ARCHITECT Insulin

REF 8K41-28

en

Insulin
8K41
F5-Y402-2 / R02
B8K4B0

Revised June 2018.

Package insert instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

WARNING: The Insulin assay value in a given specimen, as determined with assays from different manufacturers, can vary due to differences in assay methods and reagent specificity. The results reported by the laboratory to the physician must include the identity of the Insulin assay used. Values obtained with different assay methods cannot be used interchangeably. If, in the course of monitoring a patient, the assay method used for determining insulin levels serially is changed, additional sequential testing should be carried out. Prior to changing assays, the laboratory MUST confirm baseline values for patients being serially monitored.

Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA). Such specimens may show either falsely elevated or depressed values when tested with assay kits which employ mouse monoclonal antibodies. These specimens should not be assayed with the ARCHITECT Insulin assay. Refer to the section **LIMITATIONS OF THE PROCEDURE** in this package insert.

NAME

ARCHITECT Insulin

INTENDED USE

The ARCHITECT Insulin assay is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of human insulin in human serum or plasma.

SUMMARY AND EXPLANATION OF THE TEST

Insulin is a polypeptide hormone (MW 6000) composed of two nonidentical chains, A and B, which are joined by two disulfide bonds. Insulin is formed from a precursor, proinsulin (MW 9000), in the beta cells of the pancreas. In proinsulin, the A and B chains are joined by a connecting peptide, referred to as the C-peptide. Both insulin and C-peptide are stored in secretory granules of the islet cells of the pancreas and are then secreted.[1]

Insulin secretion follows two basic mechanisms, tonic secretion and biphasic secretion.[1] The basal or tonic secretion is independent of stimulation by exogenous glucose but is modulated by the fluctuations in physiological levels of glucose. The biphasic secretion is primarily a direct response from stimulation by exogenous glucose. Stimulation of insulin secretion can be caused by many factors including hyperglycemia, glucagon, amino acids, and by complex mechanisms involving growth hormone or catecholamines.[1] Increased levels of Insulin are found with obesity, Cushing's Syndrome, oral contraceptives, acromegaly, insulinoma and hyperthyroidism.[2, 3] Decreased levels of insulin are found in overt diabetes mellitus (although this may not be clearly expressed in early stages of the condition) and by part of a complex mechanism involving catecholamines.[1]

"Immunoreactive insulin" (IRI) is a term often used to refer to the component of circulating insulin and insulin-like biological activity which can be measured using antibodies against insulin. Insulinomas may produce various forms of insulin and proinsulin-like material and show total immunoreactive insulin at normal or elevated levels.[4-8] Since proinsulin and insulin both contain A and B polypeptide chains, there is a possible cross-reactivity with antibodies generated against insulin. The ARCHITECT Insulin assay shows no cross-reactivity with proinsulin (≤ 0.1% at 10^6 pg/mL). Another possible interference is brought about by insulin antibodies which develop in patients treated with bovine or porcine insulin.[9]

Immunoassays for insulin have been widely used to provide supplementary information, first, for the diagnosis of diabetes mellitus and, second, for differential diagnosis of fasting hypoglycemia to discriminate between insulinoma and factitious hypoglycemia. In these applications, the ratio of immunoreactive insulin to blood glucose (I/G) may be more valuable than the insulin level alone.[1] Furthermore, a single random blood sample may provide insufficient information due to wide variations in the time responses of insulin levels and blood glucose which are found among individuals and various clinical conditions. Other uses of insulin assays have been suggested by the finding of an increase in risk factors for coronary artery disease among healthy persons with hyperinsulinemia and normal glucose tolerance.[10]

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT Insulin assay is a one-step immunoassay to determine the presence of human insulin in human serum or plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex.

1. Sample, anti-insulin coated paramagnetic microparticles and anti-insulin acridinium-labeled conjugate are combined to create a reaction mixture. The Insulin present in the sample binds to the anti-insulin coated microparticles and anti-insulin acridinium-labeled conjugate.
2. After washing, pre-trigger and trigger solutions are then added to the reaction mixture.
3. The resulting chemiluminescent reaction is measured as relative light units (RLUs). There is a direct relationship between the amount of insulin in the sample and the RLUs detected by the ARCHITECT iSystem optics.

