assay currently being processed is completed, the STAT sample is immediately processed. When the sampling is complete, the STAT key display will return to normal (not highlighted). Open the STAT port and remove the sample.

CAUTION

Never open the STAT port during sampling (while the STAT key is highlighted). The needle can be bent or cause injury. Wait until the STAT key is not highlighted.

Before you open or close the STAT port door, check that no STAT assay is indicated on the screen (STAT key not highlighted), and that no STAT sample is being assayed.

3.11 Power OFF

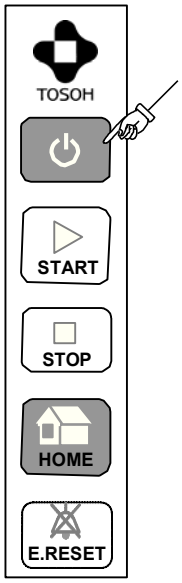
To shutdown the analyzer, press the POWER key (refer to Fig. 3-22).

The message as shown in Screen 3-16 will be displayed.

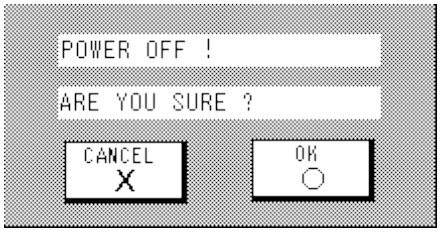
Press the OK key on the screen or press the POWER key again to confirm the shutdown process. To cancel the shutdown process, press the CANCEL key.

The column oven and the degassing unit keep on working after the shutdown. Refer to Fig.3-2 regarding turning off the main power switch.

Fig. 3-22 Power OFF Key (Power ON/OFF)



Screen 3-16 The message displayed by Power OFF Key



3.12 Interpretation of Results

Printout Format

The following two printout formats are available with this system. To change the format, select 0 or 1 on FORMAT of the PARAMETER screen. FORMAT 0 is the default factory setting.

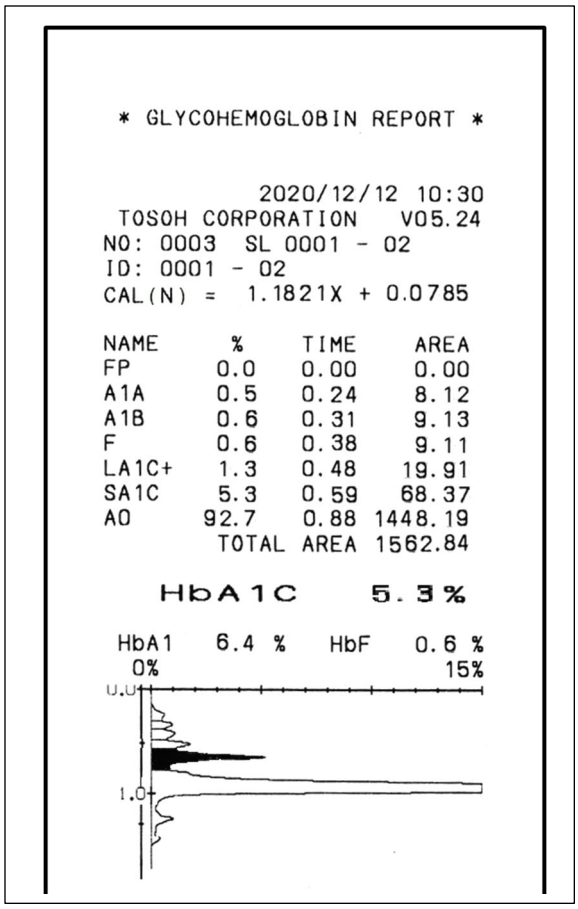
FORMAT 0
This is the most detailed format. The assay values for HbA_{1c} (s-A_{1c}), HbF, and HbA1 will be output together with a chromatogram and all peak information. To select this printout format, set 0 to the last digit for FORMAT on the PARAMETER screen.

FORMAT 1
The assay values for HbA1c (s-A_{1c}), HbF, and HbA1 will be output together with a chromatogram. To select this printout format, set 1 to the last digit for FORMAT on the PARAMETER screen.
For detailed information on Printout format, see “Chapter 4 Section 4.6: Parameter Setting”.

Assay results saved to the analyzer’s RESULT memory or to an external storage device can be printed by changing the FORMAT and running a RECALC operation.
See “Chapter 4, Section 4.9: Confirmation, Transmission to Host, and Recalculation of Saved Results”.

Fig. 3-23 Printout Examples

FORMAT 0



```
* GLYCOHEMOGLOBIN REPORT *

            2020/12/12 10:30
 TOSOH CORPORATION    V05.24
NO: 0003  SL 0001 - 02
ID: 0001 - 02
CAL(N) =  1.1821X + 0.0785

NAME      %     TIME     AREA
FP       0.0   0.00     0.00
A1A      0.5   0.24     8.12
A1B      0.6   0.31     9.13
F        0.6   0.38     9.11
LA1C+    1.3   0.48    19.91
SA1C     5.3   0.59    68.37
A0      92.7   0.88  1448.19
         TOTAL AREA  1562.84

      HbA1C    5.3%

HbA1   6.4 %   HbF   0.6 %
 0%                    15%
```

Test Report Interpretation

NO
Indicates the sample numbers (4 digits). The 0001 is automatically given to the first sample of the day and the sample numbers are assigned in succession. When the START day is changed, the numbers return to 0001.
Numbers starting from 9001 are automatically assigned to the calibrator and numbers starting from 8001 are automatically assigned to the STAT samples.

ID
When a bar code is used, the bar code number is given in the ID field.
When a bar code is not used, the rack number and sample position number is given (position and rack number).

CALIB
Shows the calibration factors with which the assay result was calibrated.
This indication “CALIB” is changed as “CAL(IN)”, “CAL(N)” or “CAL(J)”, depending on FORMAT set value (in which units the calibration was done).

NAME
Indicates the name of hemoglobin fraction identified corresponding to each peak for A_{1a}, A_{1b}, F, LA_{1c}+, SA_{1c}, A0.
P00, P01, P02, etc., are assigned to unidentified peaks and are printed below the chromatogram.
H-V0, H-V1, H-V2 and P-HV3 are assigned to variant hemoglobins. For example, typically HbS elutes in the H-V1 window. Typically HbD elutes in the H-V0 window and typically HbC elutes in the H-V2 window. HbE typically elutes in the P-HV3 window.
These H-V peaks will be reported only when the corresponding flag setting is done. See “Chapter 4, Section 4.18: FLAG Parameter Setting” for detail.

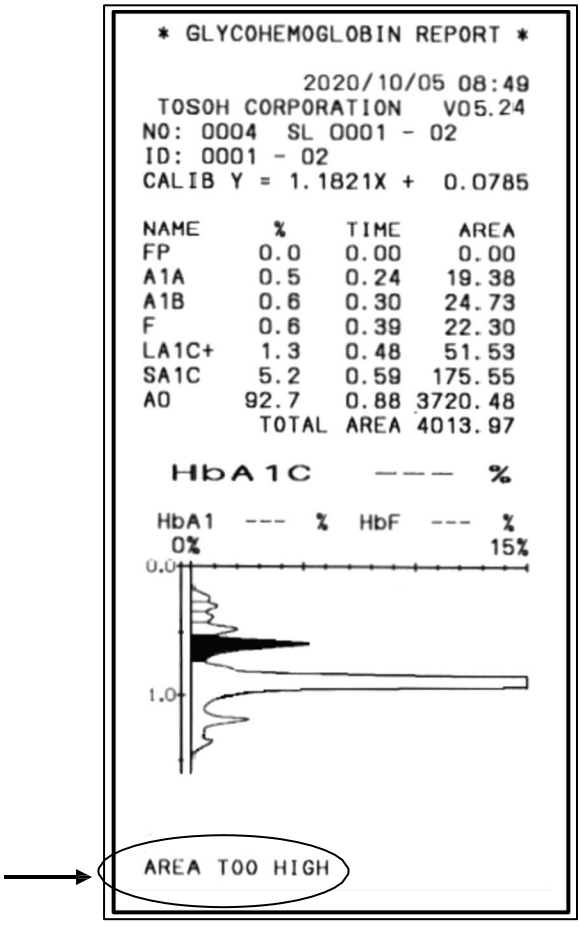
TOTAL AREA
The total of each area under the peak is printed. This corresponds to the hemoglobin concentration. The front peak (FP) is not included in the total area. The value is calculated by integrating the detector output by time. The unit is mV•s.

HbA1 (Total A_1)
The total value of A_{1a}, A_{1b} and s-A_{1c}.

CHROMATOGRAM
The fractions separated by the column are shown as they are detected. The horizontal axis is adjusted as the 15% in S-A1c concentration comes to the full scale. The vertical axis is the retention time from the time that the sample is injected into the column. The unit is in minutes. The peak identified as HbA1c (S-A1c) is shaded.

FLAG
Enter the guideline parameters needed in your lab on the FLAG screen before use. Messages are printed out when the test result meets the flag parameters. The flag is printed below the chromatogram. See figure 3-24 below
See Chapter 4, Section 4.18: FLAG Parameter Setting for further details.

Fig. 3-24 Printout Example with FLAG



DETAILED PEAK INFORMATION

If FORMAT 0 has been selected, the information for each hemoglobin fraction separated by the column is printed.

1) **%** (each peak area against the TOTAL AREA)
   This is the ratio of each peak against the total peak area (excluding FP). The front peak, FP, is always 0.0 %, since it is not related to glycohemoglobin.

2) **TIME** (elution time, retention time)
   Indicates the time at the apex of the peak.

3) **AREA**
   The peak area corresponds to the volume of each fraction. This is the value calculated by integrating the detector output by time. The unit is mV-s (millivolt-second). The TOTAL AREA, which is the sum of all individual peaks, changes depending upon the sample concentration. The acceptable range of TOTAL AREA is from 500 to 4000. However, optimal results are obtained in the TOTAL AREA range from 700 to 3000.

   When sampling whole blood directly from a primary tube, the analyzer automatically dilutes the sample by a fixed ratio of about 1:200. Samples will normally not be outside of the range indicated above, but in the case of a very low hemoglobin concentration (dialysis patients, anemia patients, etc.) the TOTAL AREA may drop below 500. In this case, transfer the blood cells to a sample cup and run the assay again in the alternative sampling position. .

4) **CHROMATOGRAM**

   The A_{1a}, A_{1b} and HbF may be eluted out with different peak shapes or not be detectable depending upon the sample. If you observe shoulders or splits around the s-A_{1c} or A0 peak, the assay condition may not be optimal. In addition, if the sample has been stored for a long time at room temperature after collection, an abnormal chromatogram may be obtained because the samples have deteriorated.

   If you observe the same phenomena with several different samples, the reagent may have deteriorated. Replace the Elution Buffers and run the assay again.
   If you observe an aberrant result with a single specific sample, the sample may have deteriorated, or hemoglobin variants may be present.

   The Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 Variant Analysis Mode can separate the major variant hemoglobins (HbD, HbS, HbC and HbE). See “Chapter 6 Section 6.4: Abnormal Chromatograms” for typical chromatograms. The chromatogram pattern for hemoglobin variants differs from that of a normal sample.

NO and ID Interpretation

The sample number (NO) and sample ID (ID) are automatically given but when the barcode on primary tube is read, the barcode ID is printed in the ID field.

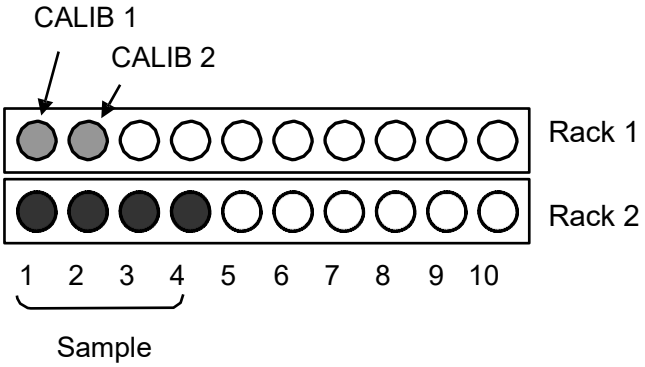
Example: CALIB. YES

The calibrator No. 1 is placed in the rack position 1-1

The calibrator No. 2 is placed in the rack position 1-2

The samples are placed in the rack positions 2-1 to 2-4

Fig. 3-25 Example



Sample NO	Sample ID	
9001	01-01	
9002	01-01	····· CALIB 1
9003	01-01	
9004	01-02	
9005	01-02	····· CALIB 2
0001	02-01	····· Sample 1
0002	02-02	····· Sample 2
0003	02-03	····· Sample 3
0004	02-04	····· Sample 4

Sample NO.: Numbers 9001- for the calibrator, numbers 8001- for the STAT samples, numbers 0001- for the test samples on the rack.
Sample ID.: The rack # and the position # or a barcode for samples.

The sample numbers start from 0001 for the first assay tested that day. When the START day is changed, the numbers return to 0001.
Specific numbers can be assigned by inputting a four-digit number in the PARAMETER screen. Take note if a sample number overlaps with a number already assayed the older result in RESULT or an external storage device will be overwritten.

3.13 List Data

List data is a table of assay result values that include the sample, NO, and ID.

The analyzer can save up to 800 test results in the RESULT memory and displays the list data referring to the RESULT memory.

You can print and transmit data of the range specified.

Press the TODAY key to specify today's data obtained on the same day as the last assay data in the RESULT memory. Those data can be collectively printed and transmitted.

In addition, IDs can be edited on the LIST screen by individually selecting test results. If the data meet the conditions specified on the FLAG screen, the FLAG code is listed in the
LIST screen and printed out in the MK field.

If LIST AUTO SAVE is set to 1 on the PARAMETER screen, the list data is automatically saved to an external storage device for each batch data (apart from the data saved to the analyzer's RESULT memory). This data is saved to the external storage device in CSV format.

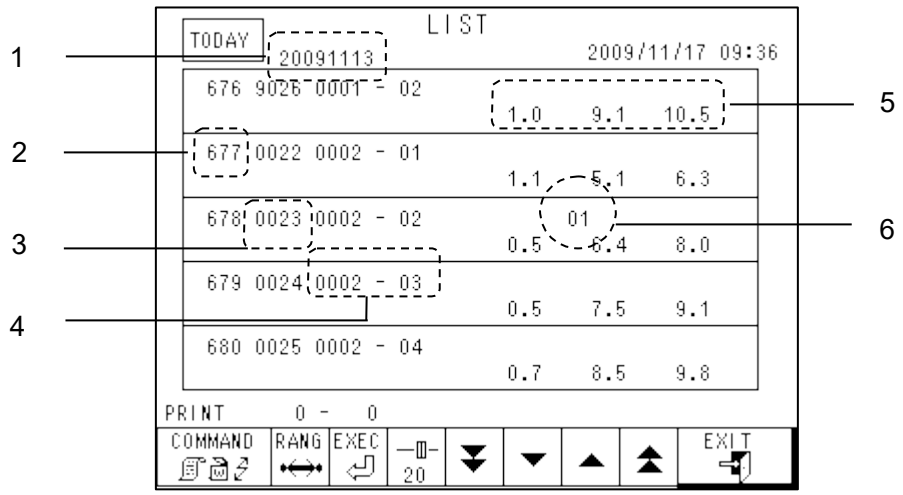
You must perform list data operations when the analyzer is in STAND-BY state.

Point

Press the TODAY key on the LIST screen to extract and display only the data obtained on the same day as the last measured assay results.

Assay results obtained in the units other than the units currently set will not be listed on the LIST screen but listed as Screen 3-19. To display those data, set the same value to the FORMAT on the PARAMETER screen as the value with which those data were obtained. See "Chapter 4 Section 4.6: Parameter Setting" for set value to the FORMAT.

Screen 3-17 LIST Screen



Display content

1. Assay date of sample

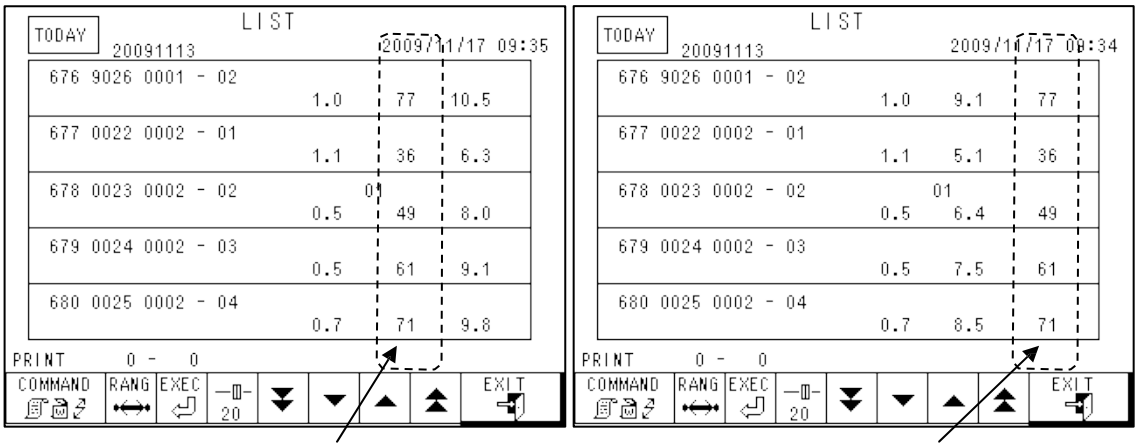
YYYYMMDD. (YYYY : Year, MM : Month, DD : Day)
If assays were done in a certain time period, this will be displayed as: Ex. 20091104－20091105

2. The number of the assay result
3. Sample number
4. Sample ID or rack position number
5. Assay results (HbF(%), HbA1c(%), HbA1(%))
6. Flag code

See “Chapter 4 Section 4.18: FLAG Parameter Setting” for details.

Assay results obtained in IFCC units are listed on the LIST screen in the format defined by “TRANS G5/7 MODE” in the PARAMETER screen. The set parameters are not normally displayed on the screen. Contact Technical Support to change for assistance.
See “Chapter 7 Section 7.2: Communication with a Host Computer” for details.

Screen 3-18 LIST Screen (examples of assay results obtained in IFCC units)



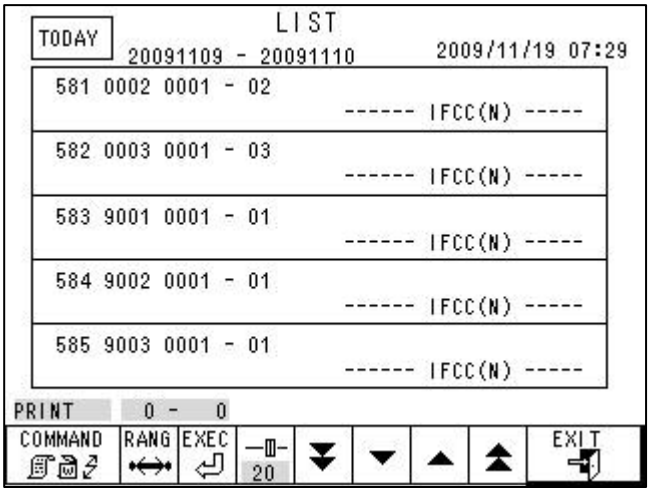
Assay results (in IFCC units)

TRANS G5/7 MODE : 18

Assay results (in IFCC units)

TRANS G5/7 MODE : 28

Screen 3-19 LIST Screen (an example of assay results obtained in IFCC units; LIST data display after FORMAT was changed to report in NGSP units.)



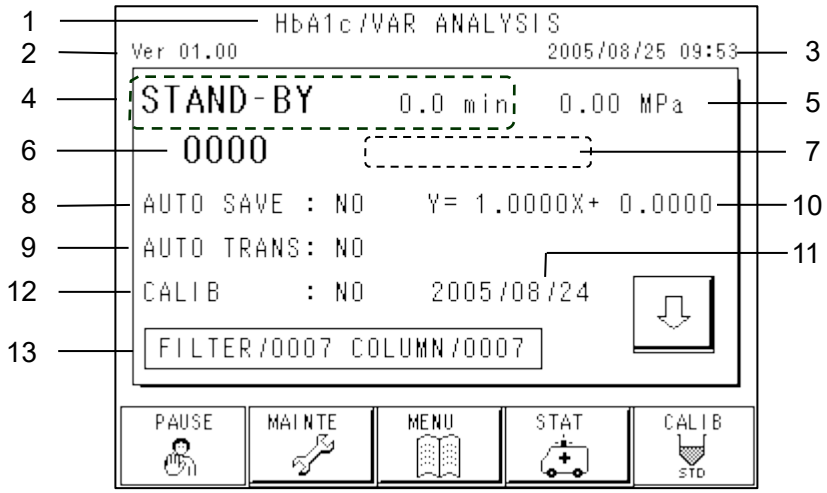
NOTES

Chapter 4 Screen Operations

4.1 Main Screen

The main screen (first screen) displayed after the analyzer is turned on.

Screen 4-1 Main Screen (first screen)



Display content

1. Title (Displays the assay mode currently in operation)
2. Program version number
3. Current date and time
4. Status and remaining processing time or elapsed time

   PUMP CLEAN: Displayed during pump cleaning
   BUFF PRIME: Displayed during buffer replacement] about 4.2 min.
   WARMING UP: Displayed during warm-up (about 4.8 min.)
   STAND-BY: In ready state (pump stopped)
   ANALYSIS: Displayed during assay
   WASH: Displayed during wash operation (about 3.0 min.)
5. Pump flow pressure: Displayed in MPa (Mega Pascals) units
6. Sample number currently under assay
7. Sample ID or rack position number currently under assay
8. Setting to auto save assay results on an external storage device

9. Setting for automatic transmissions to a host
10. Calibration factor currently in use
11. Date calibrated
12. Calibration setting
13. Number of injections for the filter and column

Key Functions

PAUSE : PAUSE (temporary stop) command
When the PAUSE key on the main screen is pressed during ANALYSIS, the key is highlighted and sampling is temporarily stopped. Pumping into the assay line continues, so the sample results currently being assayed will be output. Use this function when replacing the printer paper or performing other operations during an assay. The pause is automatically released 10 cycles (1 cycle is 1.6 minutes) after the PAUSE key is pressed.
Release the pause by pressing the PAUSE key again.

MAINTE : Displays the maintenance screen

MENU : Displays the menu screen

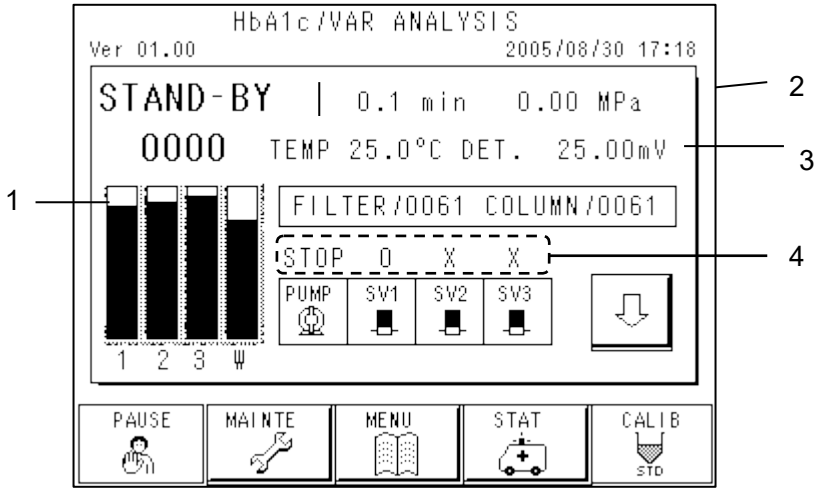
STAT : Used to set and process STAT (priority) samples

CALIB STD : Sets whether or not to perform automatic calibration.
To set automatic calibration, press and highlight the key before giving the start command.

: Displays the second screen of the MAIN screen

The following information and operation keys are displayed on the second screen.

Screen 4-2 Main Screen (Second Screen)



Display content

1. The remaining volume of the eluents (Elution Buffer No. 1, 2, and 3 and the Hemolysis & Wash solution are shown in sequence from the left)
2. Current temperature of the column oven
3. Detector output
4. The current operation status of the pump and solenoid valves

Key Functions

: Starts or stops pump run (STOP: stop pump FLOW: run pump)

: Opens or closes the valve for Elution Buffer No. 1
(o: opened x: closed GE: Gradient elution)

: Opens or closes the valve for Elution Buffer No. 2
(o: opened x: closed GE: Gradient elution)

: Opens or closes the valve for Elution Buffer No. 3
(o: opened x: closed GE: Gradient elution)


: Displays the first screen

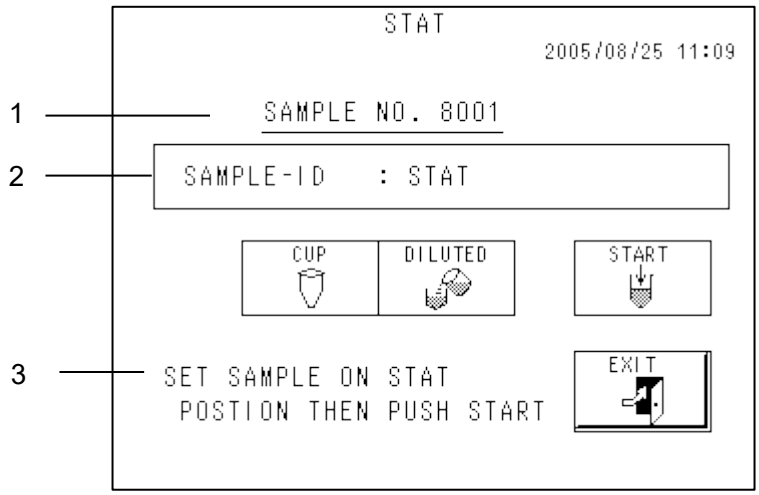
Other display content and key functions are identical to the first screen. After the MENU and other screens have been displayed, the analyzer display returns to the first screen.

4.2 STAT Main screen –

Press the STAT key on the main screen to display the STAT screen.
A sample requiring an immediate assay can be processed by placing it in the STAT position.

After acceptance of the STAT operation, press the EXIT key to return to the main screen. The STAT key will be highlighted, showing that the STAT operation has been scheduled. If you press the EXIT key on the STAT screen without pressing the START key to return to the main screen, the STAT operation will not be scheduled. After the STAT sample is assayed, the STAT key will go back to be unhighlighted.

