Access
Immunoassay Systems

TOTAL βhCG
REF 33500

Intended Use

The Access Total βhCG assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of total βhCG levels in human serum and plasma using the Access Immunoassay Systems.

Summary and Explanation

Human chorionic gonadotropin (hCG) is a glycoprotein hormone, produced by the placenta, with structural similarity to the pituitary hormones FSH, TSH, and LH. The alpha subunit (MW 15,000–20,000 daltons) is common to all of these hormones but the beta subunits differ, and confer immunological and biological specificity. Beta hCG (MW 25,000–30,000 daltons) shares several peptide sequences with beta LH, but has a unique carboxyl terminal region.[1,2,3]

Shortly after implantation of a fertilized ovum into the uterine wall, the trophoblast begins to produce hCG. The hormone maintains steroid secretions of the corpus luteum until the placenta can do so.[4] During a normal pregnancy, hCG is generally approximately 50 mIU/mL (IU/L) in the week after conception, and doubles every 1.5–3 days for the first six weeks.[5] Levels continue to rise until the end of the first trimester, then gradually fall to a lower level for the remainder of the pregnancy. After delivery, hCG returns to < 5 mIU/mL (IU/L) and is usually undetectable several days postpartum.

The hormone is an excellent marker for pregnancy. Healthy, non-pregnant individuals have low (< 5 mIU/mL [IU/L]) to undetectable hCG levels. During pregnancy, hCG concentrations increase as noted above and then show a gradual decrease after the first trimester. Unusually low or rapidly declining levels may indicate an abnormal condition such as an ectopic pregnancy or impending spontaneous abortion.[6]

Originally bioassay systems measured hCG by measuring gonadal tissue response in various animals. These methods exhibited insufficient sensitivity, were difficult to perform, and required large volumes of sample. Tests to measure urine hCG traditionally employed latex agglutination or agglutination inhibition methods. With the development of radioimmunoassay techniques for the measurement of hCG by Vaitukaitis et al. in 1972, more sensitive and rapid assays for hCG became available.[7] Subsequent development of two-site immuno-radiometric assays (IRMA) provided assays with increased sensitivity, specificity, and precision.[8]

Principles of the Procedure

The Access Total βhCG assay is a two-site immunoenzymatic ("sandwich") assay. A sample is added to a reaction vessel with rabbit anti-βhCG-alkaline phosphatase conjugate, and paramagnetic particles coated with goat anti-mouse IgG: mouse monoclonal anti-βhCG complexes. The hCG binds to the immobilized monoclonal anti-βhCG on the solid phase while, at the same time, the rabbit anti-βhCG-alkaline phosphatase conjugate reacts with different antigenic sites on the hCG. After incubation in a reaction vessel, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. Then, the chemiluminescent substrate Lumi-Phos* 530 is added to the vessel and light generated by the reaction is measured with a luminometer. The light production is directly proportional to the concentration of hCG in the sample. The amount of analyte in the sample is determined from a stored, multi-point calibration curve.

Product Information

Access Total βhCG Reagent Pack

Cat. No. 33500: 100 determinations, 2 packs, 50 tests/pack

- Provided ready to use.
- Store upright and refrigerate at 2 to 10°C.
- Refrigerate at 2 to 10°C for a minimum of two hours before use on the instrument.
- Stable until the expiration date stated on the label when stored at 2 to 10°C.
- Stable at 2 to 10°C for 28 days after initial use.
- Signs of possible deterioration are a broken elastomeric layer on the pack or control values out of range.
- If the reagent pack is damaged (i.e., broken elastomer), discard the pack.
- All antisera are polyclonal unless otherwise indicated.

R1a:	Paramagnetic particles coated with goat anti-mouse IgG: mouse monoclonal anti-βhCG complexes suspended in TRIS buffered saline, with surfactant, bovine serum albumin (BSA), < 0.1% sodium azide, and 0.1% ProClin** 300.
R1b:	Rabbit anti-βhCG alkaline phosphatase (bovine) conjugate diluted in TRIS buffered saline, with surfactant, BSA, protein (goat, rabbit, mouse), < 0.1% sodium azide, and 0.25% ProClin 300.