For additional information on system and assay technology, refer to the ARCHITECT System Operations Manual, Section 3.

REAGENTS

Kit Contents

ARCHITECT Insulin 8K41

REF	8K41-28
Σ	100
MICROPARTICLES	1 x 6.6 mL
CONJUGATE	1 x 5.9 mL

MICROPARTICLES Antibody to human insulin (mouse, monoclonal) coated microparticles in MOPS buffer with protein (bovine) stabilizer. Minimum concentration: 0.08% solids. Preservatives: sodium azide and other antimicrobial agents.

CONJUGATE Acridinium-labeled antibody to human insulin (mouse, monoclonal) conjugate in MES buffer with protein (bovine) stabilizer. Minimum concentration: 0.09 µg/mL. Preservatives: sodium azide and other antimicrobial agents.

Other Reagents

PRE-TRIGGER SOLUTION ARCHITECT Pre-Trigger Solution containing 1.32% (w/v) hydrogen peroxide.

TRIGGER SOLUTION ARCHITECT Trigger Solution containing 0.35 N sodium hydroxide.

WASH BUFFER ARCHITECT Wash Buffer containing phosphate buffered saline solution. Preservatives: antimicrobial agents.

Warnings and Precautions

- IVD
- For *In Vitro* Diagnostic Use

Safety Precautions

CAUTION: This product requires the handling of human specimens. It is recommended that all human-sourced materials be considered potentially infectious and handled in accordance with the OSHA Standard on Bloodborne Pathogens. Biosafety Level 2 or other appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.[11-14]

The following warnings and precautions apply to: MICROPARTICLES	
Contains 4-Morpholinopropanesulphonic acid and sodium azide.	
H316*	Causes mild skin irritation.
EUH032	Contact with acids liberates very toxic gas.
Response	
P332+P313*	If skin irritation occurs: Get medical advice / attention.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

* Not applicable where regulation EU 1272/2008 (CLP) or OSHA Hazard Communication 29CFR 1910.1200 (HCS) 2012 has been implemented.

The following warnings and precautions apply to: CONJUGATE	
Contains sodium azide.	
EUH032	Contact with acids liberates very toxic gas.
P501	Dispose of contents / container in accordance with local regulations.

Safety Data Sheets are available at www.abbottdiagnostics.com or contact your local representative.

For a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

Reagent Handling

- Do not use reagent kits beyond the expiration date.
- **Do not pool reagents within a kit or between kits.**
- Before loading the reagent kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may have settled during shipment. For microparticle mixing instructions, refer to the **PROCEDURE, Assay Procedure** section of this package insert.
- **Septums MUST be used to prevent reagent evaporation and contamination and to ensure reagent integrity. Reliability of assay results cannot be guaranteed if septums are not used according to the instructions in this package insert.**
  - To avoid contamination, wear clean gloves when placing a septum on an uncapped reagent bottle.
  - Once a septum has been placed on an open reagent bottle, **do not invert the bottle** as this will result in reagent leakage and may compromise assay results.
  - Over time, residual liquids may dry on the septum surface. These are typically dried salts and have no effect on assay efficacy.

For a detailed discussion of handling precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 7.

Reagent Storage

When stored and handled as directed, reagents are stable until the expiration date.

	Storage Temperature	Maximum Storage Time	Additional Storage Instructions
Unopened/ Opened*	2-8°C	Until expiration date	May be used immediately after removal from 2-8°C storage. Store in upright position.
On board	System temperature	30 days	Discard after 30 days. For information on tracking onboard time, refer to the ARCHITECT System Operations Manual, Section 5.

* Reagents may be stored on or off the ARCHITECT iSystem. If reagents are removed from the system, store them at 2-8°C (with septums and replacement caps) in an upright position. For reagents stored off the system, it is recommended that they be stored in their original trays and boxes to ensure they remain upright. **If the microparticle bottle does not remain upright (with a septum installed) while in refrigerated storage off the system, the reagent kit must be discarded.** For information on unloading reagents, refer to the ARCHITECT System Operations Manual, Section 5.