Screen 4-3 STAT Screen



Display content

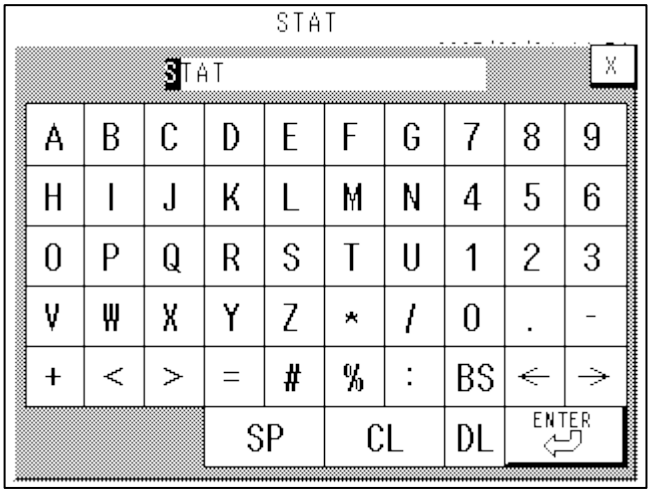
1. Number given to sample (STAT sample numbers are given sequentially starting from 8001)
2. ID number given to sample
3. Message display line

Key Functions

SAMPLE-ID : STAT	Changes the ID number
CUP	Highlighted when a sample vial is set
DILUTED	Highlighted when a diluted sample is set
START	Registers the STAT sample
EXIT	Displays the previous screen

1) Check the STAT key on the main screen and make sure that a STAT operation is not being scheduled or the STAT sample assay is not in process.
2) Press the STAT key to display the STAT screen.
3) Place a sample requiring an immediate assay into the STAT position.
4) Press SAMPLE-ID : STAT to display the ID EDIT screen. Input an ID.
5) Select cup CUP key and/or diluted sample DILUTED key.
6. Press the EXIT key to return to the main screen.
7. If the STAT sample assay is scheduled, the key on the main screen is highlighted. STAT

Screen 4-4 ID EDIT Screen

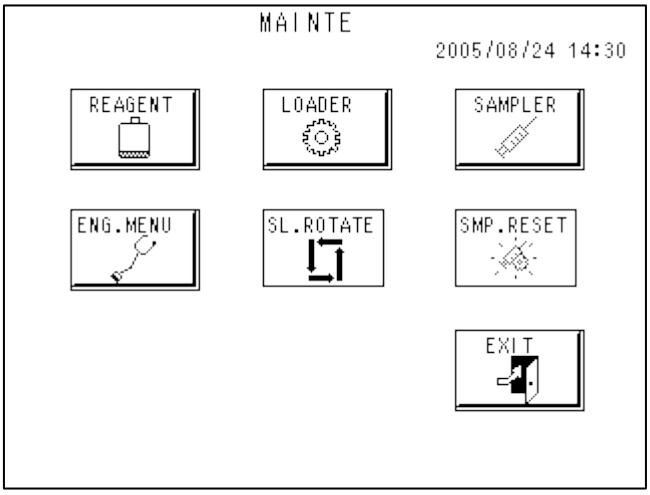


4.3 Maintenance Main Screen –

Press the 

key on the main screen to display the MAINTE screen.

Screen 4-5 MAINTE Screen



Key Functions

: Displays another screen to reset the column and filter counter or replaces the reagent

: Used by service person (nothing performs, even if pressed)

: Used by service person (nothing performs, even if pressed)

: Used by service person (nothing performs, even if pressed)

: Continuously rotates the sample loader.
Stops the loader when the key is pressed again.

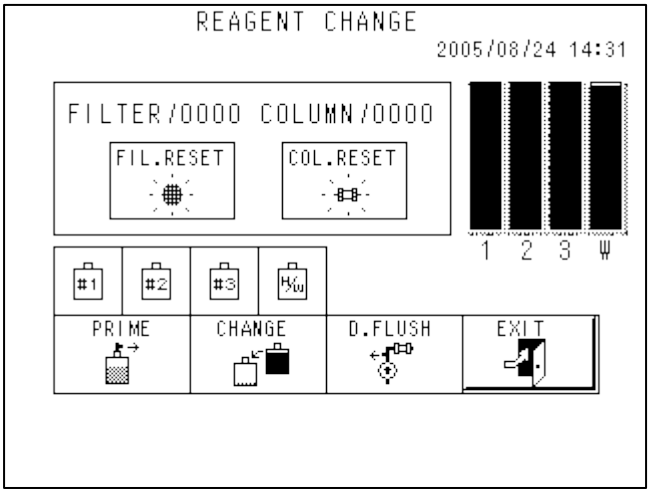
: Initializes (washes) the sampling unit

: Returns to the previous screen

4.4 Reagent Change

This key is used to reset the counter when the column or filter has been replaced, and to prime in order to purge air after replacing elution buffers, and to remove air from the pump valves.

Screen 4-6 REAGENT CHANGE Screen



Key Functions

: Sets the filter counter to 0

: Sets the column counter to 0


: Selects Elution Buffer No.1 for PRIME and CHANGE


: Selects Elution Buffer No. 2 for PRIME and CHANGE


: Selects Elution Buffer No. 3 for PRIME and CHANGE


: Selects the Hemolysis &Wash solution for PRIME and CHANGE

: Replaces reagent in the flow paths selected with the above key

: Replaces the reagent in the flow paths selected with the above key. Resets the display for the remaining volume.

: Purges the air from the drain valve when air has entered into the pump

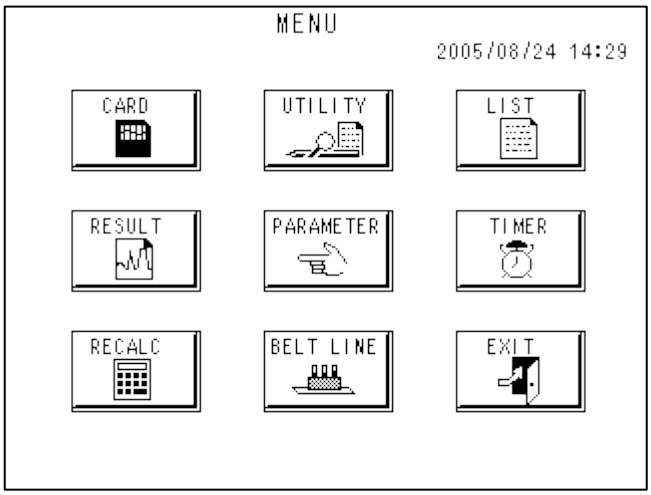
: Returns to the previous screen

4.5 Menu Main Screen

Press the 

key on the main screen to display the MENU screen.

Screen 4-7 MENU Screen



Key Functions

: Displays the card screen

: Displays the utility screen

: Displays the list data editing screen

: Displays the list of measurement results stored in analyzer

: Displays the parameter settings screen

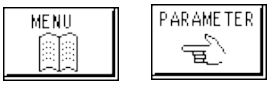
: Displays the date and timer screen

: Displays recalculation screen for test results (RESULT, External Storage device)

: Only used when LA (line automation) connecting

: Returns to the previous screen

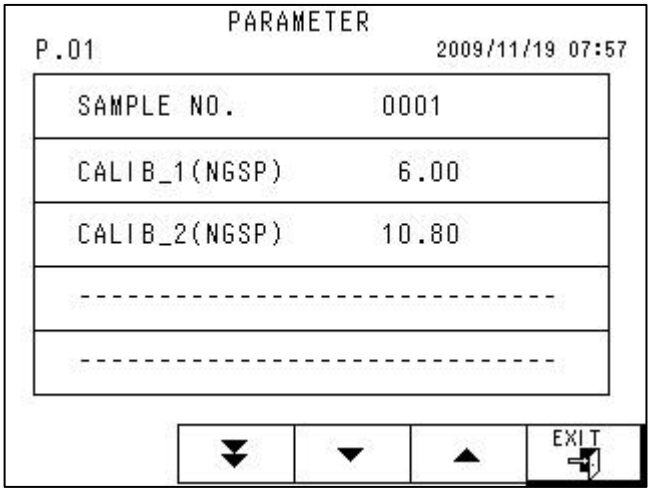
4.6 Parameter Setting



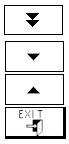
Press the 

key on the main screen to display the PARAMETER screen. Select the various parameters to change their setting.

Screen 4-8 PARAMETER Screen (page 1 of 4)

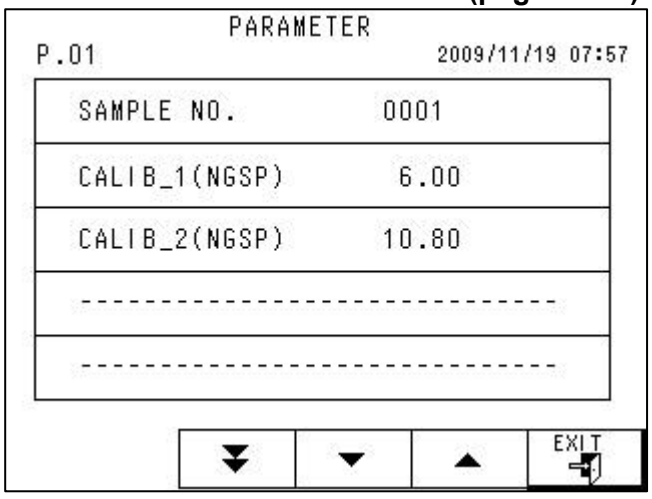


Key Functions


: Displays the page after the next page
: Displays the next page
: Displays the previous page
: Returns to the previous screen

Point There are four PARAMETER screens in total. The key functions are the same for all of the screens.

Screen 4-9 PARAMETER Screen (page 1 of 4)



Parameters (page 1 of 4)

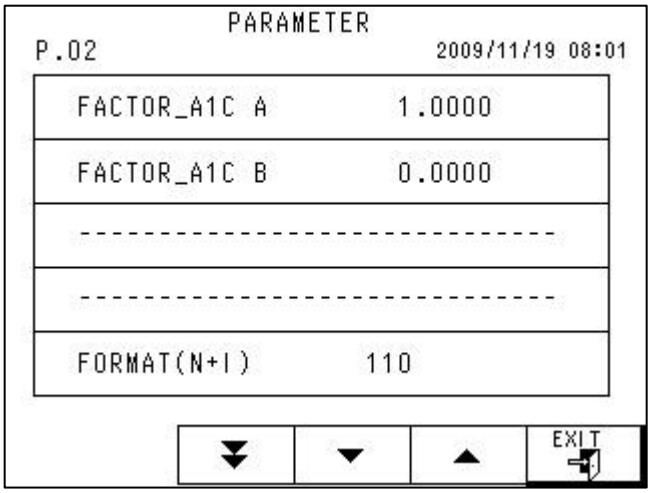
SAMPLE NO.: The first sample number on the next run (normally set automatically)
CALIB_1(XXXX): Assigned value of calibrator 1
CALIB_2(XXXX): Assigned value of calibrator 2

Point

Assigned values to be entered will be prompted with NGSP/IFCC indication as below.

For entering in NGSP units:	For entering in IFCC units:
CALIB_1(NGSP)	CALIB_1(IFCC)
CALIB_2(NGSP)	CALIB_2(IFCC)

Screen 4-10 PARAMETER Screen (page 2 of 4)



Parameters (page 2 of 4)

FACTOR_A1C A: Calibration factor A; Automatically calculated in automatic calibration mode but may be changed by key input.
FACTOR_A1C B: Calibration factor B; Automatically calculated in automatic calibration mode but may be changed by key input.
FORMAT: Comprised of 3 digits as ABC.

The last digit (C): See also “Chapter 3 Section 3.12: Interpretation of Results”

0	FORMAT 0 (Detailed peak information with the chromatogram)
1	FORMAT 1 (Basic peak information with the chromatogram)

Second digit from the last (B): Specifies assay results are reported in NGSP units (%) and/or IFCC units (mmol/mol)

0	Reported only in the units with which the calibration will be performed. Note this will be displayed as a blank when the third digit from the last was 0.
1	Reported in the both units. The units with which the calibration will be performed come first.

Third digit from the last (A): Specifies the units for calibration

0	JDS units. Shown as a blank on the screen.
1	NGSP units.
2	IFCC units. Assay results in JDS units are reported too.
3	IFCC units. Assay results in NGSP units are reported too.

Indication of “FORMAT” on the PARAMETER screen will be replaced as e.g. “FORMAT(I+N)” depending on a combination of the three digits ABC (set value) above, to clarify the units for calibration as well as the units for reporting. This indication corresponds to the FORMAT set value.

Summary table for FORMAT set value

Units for calibration	Units reported together	Printout format	Set value	Indication after entering set value
JDS units	None	FORMAT 0	000	FORMAT(J)
		FORMAT 1	001	FORMAT(J)
	IFCC units	FORMAT 0	010	FORMAT(J+I)
		FORMAT 1	011	FORMAT(J+I)
NGSP units	None	FORMAT 0	100	FORMAT(N)
		FORMAT 1	101	FORMAT(N)
	IFCC units	FORMAT 0	110	FORMAT(N+I)
		FORMAT 1	111	FORMAT(N+I)
IFCC units (Assay results in JDS units are reported too.)	None	FORMAT 0	200	FORMAT(I)
		FORMAT 1	201	FORMAT(I)
	JDS units	FORMAT 0	210	FORMAT(I+J)
		FORMAT 1	211	FORMAT(I+J)
IFCC units (Assay results in NGSP units are reported too.)	None	FORMAT 0	300	FORMAT(I)
		FORMAT 1	301	FORMAT(I)
	NGSP units	FORMAT 0	310	FORMAT(I+N)
		FORMAT 1	311	FORMAT(I+N)

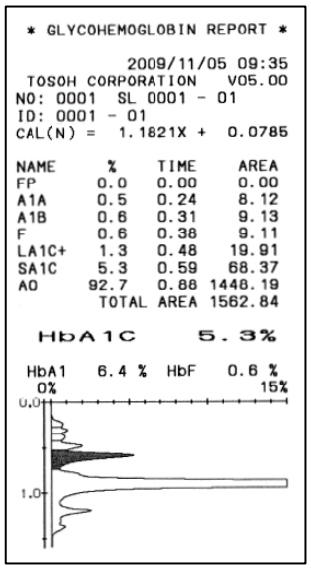
Point

The units for calibration applied are indicated as like “CAL(IN)” on assay results as below:

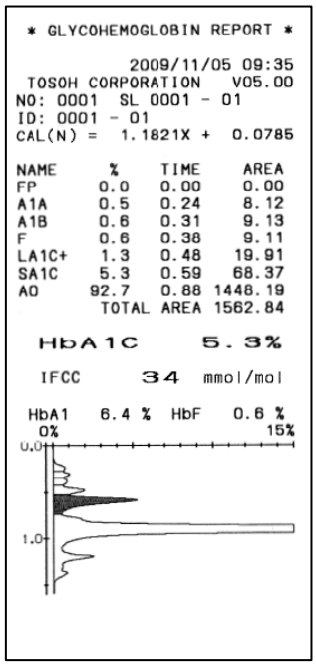
Units for calibration	Indication for calibration factors
JDS units	“CALIB Y = AX + B” or “CAL(J) = AX + B”
NGSP units	CAL(N) = AX + B
IFCC units (Assay results in JDS units are reported too.)	CAL(IJ) = AX + B
IFCC units (Assay results in NGSP units are reported too.)	CAL(IN) = AX + B

Fig. 4-1 Printout Example

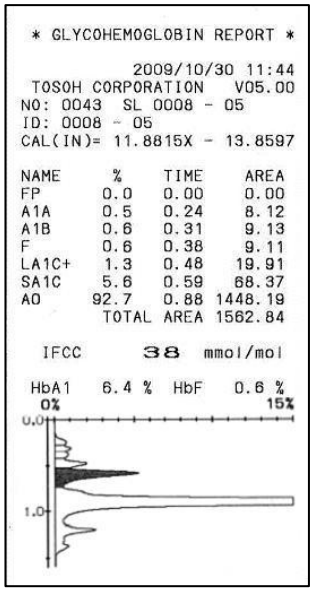
FORMAT set value : 100



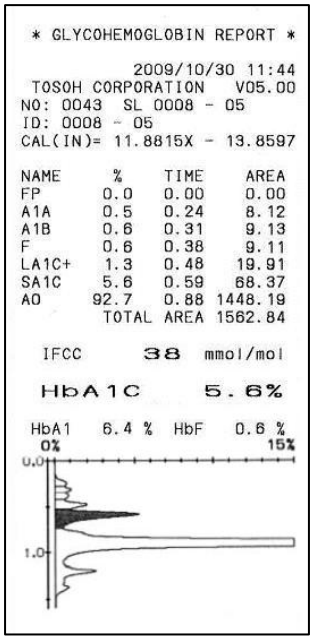
FORMAT set value : 110



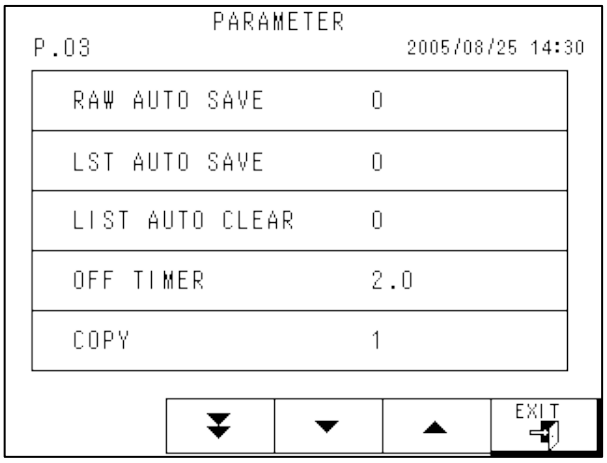
FORMAT set value : 300



FORMAT set value : 310



Screen 4-11 PARAMETER Screen (page 3 of 4)



Parameters (page 3 of 4)

RAW AUTO SAVE: Automatically saves the assay results to the external storage device (0: no save, 1: save)

LST AUTO SAVE: Automatically saves the list data to the external storage device (0: no save, 1: save)

LIST AUTO CLEAR: Clears results each time START is pressed (0: do not clear, 1: clear)

OFF TIMER: Time from STAND-BY mode entry until power shut-off. The unit is in hours. (0-3: 0 indicates no automatic power shut-off)

COPY: Number of printout copies (0-3)

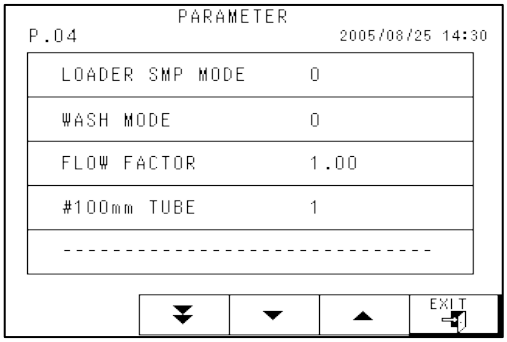
If the LIST AUTO CLEAR setting is 1, previously measured assay data saved to the RESULT section will also be deleted.

RESULT section will also be deleted.

Point

If the CARD FULL error occurs during assays, you can resave the results to an external storage device by using the SAVE key on the RECALC screen after the assay has completed. See “Chapter 4, Section 4.9: Confirmation, Transmission to Host, Recalculation of Saved Results”.

Screen 4-12 PARAMETER Screen (page 4 of 4)



Parameters (page 4 of 4)

LOADER SMP MODE: Designates the sample container type

Container	Primary tube	Sample vial
0	Whole blood	Diluted sample
1	Whole blood	Whole blood
2	Diluted sample	Diluted sample
3	Specified by host	

Point

Regardless of the LOADER SMP MODE setting, calibrators will be recognized as diluted samples and the STAT sample will be processed using the settings on the STAT screen.

WASH MODE: WASH mode settings. This parameter is not active in the Variant mode. Never change this parameter. The default value is “0”

FLOW FACTOR: Pump flow factor. Never change this parameter without instruction from Technical Support.

#100mm TUBE: Setting for the primary tube length. If you are using a combination of 75 mm and 100 mm tubes, set to 100 mm (0: 75 mm, 1: 100 mm).

Never change the FLOW FACTOR without instruction from Tosoh service personnel. Accurate results may not be obtained if this parameter is changed.

CAUTION

1. **Make sure the 100 mm TUBE is set correctly. Otherwise, the analyzer can be damaged.**
2. **If 75 mm and 100 mm primary tubes are set together, the 75 mm tubes will be pulled up after being assayed and will be forwarded as they are in this position. If these tubes are forwarded to the sampling position, the sampling needle could be bent due to this fact. Make sure to place an empty rack after the last sample so that assaying operations will stop.**

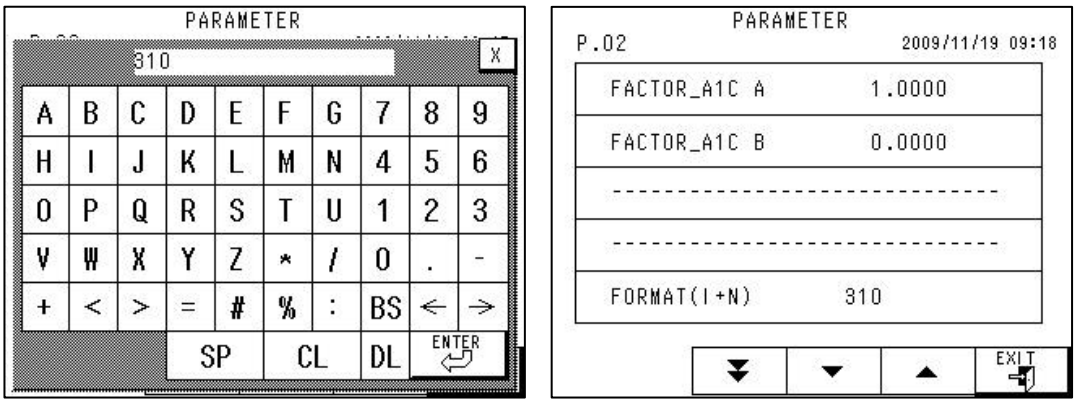
Operation Ex.

Parameter change procedure

The procedure for changing the FORMAT to 310 (calibration in IFCC units and reporting in IFCC units together with in NGSP units) is shown below. Press the keys in the designated sequence.

1) Press the screen’s FORMAT line and open the PARAMETER input screen.
2) Press the CL key to clear existing values and use the numerical keys to input “**310**”.
3) Confirm that “**310**” is displayed in the input field, press the ENTER key and close the input screen.
4) Confirm that FORMAT was set to 310 and the indication “FORMAT” was replaced with “FORMAT(I+N)”. The parameter input is now complete.

Screen 4-13 PARAMETER Input Screen **Screen 4-14 Change Example**

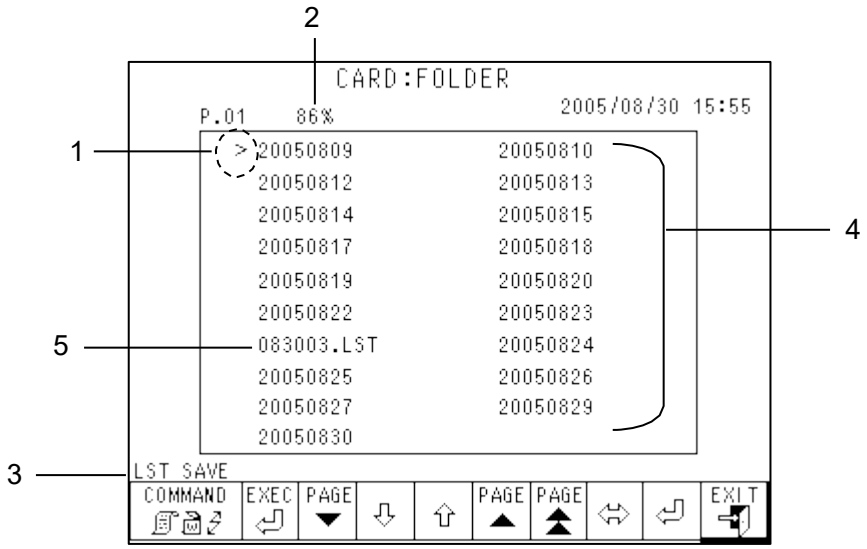


Point All settings and analyzer parameter changes should be performed in the same way, as indicated above.

4.7 Card (External Storage Device) [MENU] – [CARD]

Press the CARD key on the MENU screen to display the CARD: FOLDER screen. Use the ⇩ ⇧ ⇔ keys on that screen to select a folder (move the arrow ">"). Press the ↵ key and the list of the file will be displayed on the CARD: FILE screen. Saving list data and parameters to an external storage device, formatting an external storage device, and printing/deletion of files and folders on an external storage device are performed here.

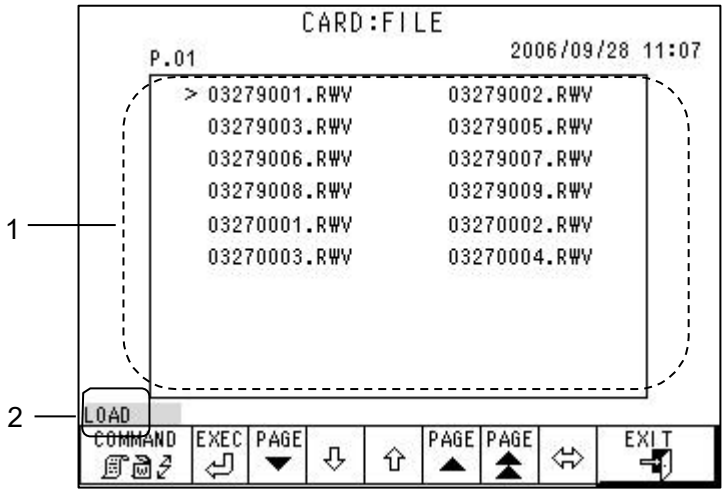
Screen 4-15 CARD: FOLDER Screen



Display content

1. The arrow shows the active field
2. Percentage of external storage device in use
3. Selected command
4. Folder (Data is stored in a folder of the assay date)
5. List data (extension: LST)

Screen 4-16 CARD: FILE Screen



Display content

1. Assay data for each sample (extension: RWV)
2. Selected command

Key functions (CARD: FOLDER / CARD: FILE screens)

COMMAND : Command key (Commands change when pressed)

Command Descriptions and Executable Statuses

Command types		WAMING-UP	STAND-BY	ANALYSIS	WASH
Command	Content				
LST SAVE	List data save (Valid only in CARD: FOLDER screen) Filename will automatically be assigned using the ID number and serial number	1	1	3	1
PRM SAVE	Parameter save (Valid only in CARD: FOLDER screen) File will be saved as SYSTEM.PRM.	3	1	3	3
LOAD	File loading Parameters and list data can be loaded	2	1	3	2
FORMAT	Format external storage device	1	1	3	1
PRINT	List of files or folders can be printed	1	1	1	1
DELETE	Selected files or folders can be deleted	1	1	3	1

1: Can be performed 2: Applies only to list data 3: Cannot be performed

EXEC : Execution key for the selected command
PAGE : Displays the next page
PAGE : Displays the previous page
PAGE : Displays prior 4 pages
: Moves the active field down
: Moves the active field up
: Moves the active field right or left
: Selects folder
EXIT : Return to the previous screen

List data deletion operation

The operation for deleting list data is indicated below.