Warnings and Precautions

- For *in vitro* diagnostic use.
- Patient samples and blood-derived products may be routinely processed with minimum risk using the procedure described. However, handle these products as potentially infectious according to universal precautions and good clinical laboratory practices, regardless of their origin, treatment, or prior certification. Use an appropriate disinfectant for decontamination. Store and dispose of these materials and their containers in accordance with local regulations and guidelines.
- Sodium azide may react with lead and copper plumbing to form highly explosive metal azides. On disposal of liquids, flush with a large volume of water to prevent azide build-up.[9]
- Xi. Irritant: 0.25% ProClin 300.

R 43: May cause sensitization by skin contact.
S 28-37: After contact with skin, wash immediately with plenty of soap and water. Wear suitable gloves.

- The Material Safety Data Sheet (MSDS) is available upon request.

Specimen Collection and Preparation

1. Serum and plasma (heparin) are the recommended samples.
2. The role of preanalytical factors in laboratory testing has been described in a variety of published literature.[10,11,12] To minimize the effect of preanalytical factors observe the following recommendations for handling, processing, and storing blood samples:[11]
   - Collect all blood samples observing routine precautions for venipuncture.
   - Allow serum samples to clot completely before centrifugation.
   - Keep tubes stoppered at all times.
   - Within two hours after centrifugation, transfer at least 500 µL of cell-free sample to a storage tube. Tightly stopper the tube immediately.
   - Store samples tightly stoppered at room temperature (15 to 30°C) for no longer than eight hours.
   - If the assay will not be completed within eight hours, refrigerate the samples at 2 to 8°C.
   - If the assay will not be completed within 48 hours, or for shipment of samples, freeze at -20°C or colder.
   - Thaw samples only once.

3. Use the following guidelines when preparing specimens:
   - Ensure residual fibrin and cellular matter has been removed prior to analysis.
   - Follow blood collection tube manufacturer's recommendations for centrifugation.
4. Each laboratory should determine the acceptability of its own blood collection tubes and serum separation products. Variations in these products may exist between manufacturers and, at times, from lot-to-lot.
5. Frozen specimens can be stored up to six months before testing.[13]

Materials Provided

R1 Access Total βhCG Reagent Packs

Materials Required But Not Provided

1. Access Total βhCG Calibrators
   Provided at zero and approximately 5, 25, 150, 500 and 1000 mIU/mL (IU/L).
   Cat. No. 33505
2. Quality Control (QC) materials: commercial control material
3. Access Substrate
   Cat. No. 81906
4. **Access, Access 2, SYNCHRON LXi:**
   Access Wash Buffer II, Cat. No. A16792
   UniCel DxI:
   UniCel DxI Wash Buffer II, Cat. No. A16793
   UniCel DxI Access Immunoassay Systems Wash Buffer II, Cat. No A79784 (Diluent pack for use with the UniCel DxI system onboard dilution feature.)

Procedural Comments

1. Refer to the appropriate system manuals and/or Help system for a specific description of installation, start-up, principles of operation, system performance characteristics, operating instructions, calibration procedures, operational limitations and precautions, hazards, maintenance, and troubleshooting.
2. Mix contents of new (unpunctured) reagent packs by gently inverting pack several times before loading on the instrument. Do not invert open (punctured) packs.
3. Use twenty-five (25) µL of sample for each determination in addition to the sample container and system dead volumes. Use twenty (20) µL of sample in addition to the sample container and system dead volumes for each determination run with the DxI system onboard dilution feature. Refer to the appropriate system manuals and/or Help system for the minimum sample volume required.
4. The system default unit of measure for sample results is mIU/mL. To change sample reporting units to the International System of Units (SI units), IU/L, refer to the appropriate system manuals and/or Help system. To manually convert concentrations to the International System, multiply mIU/mL by multiplication factor 1.

Procedure

Refer to the appropriate system manuals and/or Help system for information on managing samples, configuring tests, requesting tests, and reviewing test results.