Indications of Reagent Deterioration

When a control value is out of the specified range, it may indicate deterioration of the reagents or errors in technique. Associated test results are invalid, and samples must be retested. Assay recalibration may be necessary. For troubleshooting information, refer to the ARCHITECT System Operations Manual, Section 10.

INSTRUMENT PROCEDURE

The ARCHITECT Insulin assay file must be installed on the ARCHITECT iSystem prior to performing the assay.

For detailed information on assay file installation and viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.

For information on printing assay parameters, refer to the ARCHITECT System Operations Manual, Section 5.

For a detailed description of system procedures, refer to the ARCHITECT System Operations Manual.

Alternate Result Units

Edit assay parameter "Result concentration units" to select an alternate unit.

Conversion formula:

(Concentration in Default result unit) x (Conversion factor) = (Concentration in Alternate result unit)

Default result unit	Conversion factor	Alternate result unit
µU/mL	7.175	pmol/L

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

Verified specimen types to be used with this assay:

Specimen Types	Collection Tubes
Serum	Serum
	Serum separator tubes
Plasma	Potassium EDTA
	Sodium EDTA
	Sodium heparin
	Sodium fluoride

- Other specimen collection tube types have not been tested with this assay.
- Liquid anticoagulants may have a dilution effect resulting in lower concentrations for individual patient specimens.
- The instrument does not provide the capability to verify specimen type. It is the responsibility of the operator to verify that the correct specimen types are used in the assay.

Specimen Conditions

- Do not use specimens with the following conditions:
  - heat-inactivated
  - grossly hemolyzed
  - obvious microbial contamination
  - cadaver specimens or any other body fluids
- For accurate results, serum and plasma specimens should be free of fibrin, red blood cells, and other particulate matter. Serum specimens from patients receiving anticoagulant or thrombolytic therapy may contain fibrin due to incomplete clot formation.
- To prevent cross contamination, use of disposable pipettes or pipette tips is recommended.

Preparation for Analysis

- Follow the tube manufacturer's processing instructions for collection tubes. Gravity separation is not sufficient for specimen preparation.
- Mix thawed specimens thoroughly by low speed vortexing or by inverting 10 times. Visually inspect the specimens. If layering or stratification is observed, continue mixing until specimens are visibly homogeneous.
- To ensure consistency in results, centrifuge specimens before testing if
  - they contain fibrin, red blood cells, or other particulate matter
  - they were frozen and thawed or
  - which are hazy or cloudy in appearance
- Sample should be tested as soon as possible after drawing for the reason that the determined value may show lower levels because of insulin degrading enzyme existing in the red blood cell.
- Ensure that complete clot formation in serum specimens has taken place prior to centrifugation. Some specimens, especially those from patients receiving anticoagulant or thrombolytic therapy, may exhibit increased clotting time. If the specimen is centrifuged before a complete clot forms, the presence of fibrin may cause erroneous results.
- Transfer clarified specimen to a sample cup or secondary tube for testing. For centrifuged specimens with a lipid layer, transfer only the clarified specimen and not the lipemic material.
- Inspect all specimens for bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.

Specimen Storage

Specimen Type	Storage Temperature	Maximum Storage Time
Serum/Plasma	-10°C	≤ 7 days

If testing will be delayed, serum or plasma should be removed from the clot, serum separator, or red blood cells.

Specimens may be stored for up to 7 days at -10°C or colder prior to being tested.

Avoid multiple freeze/thaw cycles.

Specimen Shipping

- Package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.
- Do not exceed the storage limitations listed above.