1. Use the keys to move the “>” mark to the list file name that you want to delete from the CARD: FOLDER screen.
2. Press the COMMAND key until DELETE is displayed.
3. Press the EXEC key to delete the selected list.

Folders and the data stored in that folder, as well as individual data items, can be deleted by following the same procedure.

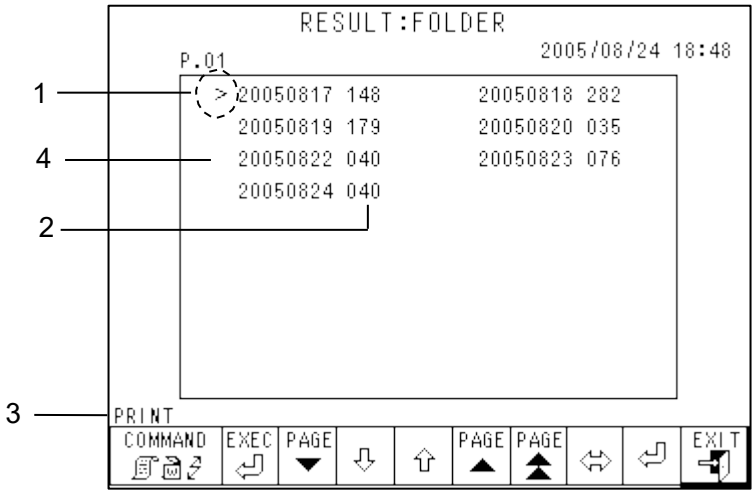
1. The commands you can perform depend on the analyzer’s operational states. When a Smart Media card is used. It’s usable capacity is 128MB or less.
2. The analyzer cannot display folder names and filenames that include double-byte characters or that exceed 12 characters. The analyzer may have an error with the external storage devices that have folder name and filenames that include double-byte characters or that exceed 12 characters.

4.8 List of Saved Data

Press the RESULT key on the MENU screen to display the RESULT: FOLDER screen. Use the ⇩ ⇧ ⇔ ↵ keys on this screen to select a folder (move the ">" mark). Press the ↵ key to display the files saved in that folder on the RESULT: FILE screen.

The file/folder lists on the RESULT screen can be printed and or deleted.

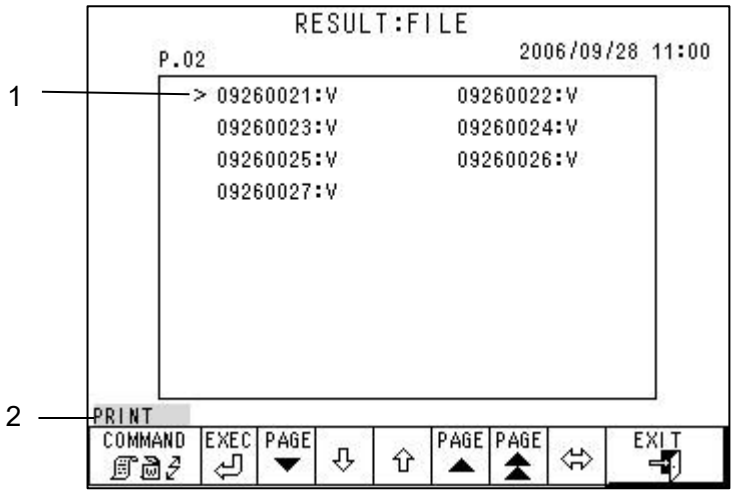
Screen 4-17 RESULT: FOLDER Screen



Display content

1. The arrow shows the active field
2. Number of saved results
3. Selected command
4. Folder - Data is stored in a folder whose name corresponds to the assay date

Screen 4-18 RESULT: FILE Screen



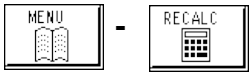
Display content

1. Assay data for each sample
2. Selected command

Key Functions

COMMAND	:	Command key (Commands change when pressed)
EXEC	:	Execution key for the selected command
PAGE	:	Displays the next page
PAGE	:	Displays the previous page
PAGE	:	Displays 4 pages prior
	:	Moves the active field (arrow: >) down
	:	Moves the active field (arrow: >) up
	:	Moves the active field (arrow: >) right or left
	:	Selects the folder
EXIT	:	Displays the previous screen

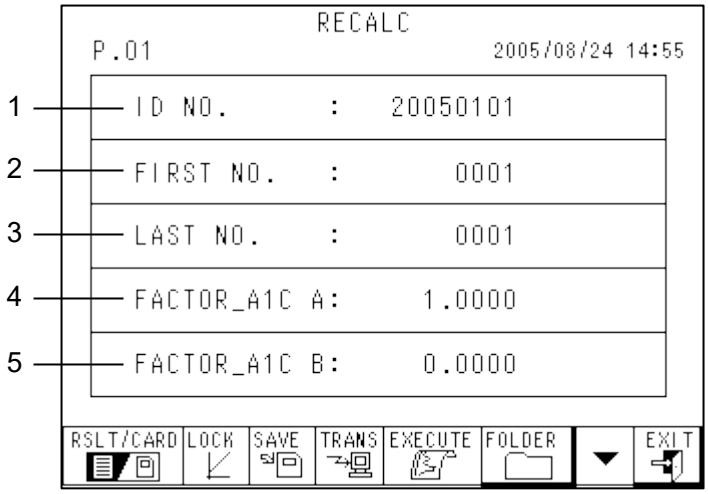
4.9 Confirmation, Transmission to Host, Recalculation of Saved Results



Press the 

key on the main screen to display the RECALC screen.
The assayed results, which are stored in the analyzer's memory (RESULT) or on an external storage device, can be printed, retransmitted to a host, and recalculated with different the calibration factors. Up to 800 test results can be stored in RESULT.

Screen 4-19 RECALC Screen



Display content

1. Assay date of sample (same as the folder name)
2. First data number of the results
3. Last data number of the results
4. FACTOR_A1C A
   Valid when recalculating results after changing the calibration factor
5. FACTOR_A1C B
   Valid when recalculating results after changing the calibration factor

Key Functions

: Selects whether the data to be processed is stored in the main unit memory (RESULT) or on an external storage device (CARD)
(Highlighted item is selected)

: When highlighted, performs recalculation using the calibration factors set in the RECALC screen

: When highlighted, saves the recalculated results to a CARD

: When highlighted, automatically transmits the recalculated results

: Starts printing and recalculation operations

: Used to check the data folders


: Not used

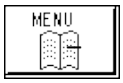
: Return to the previous screen

Point

1. Recalculated data will be printed, saved (overwriting previous results) and transmitted if the TRANS key is selected. If RESULT is selected, the data will be overwritten onto the RESULT area. If the SAVE key is selected on the RECALC screen, the data will be saved to the external storage device, regardless of whether RESULT or CARD is specified.

2. The heading will change currently set at the RECALC execution. See ”Chapter 4, Section 4.16 Entering a Heading”.

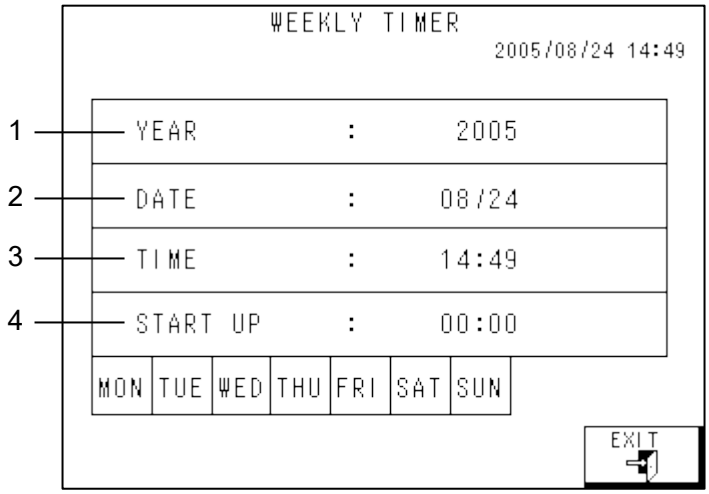
4.10 Date/Time and Weekly Timer Setting



Press the 

key on the main screen to display the WEEKLY TIMER screen. When the timer is selected, the analyzer goes in the STAND-BY mode with WARMING UP completed automatically on a specified input day every week. When the timer startup is activated, the power automatically comes on and WARMING UP is performed at the designated START UP time. The analyzer enters STAND-BY state after WARMING UP is complete. Normally, when nothing is input from the operation panel for 2 hours, the power is automatically turned off.

Screen 4-20 WEEKLY TIMER Screen



Display content

1. Year
2. Date
3. Time
4. START UP time

Key Functions

: Input the analyzer startup day of the week

: Return to the previous screen

Example setting for a weekly timer

1) Check that the current date/time shown is correct.
2) If the values are incorrect, select the value to be corrected and display the input screen.
3) Input the correct date/time and return to the WEEKLY TIMER screen.
4) Use the 

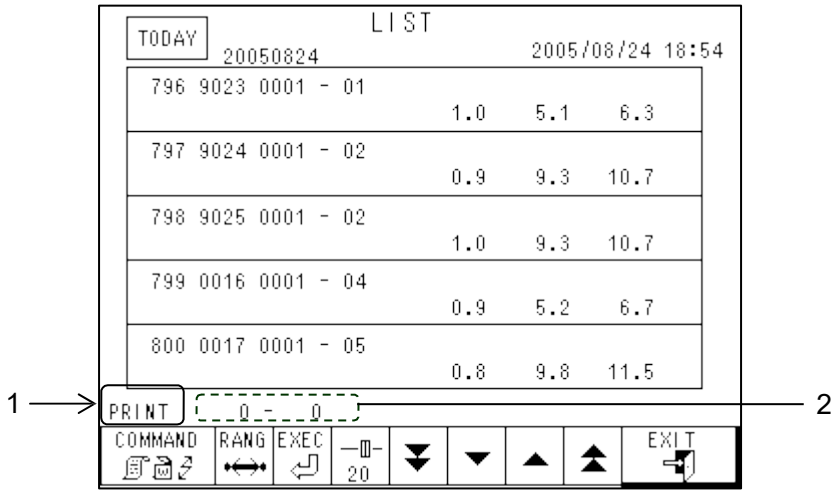
key to highlight and select the day of the week on which you want the analyzer to start up.
5) Select START UP, display the input screen, and input the time to start up.
6) Verify the specified day (highlighted) and START UP time on the WEEKLY TIMER screen.

1. The scheduled analyzer's startup day is displayed highlighted. Before starting the timer, make sure to set both START UP time and the analyzer startup day.
2. The timer period from STAND-BY to POWER OFF can be changed using the OFF TIMER parameter.

4.11 List Data Display and Bar Code Editing

Press the LIST key on the main screen to display the LIST screen.
A list of stored results can be displayed, printed, deleted, and transmitted to the host. Unreadable bar code IDs can also be input or corrected on this screen after the assay.

Screen 4-21 LIST Screen



Display content

1. Command
2. First and last number of the selected results to which the command is being applied

Key Functions

TODAY : When highlighted, only assay results which have the same date of the latest operation are selected.

COMMAND : Command key (Commands change when pressed)

Command types	
Command	Function
PRINT	Prints the selected results
DELETE	Deletes the selected results
TRANS	Transmits the selected results

RANG : Changes the data to which commands are applied

EXEC : Execution key for the selected command

20 100 END : Changes the scroll settings (can be set to 20, 100 and END)

: Scrolls down in STEP units

: Scrolls up in STEP units

: Scrolls down in single screen units

: Scrolls up in single screen units

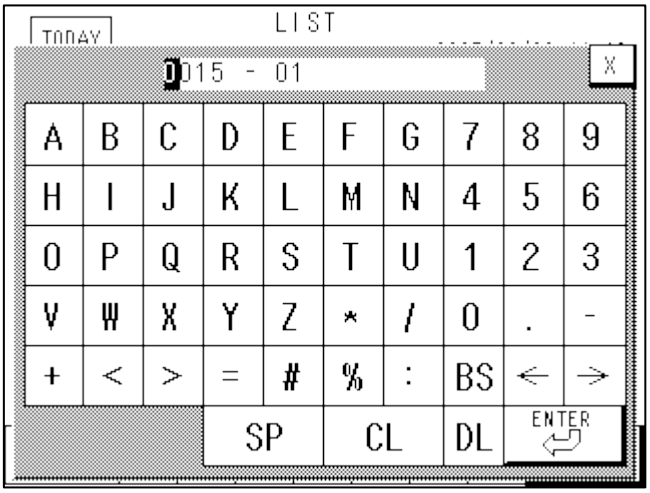
EXIT : Return to the previous screen

Operation Ex.

Example of bar code editing

1) On the LIST screen, select the sample whose bar code ID you want to change, and then display the input screen.
2) Press CL to clear the ID. Input the correct ID, press the ENTER key, confirm the input and return to the LIST screen.
3) Confirm the new bar code ID on the LIST screen.

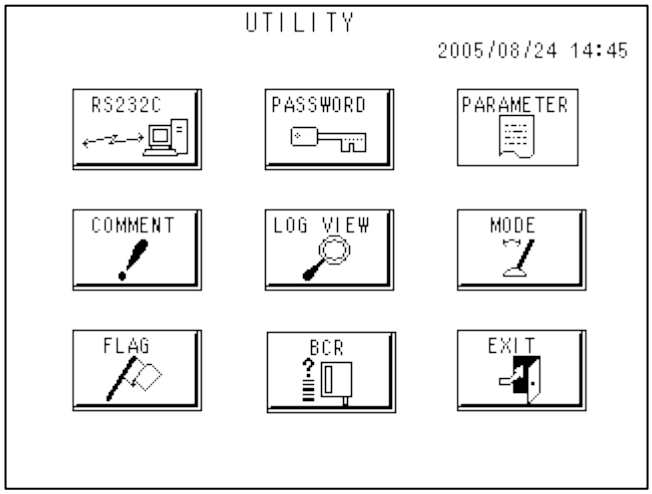
Screen 4-22 Bar Code Input Screen



4.12 Utilities  - 

Press the  key on the MENU screen to display the UTILITY screen.

Screen 4-23 UTILITY Screen



Key Functions

 : Displays RS232C settings screen

 : Password input (for service personnel)

 : Parameter Printout

 : Sets text to print in comment/header

 : Displays a list of errors, communications log, etc.

 : Change the analysis mode

 : Sets and changes flag entry parameters (FLAG file)

 : Sets and test the bar code reader

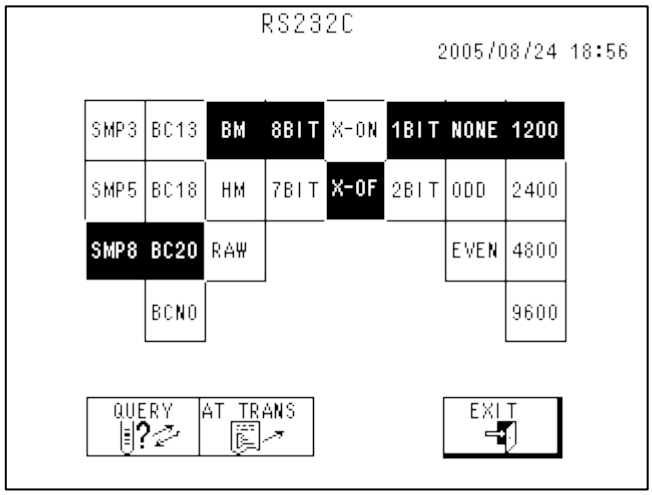
 : Return to the previous screen

4.13 Data Communication Setting 

Press the 

key on the UTILITY screen to display the RS232C screen.
To transmit data in real time, press the AT TRANS key (“auto transmit” at the bottom) to highlight.

Screen 4-24 RS232C Screen



Key Functions

SMP 3 : Handles the sample number with the last 3 digits
SMP 5 : Uses 5 digits for the sample number
SMP 8 : Uses 8 digits for the sample number
(ID number is added to the front of the number for a total of 8 digits)
BC 13 : Transmits the bar code using 13 digits
BC 18 : Transmits the bar code using 18 digits
BC 20 : Transmits the bar code using 20 digits
BC NO : Does not send the bar code ID
BM : Transmits in BASIC mode
HM : Transmits in HI-LEVEL mode
RAW : Transmits in RAW mode
8 BIT : Sets the data length to 8 bits

7 BIT : Sets the data length to 7 bits
X-ON : Sets the X parameter on (flow control on)
X-OFF : Sets the X parameter off (flow control off)
STP 1 : Sets the stop bit to 1
STP 2 : Sets the stop bit to 2
NONE : Sets the parity to none
ODD : Sets the parity to odd numbers
EVEN : Sets the parity to even numbers
1200 : Sets the baud rate to 1200 bps
2400 : Sets the baud rate to 2400 bps
4800 : Sets the baud rate to 4800 bps
9600 : Sets the baud rate to 9600 bps

: When this key is highlighted, a query with ID is performed and only designated samples are processed.

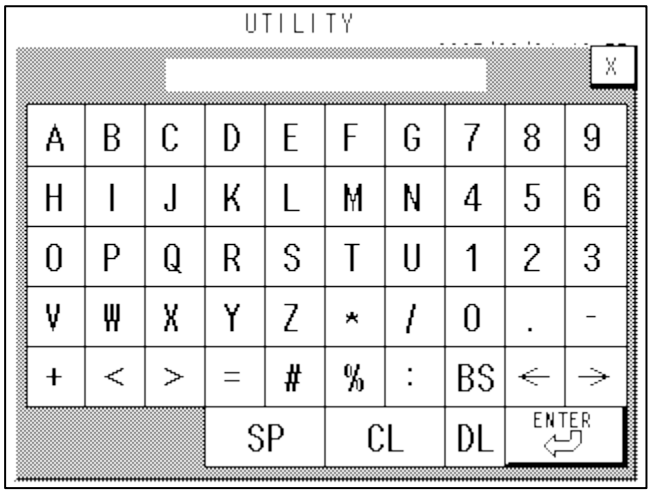
: When highlighted, results are automatically transmitted

: Return to the previous screen

4.14 Password Input for parameter initialization [MENU] - [UTILITY] - [PASSWORD]

Press the PASSWORD key on the UTILITY screen to display the PASSWORD screen. Input “CLR” on this screen to delete the parameters stored in the main unit.. During daily operations, this space is blank.

Screen 4-25 PASSWORD Screen



Operation Ex.

1. From the UTILITY screen, press the PASSWORD key to display the PASSWORD screen. Input “CLR”.
2) Turn the POWER key off.
3) Turn the main power switch off.
4) Insert an external storage device containing a SYSTEM.PRM file into the storage device socket.
5) Turn on the main power. Then, after the startup message is displayed, turn the POWER key on.
6) Parameter initialization is complete when the main screen is displayed.

The PASSWORD screen is used to initialize the parameters.
No operation except the input of “CLR” is guaranteed.
Do not enter any text except “CLR”

4.15 Parameter Printout  –  – 

Press the  key on the UTILITY screen to print out a list of parameters, as shown below.

In addition to the parameters, a list of the flag parameters, automatic calibration settings, and external communication settings will be printed.

Fig. 4-2 Parameter Printout Example

```
*****  PARAMETER    *****
          2021/08/12 09:48

PARAMETER
  SAMP NO.          6
  CALIB-1        5.8800
  CALIB-2       10.6000
  FACTOR A       1.1705
  FACTOR B       0.5220

  FORMAT          100
  RAW-SAVE          0
  LST-SAVE          0
  LIST CLR          0
  OFF TIME       3.0000

  COPY              1
  LS MODE           0
  WASHMODE          0
  FLOW           1.0700
  TUBE100           0


*** FLG PARAMETER ***
 CODE FLAG  DATA  LEVEL
      COMMENT
   2  <       4.00   1
      SA1C TOO LOW
   2  >      16.90   1
      SA1C >LINEARITY
  40  =       0.00   0
      HB-VAR DETECT
   1  <     500.00   1
      AREA TOO LOW
   1  >    4000.00   1
      AREA TOO HIGH
  25  >   20000.00   0
      SCHEDULE PM
   3  >=     25.00   1
      SA1C NOT RPTBLE
  35  <>      0.03   0
      CHECK SA1C RT
   6  >    2500.00   0
      CHANGE COLUMN
  28  >      20.00   0
      EVALUATE BASE
  43  >    9999.99   0
      HBE SUSPECTED
  27  =       0.00   0
      MISSED PEAK
  24  =       0.00   0
      CHECK PEAKS


CALIBRATION      NO


RS   8 20 8 8 N 1 N 9600
 QUERY             0
 AT TRANS          0
```

4.16 Entering a Heading  –  – 

Press the  key on the UTILITY screen to display the COMMENT screen.
The text input here will be printed at the top of the results printout (including RECALC) each time results are printed. Use this function to input the facility name, instrument serial number, etc., for assay results control.
Up to 20 characters can be input.
If you edit the heading when RECALC is performed, the new heading will be printed.

Screen 4-26 COMMENT Screen

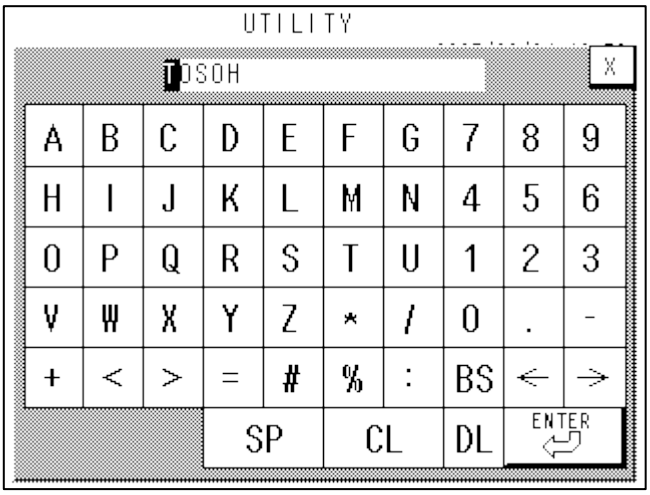
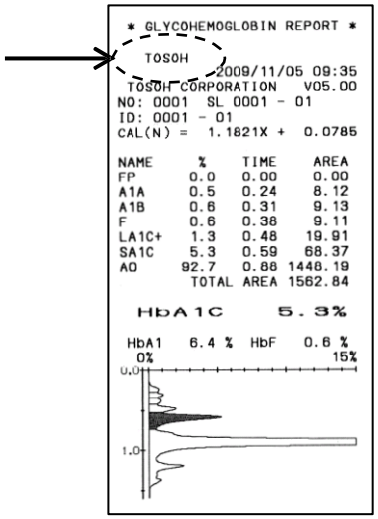


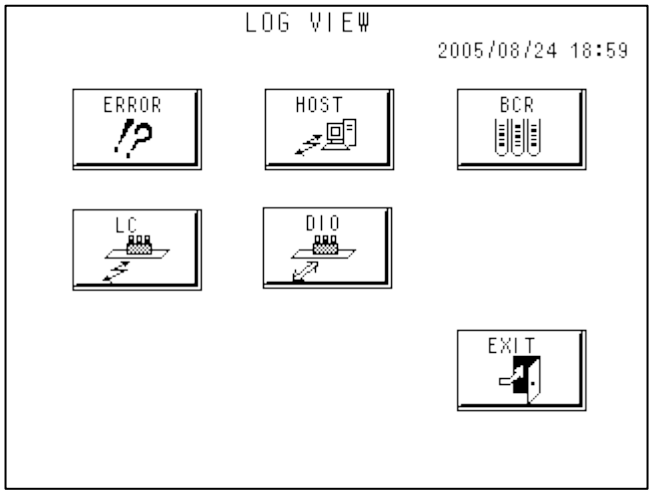
Fig. 4-3 Heading Printout Example (TOSOH)



4.17 Log File Check  –  – 

Press the  key on the UTILITY screen to display the LOG VIEW screen.

Screen 4-27 LOG VIEW Screen



Key Functions

 : Displays the analyzer error log

 : Displays a log of communications with the host computer.

 : Displays a log of scanned bar codes

 : Displays the communication log with the line controller when LA is set. When it isn't, a log of auto sampler communications is displayed.

 : Displays the DIO log when LA is set. When it isn't, a detailed log of communications with the host computer is displayed.

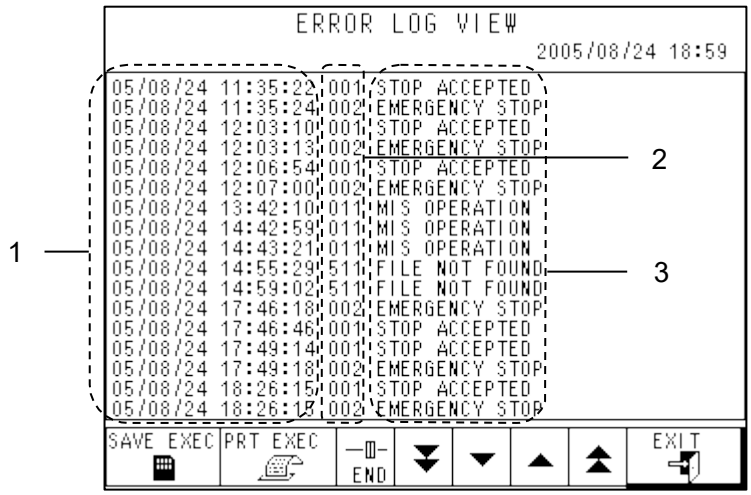
 : Return to the previous screen

Operation Ex.

The example here uses the error log.

Press the ERROR key. The next screen will be displayed.

Screen 4-28 ERROR LOG VIEW Screen



Display content

1. Date and time the error occurred
2. Error code number
3. Error message

See “Chapter 6 Section 6.3: Error messages” for detailed error messages.