For assaying samples containing < 1000 mIU/mL total βhCG, select **TβhCG2** as the test name. Select **Dil-hCG2** as the test name for assaying samples containing > 1000 mIU/mL. Alternatively, DxI users may use the DxI onboard dilution feature by selecting **d-ThCG** as the test name for assaying samples containing > 1000 mIU/mL. The same reagent pack is used for all assays.

Calibration Details

An active calibration curve is required for all tests. For the Access Total βhCG assay, calibration is required every 28 days. Refer to the appropriate system manuals and/or Help system for information on calibration theory, configuring calibrators, calibrator test request entry, and reviewing calibration data.

Quality Control

Quality control materials simulate the characteristics of patient samples and are essential for monitoring the system performance of immunochemical assays. Because samples can be processed at any time in a "random access" format rather than a "batch" format, quality control materials should be included in each 24-hour time period.[14] Include commercially available quality control materials that cover at least two levels of analyte. More frequent use of controls or the use of additional controls is left to the discretion of the user based on good laboratory practices or laboratory accreditation requirements and applicable laws. Follow manufacturer's instructions for reconstitution and storage. Each laboratory should establish mean values and acceptable ranges to assure proper performance. Quality control results that do not fall within acceptable ranges may indicate invalid test results. Examine all test results generated since obtaining the last acceptable quality control test point for this analyte. Refer to the appropriate system manuals and/or Help system for information about reviewing quality control results.

Results

Patient test results are determined automatically by the system software using a smoothing spline math model. The amount of analyte in the sample is determined from the measured light production by means of the stored calibration data. Patient test results can be reviewed using the appropriate screen. Refer to the appropriate system manuals and/or Help system for complete instructions on reviewing sample results.

Limitations of the Procedure

1. This assay is intended for early detection of pregnancy.
2. Samples can be accurately measured within the analytic range of the lower limit of detection and the highest calibrator value (approximately 0.5–1000 mIU/mL [IU/L]).
3. To accurately measure samples containing 1000–200,000 mIU/mL, select the Dil-hCG2 test. This test uses the TβhCG2 pack. When Dil-hCG2 is requested, the system autodilutes the sample and reads the resulting dose off the TβhCG2 calibration curve. The system multiplies by the dilution factor defined in the software (200) to calculate final test results.
4. For UniCel DxI systems:
   - Samples containing > 1000 mIU/mL, can be processed using the DxI onboard dilution feature.
   - The DxI system onboard dilution feature automates the dilution process, using one volume of sample with 199 volumes of UniCel DxI Access Immunoassay Systems Wash Buffer II, allowing samples to be quantitated up to 200,000 mIU/mL.
   - The system reports the results adjusted for the dilution.
   - If the sample contains less than 800 mIU/mL, the system will report results as < 800 mIU/mL.
5. Samples containing > 1000 mIU/mL can also be processed via **off-line pre-dilution** following these steps:
   - Dilute one volume of sample with 199 volumes of Wash Buffer (1/200) or dilute per laboratory dilution protocol. NOTE: Dilution with alternate buffers may cause erroneous results.
   - Type in the pre-dilution factor when entering the test request. Order the TβhCG or Dil-hCG2 test.
   - The system will automatically multiply the result by the pre-dilution factor and report that value. **NOTE: If the system reports a pre-diluted Dil-hCG2 result as < 1000 mIU/mL (IU/L), redilute the sample such that it will read between 1000 and 200,000 mIU/mL (IU/L). A neat sample reading < 1000 mIU/mL (IU/L) in the Dil-hCG2 assay should be retested in the TβhCG2 assay.**
   - If the pre-dilution option is not selected, multiply the calculated value by the dilution factor 200 (or by another selected factor) after assaying the diluted sample using the Access Total βhCG assay.
   - If the calculated value of the diluted sample using the Access Total βhCG assay is < 5 mIU/mL (IU/L), re-dilute one volume of the neat sample with 99 volumes of Wash

Buffer (1/100) and re-assay, remembering to multiply the calculated value by the dilution factor 100.

- Refer to the appropriate system manuals and/or Help system for additional instructions on processing pre-diluted samples.