PROCEDURE

Materials Provided

8K41 ARCHITECT Insulin Reagent Kit

Materials Required but not Provided

- ARCHITECT Insulin Assay file obtained from the ARCHITECT iSystem e-Assay CD-ROM found on www.abbottdiagnostics.com.
- 8K41-03 ARCHITECT Insulin Calibrators
- 8K41-12 ARCHITECT Insulin Controls
- ARCHITECT Pre-Trigger Solution
- ARCHITECT Trigger Solution
- ARCHITECT Wash Buffer
- ARCHITECT Reaction Vessels
- ARCHITECT Sample Cups
- ARCHITECT Septum
- ARCHITECT Replacement Caps
- Pipettes or pipette tips (optional) to deliver the volumes specified on the patient or control order screen.

For information on materials required for maintenance procedures, refer to the ARCHITECT System Operations Manual, Section 9.

Assay Procedure

- Before loading the reagent kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may have settled during shipment. After the first time the microparticles have been loaded, no further mixing is required.
  - **Invert the microparticle bottle 30 times.**
  - Visually inspect the bottle to ensure microparticles are resuspended. If microparticles are still adhered to the bottle, continue to invert the bottle until the microparticles have been completely resuspended.
  - **If the microparticles do not resuspend, DO NOT USE. Contact your local Abbott representative.**
  - Once the microparticles have been resuspended, place a septum on the bottle. For instructions about placing septums on bottles, refer to the **Reagent Handling** section of this package insert.
- Load the reagent kit on the ARCHITECT iSystem.
  - Verify that all necessary reagents are present.
  - Ensure that septums are present on all reagent bottles.
- Order calibration, if necessary.
  - For information on ordering calibrations, refer to the ARCHITECT System Operations Manual, Section 6.
- Order tests.
  - For information on ordering patient specimens and controls and for general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
- Minimum sample cup volume is calculated by the system and printed on the Orderlist report. To minimize the effects of evaporation, verify adequate sample cup volume is present prior to running the test.

  Maximum number of replicates sampled from the same sample cup: 10
  - Priority:

    Sample volume for first test: 150 µL

    Sample volume for each additional test from same sample cup: 24 µL
  - ≤ 3 hours on board:

    Sample volume for first test: 150 µL

    Sample volume for each additional test from same sample cup: 24 µL
  - > 3 hours on board: additional sample volume is required
  - If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.

- Prepare ARCHITECT Insulin Calibrators and Controls.
  - Mix calibrator(s) and controls by gentle inversion before use.
  - Hold bottles **vertically** and dispense recommended volumes into each respective sample cup.
  - Recommended volumes:

    for each calibrator: 4 drops

    for each control: 4 drops
- Load samples.
  - For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5.
- Press RUN.
- For additional information on principles of operation, refer to the ARCHITECT System Operations Manual, Section 3.
- For optimal performance, it is important to perform routine maintenance as described in the ARCHITECT System Operations Manual, Section 9. Perform maintenance more frequently when required by laboratory procedures.

Specimen Dilution Procedures

Specimens with an insulin value exceeding 300 µU/mL are flagged with the code "> 300.0" and may be diluted using either the Automated Dilution Protocol or the Manual Dilution Procedure.

Automated Dilution Protocol

The system performs a 1:2 dilution of the specimen and automatically calculates the concentration of the specimen before dilution and reports the result.

Manual Dilution Procedure

Suggested dilution: 1:10

1. Add 20 µL of the patient specimen to 180 µL of ARCHITECT Insulin Calibrator A (8K41-03).
2. The operator must enter the dilution factor in the Patient or Control order screen. The system will use this dilution factor to automatically calculate the concentration of the sample before dilution and report the result. The result should be > 3.0 µU/mL before the dilution factor is applied.

To avoid contamination of Calibrator A, dispense several drops of Calibrator A into a clean test tube prior to pipetting.

For detailed information on ordering dilutions, refer to the ARCHITECT System Operations Manual, Section 5.

Calibration

- Test Calibrators A-F duplicate. The calibrators should be priority loaded.

  A single sample of each control level must be tested to evaluate the assay calibration. Ensure that assay control values are within the ranges specified in the respective control package insert.
- Calibration Range: 0 - 300 µU/mL.
- Once an ARCHITECT Insulin calibration is accepted and stored, all subsequent samples may be tested without further calibration unless:
  - A reagent kit with a new lot number is used or
  - Controls are out of range.
- For detailed information on how to perform an assay calibration, refer to the ARCHITECT System Operations Manual, Section 6.