Key Functions

SAVE EXEC : Stores the log list on an external storage device

PRT EXEC : Prints the log list on the printer

20 100 END : Changes the scroll settings (can be set to 20, 100 and END)

: Scrolls down in STEP units

: Scrolls up in STEP units

: Scrolls down in single screen units

: Scrolls up in single screen units

EXIT : Return to the previous screen

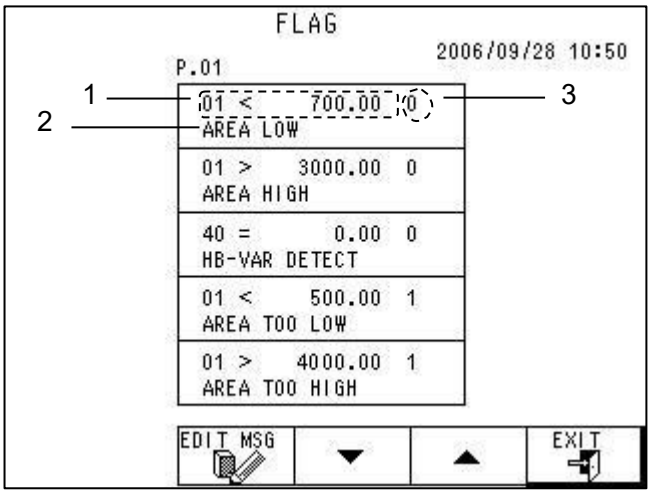
4.18 FLAG Parameter Setting  –  – 

Press the  key on the UTILITY screen to display the FLAG screen.

The analyzer checks results according to the flag parameters set on this screen. Flags are printed with the results. If the flag level is set to 0, the assay values are printed out with the flag message. If the level is set to 1, the assay value is not reported.

For RECALC, the determination is made in accordance with the current FLAG conditions.

Screen 4-29 FLAG Screen



Display content

1. Criteria (code/condition/num. value)
2. Flag message output when result meets condition
3. Flag Level

   (Level 0: The assay values are displayed/printed or transmitted to the host with Flag.)

   (Level 1: “---” is displayed or printed in the field of the assay result with Flag. But a blank or “0” is transmitted to the host computer with Flag.)

Key Functions

EDIT MSG : Displays the message editing screen

▼ : Scrolls down in single screen units

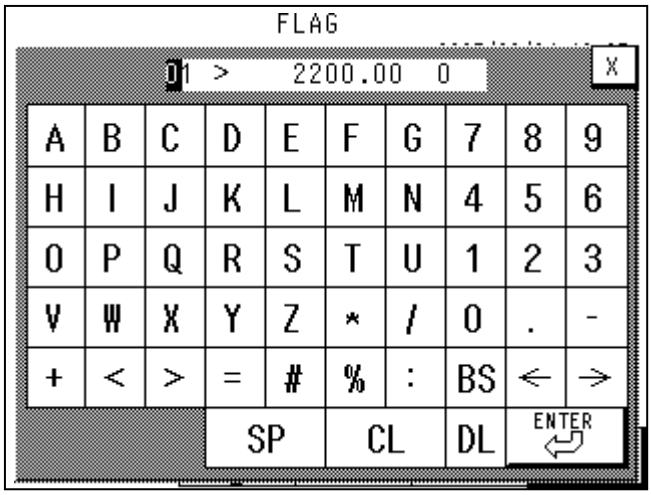
▲ : Scrolls up in single screen units

EXIT : Return to the previous screen

Input Ex.

1) Press the input line on the screen to select. (The field is blank when the settings are new.)
2) The numerical value input screen is displayed. Input the values for the “flag code”, “flag condition”, "flag values (number)” and “flag level” (in that order). Press the ENTER key to close the numerical value input screen.
3) Press the EDIT MSG key to highlight.
4) Press the input line on the screen and open the message input screen.
5) Input the text that you want to display when the criteria conditions are met and press the ENTER key to return to the FLAG screen.
6) Verify the content again on the FLAG screen. To modify an input message, input and correct from step 3).
7) RECALC the previously assayed data and verify settings.
8) If you want to remove a set condition, select the line, enter 0 = 0 and press the ENTER key.

Screen 4-30 Numerical Value Input Screen



Flag conditions

>	Result is greater than the assigned cut-off value
<	Result is smaller than assigned cut-off value
> =	Result is greater than or equal to the assigned cut-off value
< =	Result is smaller than or equal to the assigned cut-off value
=	Result is equal to the assigned cut-off value

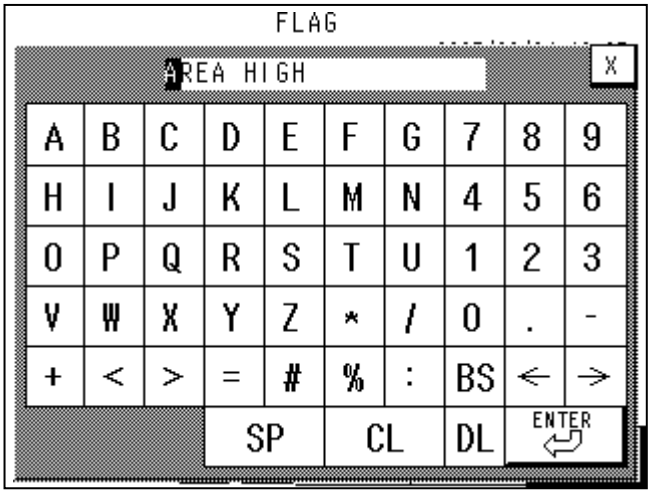
Flag codes (items]

1	TOTAL AREA
2	SA1c%
3	F%
4	HbA1
5	FILTER COUNT
6	COLUMN COUNT
7	Number of theoretical plates
8	Unidentified peak between LA1c and SA1c when data =0 Unidentified peak between SA1c and A0 when data =1
9	Number of peaks
10	Sample number

Flag codes 11-20: When +10 is added to the above code (11, 12, 13, ...), the analyzer will perform the flag error check only when the calibrator is processed.

In addi	Unknown peak(s) found in the chromatogram - Check Peaks
25	Schedule PM
27	One or more indispensable peak(s) do NOT exist: A1A, A1B, F, LA1c+, SA1c and A0
28	Stability of the baseline – Evaluate Baseline
35	Retention time of SA1c peak – Check SA1c RT
36	Retention time of A0 peak – Check A0 RT
40	Hb Variant Detected
42	LA1c+ Value – LA1c High
43	HbE suspected
45	Detects a sample which had a higher P-HV3 value than or equal to the set value when set as “45 >= x.x”

Screen 4-31 Message Input Screen



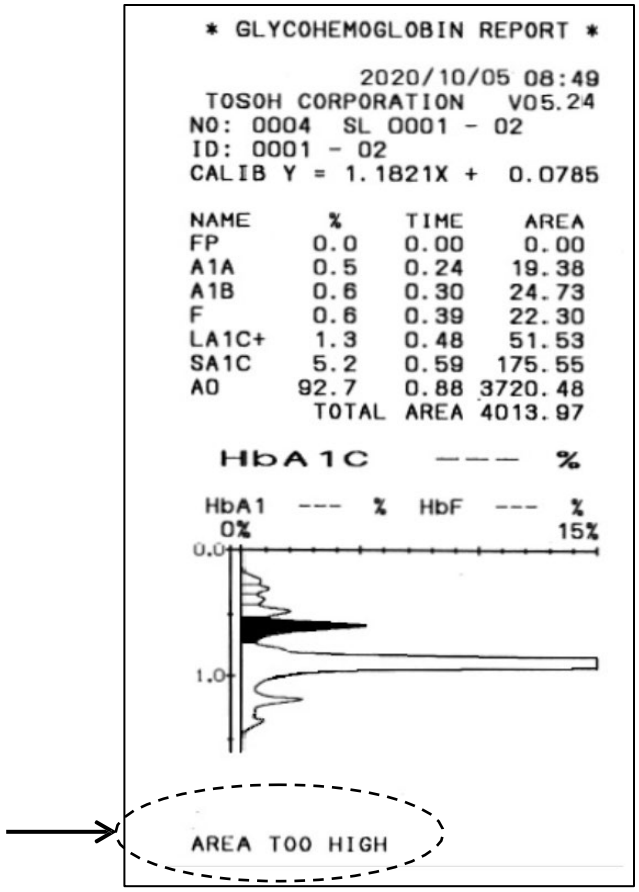
1. Upon installation, the following flags are set

02 < 4.0	1	SA1C TOO LOW	
02 > 16.9	1	SA1C>LINEARITY40 = 00	HB-VAR DETECT
01 < 500	1	AREA TOO LOW	
01 > 4000	1	AREA TOO HIGH	
25 >20000	0	SCHEDULE PM	
03 >= 25	1	SA1C NOT RPTABLE	
35 <> 0.03	0	CHECK SA1C RT	
06 > 2500	0	CHANGE COLUMN	
28 = 20	0	EVALUATE BASE	
43 > 9999.99	0	HBE SUSPECTED	
27 = 0	0	MISSED PEAK	
24 = 0	0	CHECK PEAKS	

2. Flag levels:
   Level 0: The value falls within an acceptable range, but the data should be handled with care.
   Level 1: The value is out of the acceptable range. Try assaying again.

3. If the same sample meets two or more flag conditions, all relevant flag messages will be printed on the report. However, only one flag code is transmitted host and is displayed on the LIST screen. The Level 1 flags will be given priority over the Level 0 flags. A flag set lower in the table has higher priority

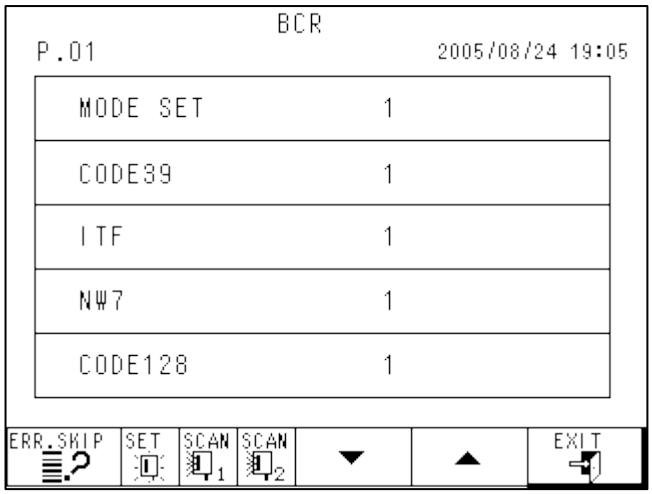
Fig. 4-4 Printout Example (AREA HIGH)



4.19 Bar Code Reader Setting and Reading Check

Press the BCR key on the UTILITY screen to display the BCR screen.
You can make bar code settings and perform a reading check on this screen.

Screen 4-32 BCR Screen (P.01)



Key Functions

- ERR.SKIP : Skips unreadable bar-coded samples during an assay (highlighted when pressed)
- SET : Inputs conditions (bar code specifications you want to use) into the bar code reader.
- SCAN1 : Checks reading capability of bar code reader (by scanning)
- SCAN2 : Checks reading capability of bar code reader for LA (by scanning)
- ▼ : Displays the next page
- ▲ : Displays the previous page
- EXIT : Return to the previous screen

Parameters

MODE SET:	Determines whether or not to set the bar code reader (0: do not set, 1: set)
CODE39:	Sets use of CODE 39 (0: do not use, 1: use)
ITF:	Sets use of ITF (0: do not use, 1: use)
NW-7:	Sets use of NW-7 (Codabar) (0: do not use, 1: use)
CODE128:	Sets use of CODE128 (0: do not use, 1: use)
JAN:	Sets use of JAN (UPC/EAN) (0: do not use, 1: use)
INDUST-2OF5:	Sets use of INDUSTRIAL 2 of 5 (0: do not use, 1: use)
COOP-2OF5:	Sets use of COOP 2 of 5 (0: do not use, 1: use)

Up to four types of codes can be used at once.

CODE39 STR&STP:	Sets transmission of start/stop character (*) with code39 (0: do not transmit, 1: transmit)
CODE39 CHK-DIG:	Sets inspection for check digits (modulus43) with code39 (0: do not inspect, 1: inspect)
CODE39 CD OUT:	Sets transmission of check digits with code39 (0: do not transmit, 1: transmit)
CODE39 MIN:	Sets the minimum number of check digits with code39 (3 - 20)
CODE39 MAX:	Sets the maximum number of check digits with code39 (3 - 20)
ITF CHK-DGT:	Sets inspection for check digits (modulus10/weight 3) with ITF (0: does not inspect, 1: inspect)
ITF CD OUT:	Sets transmission of check digits with ITF (0: do not transmit, 1: transmit)
ITF MIN:	Sets the minimum number of check digits with IFT (2 ~ 20)
ITF MAX:	Sets the maximum number of check digits with IFT (2 ~ 20)
NW-7 STR&STP:	Sets transmission of start/stop character with NW-7 (0: do not transmit, 1: transmit)
NW-7 S/L CHAR:	Sets the type of start/stop character transmitted with NW-7 (0: lower case, 1: upper case)

NW-7 CHK-DIG: Sets inspection for check digits (modulus10/weight2) with NW-7 (0: do not inspect; 1: inspect)

NW-7 CD TYPE: Sets the check-digit type for inspection with NW-7 (0: modulus16, 1: modulus11, 2: modulus10/weight2, 3: modulus10/weight3, 4: 7 check DR, 5: modulus11-A, 6:modulus10/weight2-A)

NW-7 CD OUT: Sets transmission of check digits with NW-7 (0: do not transmit, 1: transmit)

NW-7 MIN: Sets the minimum number of check digits with NW-7 (3 - 20)

NW-7 MAX: Sets the maximum number of check digits with NW-7 (3 - 20)

CODE128 DBL CHAR: Sets check of double character start pattern for CODE128 (0: do not check; 1: check)

CODE128 MIN: Sets the minimum number of check digits with code 128 (1-20)

CODE128 MAX: Sets the maximum number of check digits with code 128 (1-20)

JAN UPC-E: Sets use of UPC-E with JAN (0: do not use, 1: use)

JAN JAN8: Sets use of JAN8 with JAN (0: do not use, 1: use)

JAN JAN13: Sets use of JAN13 with JAN (0: do not use, 1: use)

JAN UPC-A OUT: Sets the number of output digits for UPC-A used with JAN (0: 13 digits, 1: 12 digits)

JAN UPC-E ZERO: Sets addition of UPC-E system code "0" with JAN (0: no addition, 1: add)

INDUST-2OF5 MIN: Sets the minimum number of check digits with INDUSTRIAL 2 of 5 (1-20)

INDUST-2OF5 MAX: Sets the maximum number of check digits with INDUSTRIAL 2 of 5 (1-20)

COOP-2OF5 MIN: Sets the minimum number of check digits with COOP 2 of 5 (1-20)

COOP-2OF5 MAX: Sets the maximum number of check digits with COOP 2 of 5 (1-20)

Chapter 5 Maintenance Procedure

5.1 Daily Care

Use a cloth dampened with a neutral cleaner to wipe stains from the analyzer's plastic components on the front side (needle cover, etc.).

CAUTION

Do not use organic solvents such as ethanol to clean the plastic components. Doing so could warp or discolor such components.

Use a cloth dampened with a neutral cleaner to wipe blots and stains on metallic components as well. If contamination is severe, wipe using a cloth soaked in ethanol.
Water remaining on metallic surfaces will cause rust.

Lightly wipe away blots and stains on the sample loader belt, display, and key sheet with a cloth soaked in ethanol.

5.2 Daily Checklist

- Pre-assay Checklist

The following table provides a checklist of procedures to be performed on a daily basis before starting analysis (pressing START KEY)

No.	Items to Check	Content	Refer to section
1	Calibration settings	Check the CALIB key display	3.6
2	Column	Check counter → replace	5.6
3	Filter	Check counter → replace	5.7
4	Elution buffers	Check volume → replace	5.3
5	Hemolysis & Wash Solution	Check volume → replace	5.3
6	Smart Media	Check remaining volume → replace or initialize	4.7
7	Printer paper	Check volume → replace	5.8
8	Waste eluent bottle	Check waste volume → treat waste	3.5.6
9	Tube leakage	Check flow path → Tighten	

- Be sure to check the following items before starting analysis

No.	Items to check/replace	Maintenance schedule	Refer to
1	Column	2500 tests	5.6
2	Filter	400 tests	5.7
3	Suction filter	Every 6 months	5.9
4	Sampling needle	When bent or broken	5.10
5	Needle O-ring	Annually	5.11

- The following items are checked by field service personnel.

No.	Items to check / replace	Service frequency (guide or target)
1	Check the bar code reader	Annually
2	Check the end marker sensor	
3	Check the rack holder and the sample holder	
4	Check the sample sensor	
5	Check needle descent position	
6	Clean dilution port and wash assembly	
7	Check the screws of sampling unit	
8	Check the screw of the parts driving the valves	
9	Check the column oven temperature	
10	Check the solenoid valve's action (3 locations)	
11	Check vacuum pump's action	
12	Replace the rotor seal of the injection valve	
13	Replace the rotor seal of the AS valve	
14	Wash or replacement of the pump check valves	
15	Replace the plunger seal	
16	Lubrication of pump drive unit	
17	Replace the Teflon® tip of syringe	
18	Replace the sample loop	Annually or every 20,000 sample injections
19	Replace the valve stator face	When dirty or worn
20	Replace the drain valve packing	When worn

5.3 Elution Buffer and Hemolysis & Wash Solution Replacement

Replace elution buffers and Hemolysis & Wash solution as early as possible when remaining volumes are low. The remaining volumes of buffers are displayed in a graph on the main screen (second screen) by pressing the ⇩ key in the main screen (first screen). Since the graphical display is only an indication, there may be some difference with the actual remaining amount depending on usage conditions.

Procedure

1) If the analyzer is not in STAND-BY state, wait for the assay to end and STAND-BY to be displayed. You can also change the state to STAND-BY state by pressing the STOP key.
2) Replace the buffer or Hemolysis & Wash solution.
3) Confirm that the end of the tube reaches the bottom of the container.
4) For buffers, be sure to securely fasten the bottle cap to make a tight seal.
5) Tightly seal the bottle cap for the Hemolysis & Wash solution as well. However, do not completely seal these bottles with paraffin film or other seals. A complete seal may cause poor fluid pumping.

Fig.5-1 Elution Buffers

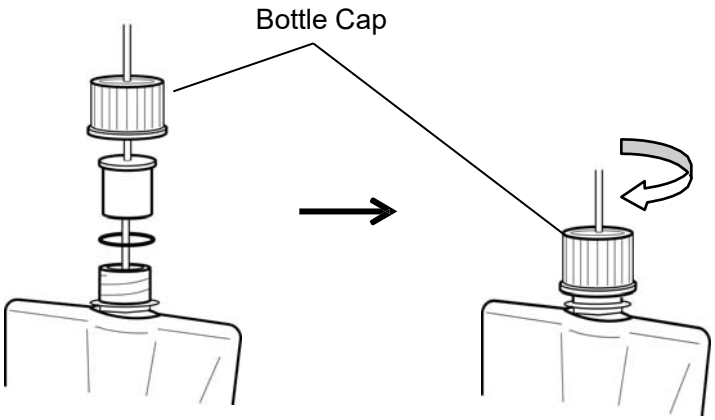
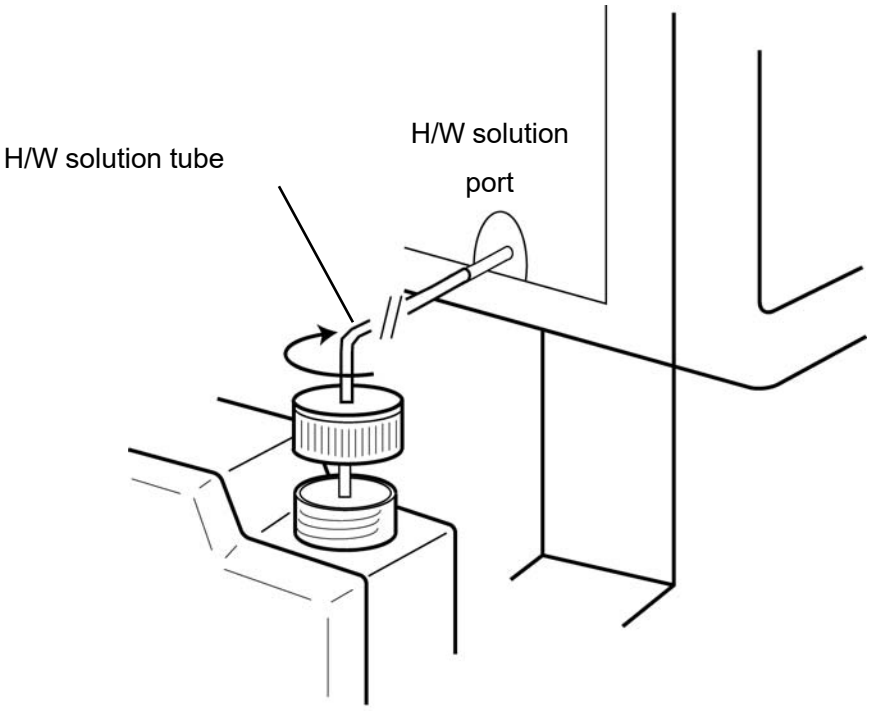
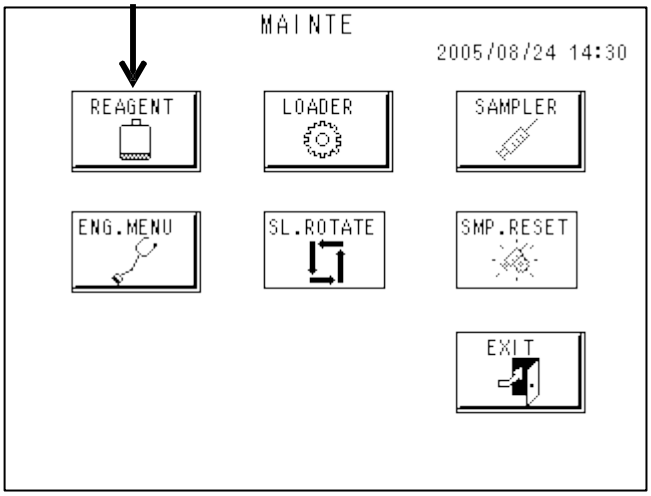


Fig. 5-2 Hemolysis & Wash Solution Tube Connection



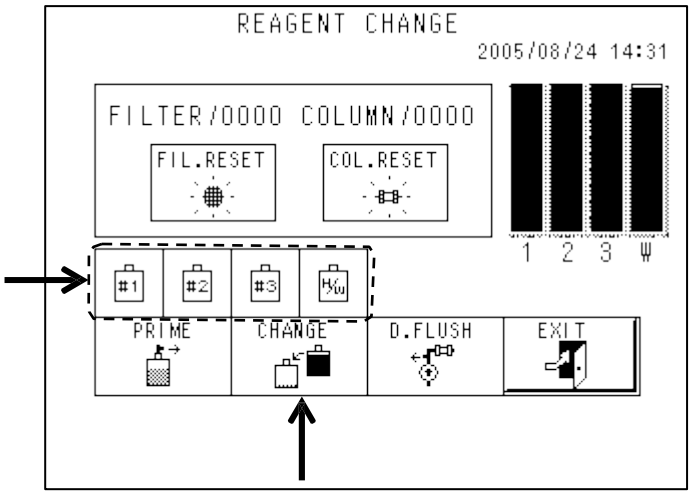
6. Press the  key in the MAINTE screen.

Screen 5-1 MAINTE Screen



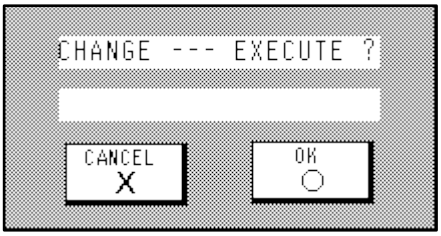
7) Highlight the keys of the reagents which you want to replace. (Example: Highlight key #1 and #2 when you want to replace buffer No.1 and 2.)

Screen 5-2 REAGENT CHANGE Screen



8) Press the CHANGE key. A confirmation message will be displayed. If everything is all right, press the OK key.

Screen 5-3 CHANGE Message



9) The reagents in the flow line of the analyzer will automatically be replaced with the new reagents.

10) Operations are complete when the "CHANGING..." message disappears. Confirm that the graph for the replaced reagent returns to 100%.

Point

Approximately 5 mL of each eluent will be consumed when CHANGE is performed.

1. Only use reagents specified for analyzer.
2. Never use expired reagents.
3. Do not reuse remaining elution buffer or Hemolysis & Wash solution or mix remaining reagent with a different or new one. Handle the remaining solutions as general waste fluid and dispose of them according to your facility's procedures. The elution buffers and Hemolysis & Wash solution contain sodium azide as a preservative. Dispose of the reagents using large volumes of water.
4. When using buffers in aluminum packs, tighten the cap until it is firmly shut. A loose cap could cause higher buffer concentrations and unreliable results. In addition, the remaining volume cannot be checked visually if the cap is loose.
5. The counter for the remaining volume of each buffer is adjusted based on the standard packaging size. Therefore, do not use any other container since no exact remaining volume can be displayed. To change the size, contact service representative.

5.4 Elution Buffer Priming

The analyzer automatically performs priming or purging with all elution buffers when the power is turned on and when it has been in STAND-BY state for 90 minutes or more. It replaces the buffer in the flow lines, and then starts the pump run and assay.

However, if the analyzer has been shut down for a long period of time, air may have entered into the flow lines or the buffer concentration in the flow path may have increased. As a result, you may experience problems such as unstable pumping pressure, abnormal chromatograms (unidentified peak P00 may appear), and an abnormal assay value for the control.

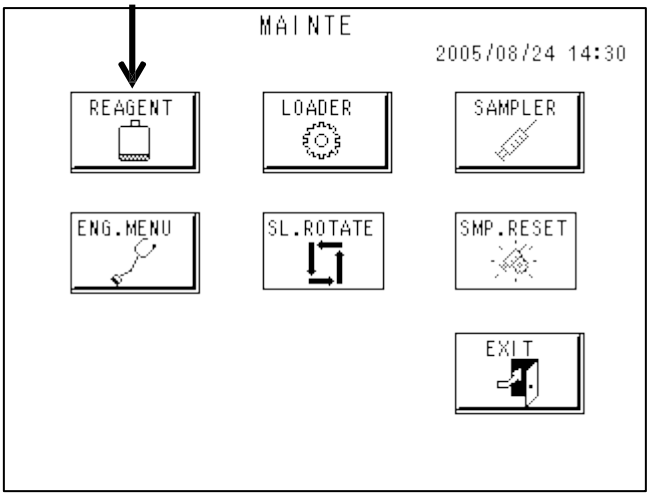
If this happens, perform a manual priming of the buffers, and then perform the DRAIN FLUSH described in the next section. Manual pumping of elution buffer No. 1 for approximately 20 minutes should resolve the problem in most cases.