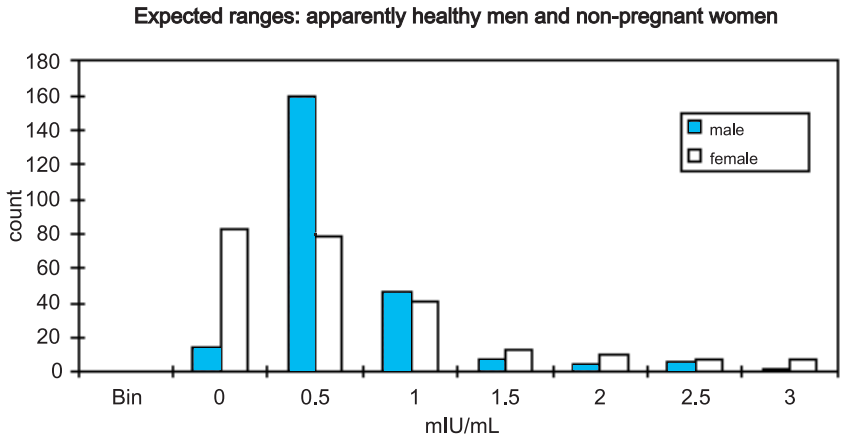
6. DO NOT reuse small sample volumes that have been resident on the analyzer for more than 1 hour.
7. The Access Total βhCG assay has no discernible "hook effect" at 1,000,000 mIU/mL.
8. For assays employing antibodies, the possibility exists for interference by heterophile antibodies in the patient sample. Patients who have been regularly exposed to animals or have received immunotherapy or diagnostic procedures utilizing immunoglobulins or immunoglobulin fragments may produce antibodies, e.g. HAMA, that interfere with immunoassays. Additionally, other heterophile antibodies such as human anti-goat antibodies may be present in patient samples.[15,16]

   Such interfering antibodies may cause erroneous results. Carefully evaluate the results of patients suspected of having these antibodies.
9. The role of preanalytical factors in laboratory testing has been described in a variety of published literature.[10,11,12] Following blood collection tube manufacturers' specimen collection and handling recommendations will help to reduce preanalytical error.
10. The Access Total βhCG results should be interpreted in light of the total clinical presentation of the patient, including: symptoms, clinical history, data from additional tests, and other appropriate information.
11. If the total βhCG level is inconsistent with clinical presentation, results should be confirmed by an alternate hCG method or a urine-based assay.[17]
12. Trophoblastic or nontrophoblastic neoplastic conditions should be ruled out before reporting results.

Expected Values

1. Each laboratory should establish its own reference ranges to assure proper representation of specific populations.
2. Total βhCG concentrations were measured in human serum samples collected from apparently healthy adult males and non-pregnant females using the Access Total βhCG assay. The observed range of total βhCG concentrations are shown below.

Reference Group	n	Median (mIU/mL)	95% Range (mIU/mL)
Males	250	< 0.5	< 0.5–2.67
Non-pregnant females	250	< 0.5	< 0.5–2.90



3. Representative hCG ranges during normal pregnancy are summarized below.[1] Because other clinical reference citations may show different values, each laboratory should establish its own reference ranges.

Approximate Gestational Age (weeks)	Approximate hCG Range (mIU/mL, IU/L)	Approximate Gestational Age (weeks)	Approximate hCG Range (mIU/mL, IU/L)
0.2–1	5–50	4–5	1,000–50,000
1–2	50–500	5–6	10,000–100,000
2–3	100–5,000	6–8	15,000–200,000
3–4	500–10,000	8–12	10,000–100,000

Specific Performance Characteristics

Methods Comparison

A comparison of serum total βhCG values using the Access Total βhCG assay on the Access Immunoassay system and a commercially available immunoassay kit gave the following statistical data using Deming calculations:

n	Range of Observations (mIU/mL)	Intercept (mIU/mL)	Slope	Correlation Coefficient (r)
119	1.82–939.50	-6.56	0.914	0.981
56	1.82–68.9	1.42	0.804	0.970