Quality Control Procedures

The recommended control requirement for the ARCHITECT Insulin assay is that a single sample of each control level be tested once every 24 hours each day of use. If the quality control procedures in your laboratory require more frequent use of controls to verify test results, follow your laboratory-specific procedures.

Additional controls may be tested in accordance with local, state, and/or federal regulations or accreditation requirements and your laboratory's quality control policy.

Each laboratory should establish control ranges to monitor the acceptable performance of the assay. If a control is out of its specified range, the associated sample results are invalid and the samples must be retested. Recalibration may be indicated.

Verification of Assay Claims

For protocols to verify package insert claims, refer to the ARCHITECT System Operations Manual, Appendix B.

RESULTS

Calculation

The ARCHITECT Insulin assay utilizes a 4 Parameter Logistic Curve fit data reduction method (4PLC, Y-weighted) to generate a calibration curve.

For information on alternate result units, refer to the **INSTRUMENT PROCEDURE, Alternate Result Units** section of this package insert.

Flags

Some results may contain information in the Flags field. For a description of the flags that may appear in this field, refer to the ARCHITECT System Operations Manual, Section 5.

Measurement Range (Reportable Range)

The measurement range for the ARCHITECT Insulin assay is 1.0 µU/mL to 300.0 µU/mL.

LIMITATIONS OF THE PROCEDURE

- If the insulin results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- For diagnostic purposes, results should be used in conjunction with other data; e.g., symptoms, results of other tests, clinical impressions, etc.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays. Patients routinely exposed to animals or to animal serum products can be prone to this interference, and anomalous values may be observed. Additional information may be required for diagnosis.[15]
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA).[16, 17] Specimens containing HAMA may produce anomalous values when tested with assay kits (such as ARCHITECT Insulin) that employ mouse monoclonal antibodies.[17]
- Insulin levels may be measured lower in patients with insulin autoimmune syndrome or familial high pro-insulinemia.
- Hemolyzed samples should not be used, since enzymatic degradation of insulin may occur and result in lower assay values.[18, 19] However, purified hemoglobin up to 500 mg/dL has been shown not to interfere.
- Specimens from patients treated with bovine or porcine insulin may contain insulin antibodies which could show interference in the assay.[9]

EXPECTED VALUES

It is recommended that each laboratory establish its own normal range. The reference ranges vary between countries due to differences in body size and nutrition.

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

The ARCHITECT Insulin assay precision is ≤ 7% total CV. A study was performed as described in the National Committee for Clinical Laboratory Standards (NCCLS) Protocol EP5-A2.[20] Seven samples consisting of four serum based panels and three Insulin Controls were assayed in replicates of two at two separate times per day for twenty days (n=80 for each sample), using three lots of reagents. Data from this study are summarized in the following table.

Sample	Lot	Mean insulin (µU/mL)	Repeatability SD	Repeatability %CV	Within-laboratory SD	Within-laboratory %CV
Low Control	1	7.47	0.270	3.6	0.334	4.5
	2	7.61	0.322	4.2	0.395	5.2
	3	7.64	0.266	3.5	0.360	4.7
Medium Control	1	38.35	0.785	2.0	0.889	2.3
	2	37.80	0.647	1.7	1.041	2.8
	3	38.47	0.792	2.1	0.910	2.4
High Control	1	119.41	2.135	1.8	2.456	2.1
	2	118.56	2.198	1.9	2.507	2.1
	3	121.10	2.447	2.0	2.795	2.3
Panel 1	1	8.35	0.260	3.1	0.354	4.2
	2	8.66	0.261	3.0	0.399	4.6
	3	8.76	0.298	3.4	0.311	3.6
Panel 2	1	18.24	0.738	4.0	0.816	4.5
	2	18.38	0.381	2.1	0.656	3.6
	3	18.68	0.395	2.1	0.551	3.0
Panel 3	1	53.73	1.007	1.9	1.333	2.5
	2	53.19	1.185	2.2	1.528	2.9
	3	55.08	1.261	2.3	1.392	2.5
Panel 4	1	164.51	2.810	1.7	3.111	1.9
	2	164.19	3.286	2.0	3.540	2.2
	3	168.47	3.950	2.3	3.950	2.3

Recovery

Known amounts of human insulin were added to normal human serum and plasma samples. The concentration of insulin was determined using the ARCHITECT Insulin assay and the resulting percent recovery was calculated.