Perform manual priming using the following procedure.

Procedure

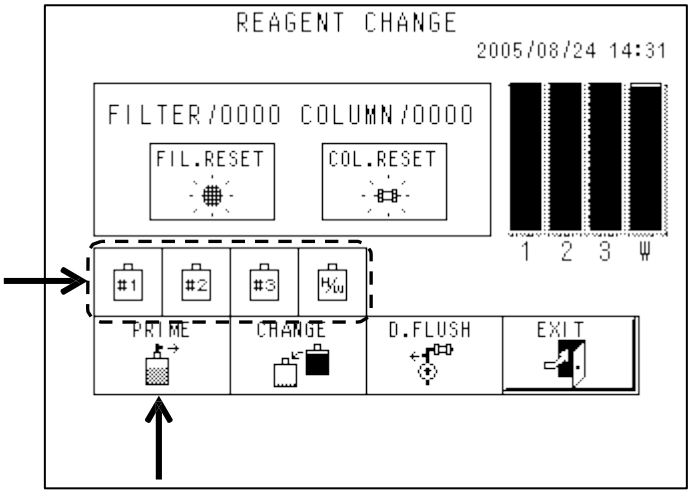
1) If the analyzer is not in STAND-BY state, wait for the assay to end and STAND-BY to be displayed. You can also press the STOP key to switch the analyzer into STAND-BY state.
2) On the MAINTE screen, press the REAGENT key.

Screen 5-4 MAINTE Screen



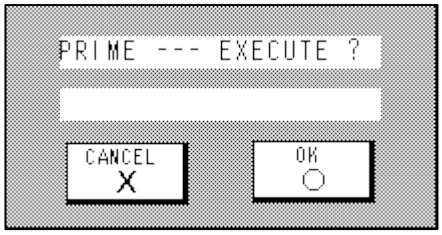
3) Highlight the key for the reagent to be primed.
(Example: Highlight key #1 and #2 for buffer No. 1 and 2 to prime them.)

Screen 5-5 REAGENT CHANGE Screen



4) Press the PRIME key. A confirmation message will be displayed. If everything is all right, press the OK key.

Screen 5-6 PRIME Message Screen



5) The reagent in the flow lines of the analyzer will automatically be replaced.
6) The operation is complete when the "PRIMING..." display disappears.

Point **Approximately 5 mL of each buffer will be consumed when PRIME is performed**.

PRIME replaces the buffers in the lines without resetting to 800 mL.

CHANGE replaces the buffers and resets the graph.

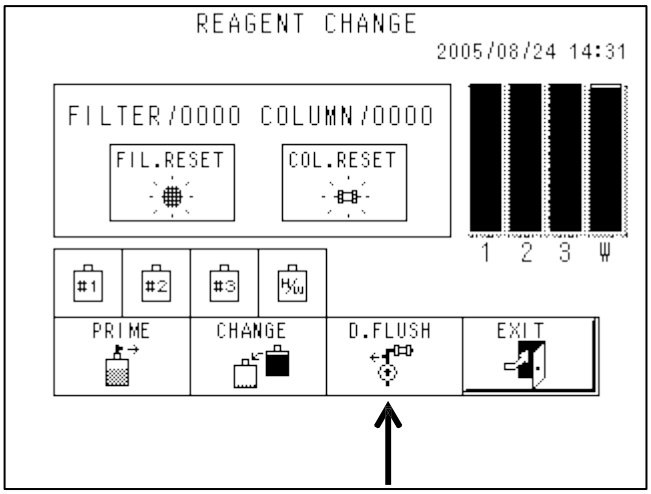
5.5 Pump Air Removal

If the pump runs, but the pressure will not rise or stabilize even though sufficient buffer is delivered, air may be trapped in the liquid end of the pump.
When this occurs, use the following procedure to remove the air from the pump.

Procedure

1) If the analyzer is not in STAND-BY state, wait for the assay to end and STAND-BY to be displayed. You can also change the state to STAND-BY state by pressing the STOP key.
2) From the MAINTE screen, press the REAGENT key.
3) Press the D.FLUSH key.

Screen 5-7 REAGENT CHANGE Screen



4) The following message will be displayed requesting that the drain valve be opened. Open the door on the left side of the analyzer and turn the drain valve 90 degrees in the counterclockwise direction to open the valve. Be careful not to turn the valve more than 90 degrees.

Screen 5-8 OPEN DRAIN VALVE Message

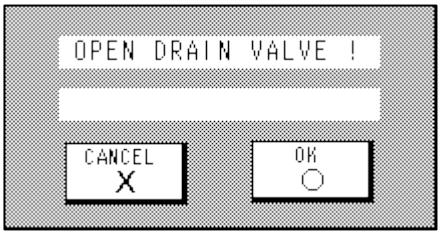
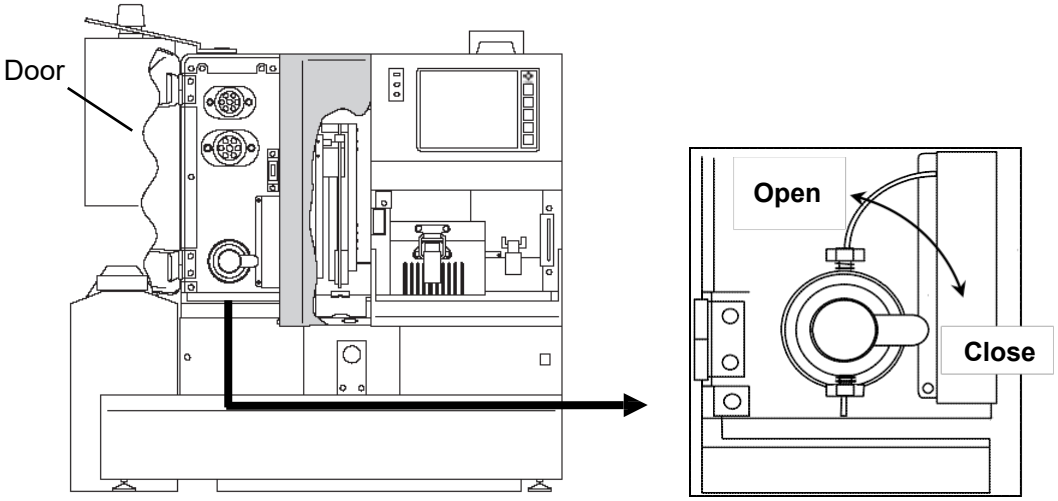
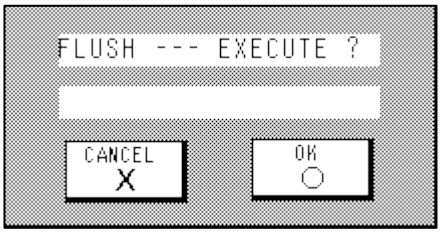


Fig. 5-3 Drain Valve



5) Press the OK key.
6) The confirmation message will be displayed. If everything is all right, press the OK key.

Screen 5-9 FLUSH Message Screen



7) Since air trapped in the pump will be automatically removed, wait until the "FLUSHING..." message disappears.
8) A message will be displayed requesting that the drain valve be closed. Turn the valve back 90 degrees in the clockwise direction to securely close it.
9) Return to the Main Screen (second screen), press the PUMP key and operate the pump.
10) If the pressure was stabilized within a range less than the original pressure (which is indicated on the column inspection report) + 4 MPa, air removal is completed. Press the PUMP key again to stop.
11) If the pressure does not rise or is unstable, stop the pump and follow the air removal procedure again.

Point Approximately 5 mL of each buffer will be consumed when DRAIN FLUSH is performed.

During the above procedure, always open the drain valve in accordance with the instructions on the screen message. If the valve is not opened, the flushing buffer to remove the air will flow backward into the buffer bottle and reliable results may not be obtained.

5.6 Column Replacement

We recommend column replacement on a regular basis.
Replace the column in the following cases.

1. When the pressure is more than the pressure (which is indicated on the column inspection report) + 4 MPa and the pressure is not reduced by filter replacement.
2. When peaks on the chromatogram (particularly the shaded S-A1c peak) have become broad or broken into two fractions. (Caution: If this phenomenon is observed only with a specific sample, column deterioration may not be the cause. Other factors, such as a hemoglobin variant, could be the cause.)
3. When assay results for quality control samples are consistently out of the assigned ranges even after re-calibration.
4. When the CALIB ERROR persistently occurs.

Please contact Technical Support if the above issues are not resolved after column replacement.

Caution **The filter has been in contact with blood samples. Wear protective clothing (glasses, gloves, mask, etc.) and take sufficient care to prevent infection during replacement and handling.**

Point When a calibration error occurs or control results are not acceptable, it may be necessary to replace the column.

Procedure

1. If the analyzer is not in STAND-BY state, wait for the assay to end and STAND-BY to be displayed. You can also change the state to STAND-BY state by pressing the STOP key.

2. Open the door below the display, remove the latch, and open the column oven.

Fig. 5-4 Front View

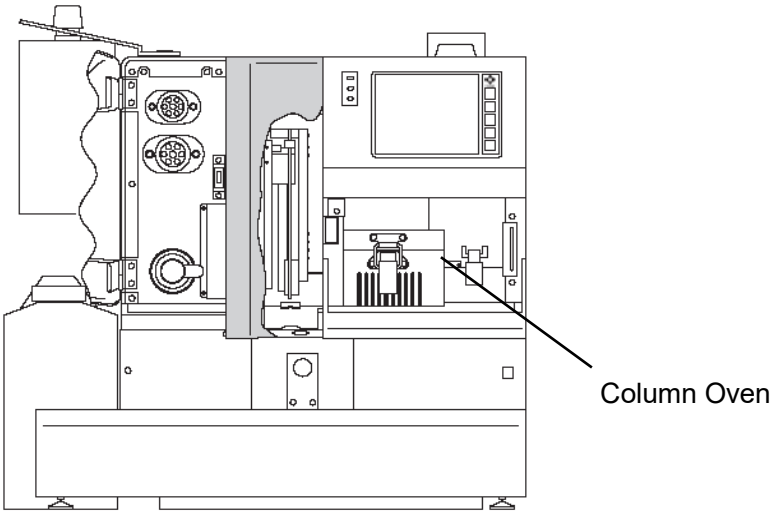
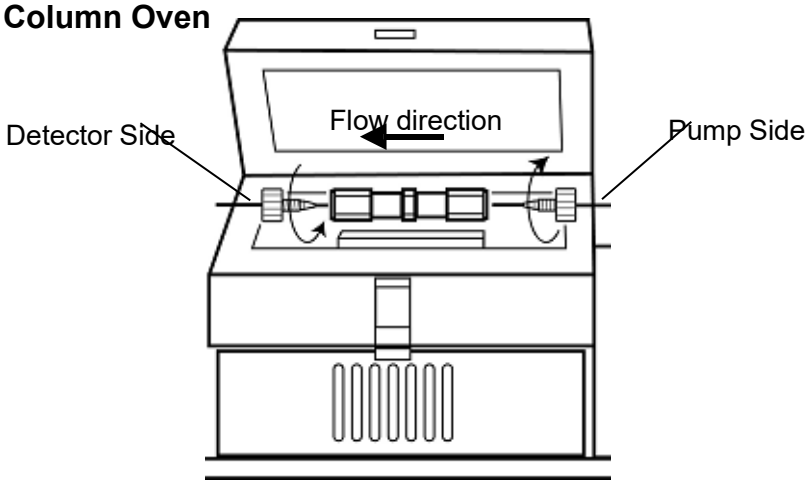


Fig. 5-5 Column Oven



3. Next, remove the old column.

4. Confirm that the SV1 key is open (O) on the main screen (second screen).

5. Place lab wipes on the filter side (right side) of the column flow line.

6. Press the PUMP key to start the pump.

7. Remove the protective plugs of the column. Retain the protective plugs because they are necessary for long-term storage of the column.

8. Connect the new column to the pump (inlet) side only, taking care of the flow direction shown by the arrow on the label, which should be right to left, and let the buffer flow into the column. When buffer comes out of the open end of the column, press the PUMP key to stop the flow.

9. Connect the column outlet to the detector side (left side) and press the PUMP key to start the pump. The fluid will begin flowing.

10. Make sure that the pressure falls within a range less than the original pressure (which is indicated on the column inspection report) + 4 MPa and that there are no leaks from the column connections.

11. Place the column in the aluminum block, close the column oven cover, and lock the latch.

12. Press the PUMP key to stop the pump.

13. Before calibrating the newly installed column, run at least three whole blood samples to make sure that all specifications are inline. If all specifications are in line, calibrate the system and run controls.

Caution **The used column has been in contact with blood samples. Therefore, wear protective clothing (glasses, gloves, mask, etc.) when handling. Dispose of the column as infectious waste in accordance with your facility's waste disposal procedures.**

1. Be sure not to use any other column than the column for the HLC-723G8.
2. After connecting a new column, reset (zero) the column counter in the REAGENT CHANGE screen.
3. Securely insert the inlet tube to the end with no space at the connections.

5.7 Filter Replacement

Replace the filter in the following cases.

1. When the filter counter reaches 400 injections.
2. When the pressure is more than what is indicated on the column inspection report + 4 MPa.

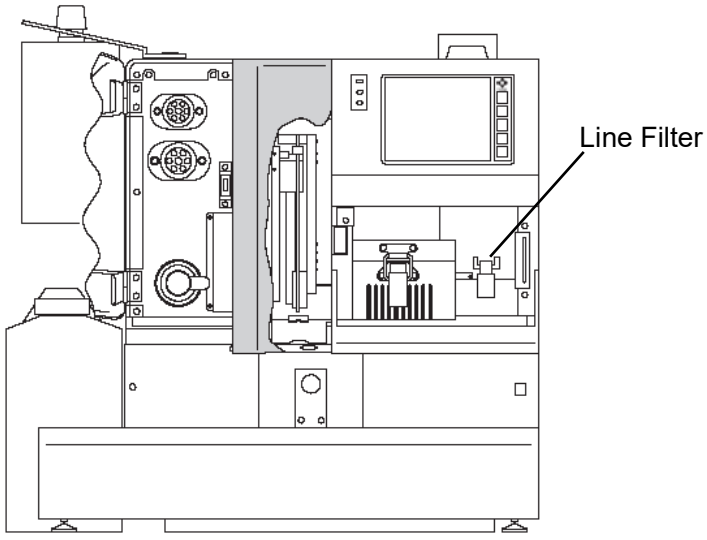
Caution **The filter has been in contact with blood samples. Wear protective clothing such as glasses, gloves, mask, etc., and take sufficient care to prevent infection during replacement and handling.**

Procedure

1. If the analyzer is not in STAND-BY state, wait for the assay to end and STAND-BY to be displayed. You can also change the state to STAND-BY state by pressing the STOP key.

2. Open the door below the display.

Fig. 5-6 Front View



3) Confirm on the main screen (the second screen) that the SV1 key is open (O).

4) Remove the filter outlet (top) flow line.

5) Turn the top of the filter holder assembly by turning it counterclockwise and remove the filter holder by pulling it straight out.

6) Lightly press the top of the holder to take out the old filter element. Place the new element with great care of surface of filter. The gray colored surface is the outlet (up) side.

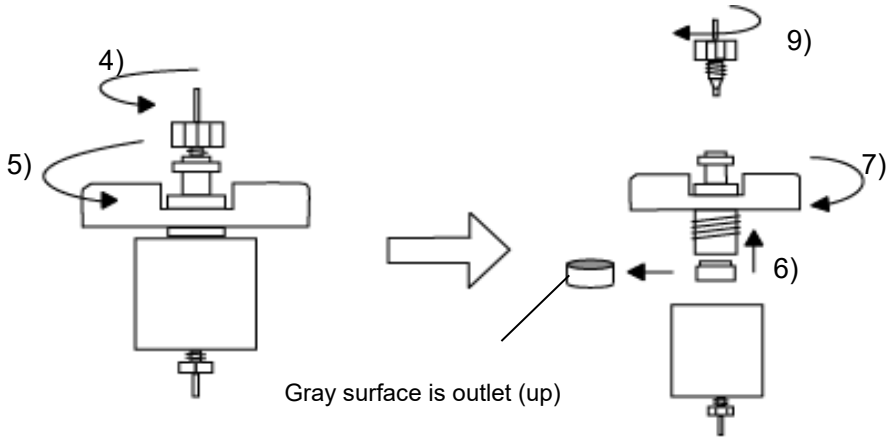
7) Firmly tighten the top of the filter holder assembly by hand until no further tightening is possible.

8) Place a lab wipe at the filter holder outlet and run the pump by pressing the PUMP key to remove the air inside the element. Check that no more bubbles come from the outlet side, and then press the PUMP key to stop the pump.

9) Connect the outlet side flow tube.

10) Press the PUMP key again to start the elution buffer delivery. Make sure that the pressure falls within a range less than the original pressure (which is indicated on the column inspection report) + 4 MPa and that there are no leaks from the filter housing components and tube connections. If a leak is found, tighten the assembly further.

Fig. 5-7 Filter Replacement



Caution **Be certain to remove the filter outlet flow line before turning the filter holding assembly. Failure to properly remove the filter outlet flow line may result in damage to the tubing or fitting. If damage occurs, the tubing and fitting will need to be replaced.**

Caution **The used filter has been in contact with blood samples. Therefore, wear protective clothing (goggles, gloves, mask, etc.), and take sufficient care to prevent infection during filter replacement and handling. In addition, dispose of the used filter as infectious waste according to the procedures in your facility.**

1. After installing a new filter, reset (zero) the filter counter on the REAGENT CHANGE screen.
2. Once the filter is tightened it will become deformed and cannot be used again.

5.8 Printer Paper Replacement

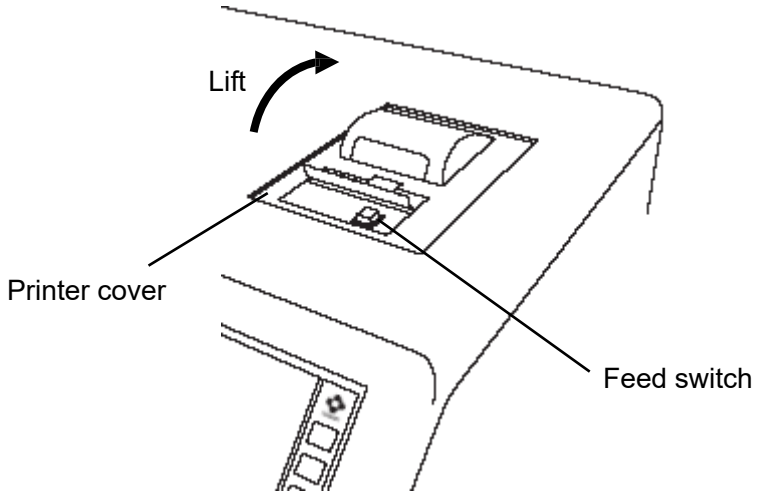
Use printer paper dedicated to the G8 analyzer.

Each roll has a width of 60 mm and a length of 42 m. When FORMAT 0 is used as the printout format, results for approximately 350 samples can be printed.

Procedure

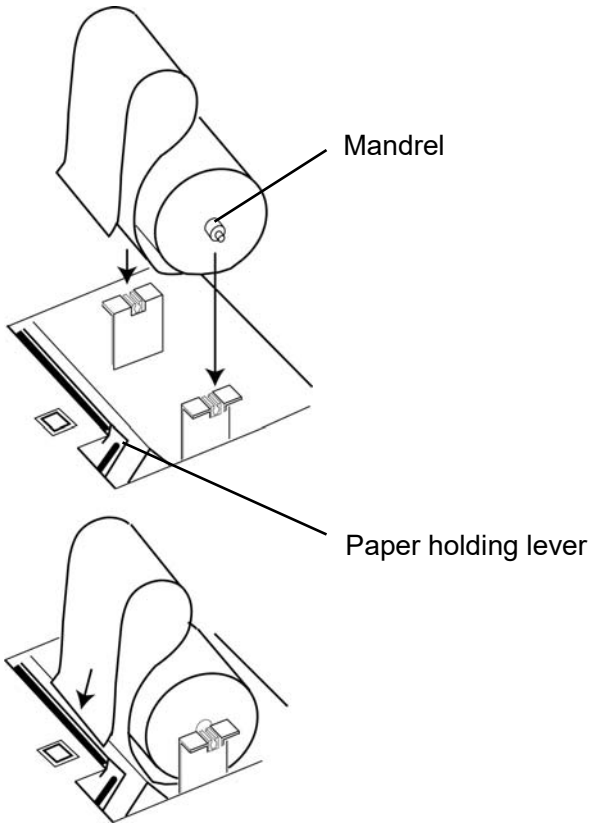
1) Lift the printer cover (upper lid) to the back to open.

Fig. 5-8 Printer



2) Push the paper holding lever down to the very front and wrap the remaining paper onto the roll.
3) Lift the roll up and remove the mandrel.
4) Insert the mandrel into the new roll and set it with great care for the direction.
5) Return the paper holding lever to the very back and insert the paper into the printer as shown in Fig. 5-9. The paper will automatically be fed. Since the lever has a two-step stop, be sure to position it at the very back.

Fig. 5-9 Printer Paper Placements



6) Check for twisted paper. If the paper is twisted, push the paper holder lever to the front, adjust the paper, and return the lever to the back.

If you do not return the paper holding lever to its original position, a "PRINTER OFF LINE" error will occur.

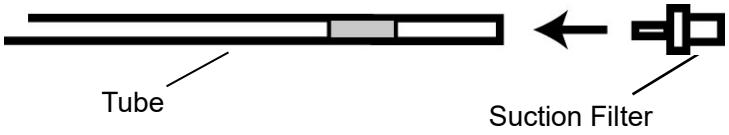
5.9 Suction Filter Replacement - every 6 months

The suction filter is attached to the inlet end of the elution buffer tube inserted in the elution buffer bag in order to remove foreign particles. If the suction filter is clogged, the pump will not operate normally and reliable results may not be obtained. Make sure to periodically replace the filter. Replace all three filters at the same time.
Foreign particles inside the filter cannot be removed by cleaning. Replace the used filter with a new one.

Procedure

1) If the analyzer is not in STAND-BY state, wait for the assay to end and STAND-BY to be displayed. You can also change the state to STAND-BY state by pressing the STOP key.
2) Loosen the bottle caps of the elution buffers.
3) Pull out the elution buffer tube and remove the old suction filters.
4) Securely attach the new suction filters, re-insert the tube into the pack, and close the caps.

Fig. 5-10 Suction Filter Attachment



5) After all three filters have been replaced, perform PRIME for Elution Buffer No. 1, 2, and 3 on the REAGENT CHANGE screen.
See “Chapter 5, Section 5.3 Elution Buffer and Hemolysis & Wash Solution Replacement” for details about the PRIME operation.

Used suction filters can be disposed as general nonflammable waste according to the procedures at your facility.

5.10 Sampling Needle Replacement

Caution **Replace the sampling needle if it is bent or broken. Use the following procedure to replace the sampling needle.**

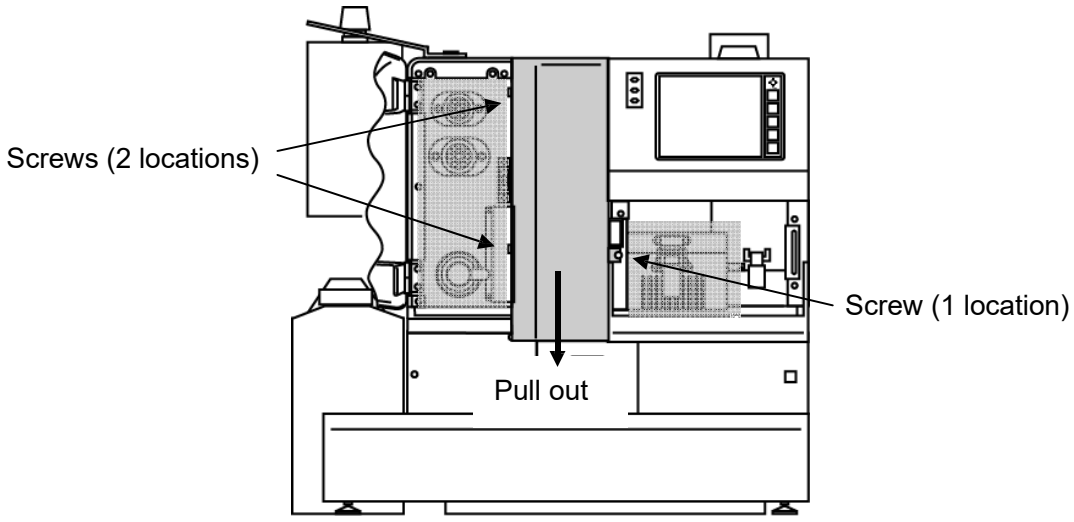
Access to the inside of the analyzer is needed to replace the sampling needle. Be sure that only personnel who have been trained by Tosoh or its representatives perform these operations. Be sure to wear protective clothing (goggles, gloves, mask, etc.) and take sufficient care to prevent infection during handling. Take care not to touch the end of the sampling needle during handling.

Procedure

1) Turn the POWER key and main power switch off to stop the analyzer operations during needle replacement. The sampling needle unit cannot be drawn unless the POWER key is off.

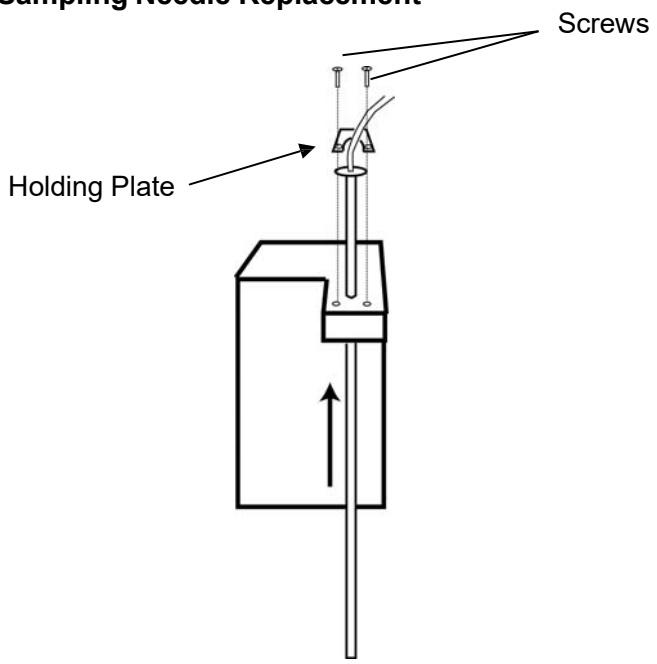
Caution **The analyzer may be broken or cause injury if the needle is forcibly moved.**

Fig. 5-11 Front View



2) Open the left-side door and loosen two needle cover screws indicated in Fig. 5-11. You do not need to remove the screws.
3) Open the door below the display and loosen one needle screw indicated in Fig. 5-11.
4) Grasp the needle cover, push it inward while taking care not to break it, and remove it from the needle screw indicated in 3) above.
5) Once you verify that the cover has been removed from the screws shown in Fig. 5-11, remove the cover by pulling it straightforward.
6) You will see the sampling needle unit back in the middle. Grasp the upper part of the sampling needle unit by hand and slowly pull the unit forward as much as possible.
7) Since a small volume of reagent will spill during replacement, place a lab wipe under the sampling needle tip.
8) By hand, loosen and remove the joint connected to the 3-way block of the sampling needle flow line.
9) Remove the screws on the upper section of the sampling needle. Be careful not to drop the screws or the holding plate inside the machine during this operation. See Fig. 5-12
10) Remove the tube from the black clip.