A comparison of total βhCG values obtained by assaying paired serum and plasma samples using the Access Total βhCG assay on the Access Immunoassay system gave the following statistical data using Deming calculations:

n	Range of Observations (mIU/mL)	Intercept (mIU/mL)	Slope	Correlation Coefficient (r)
148	0.59–961.08	-1.75	0.957	0.995

Dilution Recovery (Linearity)

Multiple dilutions of two samples containing elevated hCG levels with Access Total βhCG Calibrator S0 (zero) resulted in the following data:

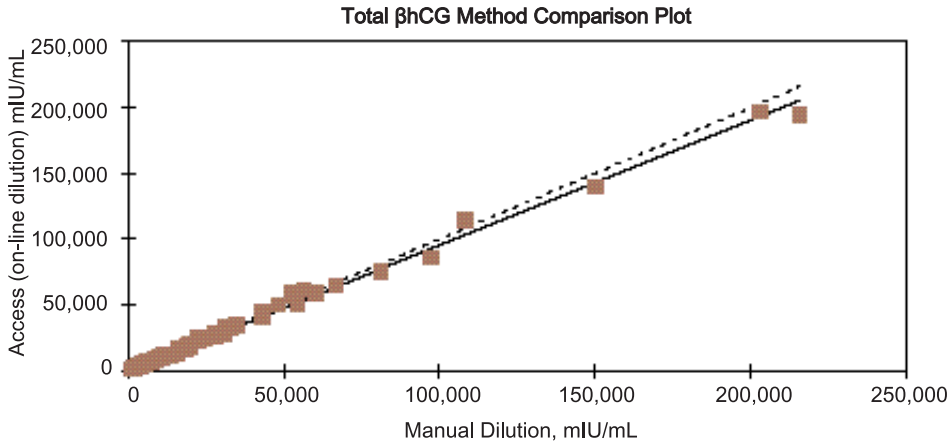
Sample 1	Expected Concentration (mIU/mL)	Determined Concentration (mIU/mL)	Recovery (%)
Neat	N/A	524.87	N/A
1/1.2	437.39	438.18	100
1/2	262.44	253.79	97
1/4	131.22	127.16	97
1/8	65.61	58.83	90
1/16	32.80	31.70	97
1/32	16.40	16.57	101
		Mean % Recovery	**97**

Sample 2	Expected Concentration (mIU/mL)	Determined Concentration (mIU/mL)	Recovery (%)
Neat	N/A	739.83	N/A
1/1.2	616.53	618.32	100
1/2	369.92	362.90	98
1/4	184.96	171.73	93
1/8	92.48	83.38	90
1/16	46.24	47.15	102
1/32	23.12	24.74	107
		Mean % Recovery	**98**

Instrument vs. off-line dilution correlation

The following Deming regression analysis was obtained from studies evaluating off-line (manual) dilution protocols versus the Access system dilution protocol.

n	Range of Observations (mIU/mL)	Adjusted Intercept (mIU/mL)	Slope	Correlation Coefficient (r)
105	1037–196,361	497	0.949	0.998
92	1037–49,948	-167.79	1.002	0.997
64	1037–10,267	-10.45	0.975	0.993



Imprecision

This assay exhibits total imprecision of less than 10% across the assay range. One study, using commercially available human serum based control material generating a total of 20 assays, 3 replicates per assay, over 14 days provided the following data, analyzed via analysis of variance (ANOVA).[18,19]

Sample	Grand Mean (n=60) (mIU/mL)	Within Run SD	Within Run (%CV)	Total SD	Total Imprecision (%CV)
Low	6.95	0.15	2.15	0.17	2.42
Medium	22.35	0.37	1.67	0.63	2.81
High	321.17	4.29	1.34	10.85	3.38

Analytical Specificity/Interferences

Samples containing up to 10 mg/dL (171 µmol/L) bilirubin, lipemic samples containing the equivalent of 1800 mg/dL (20.32 mmol/L) triglycerides, and hemolyzed samples containing up to 500 mg/dL (5 g/L) hemoglobin do not affect the concentration of total βhCG assayed. In

addition, samples with 3 g/dL (30 g/L) of human albumin added to the endogenous albumin in the samples do not affect the concentration of total βhCG assayed.