Sample Type	Endogenous Level (µU/mL)	Insulin Added (µU/mL)	Insulin Observed (µU/mL)	Percent Recovery
Serum				
1	4.79	19.67	23.22	93.6
	4.79	60.57	60.30	91.6
	4.79	199.23	188.38	92.1
2	13.72	19.67	32.44	95.1
	13.72	60.57	72.58	97.2
	13.72	199.23	200.24	93.6
3	11.53	19.67	30.23	95.1
	11.53	60.57	68.07	93.4
	11.53	199.23	192.99	91.1
4	5.01	19.67	23.86	95.8
	5.01	60.57	62.33	94.6
	5.01	199.23	190.64	93.2
5	2.04	19.67	20.52	93.9
	2.04	60.57	59.12	94.2
	2.04	199.23	186.72	92.7
Plasma				
1	6.00	19.67	25.26	97.9
	6.00	60.57	64.80	97.1
	6.00	199.23	193.50	94.1
2	6.23	19.67	25.77	99.3
	6.23	60.57	67.78	101.6
	6.23	199.23	201.71	98.1
3	8.77	19.67	27.59	95.7
	8.77	60.57	66.30	95.0
	8.77	199.23	194.45	93.2
4	8.17	19.67	26.94	95.4
	8.17	60.57	63.57	91.5
	8.17	199.23	195.50	94.0
5	6.11	19.67	24.54	93.7
	6.11	60.57	62.93	93.8
	6.11	199.23	190.73	92.7

$$\% \text{ Recovery} = \frac{\text{Insulin Observed (µU/mL)} - \text{Endogenous Level (µU/mL)}}{\text{Insulin Added (µU/mL)}} \times 100$$

Analytical Sensitivity

Analytical sensitivity is defined as the lower limit of detection and is estimated as the mean of the blank sample plus 2 times the SD obtained from the blank sample. The ARCHITECT Insulin assay is designed to have a sensitivity of ≤ 1.0 µU/mL.

Specificity

The specificity of the ARCHITECT Insulin assay was determined by testing sera containing the compounds listed below. These compounds showed less than 10% interference in the ARCHITECT Insulin assay at the levels indicated.

Test Compound	Test Concentration
Bilirubin	20 mg/dL
Hemoglobin	500 mg/dL
Total Protein	12 g/dL
Triglycerides	3000 mg/dL

The cross-reactivity with Proinsulin (1,000,000 pg/mL), with C-Peptide (10,000,000 pg/mL) and with Glucagon (10,000,000 pg/mL) was determined as below in the ARCHITECT Insulin assay.

Substance	Concentration	Cross-reactivity (%)
Proinsulin	10^6 pg/mL	≤ 0.1
C-Peptide	10^7 pg/mL	≤ 0.001
Glucagon	10^7 pg/mL	≤ 0.001

Carryover

No detectable carryover (less than 0.5 µU/mL) was observed when a sample containing 15,000 µU/mL of insulin was assayed.