Fig. 5-12 Sampling Needle Replacement



11) Slowly lift up the sampling needle to remove.
12) Insert the new sampling needle and secure the upper plate with the screws. When you do so, make sure that the needle tip hole is oriented forward.
13) Fix the flow line by the black clip so that it doesn't twist, and then securely connect the joint to the 3-way block.
14) Move the sampling needle unit back and forth and confirm that the flow line does not catch on anything. If necessary, loosen the screws, turn the sampling needle, and change the stay direction to prevent the flow line from catching on anything.
15) Push the sampling needle unit back, close the sampling unit cover by following the procedure in reverse, and secure the screws.
16) Turn on the main power and return the analyzer to STAND-BY state.
17) Assay a dummy sample or control to confirm that the sample aspiration is processed correctly (see the total area in the result should be about the same as before the sampling needle replacement).

If the needle becomes bent immediately after replacement, check that the primary tubes match the sample rack or sample rack adapter.
If the needle placement is clearly off center of the primary tube, it must be adjusted. Cancel the assay and contact your local representative.

Caution **Dispose of the used sampling needle as infectious waste according to the procedures at your facility.**

Chapter 6 Troubleshooting

6.1 Assay Precautions

- **Column**
  - Be sure to read the Instructions for Use enclosed in the column box, as well as this manual.
  - Be sure not to use any other column for the HLC-723G8.
  - Store columns in a refrigerator before use.
  - Do not bump the column.
  - Alphabetical lot number, such as A and B, are shown on the box label of the column. Be sure to match this number with the lot number for the elution buffer.
  - Do not use tools to disassemble a column.

- **Elution Buffers**
  - Be sure to read the Instructions for Use enclosed in the elution buffer box, as well as this manual.
  - Be sure not to use any other buffer than the buffer for the HLC-723G8. Use the elution buffers before the expiration date indicated on the label.
  - For G8 Variant Elution Buffer No. 1, No. 2, and No. 3be sure the lot number matches the column lot number.
  - Do not refill the elution buffer or use it without ensuring that the lot numbers are the same.

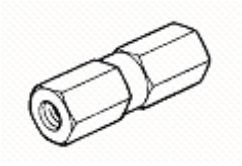
- **Hemolysis & Wash Solution**
  - Be sure to read the Instructions for Use enclosed in the Hemolysis & Wash solution box, as well as this manual.
  - Be sure to use the Hemolysis & Wash solution designated for the HLC-723G8/HLC-723GHbV by TOSOH. Use the Hemolysis & Wash solution before the expiration date indicated on the label.
  - There are no differences between lots for the Hemolysis & Wash solution.

- **Long-term shutdown**
  - If the analyzer is to be shut off for one week or more, replace the reagents in the analyzer flow line with purified water, using the procedure below.

Procedure

1. Remove the column and connect the open ends of the flow line with a union.

Fig. 6-1 Union (P/N: 0006163)



2. Move all suction tubes in the elution buffers and Hemolysis & Wash solution to a bottle containing purified water, and then prime all liquids on the REAGENT CHANGE screen.
3. Pump for approximately 10 minutes by using the pump key in the main screen (the second screen) in order to replace all reagents in the tubes with purified water.

1. Do not wash the flow line for the Hemolysis & Wash solution with elution buffers.
2. Absolutely do not insert the suction tube for the elution buffer in the Hemolysis & Wash Solution container to wash the tubes.
3. Attach the protective plugs to the column end and store in a cool place, such as a refrigerator, to prevent the inside of the column from drying out.

- **Operating Condition Changes**
  - Changes in assay parameters are invalid until the current assay (during ANALYSIS state) is complete. Make changes when the analyzer is in the STAND-BY state.

6.2 General System Failures

- **Power will not come on**
  - Is the power cord properly connected?
  - Is the main power switched on?
  - Was the POWER key pressed?

- **The external storage device cannot be read or written onto**
  - Is the external storage device correctly inserted in the external storage device socket?
  - Are you using an external storage device other than a Smart Media card or USB?
  - Is the external storage device correctly inserted in the storage device socket?
  - Are you using an external storage device other than a Smart Media card or USB stick?
  - Does the external storage device have adequate free space available?
  - Is the external storage device write-protected?
  - Is a card up to 128 MB being used?
  - Are you using a USB stick with a security function?
  - Are you using a USB stick formatted to a format other than FAT32?

- **Analyzer will not start with timer startup**
  - Is the date (year, month, and day) properly set?

    See “Chapter 4 Section 4.10: Date/Time and Weekly Timer Setting”.

- **Only abnormal chromatograms appear**
  - Is the sample volume sufficient?

    1 mL or more of whole blood is required with primary tubes and 150 µL or more is required with vials (diluted samples). The calibrator CALIB-1 is injected 3 times and CALIB-2 is injected 2 times. A volume of 500 µL or more of each calibrator is therefore required.
  - Is the buffer being pumped properly?

    Verify the pressure on the main screen.

    If the pressure is lower than the column pressure indicated on the column inspection report or if it looks unstable, refer to “**Chapter 5. Section 5.5: Pump Air Removal**” and remove the air from the pump.
  - Is there sufficient Hemolysis & Wash solution?
  - Do the column and/or filter need replacement? Does the column lot number agree with the elution buffer lot number? Has the expiration date passed?
  - Do the buffer label colors agree with the colors of the tubing labels?

- **Frequent bar code reading errors**
  - Is the printing quality sufficient?
  - Is it printed on a white label?
  - Are you using a bar code set in the bar code parameter? Are the labels clean and unwrinkled?

    See “Chapter 3 Section 3.7: Samples – Bar Code Label Confirmation”.
  - Are the samples set as the bar code labels oriented toward the bar code reader?
  - Are the labels properly affixed?

    Attach the labels at least 20 mm from the bottom of primary tubes and with less than 5° of rotation.

    At least 5 mm of space (margin) is required to the left and right in the bar code.

- **Errors with sample vials (Z1 error)**
  - Was the sample sensor bent downward because the rack was moved forcibly?

If a Tosoh rack is being used

- Is a vial adapter attached to the rack onto which the vial has been placed?

If a SYSMEX® rack is being used

- Is a vial adapter attached to the sample rack onto which the vial has been placed?
- Is a SYSMEX® rack with a proper adapter attached (13mm diameter, etc.) being used?

- **Sampling needle is bent or broken**
  - Are the primary tubes properly installed in the rack to stand straight?
  - Is the end marker properly attached?

    If the end marker is incorrectly installed, damage will occur when the analyzer moves the rack.

  - Is the parameter for a #100 mm tube properly set?

    See “Chapter 4, Section 4.6: Parameter Setting” and check the settings.

If a Tosoh rack is being used

- Has the primary tube holder (spring) become weak?

  Make sure the tubes are held in place so they don’t rattle.

If a SYSMEX® rack is being used

- Is a vial adapter attached to the sample rack onto which the vial has been placed?
- Is a SYSMEX® rack with a proper adapter attached (13mm diameter, etc.) being used?

  A sample rack adapter must be attached to the rack securely when using 12 ~ 14mm diameter primary tubes.

- **Some samples cannot be assayed**
  - Is the query mode set?

    Referring to “Chapter 4 Section 4.13: Data Communication Setting”, confirm 

key status.

    Samples are skipped when using a query mode if the test request from the host computer is not directed.

    If the bar code affixed to the sample is not properly read, the sample will be skipped when 

is set (highlighted) on the BCR screen. See “Chapter 4 Section 4.19: Bar Code Reader Setting and Reading Check”.

    Contact the Technical Support when successive samples are not detected.

6.3 Error Messages

When consulting with Technical Support about a problem, please note the error message and error number. In addition, if you follow the suggested solutions in this section and are still unable to resolve the error, or if you encounter an error message that is not noted, contact Technical Support.

General Error Messages

With these errors, the assay stops and the analyzer immediately enters STAND-BY state.

100 PRESSURE HIGH

The pump pressure exceeded the upper limit (15 MPa) set in the PRES HIGH parameters.

When the filter or column replacement period has been exceeded, first replace the filter or column. If the pressure is still high, remove the inlet and outlet flow line around the column and filter, and determine which part is the cause of the high pressure. Then, contact a Technical Support representative.

The target pressure within a range less than the pressure (which is indicated on the column inspection report) +4 MPa.

101 PRESSURE LOW

The pressure will not rise because the pump is unable to run due to air bubbles in the pump check valve. If the elution buffer is empty, place a new elution buffer and execute REAGENT CHANGE. Next, execute DRAIN FLUSH. See “Chapter 5 Section 5.5: Pump Air Removal”.

Execute manual pumping using the PUMP key in the main screen (second screen), and open and close the drain valve 2 or 3 times. If the pressure rises when the drain valve is closed, the operation is complete. If the pressure still does not rise or stabilize, execute DRAIN FLUSH again. In addition, confirm that the drain valve is securely closed.

102 PRES LIMIT OVER

The pump pressure has risen abnormally, then the shutdown circuit to be activated. Turn the main power switch off and remove the cause of the pressure increase. (Refer to “100 PRESSURE HIGH”)

718 INJ.VALVE ERROR

The injection valve is operating abnormally. The rotor seal of the valve requires replacement. If the error occurs many times, contact Technical Support.

Errors resulting in STAND-BY status after stopping an assay and performing WASH.

200 AREA LOW ERROR

Three successive results below the lower limit of the Total Area (50) occur. If the error message is present when sufficient volume of sample is set in the rack, the problem may be caused by an empty reagent (Hemolysis & Wash solution). Check the remaining volume of Hemolysis & Wash solution and start the assay again.

201 CALIB ERROR

Assay results for the calibrators were unsatisfactory.

Refer to “Chapter 3, Section 3.6: Calibration”. Check the dilution method, and the column and filters. Verify that the reagents have not expired.

Do the values for CALIB-1 and CALIB-2 in the PARAMETER screen agree with the assigned values (refer to the Instructions for Use or the label of the calibrator)? Are the units for calibration appropriate (refer to “Chapter 3 Section 3.7: Samples - Units for reporting and calibration”).

680 CALIB POS ERROR

The calibrator bar code was not able to read or the placement order was incorrect.

702 BC COMM ERROR

This is an abnormality in communications with the bar code reader, possibly caused by poor contact at an internal cable or another such problem.

Contact Technical Support if the problem occurs repeatedly.

703 AS COMMAND ERROR

Communications with the sampling assembly is abnormal. Contact Technical Support if the problem occurs repeatedly.

Errors resulting in STAND-BY status after stopping an assay and performing WASH

704 SAMPLE NOT FOUND

This error occurs when an empty rack, with no samples, is set and the START command is input.

If this error occurs even when samples are in place, there could be a sensor problem. Contact Technical Support.

705 RACK POS ERROR

(Rack position error)

The sample rack was not properly transferred.

Set the rack in the correct position and start again.

If you touch or move a rack during an assay run, this error may occur.

Do not touch the racks or primary tubes during an assay run.

710 Z1-AXIS ERROR

An abnormality occurred in the up and down movement of the sampling needle.

If this occurs during a STAT assay, check that the container setting (CUP or TUBE) is correctly set.

The error also occurs when the sample vial was not recognized as a primary tube, due to the disoriented sample sensor.

Errors that do not interrupt the assay run.

When the following errors occur, a message will be displayed, but the assay will continue.

120 STAT DOOR OPEN

The door on the STAT port is open. Close the door.

130 FILTER COUNT OVER

The filter count indicates the filter life has been reached.

A message will be displayed only if the alarm is set. Change filter at 400 injections.

131 COLUMN COUNT OVER

The column count indicates the column life has been reached.

A message will be displayed only if the alarm is set. Change column at 2500 injections.

140 BUFFER EMPTY

The remaining reagent is low. A message will be displayed only if the alarm is set.

220 NO PEAK DETECT

No peaks could be detected. This problem could be caused by different scenarios. Insufficient sample uptake due to a coagulated sample may have been processed or a short sample was processed.

221 #### NOT DETECT (#### is the peak ID)

A specific peak (hemoglobin fraction) could not be detected. When this occurs repeatedly with some samples, the elution buffer may have become concentrated, resulting in unidentified peak detection on chromatograms. Never mix the buffers.

When the error only occurs with specific samples, a hemoglobin variant may be present.

Errors which do not interrupt assays

640 QUERY NO RESPONSE

No response was received from the host in the query mode. Check the communication cable or the host computer settings.

670 SKIP: ############

The sample shown by ############ (ID) was not assayed because the bar code could not be read.
Verify the bar code label.
An ID number exceeding initial 12 digits is abbreviated as "_".

Errors which do not interrupt assays

The following messages are displayed on the STATUS screen but not printed.

001 STOP ACCEPTED

Instruction to stop assay is received by pressing the STOP key once during an assay.

002 EMERGENCY STOP

Instruction to make an immediate stop is received by pressing the STOP key twice during an assay.

010 SYSTEM RUNNING

Instruction that can't be processed during assay is received. For example, this occurs when operations such as recalculation are requested during an assay.

400 PAPER EMPTY

There is no printer paper. Install a new paper roll.

401 PRINTER OFF LINE

The printer paper holding lever is lifted up. Set the lever correctly.

500 CARD NOT READY

There is no external storage device. Insert a formatted external storage device into the socket.

501 WRITE PROTECT

The Smart Media card is write-protected. Peel off the write-protect sticker on the card.

510 CARD FULL

The external storage device is full. Prepare a new, formatted external storage device.

511 FILE NOT FOUND

A nonexistent file in the external storage device is attempted to be read.

530 CARD HARD ERROR

There is a problem with the socket or external storage device. This error also occurs when a USB stick cannot be written due to write protect. Replace with a new, formatted external storage device and try again. If the storage device cannot be formatted, there may be a problem with the socket itself. Contact Technical Support.

Error Messages and Their Meanings

Error Level 0: Warning 1: Enter STAND-BY state 2: Enter WASH state
Alarm Level 0: Beep for 1 sec 1: Beep for 30 sec and turn on ERROR LED & Patolight® (optional)
Print 0: No 1: Yes

Error Messages	Explanation	Countermeasure	Error Level	Alarm Level	Print
Operation errors					
001 STOP ACCEPTED	STOP was executed		0	0	0
002 EMERGENCY STOP	EMERGENCY STOP was executed		0	0	0
010 SYSTEM RUNNING	Command could not be executed during assay	Re-execute after assay is complete	0	0	0
011 MIS OPERATION	Command was not allowed	Feed correct command	0	0	0
020 #9999 PARAM ERROR	Parameters are not correct	Re-install the backup parameters stored on an external storage device	0	0	1
030 UNMATCH MODE DATA	Different mode data was attempted to be read	Set the proper data	0	0	0
040 SAMPLING BUSY	ERROR RESET operation is not possible due to sample processing through LA line.	Execute ERROR RESET after sample processing through LA line is complete	0	0	0
050 EXCEEDED 4 KINDS	More than 4 types of bar codes were input	Designate up to 4 bar codes types	0	0	0
Status monitoring errors					
100 PRESSURE HIGH	Pump pressure exceeded upper limit (PRES-HIGH)	Inspect for clogging at column and filter	1	1	1
101 PRESSURE LOW	Pump pressure fell below lower limit (PRES-LOW)	Execute air removal	1	1	1
102 PRES LIMIT OVER	Pump pressure abnormality was detected	Inspect for clogging at filter. Main power must be shut off then turned on again to re-start operations.	1	1	1
110 TEMP UNSTABLE	Column temperature will be not stabilized. (exceeds COL.T-RANGE)	Inspect temperature control. Check that TEMP parameters are correct.	2	1	1
111 TEMP LIMIT OVER	Temperature abnormality was detected	Inspect temperature control. Main power must be shut off then turned on again to re-start operations.	2	1	1
120 STAT DOOR OPEN	The STAT door is open	Close the door	0	1	1
130 FILTER COUNT OVER	The injection limit for filter (input value) has been exceeded	Replace the filter	0	1	1
131 COLUMN COUNT OVER	The injection limit for column (input value) has been exceeded	Replace the column	0	1	1
140 BUFFER EMPTY	Buffer volume is low. (get below the limit input)	Replace eluent	0	1	1
150 GRAD SENSOR ERROR	The GRAD sensor on the pump malfunctioned.	Check the GRAD sensor.	0-STD 2-other	1	1

Error Messages	Explanation	Countermeasure	Error Level	Alarm Level	Print
Data processing errors					
200 AREA LOW ERROR	The peak area which does not reach the minimum required area (50) occurred three times in series.	Check the samples, buffers, and Hemolysis & Wash Solution	2	1	1
201 CALIB ERROR	Calibration results were out of the acceptable range	Check the samples, buffers, and Hemolysis & Wash Solution	2	0	1
211 PEAK PATTERN ERROR	Peaks were not separated well	Check the samples, buffers, and Hemolysis & Wash Solution	0	0	1
220 NO PEAK DETECT	Peaks were not detected	Check the samples, buffers, and Hemolysis & Wash Solution	0	0	1
221 #####NOT DETECT	The ##### peak could not be detected	Check the samples, buffers, and Hemolysis & Wash Solution	0	0	1
230 RAW DATA FULL	No more available space for data collection		0	0	1
231 NO RAW DATA	No raw data have been stored		0	0	1
Communication errors					
300 MJ COMM ERROR (PE)	Parity error occurred in displayed device data communication	Check connection	0	1	1
301 MJ COMM ERROR (FE)	Framing error occurred in displayed device data communication	Check connection	0	1	1
302 MJ COMM ERROR (OR)	Overrun error occurred in displayed device data communication	Check connection	0	1	1
303 MJ COMM ERROR (BF)	Buffer full error occurred in displayed device data communication	Check connection	0	1	1
304 MJ COMM ERROR (OL)	Overly long data error occurred in displayed device communication	Check connection	0	1	1
305 MJ COMM ERROR (RE)	Retry error occurred in displayed device data communication	Check connection	0	1	1
306 MJ COMM ERROR (ST)	Timeout error for sending occurred in displayed device data communication	Check connection	0	1	1
307 MJ COMM ERROR (RT)	Timeout error for receiving occurred in displayed device data communication	Check connection	0	1	1
308 MJ COMM ERROR (NR)	A no response error occurred in displayed device data communication	Check connection	0	1	1
310 EXB COM ERROR (PE)	Parity error occurred in BCR communication for LA line	Check connection	0	1	1
311 EXB COM ERROR (FE)	Framing error occurred in BCR communication for LA line	Check connection	0	1	1

Error Messages	Explanation	Countermeasure	Error Level	Alarm Level	Print
312 EXB COM ERROR (OR)	Overrun error occurred in BCR communication for LA line	Check connection	0	1	1
313 EXB COM ERROR (BF)	Buffer full error occurred in BCR communication for LA line	Check connection	0	1	1
314 EXB COM ERROR (OL)	Overly long data error occurred in BCR communication for LA line	Check connection	0	1	1
315 EXB COM ERROR (RE)	Retry error occurred in BCR communication for LA line.	Check connection	0	1	1
316 EXB COM ERROR (ST)	Timeout error for sending occurred in BCR communication for LA line	Check connection	0	1	1
317 EXB COM ERROR (RT)	Timeout error for receiving occurred in BCR communication for LA line	Check connection	0	1	1
318 EXB COM ERROR (NR)	No response error occurred in BCR communication for LA line	Check connection	0	1	1
320 LCD COM ERROR (PE)	Parity error occurred in LCD communication through KEY	Check connection	0	1	1
321 LCD COM ERROR (FE)	Framing error occurred in LCD communication through KEY	Check connection	0	1	1
322 LCD COM ERROR (OR)	Overrun error occurred in LCD communication through KEY	Check connection	0	1	1
323 LCD COM ERROR (BF)	Buffer full error occurred in LCD communication through KEY	Check connection	0	1	1
324 LCD COM ERROR (OL)	Overly long data error occurred in LCD communication through KEY	Check connection	0	1	1
325 LCD COM ERROR (RE)	Retry error occurred in LCD communication through KEY	Check connection	0	1	1
326 LCD COM ERROR (ST)	Timeout error for sending occurred in LCD communication through KEY	Check connection	0	1	1
327 LCD COM ERROR (RT)	Timeout error for receiving occurred in LCD communication through KEY	Check connection	0	1	1
328 LCD COM ERROR (NR)	No response error occurred in LCD communication with KEY	Check connection	0	1	1
330 AS COMM ERROR (PE)	Parity error occurred in AS communication	Check connection	0	1	1
331 AS COMM ERROR (FE)	Framing error occurred in AS communication	Check connection	0	1	1
332 AS COMM ERROR (OR)	Overrun error occurred in AS communication	Check connection	0	1	1
333 AS COMM ERROR (BF)	Buffer full error occurred in AS communication	Check connection	0	1	1
334 AS COMM ERROR (OL)	Overly long data error occurred in AS communication	Check connection	0	1	1
335 AS COMM ERROR (RE)	Retry error occurred in AS communication	Check connection	0	1	1

Error Messages	Explanation	Countermeasure	Error Level	Alarm Level	Print
336 AS COMM ERROR (ST)	Timeout error for sending occurred in AS communication	Check connection	0	1	1
337 AS COMM ERROR (RT)	Timeout error for receiving occurred in AS communication	Check connection	0	1	1
338 AS COMM ERROR (NR)	No response error occurred in AS communication	Check connection	0	1	1
340 HOST COMM ERR(PE)	Parity error occurred in HOST communication	Check the connections and communication specifications	0	1	1
341 HOST COMM ERR (FE)	Framing error occurred in HOST communication	Check the connections and communication specifications	0	1	1
342 HOST COMM ERR (OR)	Overrun error occurred in HOST communication	Check the connections and communication specifications	0	1	1
343 HOST COMM ERR (BF)	Buffer full error occurred in HOST communication	Check the connections and communication specifications	0	1	1
344 HOST COMM ERR (OL)	Overly long data error occurred in HOST communication	Check the connections and communication specifications	0	1	1
345 HOST COMM ERR (RE)	Retry error occurred in HOST communication	Check the connections and communication specifications	0	1	1
346 HOST COMM ERR (ST)	Timeout error for sending occurred in HOST communication	Check the connections and communication specifications	0	1	1
347 HOST COMM ERR (RT)	Timeout error for receiving occurred in HOST communication	Check the connections and communication specifications	0	1	1
348 HOST COMM ERR (NR)	No response error occurred in HOST communication	Check the connections and communication specifications	0	1	1
350 LC COMM ERROR (PE)	Parity error occurred in LA communication	Check connections and communication specifications	0	1	1
351 LC COMM ERROR (FE)	Framing error occurred in LA communication	Check the connections and communication specifications	0	1	1
352 LC COMM ERROR (OR)	Overrun error occurred in LA communication	Check the connections and communication specifications	0	1	1
353 LC COMM ERROR (BF)	Buffer full error occurred in LA communication	Check the connections and communication specifications	0	1	1
354 LC COMM ERROR (OL)	Overly long data error occurred in LA communication	Check the connections and communication specifications	0	1	1
355 LC COMM ERROR (RE)	Retry error occurred in LA communication	Check the connections and communication specifications	0	1	1
356 LC COMM ERROR (ST)	Timeout error for sending occurred in LA communication	Check the connections and communication specifications	0	1	1
357 LC COMM ERROR (RT)	Timeout error for receiving occurred in LA communication	Check the connections and communication specifications	0	1	1
358 LC COMM ERROR (NR)	No response error occurred in LA communication	Check the connections and communication specifications	0	1	1
360 LCD COM ERROR (??)	An unknown error occurred in LCD communication through KEY	Check connection	0	1	1

Error Messages	Explanation	Countermeasure	Error Level	Alarm Level	Print
361 LCD COM ERROR (01)	An 01 error (display processing) occurred in LCD communication through KEY	Check connection	0	1	1
362 LCD COM ERROR (02)	An 02 error (overrun/framing error) occurred in LCD communication through KEY	Check connection	0	1	1
363 LCD COM ERROR (03)	An 03 error (parity error) occurred in LCD communication through KEY	Check connection	0	1	1
364 LCD COM ERROR (04)	An 04 error (sum check error) occurred in LCD communication through KEY	Check connection	0	1	1
365 LCD COM ERROR (05)	An 05 error (address error) occurred in LCD communication through KEY	Check connection	0	1	1
366 LCD COM ERROR (06)	An 06 error (count error) occurred in LCD communication	Check connection	0	1	1
367 LCD COM ERROR (07)	An 07 error (screen error) occurred in LCD communication through KEY	Check connection	0	1	1
368 LCD COM ERROR (08)	An 08 error (format error) occurred in LCD communication through KEY	Check connection	0	1	1
369 LCD COM ERROR (09)	An 09 error (received data over) occurred in LCD communication through KEY	Check connection	0	1	1
370 LCD COM ERROR (0B)	An 0B error (retry command error) occurred in LCD communication through KEY	Check connection	0	1	1
371 LCD COM ERROR (0F)	An 0F error (ETX error) occurred in LCD communication through KEY	Check connection	0	1	1
372 LCD COM ERROR (10)	A 10 error (DLE error) occurred in LCD communication through KEY	Check connection	0	1	1
373 LCD COM ERROR (11)	An 11 error (character error) occurred in LCD communication through KEY	Check connection	0	1	1
374 LCD COM ERROR (12)	An 12 error (command error) occurred in LCD communication through KEY	Check connection	0	1	1
Printer errors					
400 PAPER EMPTY	Printer is out of paper	Replace the paper roll	0	0	0
401 PRINTER OFF LINE	Printer lever is not set	Set the printer lever	0	0	0
420 PRINTER ERROR	Printer is broken	Inspect the printer	0	0	0