No significant cross reactivity (< 0.5 mIU/mL [IU/L]) was observed when hLH, hFSH, or hTSH were added to the Access Total βhCG Calibrator S0 (zero) at 1000 mIU/mL (IU/L), 1000 mIU/mL (IU/L), 1 mIU/mL (IU/L), respectively. The molar percent specificity, based on equivalent moles of hCG and the free βhCG subunit, was measured in multiple reagent lots using a preparation of 10 mIU/mL (IU/L) of the WHO 75/551 free βhCG subunit in Access Total βhCG Calibrator S0 (zero). The mean was 165% (Range of Observations 142%–184%, n=115).

Analytical Sensitivity

The lowest detectable level of hCG distinguishable from zero (Access Total βhCG Calibrator S0) with 95% confidence is 0.5 mIU/mL (IU/L). This value is determined by processing a complete six point calibration curve, controls, and 10 replicates of the zero calibrator in multiple assays. The analytical sensitivity value is interpolated from the curve at the point that is two standard deviations from the mean measured zero calibrator signal.

Access
Immunoassay Systems

TOTAL βhCG CALIBRATORS
REF 33505

Intended Use

The Access Total βhCG Calibrators are intended to calibrate the Access Total βhCG assay for the quantitative determination of total βhCG levels in human serum and plasma using the Access Immunoassay Systems.

Summary and Explanation

Quantitative assay calibration is the process by which samples with known analyte concentrations (i.e., assay calibrators) are tested like patient samples to measure the response. The mathematical relationship between the measured responses and the known analyte concentrations establishes the calibration curve. This mathematical relationship, or calibration curve, is used to convert RLU (Relative Light Unit) measurements of patient samples to specific quantitative analyte concentrations.

Traceability

The measurand (analyte) in the Access Total βhCG Calibrators is traceable to the WHO 3rd International Standard 75/537.[20] Traceability process is based on EN ISO 17511.

The assigned values were established using representative samples from this lot of calibrator and are specific to the assay methodologies of the Access reagents. Values assigned by other methodologies may be different. Such differences, if present, may be caused by inter-method bias.

Product Information

Access Total βhCG Calibrators
Cat. No. 33505: S0–S5, 4.0 mL/vial

- Provided ready to use.
- Store at -20°C or colder.
- Thaw at room temperature and mix contents by gently inverting before use. Avoid bubble formation.
- Return calibrators to -20°C or colder after each use.
- Stable until the expiration date stated on the label when stored at -20°C or colder.
- Signs of possible deterioration are control values out of range.
- Refer to calibration card for exact concentrations.

S0:	Buffered bovine serum albumin (BSA) matrix with surfactant, < 0.1% sodium azide, and 0.5% ProClin** 300. Contains 0.0 mIU/mL (IU/L) hCG.
S1, S2, S3, S4, S5:	hCG at levels of approximately 5, 25, 150, 500 and 1000 mIU/mL (IU/L), respectively, in buffered BSA matrix with surfactant, < 0.1% sodium azide, and 0.5% ProClin 300.
Calibration Card:	1

Warnings and Precautions

- For *in vitro* diagnostic use.
- Human source material used in the preparation of the reagent has been tested and found negative or non-reactive for Hepatitis B, Hepatitis C (HCV), and Human Immunodeficiency Virus (HIV-1 and HIV-2). Because no known test method can offer complete assurance that

infectious agents are absent, handle reagents and patient samples as if capable of transmitting infectious disease.[21]

- Human source material purified from the urine of pregnant women. Treat as potentially infectious.[21]
- Sodium azide may react with lead and copper plumbing to form highly explosive metal azides. On disposal of liquids, flush with a large volume of water to prevent azide build-up.[9]
- Xi. Irritant: 0.5% ProClin 300.

R 43: May cause sensitization by skin contact.
S 28-37: After contact with skin, wash immediately with plenty of soap and water. Wear suitable gloves.

- The Material Safety Data Sheet (MSDS) is available upon request.

Procedure

Refer to the appropriate system manuals and/or Help system for information on calibration theory, configuring calibrators, calibrator test request entry, and reviewing calibration data.