BIBLIOGRAPHY

1. Travis JC. *Clinical Radioimmunoassay: State-of-the-Art.* Anaheim, CA: Scientific Newsletters/Radioassay-Ligand Assay Publ; 1980:89-92.
2. Jacobs DS, editor. *Laboratory Test Handbook*. Cleveland, OH: Lexi-Comp/Mosby; 1988:139.
3. DeVisscher M, editor. *Comprehensive Endocrinology: The Thyroid Gland*. New York, NY: Raven; 1980:289.
4. Robbins DC, Tager HS, Rubenstein AH. Biologic and clinical importance of proinsulin. *N Engl J Med* 1984;310(18):1165-1175.
5. Creutzfeldt W, Arnold R, Creutzfeldt C, et al. Biochemical and morphological investigations of 30 human insulinomas. *Diabetologia* 1973;9(3):217-231.
6. Creutzfeldt C, Track NS, Creutzfeldt W. In vitro studies of the rate of proinsulin and insulin turnover in seven human insulinomas. *Eur J Clin Invest* 1973;3(5):371-384.
7. Gorden P, Freychet P, Nankin H. A unique form of circulating insulin in human islet cell carcinoma. *J Clin Endocrinol Metab* 1971;33(6):983-987.
8. Alsever RN, Roberts JP, Gerber JG, et al. Insulinoma with low circulating insulin levels: the diagnostic value of proinsulin measurements. *Ann Intern Med* 1975;82(3):347-350.
9. Tietz NW, editor. *Clinical Guide to Laboratory Tests.* 2nd ed. Philadelphia, PA: WB Saunders; 1990:333.
10. Zavaroni I, Bonora E, Pagliara M, et al. Risk factors or coronary artery disease in healthy persons with hyperinsulinemia and normal glucose tolerance. *N Engl J Med* 1989;320(11):702-706.
11. US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, Bloodborne pathogens.
12. US Department of Health and Human Services. *Biosafety in Microbiological and Biomedical Laboratories*. 5th ed. Washington, DC: US Government Printing Office; December 2009.
13. World Health Organization. *Laboratory Biosafety Manual*. 3rd ed. Geneva: World Health Organization; 2004.
14. Clinical and Laboratory Standards Institute (CLSI). *Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline—Fourth Edition.* CLSI Document M29-A4. Wayne, PA: CLSI; 2014.
15. Boscato LM, Stuart MC. Heterophilic antibodies: a problem for all immunoassays. *Clin Chem* 1988;34(1):27-33.
16. Schroff RW, Foon KA, Beatty SM, et al. Human anti-murine immunoglobulin responses in patients receiving monoclonal antibody therapy. *Cancer Res* 1985;45(2):879-885.

17. Primus FJ, Kelley EA, Hansen HJ, et al. “Sandwich”-type immunoassay of carcinoembryonic antigen in patients receiving murine monoclonal antibodies for diagnosis and therapy. *Clin Chem* 1988;34(2):261-264.
18. Ziegler M, Michael R, Hommel H, et al. The interference of hemolysis on radioimmunoassay of insulin and its prevention by pre-incubation with anti-insulin serum. *J Clin Endocrinol Metab* 1972;35(2):317-318.
19. Brodal BP. Evidence of an enzymatic degradation of insulin in blood in vitro. *Eur J Biochem* 1971;18(2):201-206.
20. National Committee for Clinical Laboratory Standards (NCCLS). *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline—Second Edition.* NCCLS Document EP5-A2. Wayne, PA: NCCLS; 2004.

Key to Symbols

	Consult instructions for use
	Manufacturer
	Sufficient for
	Temperature limitation
	Use by/Expiration date
CONJUGATE	Conjugate
CONTAINS: AZIDE	Contains Sodium Azide. Contact with acids liberates very toxic gas.
CONTROL NO.	Control Number
DISTRIBUTED IN THE USA BY	Distributed in the USA by
INFORMATION FOR USA ONLY	Information needed for United States of America only
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
MICROPARTICLES	Microparticles
PRE-TRIGGER SOLUTION	Pre-Trigger Solution
PRODUCED FOR ABBOTT BY	Produced for Abbott by
PRODUCT OF JAPAN	Product of Japan
REACTION VESSELS	Reaction Vessels
REAGENT LOT	Reagent Lot
REF	List Number
REPLACEMENT CAPS	Replacement Caps
SAMPLE CUPS	Sample Cups
SEPTUM	Septum
SN	Serial number
TRIGGER SOLUTION	Trigger Solution
WASH BUFFER	Wash Buffer


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