Error Messages	Explanation	Countermeasure	Error Level	Alarm Level	Print
Card errors					
500 CARD NOT READY	No external storage device is set	Set the external storage device	0	0	0
501 WRITE PROTECT	The Smart Media card is write-protected	Peel off the sticker on the Smart Media card.	0	0	0
510 CARD FULL	The external storage device is full	Insert a new, formatted external storage device	0	0	0
511 FILE NOT FOUND	The file could not be found	Insert the proper external storage device. Input the correct number.	0	0	0
520 CARD DATA ERROR	External storage device data is corrupted	Format the external storage device to re-use	0	0	0
530 CARD HARD ERROR	External storage device could not be accessed or the USB stick is write-protected	Inspect the external storage device and socket or remove write protection from the USB stick	0	0	0
Control and monitoring errors					
600 AS NO RESPONSE	Autosampler is not responding	Check connections. Turn the main power off then on to re-start.	2	1	1
610 SAMPLER BUSY	AS is currently operating and cannot accept any commands	Wait for operation to end	2	1	1
620 SAMPLE NOT INJECT	Assay of previous sample is not yet complete, so sample was not processed		0	0	1
630 BELT BCR NO RESP	BCR for LA line is not responding	Check connections	0	0	1
631 BELT BCR SET ERROR	Setting error occurred in the BCR for LA line	Check connections	0	0	1
632 BCR SET ERROR	BCR setting error occurred	Check connections	0	0	1
640 QUERY NO RESPONSE	No response is received for order query to host	Check the host	0	1	1
650 BELT ID UNMATCH	Sample ID sent by HOST does not agree with the sample ID read by BCR	Check LA line	0	1	1
660 BELT LINE ABORT	Error occurred at LA line or analyzer during connecting to HOST. No sample processing was executed.	Remove the cause of the error	0	1	1
670 SKIP:############	Assay was not done for the sample indicated by the ID because the bar code could not be read or some other problem occurred (ID number exceeding initial 12 digits will be abbrev. as "_")	Inspect bar code label etc.	0	0	1
680 CALIB POS ERROR	The calibrator position is wrong	Inspect the calibrator position, bar code label, etc.	2	1	1

Error Messages	Explanation	Countermeasure	Error Level	Alarm Level	Print
AS errors					
701 PULSE ERROR	Pulse data was abnormal	Check the pulse parameters	2	1	1
702 BC COMM ERROR	A communication error occurred in the BCR with AS	Check the BCR connection	2	1	1
703 AS COMMAND ERROR	The AS received an invalid command	Check the AS connection	2	1	1
704 SAMPLE NOT FOUND	Sample could not be detected	Start assay after setting samples	2	1	1
705 RACK POS ERROR	The rack transfer lever cannot return due to the presence of an incoming rack	Remove the rack	2	1	1
706 SYRINGE-L ERROR	Operation error in syringe-L	Inspect syringe-L. Execute SMP.RESET.	2	1	1
707 SYRINGE-S ERROR	Operation error in syringe-S	Inspect syringe-S. Execute SMP.RESET.	2	1	1
708 X1-AXIS ERROR	Operation error in X1-axis	Inspect X1-axis. Execute SL.ROTATE.	2	1	1
709 Y1-AXIS ERROR	Operation error in Y1-axis	Inspect Y1-axis. Execute SMP.RESET.	2	1	1
710 Z1-AXIS ERROR	Operation error in Z1-axis	Inspect Z1-axis. Execute SMP.RESET.	2	1	1
711 LINE VALVE ERROR	Operation error in switching valve (AS valve)	Inspect valve on line. Execute SMP.RESET.	2	1	1
712 X2-AXIS ERROR	Operation error in X2-axis	Inspect X2-axis Execute SL.ROTATE	2	1	1
713 X3-AXIS ERROR	Operation error in X3-axis	Inspect X3-axis. Execute SL.ROTATE.	2	1	1
714 Y2-AXIS ERROR	Operation error in Y2-axis	Inspect Y2-axis. Execute SL.ROTATE.	2	1	1
715 Y3-AXIS ERROR	Operation error in Y3-axis	Inspect Y3-axis. Execute SL.ROTATE.	2	1	1
716 Y4-AXIS ERROR	Operation error in Y4-axis	Inspect Y4-axis. Execute SL.ROTATE.	2	1	1
717 Y5-AXIS ERROR	Operation error in Y5-axis	Inspect Y5-axis. Execute SL.ROTATE.	2	1	1
718 INJ VALVE ERROR	Operation error in injection valve	Inspect injection valve. Execute SMP.RESET.	1	1	1
722 SOFT ERROR	An AS control error occurred	Turn the main power off then on	2	1	1
723 SAMPLE MISMATCH M	Sample position transmitted from AS does not match position at main unit	Turn the main power off then on	2	1	1
724 SAMPLE MISMATCH A	Sample position transmitted from main unit does not match position at AS	Turn the main power off then on	2	1	1
725 SAMPLE RACK FULL	The sample rack is full on the transport side	Remove rack	0	1	0

Error Messages	Explanation	Countermeasure	Error Level	Alarm Level	Print
730 TUBE MIXING ERROR	The rack moved at mixing or bar code reading (100SL-GA)	Inspect the tube condition	2	1	1
LA line control errors					
800 BL BC UNMATCH	ID transmitted from LA does not match ID read by the BCR for LA line	Inspect BCR and bar code label	0	1	1
801 BL BC READ ERROR	Bar code could not be read by the BCR for LA line	Inspect BCR and bar code label	0	1	1
802 BELT LINE ERROR	Trouble signal was received from LA line	Inspect transport line	0	1	1
803 BL ID TRANS ERROR	ID was transmitted when assay was not accessible	Inspect transport line	0	1	1
804 BL ID NOT ACCEPT	Samples came in even though ID was not received	Inspect transport line	0	1	1
805 BELT LINE DOWN	LA line connection signal was off or communication from LA line was interrupted	Inspect transport line	0	1	1
806 BL COMM ERROR	LA communication error occurred	Check connection	0	1	1
807 BL ANAL START	Assay start command was received from LA line		0	0	1
808 BL ANAL STOP	Assay stop command was received from LA line		0	0	1
809 BL MODE CHG ERR	There was an error to change command in the mode setting	Inspect transport line	0	0	1
810 BL SAMP SIG ERR	The SMPOK signal from LA line during sampling is off	Inspect transport line	2	1	1

6.4 Abnormal Chromatograms

Although the percentage of each hemoglobin component may vary slightly from patient to patient, most whole blood samples will contain six fractions: A_{1a}, A_{1b}, F, L-A_{1c+}, s-A_{1c}, and A_0. A normal chromatogram is shown below in Figure 6-2.

Chromatograms from patients with hemoglobin variants or unknown peaks not recognized by the analyzer are occasionally seen during routine testing. These patterns may indicate interferences or problems with the assay. Therefore, it is important to use caution when troubleshooting. Review all chromatograms to determine whether the results are valid. In most cases, results for the s-A_{1c}% are reportable. In some cases, the s-A_{1c}% may be invalid depending on the hemoglobinopathy present, the flow rate, and the condition of the column and reagent system.

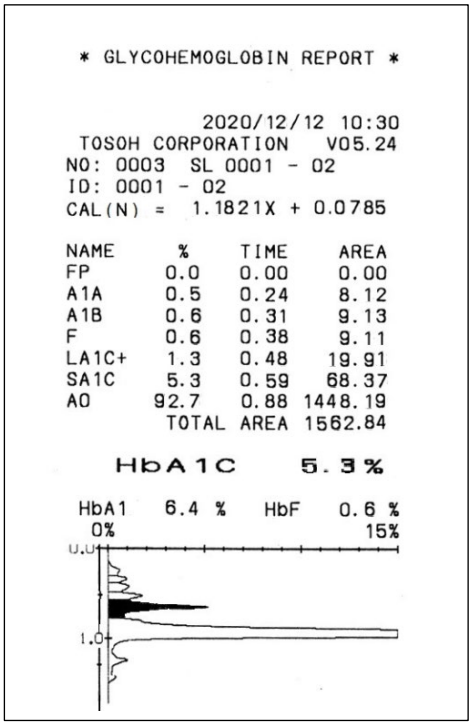
Mathematical algorithms used in the software exclude hemoglobin variant peaks when calculating the Total Area. The s-A_{1c}% is usually not affected in such situations, although chromatograms should be carefully reviewed. Variant hemoglobins HbS (HV-1 peak), HbD (HV-0 peak) and HbC (HV-2) elute after the A_0 peak. The HbE (P-HV3 peak) appears between s-A_{1c} and HbA_0.The s-A_{1c}% is reportable on the G8 when these hemoglobins are present in the heterozygous state with HbA.

Glycemic monitoring for patients displaying any homozygous hemoglobin other than HbAA such as HbSS, HbCC or the double heterozygous HbSC, cannot be performed using HbA_{1C} because there is no HbA present. Alternative testing is mandatory for these types of patients.

Remember that all abnormal chromatograms are not necessarily the result of abnormalities in the patient sample. Analyzer problems such as a malfunctioning pump or sampling unit, a column that should be replaced or reagents that are incorrectly placed or have been depleted can also cause abnormal chromatograms. In these cases, sequential chromatograms are usually all affected from the point that the problem began.

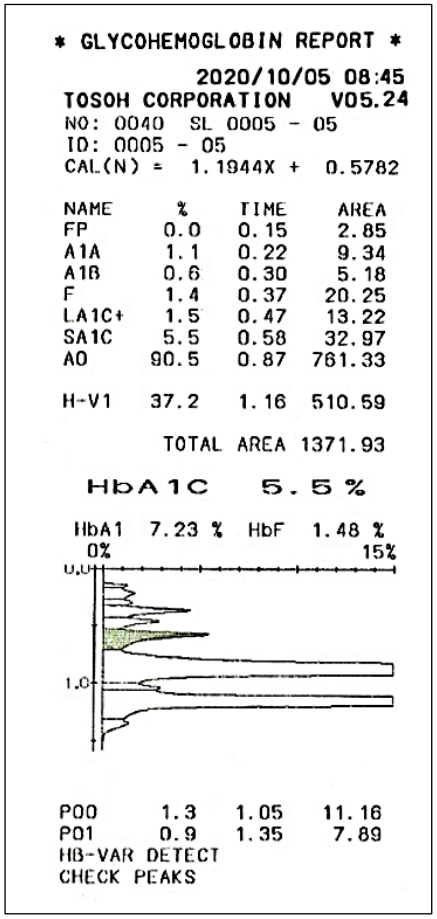
See Figure 6-3 through Figure 6-15 for examples of abnormal chromatograms. Refer to Troubleshooting Flow Carts Fig. 6-16 for additional information.

Fig. 6-2 Normal Chromatogram
HbA_{1c} is reportable



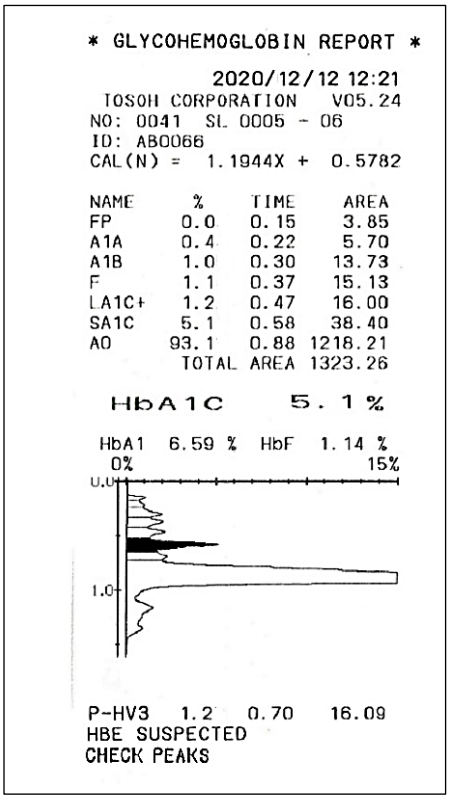
```
* GLYCOHEMOGLOBIN REPORT *

                2020/12/12 10:30
 TOSOH CORPORATION    V05.24
NO: 0003  SL 0001 - 02
ID: 0001 - 02
CAL(N) =  1.1821X + 0.0785

NAME      %     TIME     AREA
FP      0.0    0.00     0.00
A1A     0.5    0.24     8.12
A1B     0.6    0.31     9.13
F       0.6    0.38     9.11
LA1C+   1.3    0.48    19.91
SA1C    5.3    0.59    68.37
A0     92.7    0.88  1448.19
         TOTAL AREA  1562.84

        HbA1C     5.3%

HbA1   6.4 %   HbF   0.6 %
 0%                    15%
```

Fig. 6-3 Hemoglobin Variant (AS)
HbA_{1c} is reportable



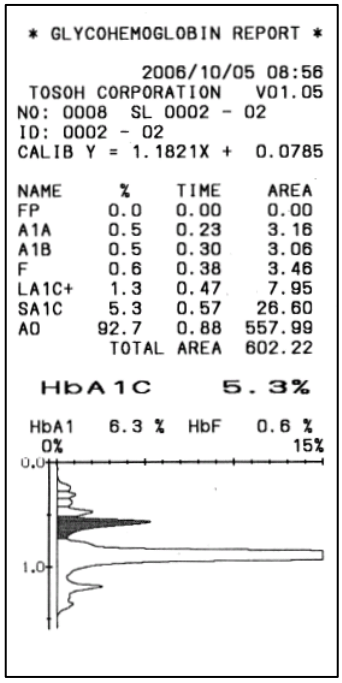
```
* GLYCOHEMOGLOBIN REPORT *

                2020/10/05 08:45
TOSOH CORPORATION    V05.24
NO: 0040  SL 0005 - 05
ID: 0005 - 05
CAL(N) =  1.1944X +  0.5782

NAME      %     TIME     AREA
FP      0.0    0.15     2.85
A1A     1.1    0.22     9.34
A1B     0.6    0.30     5.18
F       1.4    0.37    20.25
LA1C+   1.5    0.47    13.22
SA1C    5.5    0.58    32.97
A0     90.5    0.87   761.33

H-V1   37.2    1.16   510.59

         TOTAL AREA  1371.93

        HbA1C     5.5%

HbA1  7.23 %  HbF   1.48 %
 0%                    15%

P00     1.3    1.05    11.16
P01     0.9    1.35     7.89
HB-VAR DETECT
CHECK PEAKS
```

Fig. 6-4 Hemoglobin Variant (AE)
HbA_{1c} is reportable



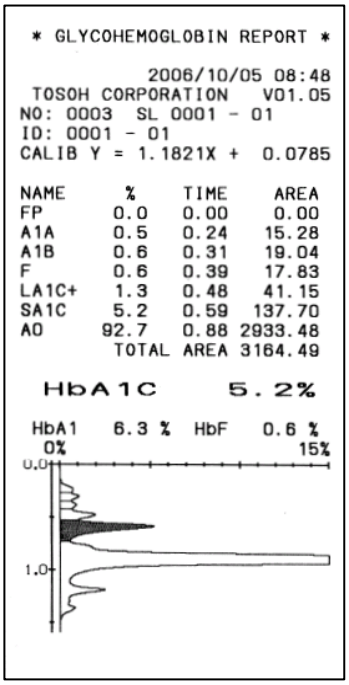
```
* GLYCOHEMOGLOBIN REPORT *

                2020/12/12 12:21
 TOSOH CORPORATION    V05.24
NO: 0041  SL 0005 - 06
ID: ABO066
CAL(N) =  1.1944X +  0.5782

NAME      %     TIME     AREA
FP      0.0    0.15     3.85
A1A     0.4    0.22     5.70
A1B     1.0    0.30    13.73
F       1.1    0.37    15.13
LA1C+   1.2    0.47    16.00
SA1C    5.1    0.58    38.40
A0     93.1    0.88  1218.21
         TOTAL AREA  1323.26

        HbA1C     5.1%

HbA1  6.59 %  HbF   1.14 %
 0%                    15%

P-HV3   1.2    0.70    16.09
HBE SUSPECTED
CHECK PEAKS
```

Fig. 6-5 Total Area is less than optimum but within acceptable range
HbA_{1c} is reportable



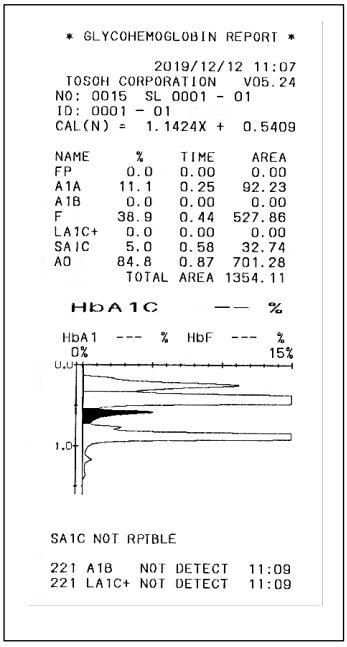
```
 * GLYCOHEMOGLOBIN REPORT *

            2006/10/05 08:56
 TOSOH CORPORATION    V01.05
NO: 0008  SL 0002 - 02
ID: 0002 - 02
CALIB Y = 1.1821X +  0.0785

NAME      %     TIME     AREA
FP       0.0   0.00     0.00
A1A      0.5   0.23     3.16
A1B      0.5   0.30     3.06
F        0.6   0.38     3.46
LA1C+    1.3   0.47     7.95
SA1C     5.3   0.57    26.60
A0      92.7   0.88   557.99
          TOTAL AREA   602.22

HbA1C      5.3%

HbA1   6.3 %  HbF   0.6 %
 0%                   15%
0.0
1.0
```

Fig. 6-6 Total Area is more than optimum but within acceptable range
HbA_{1c} is reportable



```
 * GLYCOHEMOGLOBIN REPORT *

            2006/10/05 08:48
 TOSOH CORPORATION    V01.05
NO: 0003  SL 0001 - 01
ID: 0001 - 01
CALIB Y = 1.1821X +  0.0785

NAME      %     TIME     AREA
FP       0.0   0.00     0.00
A1A      0.5   0.24    15.28
A1B      0.6   0.31    19.04
F        0.6   0.39    17.83
LA1C+    1.3   0.48    41.15
SA1C     5.2   0.59   137.70
A0      92.7   0.88  2933.48
          TOTAL AREA  3164.49

HbA1C      5.2%

HbA1   6.3 %  HbF   0.6 %
 0%                   15%
0.0
1.0
```

Fig. 6-7 HbF is high
HbA_{1c} is not reportable



```
 * GLYCOHEMOGLOBIN REPORT *

            2019/12/12 11:07
 TOSOH CORPORATION    V05.24
NO: 0015  SL 0001 - 01
ID: 0001 - 01
CAL(N) =  1.1424X +  0.5409

NAME      %     TIME     AREA
FP       0.0   0.00     0.00
A1A     11.1   0.25    92.23
A1B      0.0   0.00     0.00
F       38.9   0.44   527.86
LA1C+    0.0   0.00     0.00
SA1C     5.0   0.58    32.74
A0      84.8   0.87   701.28
          TOTAL AREA  1354.11

HbA1C      -- %

HbA1   --- %  HbF   --- %
 0%                   15%
0.0
1.0

SA1C NOT RPTBLE

221 A1B   NOT DETECT  11:09
221 LA1C+ NOT DETECT  11:09
```

Fig. 6-8 Total Area is less than 500 HbA_{1c} is not reportable

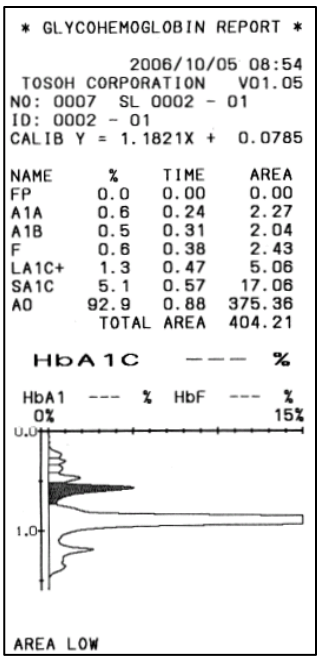


Fig. 6-9 Total Area is above 4000 HbA_{1c} is not reportable

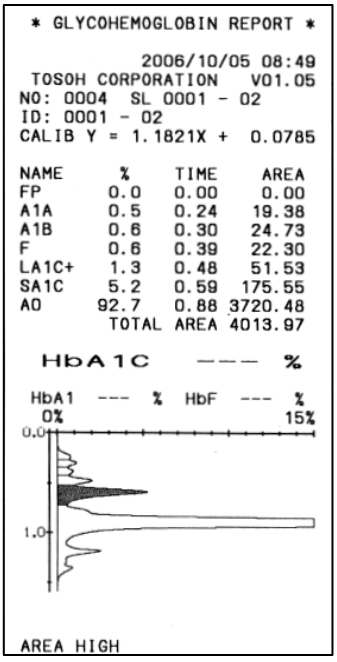


Fig. 6-10 Insufficient Sample Suction HbA_{1c} is not reportable

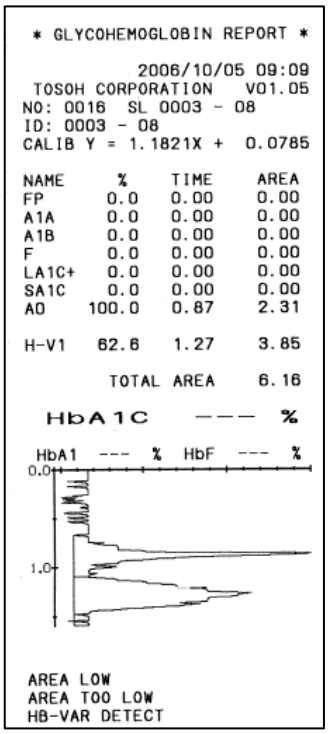


Fig. 6-11 Defective Pump Delivery HbA_{1c} is not reportable

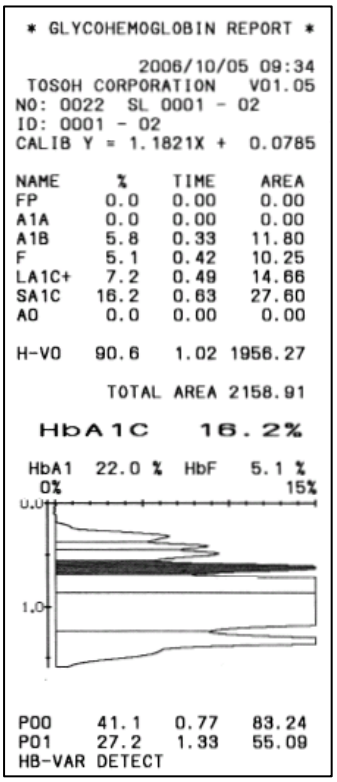


Fig. 6-12 Switched Elution Buffers No. 1 and 2 HbA_{1c} is not reportable

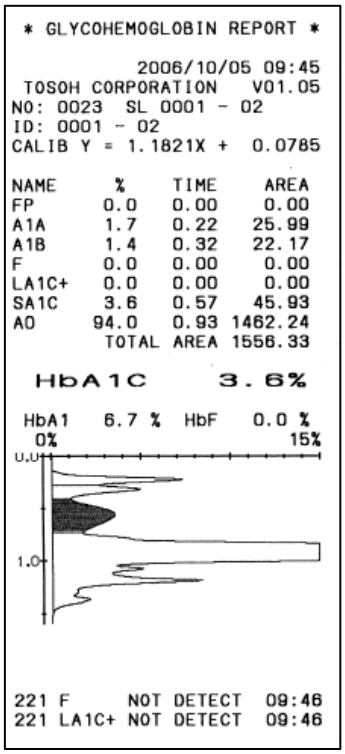


Fig. 6-13 Switched Elution Buffers No. 2 and 3 HbA_{1c} is not reportable

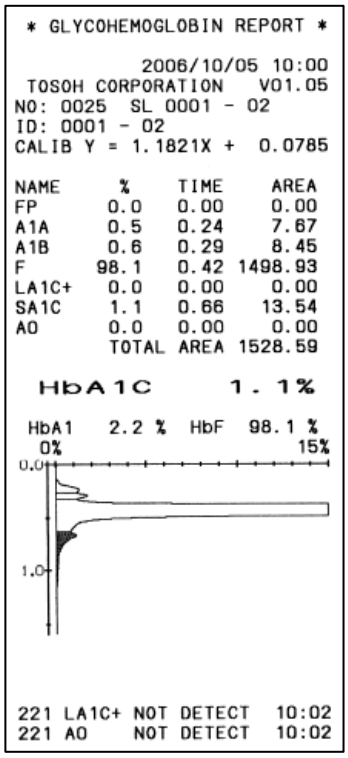


Fig. 6-14 Low Flow Rate HbA_{1c} is not reportable

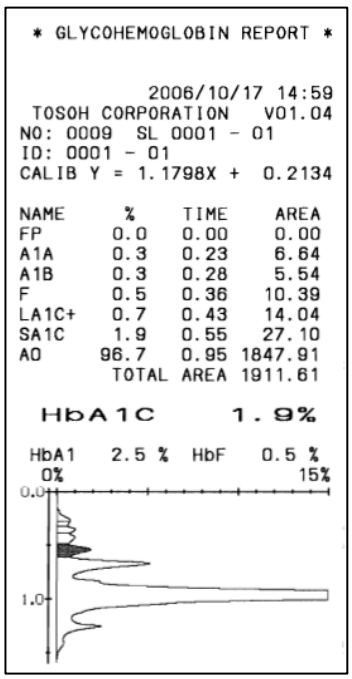


Fig. 6-15 High Flow Rate HbA_{1c} is not reportable

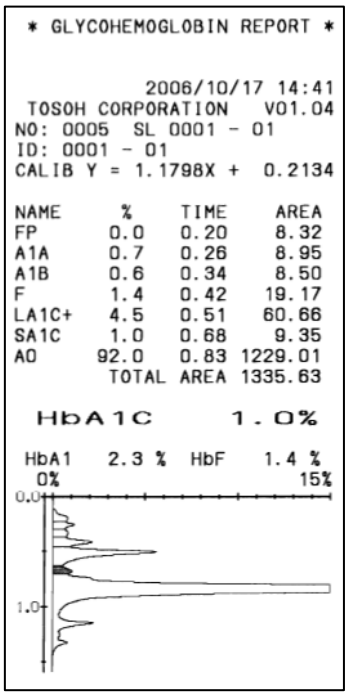
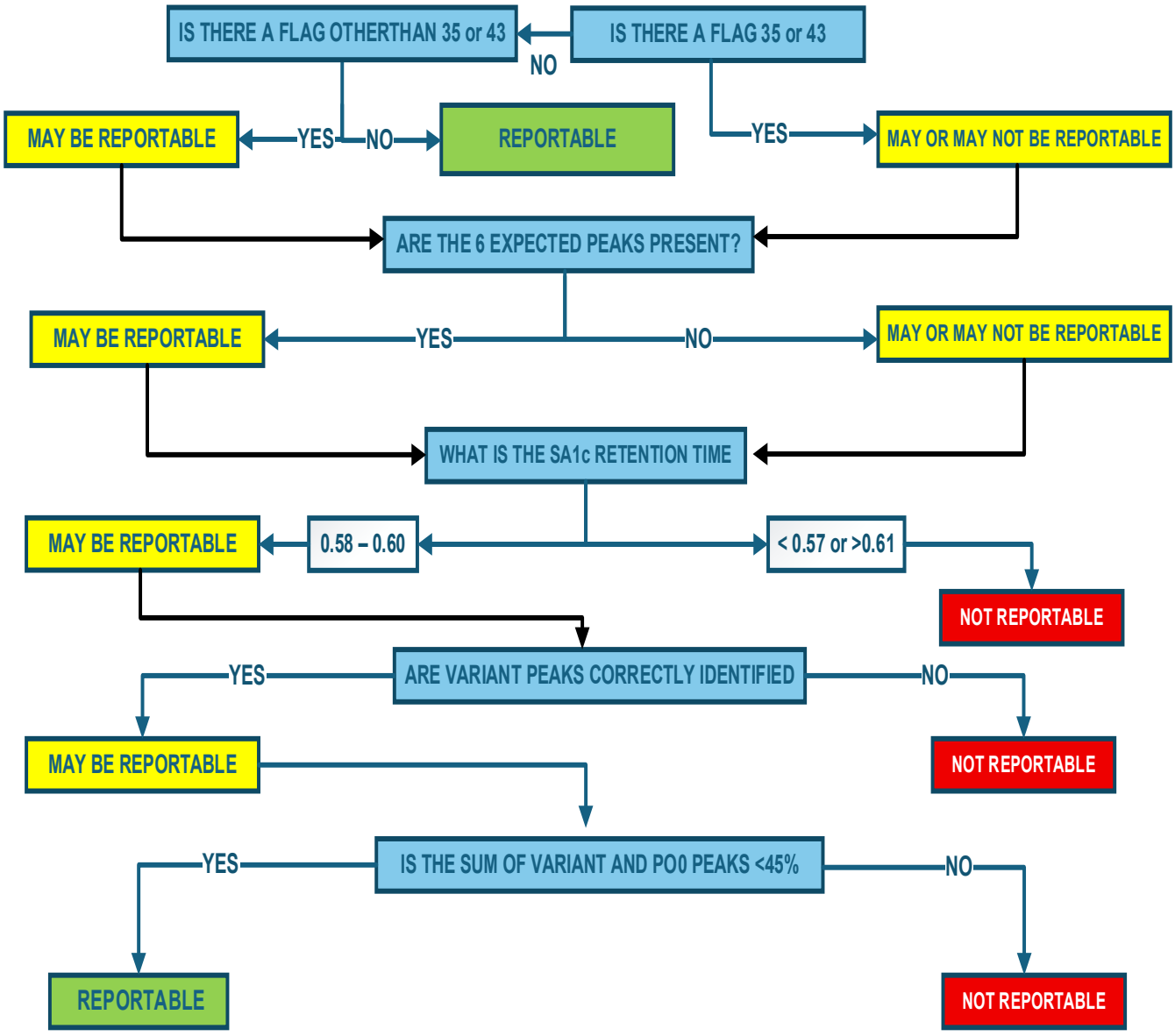


Fig. 6-16 G8 CHROMATOGRAM REVIEW FLOW CHART



NOTES

Chapter 7 Data Management

7.1 Data Management Details

7.2

The analyzer's system program and assay parameters are backed up by the internal battery.
When a system program version has been upgraded or some problem has corrupted the system program, use the following procedure to reload the program and other data from the storage device socket.