Calibration Details

The Access Total βhCG Calibrators are provided at six levels – zero and approximately 5, 25, 150, 500 and 1000 mIU/mL – prepared gravimetrically from purified hCG and buffered BSA matrix. Assay calibration data are valid up to 28 days.

Calibrators run in duplicate.

Limitations of the Procedure

If there is evidence of microbial contamination or excessive turbidity in a reagent, discard the vial.

References

1 Hohnadel DC, Kaplan LA. Beta-hCG. Methods in clinical chemistry. Edited by Pesc, AJ and Kaplan LA. St. Louis, MO: The C.V. Mosby Company, 1987.

2 Birken S. Chemistry of human choriogonadotropin. Annales d'endocrinologie 1984; 45: 297-305.

3 Human reproduction unit, WHO report of meeting. Assay of protein hormones related to human reproduction: problems of specificity of assay methods and reference standards. Acta Endocrinology 1972; 71: 625-637.

4 Kardana A, et al. The heterogeneity of hCG. Endocrinology 1991; 129: 1541-1567.

5 Vaitukaitis JL. Recent progress in hormone research 1976; 32: 289.

6 Sokolove PJ, Faix JD. Agreement of intact and beta chain-specific HCG assays in abnormal pregnancy. Journal of Clinical Immunoassay, Fall, 1991; 14, No. 3: 196-199.

7 Vaitukaitis JL, Braunstein GD, Ross GT. A radioimmunoassay which specifically measures human chorionic gonadotropin in the presence of human lutenizing hormone. American Journal of Obstetrics and Gynecology 1972; 113: 751-758.

8 Norman RJ, Buck RH, Joubert SM. Comparison of human chorionic gonadotrophin concentrations in the sera of patients with normal and abnormal pregnancy measured by radioimmunoassay and immunoradiometric assay. South African Medical Journal April, 1989; 75: 318-319.

9 DHHS (NIOSH) Publication No. 78-127, August 1976. Current Intelligence Bulletin 13 - Explosive Azide Hazard. Available http://www.cdc.gov/niosh.

10 Blood Human Chorionic Gonadotropin (hCG) Assays: What Laboratorians Should Know About False-Positive Results. Food and Drug Administration Center for Devices and Radiological Health Medical Device Reporting, 2009.
http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/TipsandArticlesonDeviceSafety/ucm109390.htm

11 Approved Guideline – Fourth Edition, Procedures for the Handling and Processing of Blood Specimens for Common Laboratory Tests, H18-A4. 2010. Clinical and Laboratory Standards Institute.

12 Approved Standard – Sixth Edition, Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture, H3-A6. 2007. Clinical and Laboratory Standards Institute.

13 O'Connor JF, et al. Recent advances in the chemistry and immunochemistry of human chorionic gonadotropin: impact on clinical measurements, Endocrine Reviews 1994; 15, No. 5: 650-683.

14 Cembrowski GS, Carey RN. Laboratory quality management: QC⇌QA. ASCP Press, Chicago, IL, 1989.

15 Kricka L. Interferences in immunoassays – still a threat. Clin Chem 2000; 46: 1037–1038.

16 Bjerner J, et al. Immunometric assay interference: incidence and prevention. Clin Chem 2002; 48: 613–621.

17 Cole, LA. Phantom hCG and Phantom Choriocarcinoma. Gynecol Oncol, 1998; 71:325–9.

18 Tentative Guideline – User evaluation of precision performance of clinical chemistry devices, EP5-T, 4, N8, 1984. National Committee for Clinical Laboratory Standards.

19 Krouwer JS, Rabinowitz R. How to improve estimates of imprecision. Clinical Chemistry 1984; 30: 290-292.

20 Standardization of protein immunoprocedures. Scand J Clin Lab Invest 1993; 53 (Suppl 216); 42–78.

21 HHS Publication, 4th ed., April 1999. Biosafety in Microbiological and Biomedical Laboratories. Available http://www.cdc.gov/od/ohs/biosfty/bmbl4/bmbl4toc.htm

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