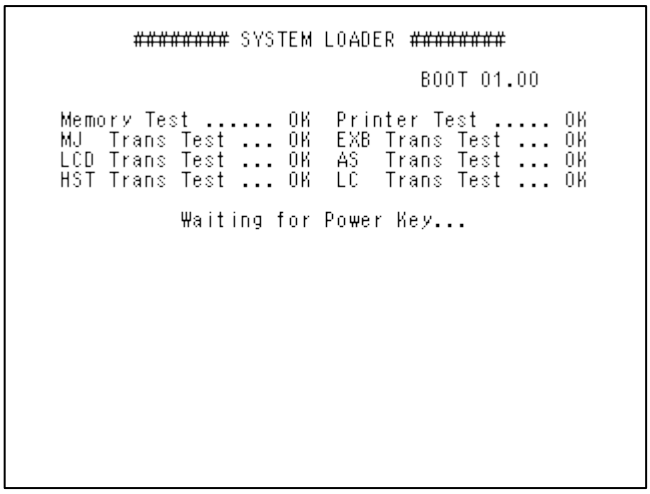
System and AS program Downloading

Procedure

1) Turn off the main power switch on the left lower side of the analyzer.
2) Insert the system external storage device into the smart media socket.
3) Turn on the main power switch.
4) Screens 7-1 and 7-2 will be displayed and then the screen will go temporarily dark.

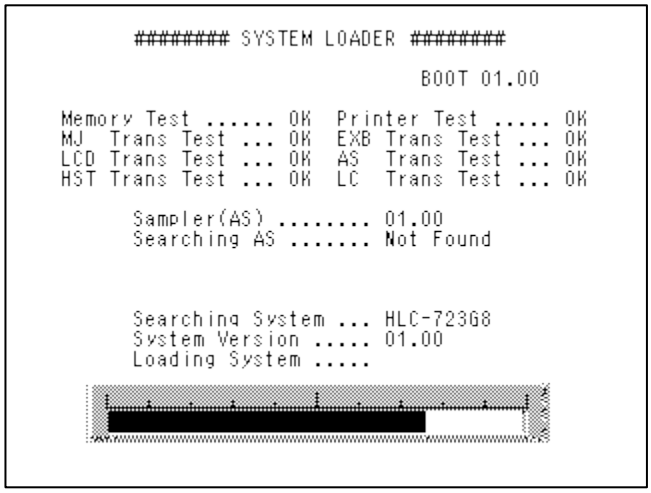
Screen 7-1 Just After Main Power Is Turned On

Screen 7-2 Just before Power Key is Pressed



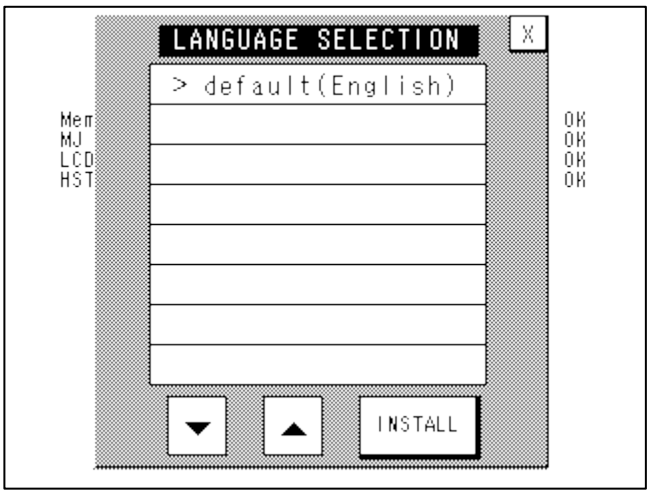
5) Press the POWER KEY.
6) Screen 7-3 will be displayed and the AS program and system program are loaded one after the other. (This takes about 6 minutes.)

Screen 7-3 System Loader Screen



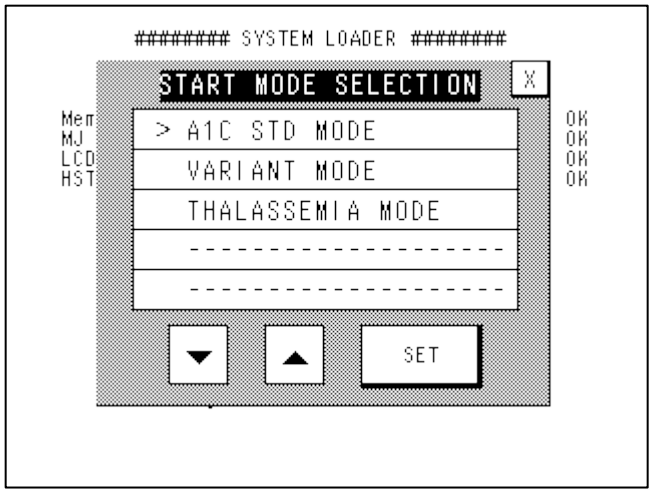
7) Once the system has been loaded, the Language Selection screen will be displayed.

Screen 7-4 Language Selection Screen



8) Select “default” and press the INSTALL key.
9) When loading is complete, the analyzer automatically starts up and enters the WARMING UP state. After confirming that the analyzer has entered into the WARMING UP state, remove the system external storage device from the socket.
10) After Screen 7-4 has been displayed, Screen 7-5 will automatically be displayed.

Screen 7-5 Assay Mode Selection Screen



11) Check that **VARIANT MODE** is selected and then press the SET key.
12) The system loader screen appears. When loading is complete, the analyzer automatically starts up and enters the WARMING UP state.
13) Remove the system external storage device.

The AS program (filename: **AS.MOT**) and system program (filename: **SYSTEM.MOT**) are required to operate the analyzer. Both of these programs are stored in the accessory system external storage device.

When the main power is turned on, the analyzer searches the files on the external storage device in the socket. If the AS and system program are found, they are automatically loaded in the internal memory of the analyzer. During a system upgrade, or when “CLR” is entered as the password (Refer to Chapter 4, Section 4.14: Password Input), the assay parameters are overwritten and returned to their initial values. If the assay parameters have been saved beforehand (filename: **SYSTEM.PRM**), by loading back the saved parameters from it the analyzer is ready to operate as it has been. To save the assay parameters on an external storage device, see next section.

Assay Parameter Storage and Loading

Procedure

[Storage]

1) Confirm that the analyzer is in STAND-BY state.
2) Insert a formatted external storage device into the socket.
3) Press the CARD key on the MENU screen.
4) Display PRM SAVE using the COMMAND key.
5) Press the EXEC key.
6) Confirm that the stored assay parameter file (**SYSTEM.PRM**) is displayed.

[Loading]

1) Confirm that the analyzer is in STAND-BY state.
2) Insert the external storage device containing the assay parameters (**SYSTEM.PRM**) into the socket.
3) Press the CARD key on the MENU screen.
4) Display LOAD using the COMMAND key.
5) Press the EXEC key.
6) The assay parameters stored on the external storage device will be loaded and stored in the analyzer.

The filename valid for storing/loading the assay parameters is **SYSTEM.PRM** only. If there is already the **SYSTEM.PRM** file on the external storage device, it will be overwritten by new contents when performing assay parameters storage.

Point

When the analyzer is installed and the assay parameters are set, store the parameter file (**SYSTEM.PRM**) on the external storage device. Refer to Chapter 4, Section 4.7: Card (External storage device) for details.

7.2 Communication with a Host Computer

Results can be sent to a host computer using the RS-232C port (EIA-232 / EIA-574). Real-time transfer of each data set (every 1.6 minutes) or batch transfer of the transmitted list data using the recalculation function are both possible.

The outline of the host communications is shown below. Refer to the "Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 Host connection specifications" for detailed communication specifications and various settings. (This manual can be obtained from one of our sales representatives.)

(1) Communication start

When communicating with a host computer, press to highlight AT TRANS

key on the RS232C screen.

Each time results are output, they will be transmitted in the designated format (real-time transfer).

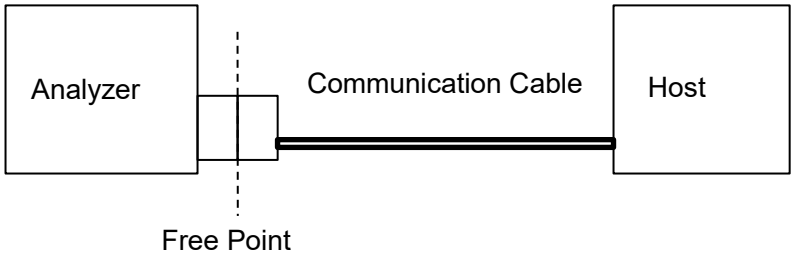
Batch transmission is possible by selecting TRANS using the COMMAND key after designating a data range from the list screen. A specific result can also be designated and re-transmitted from the RECALC screen.

(2) Communication specifications

Item	Specification
Transmission method	RS-232C, start-stop transmission, half-duplex
Rate	1200, 2400, 4800, 9600 bps
Transmitted code	ASCII
Data length	7 bit, 8 bit
Parity	Even, odd, none
Stop bits	1 bit, 2 bit

When the raw data transmission mode is selected (RAW mode), be sure to select 9600 bps due to the large volume of data.

(3) Connection



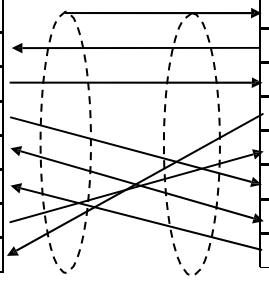
(4) Connector

A **D-Sub 9P** (male) is installed on the analyzer side as the connector.
The connector on the communication cable which connects to the analyzer is a **D-Sub 9S** (female).

(5) Pin Assignment

Analyzer Side (9 pin) Host Side (Ex. 25 pin)

Signal name	Pin No.
Receive data (RxD)	2
Transmit data (TxD)	3
Data terminal ready (DTR)	4
Signal GND (GND)	5
Data set ready (DSR)	6
Request to send (RTS)	7
Clear to send (CTS)	8



Pin No.	Signal name
1	Frame GND (FG)
2	Transmit data (TxD)
3	Receive data (RxD)
4	Request to send (RTS)
5	Clear to send (CTS)
6	Data set ready (DSR)
7	Signal GND (GND)
20	Data terminal ready (DTR)

(6) Communication Modes

There are two communication modes: the query mode, in which the analyzer queries a test order to the host using the sample ID after reading the bar code, and the result transmission mode, in which the analyzer transmits results to the host every time results are obtained. Various formats compatible with applications and the previous models (GHbV (A1c2.2 Plus)) are available for the result transmission mode. Non-handshake and handshake protocols are available as the basic transmission method. In addition, flow control is available as an option using X-ON/OFF code for the non-handshake protocol.

(7) Communication Formats

There are three available communication formats: G8 format (standard), and GHbV (A1c2.2 Plus) compatible format. Select the desired format using **TRANS G5/7 MODE** on the PARAMETER screen of the analyzer. With this parameter, data format (in JDS units, NGSP units, Mono S units or IFCC units) for transmitting assay results to the host is also defined as below.

TRANS G5/7 MODE is comprised of two digits as AB.

The last digit (B) defines communication format.

- Setting value 8: G8 format (default setting)
- Setting value 7: G7 model compatible format
- Setting value 6: GHbV (A1c2.2 Plus) model compatible format (When 5 digits are selected for the sample number, except when the sample is STAT or CALIB, the sample number is extended by adding a 0 to the top digit of the sample #)
- Setting value 5: GHbV (A1c2.2 Plus) model compatible format

Second digit from the last (A) is used when assay results in IFCC units are transmitted to the host. 0-3 can be set to this, but refer to “Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 Host connection specifications“ for details, which is provided fro the Tosoh sales representative upon request. When 1-3 is set to this digit, assay results in IFCC units are displayed on the LIST screen.

The parameter settings are made by the Clinical Support Specialist or service personnel and the set parameters are not normally displayed on the screen.

(8) BASIC mode, HI-LEVEL mode, and RAW mode

There are two modes in all communication formats: BASIC and HI-LEVEL. The primary difference in these modes is the transmission protocol. The non-handshake protocol is used in BASIC mode and the handshake protocol is used in the HI-LEVEL mode. In addition, the RAW mode (chromatographic data transmission) is available in the G7 and G8 formats, and is used with the same protocol as the HI-LEVEL mode. The various modes correspond to the following selection keys in the RS-232C screen of the analyzer.

BM key: BASIC mode
HM key: HI-LEVEL mode
RAW key: RAW mode (the protocol is the same as the HI-LEVEL mode)

(9) Query to host

When executing a query to a host, set the QUERY key on the RS-232C settings screen to ON (highlighted).
When analyzing all samples set on the loader without using the query mode, set the QUERY key to OFF (not highlighted).

7.3 Specifications

Main Specifications

Analytes:	HbA1c (SA1c), HbF, HbA1
Applicable samples:	Whole blood and diluted samples
Assay principle:	Ion exchange high performance liquid chromatography
Processing throughput:	1.6 min/sample (Variant Analysis Mode)
Detection method:	2-wavelength absorbance (detection wavelength: 415 nm)
Sampling unit	
Sampling volume:	3 µL for whole blood and 80 µL for diluted samples
Sample rack:	10 primary tubes or cups per rack
Sample loading capacity:	90 samples or 290 samples
Sample suction:	Nozzle suction
Sample injection:	Sample loop (4 µL)
Sample dilution:	Dilution by Hemolysis & Wash solution in the dilution port
Sample tubes or vials:	12-15mm diameter × 75-100mm primary tubes Sample cups (using adapter)
Sample ID recognition:	Bar code with maximum of 20 digits
Bar code standards:	NW-7 (Codabar), CODE39, ITF and CODE128 (initial setting), or JAN (UPC/EAN), Industrial 2 of 5 and COOP 2 of 5 (requires setting change)
Operation unit	
Display:	320 x 240 dot matrix monochromatic LCD
Input:	Pressure-sensitive touch panel / sheet keys
Output:	Thermal printer
Storage:	Smart Media card or USB stick For details about the usable external storage device and the number of sets of assay results that can be stored, refer to “Chapter 2, Section 2.3: Units and Functions, 4. Storage device”
Pump unit:	Single plunger pump (Max transport pressure: 15 MPa)
Column Temperature control:	Electronic cooling (Temperature: approx. 25°C)

Data processing unit:	RS-232C serial communication port (bi-directional)
	Data storage by internal memory (for up to 800 samples)
	Recalculation (reprinting) of achieved result
	Automatic startup by timer
	Error flag function for abnormal results
Calibration:	2-point method for HbA1c

Dimensions (prongs not included)

Main unit and 90SL combination:	530 (W) x 515 (D) x 482 (H) mm
Main unit and 290SL combination:	1120 (W) x 530 (D) x 482 (H) mm

Weight

Main unit:	approx. 26.5 kg
Sample Loader 90SL:	approx. 7.5 kg
Sample Loader 290SL:	approx. 25.0 kg

Operating Environment Conditions

Power supply / consumption (common to 90SL model and 290SL model):

	AC100 - 240 V, 50 / 60 Hz, 180 VA
- EU Area:	AC230 V, 50 Hz, 180 VA
- USA and Canada Area:	AC120 V, 60 Hz, 180 VA

Temperature:	15°C - 30°C
Humidity:	20% - 80% R.H. (without condensation)
Over voltage category:	II
Pollution degree:	2
Altitude:	up to 2,000 m
Electrical power quality:	Typical commercial or hospital environment
Dust:	Typical office level

Environment of Transportation and Storage

Temperature:	5°C - 50°C
Humidity:	80% R.H. or less (without condensation)
Others:	Keep dry and store indoors

Standard Conformity

EMC standard:	IEC60601-1-2: 2001
CISPR11 class and group categories:	Class A, Group 1
FCC:	Part 15, Sub Part B Class A

EN61010-1: 2001 (2nd Edition)

EN61010-2-081:2002, +A1: 2003, EN61010-2-101: 2002

UL61010-1, CAN/CSA C22.2 No. 61010-1-04

Bar code reader:	Class 1: IEC60825-1: 1994

Refer to Host Connection Specifications for more details.

Chapter 8 Warranty

This product has passed a rigorous inspection by Tosoh engineers. In the event of a malfunction, the product will be repaired according to the restrictions in this warranty policy. Contact Tosoh Technical Support for details at 800-248-6764.

Warranty Restrictions

Warranty period:
This warranty is valid for 1 year from the date of installation.

Warranty contents:
If a defect in the structure of the product causes a breakdown in spite of use according to the directions in the Operator's Manual, the product will be repaired free of charge.

Consumable parts and tubings are not included in the warranty.

A service contract for repair after the warranty period is available. Please contact your Tosoh System Sales Specialist or your Tosoh Field Service Engineer for conditions and costs. The option is available to purchase a service contract at the time of instrument purchase for a discount. This contract would be in effect after the warranty period.

The warranty period for repaired or replaced parts covered by the original warranty is the same as the original warranty, provided the part was repaired or replaced by Tosoh or its authorized agent.

Conditions invalidating the warranty:

A charge for repair of the product will be levied, even within the warranty period, if a breakdown or damage is caused by:

- Incorrect use or improper installation conditions.
- Independent repair, adjustment or remodeling of parts, circuits, software or othercomponents of the product by the customer.
- Movement or transport of the product after installation.
- Dropping the product or otherwise strongly striking the product.
- Fire, earthquake or other natural disasters.
- Use of an incorrect power source (voltage or frequency) or an abnormal voltage.
- Use of supplies or consumables not authorized by Tosoh.
- Repair, adjustment, or remodeling done by parties other than Tosoh or Tosoh‘s authorized agent.
- Damage caused by negligence or misuse by the customer including liquid spills intothe analyzer or dropping of foreign objects into the mechanical sample loader.

Notes:

Consumables listed as accessories in the Operator’s Manual for the Tosoh G8 Automated HPLC Analyzer are not included under the warranty. Use of consumable/expendables not supplied by Tosoh will void the analyzer warranty. Repair after the expired warranty period, if not covered by a service contract will incur a fee for time and materials. Details are available from your Tosoh System Sales Specialist or your Tosoh Field Service Engineer.

SUPPLEMENT TO OPERATOR'S MANUAL

WARRANTY AND RELATED TERMS

THIS SUPPLEMENT CONTAINS IMPORTANT INFORMATION REGARDING OUR WARRANTY. PLEASE READ IT CAREFULLY AND KEEP THIS SUPPLEMENT WITH YOUR OPERATOR'S MANUAL.
If the analyzer fails to meet the warranty set forth in the Operator's Manual during the warranty period, Tosoh Bioscience's sole liability and your exclusive remedy shall be limited to, at Tosoh Bioscience's option, either the repair or replacement of the analyzer, provided that Tosoh Bioscience's investigation and inspection disclose that (i) such defect or non-conformity developed under normal and proper use (including use of only Tosoh Bioscience authorized reagents) and (ii) the analyzer is covered under the warranty set forth in the Operator's Manual

THE WARRANTIES SET FORTH IN THE OPERATOR'S MANUAL, AS SUPPLEMENTED BY THIS SUPPLEMENT, ARE THE SOLE AND EXCLUSIVE WARRANTIES PROVIDED FOR THE ANALYZER AND REAGENTS (THE "PRODUCTS"). EXCEPT FOR SUCH WARRANTIES, TOSOH BIOSCIENCE MAKES NO AND DISCLAIMS ALL OTHER REPRESENTATIONS, GUARANTIES, CONDITIONS AND WARRANTIES OF ANY KIND WHATSOEVER, WHETHER DIRECT OR INDIRECT, EXPRESS OR IMPLIED, OR ARISING UNDER ANY STATUTE, ORDINANCE, COMMERCIAL USAGE OR OTHERWISE, INCLUDING WITHOUT LIMITATION ANY WARRANTY OR REPRESENTATION AS TO SUITABILITY, DURABILITY, DESIGN, OPERATION, OR CONDITION OF THE PRODUCTS (OR ANY PART THEREOF), OR THE MERCHANTABILITY OF THE PRODUCTS OR THEIR FITNESS FOR A PARTICULAR PURPOSE, OR AGAINST INFRINGEMENT OF INTELLECTUAL PROPERTY. SPECIFICALLY, TOSOH BIOSCIENCE DOES NOT WARRANT THAT THE PRODUCTS WILL MEET YOUR REQUIREMENTS. IF ANY IMPLIED WARRANTIES APPLY AS A MATTER OF LAW, THEY ARE LIMITED IN DURATION TO THE LENGTH OF THE APPLICABLE WARRANTY SET FORTH IN THE OPERATOR'S MANUAL.

Should warranty repair or service of the analyzer or any component thereof be necessary, it must be provided by Tosoh Bioscience or its authorized agents. Please contact us at 800-248-6764 for repair or service.

Your sole and exclusive remedy for Tosoh Bioscience's negligence, breach of warranty, breach of contract or for any other liability in any way connected with or arising out of the Products or warranty service furnished on the analyzer shall be the repair or replacement of non-conforming Products, or, if Tosoh Bioscience is unable or chooses not to repair or replace non-conforming Products, the crediting of the purchase price that has been paid for the non-conforming Products and the cancellation of any obligation to pay the unpaid portions of the purchase price of the non-conforming Products. (If Products were sold by Tosoh Bioscience to a distributor such crediting will be to the distributor's account.)

Tosoh Bioscience's liability with respect to any Product shall in no event exceed the purchase price paid to Tosoh Bioscience for such Product. IN NO EVENT SHALL TOSOH BIOSCIENCE BE LIABLE FOR COSTS OF PROCUREMENT OF SUBSTITUTE GOODS OR SERVICES, LOSS OF USE OR PROFITS OR ANY OTHER SPECIAL, INCIDENTAL, INDIRECT, PUNITIVE OR CONSEQUENTIAL DAMAGES, ARISING OUT OF OR RELATED TO THE USE OR PERFORMANCE OF THE PRODUCTS, HOWEVER CAUSED AND ON ANY THEORY OF LIABILITY, WHETHER IN AN ACTION FOR CONTRACT OR TORT (INCLUDING NEGLIGENCE) OR OTHERWISE, AND WHETHER OR NOT TOSOH BIOSCIENCE HAS BEEN ADVISED OF THE POSSIBILITY OF SUCH DAMAGES. EACH LIMITATION OF LIABILITY OR LIMITED OR EXCLUSIVE REMEDY SET FORTH HEREIN IS INDEPENDENT OF ANY OTHER LIMITATION OF REMEDY AND IF ANY SUCH LIMITATION OF REMEDY FAILS OF ITS ESSENTIAL PURPOSE OR IS OTHERWISE HELD TO BE UNENFORCEABLE, THAT SHALL NOT AFFECT THE VALIDITY OF ANY OTHER SUCH LIMITATION OF REMEDY.