HAMA IgG Test System

REF 6401

IVD

CE

Rx Only

INTENDED USE

The ZEUS HAMA IgG ELISA Test System is a direct enzyme-linked immunosorbent assay for the detection and semi-quantitation of human antibodies to mouse IgG (HAMA). The presence of human anti-mouse antibody (HAMA) has been associated with patients receiving injections of murine monoclonal antibody for diagnostic and/or therapeutic purposes.

SIGNIFICANCE AND BACKGROUND

The ZEUS HAMA IgG ELISA Test System is a direct enzyme-linked immunosorbent assay for the detection and semi-quantitation of human humoral antibodies to mouse IgG (1). Significant levels of human anti-mouse IgG antibody (HAMA) have been associated with patients receiving injections of murine monoclonal antibody (MAb) (2 - 6).

The use of radioimmunotherapy has significantly increased the number of patients with HAMA titers. Circulating levels of HAMA can complex the injected antibody and adversely affect the imaging and/or therapy that was intended (5). In addition, HAMA has been shown to significantly interfere with many commercial assays utilizing murine MAbs, resulting in both false-positive and false-negative results (7 - 12).

The ZEUS HAMA IgG ELISA Test System may be performed manually or with existing microtiter equipment. Results, which are read at 450nm, are available in less than 1 hour. The test has been calibrated with baboon anti-mouse IgG serum and has a sensitivity of 37 ng/mL. Final patient values are reported as nanograms of precipitable antibody equivalents per mL. It is recommended that baseline HAMA levels are determined prior to the initiation of therapy with murine-derived proteins.

PRINCIPLE OF THE ASSAY

The ZEUS ELISA HAMA IgG Test System is designed to detect human anti-mouse antibody (HAMA). Mouse IgG conjugated to horseradish peroxidase enzyme (conjugate) is added to the microwell which has been coated with mouse IgG whole molecule. Diluted test sample is then added and incubated. If antibody to the mouse IgG is present in the test sample, antigen-antibody complexes are formed. If antibody is not present in the test sample, the unbound conjugate will be removed in the subsequent washing step. Enzyme substrate is then added to the microwell. If bound conjugate is present, the substrate will be reduced; the reduced end-product oxidizes the colorless chromogen resulting in a colored end-product. Acid is added to stop the reaction and fix the color. The absorbance is measured with a microwell strip reader at a wavelength of 450nm. The absorbance of the solution is directly proportional to the amount of bound conjugate and, therefore, to the concentration of precipitable antibody present in the sample.

TEST SYSTEM COMPONENTS

Materials Provided:

Each Test System contains the following components in sufficient quantities to perform the number of tests indicated on the packaging label. **NOTE: Reagents from different lot numbers must not be interchanged.**

PLATE		1. Plate: 96 wells configured in twelve, 1x8-well, strips coated with whole mouse IgG. The strips are packaged in a strip holder and sealed in an envelope with desiccant.
CONJ		2. Conjugate: 10X concentrated enzyme conjugate in PBS-buffered protein solution containing gentamicin sulfate. One, 2mL, amber bottle.
CONTROL	+	3. Positive Control: One, 2mL, bottle containing Baboon anti-mouse serum diluted with specimen diluent, containing 100 - 150ng of precipitable antibody equivalents per mL.
CAL		4. Calibrator: One, 3mL, bottle containing Baboon anti-mouse IgG serum containing 220ng of precipitable antibody equivalents per mL.
DIL	SPE	5. Specimen Diluent: One, 30mL, green-capped, bottle containing buffered human serum containing 0.005% gentamicin sulfate and 0.02% thimerosal.
SOLN	TMB	6. TMB: Two, 15mL, amber-capped, amber bottle containing 3, 3', 5, 5' - tetramethylbenzidine (TMB). Ready to use.
SOLN	STOP	7. Stop Solution: One, 15mL, red-capped, bottle containing 1M H_2SO_4, 0.7M HCl. Ready to use.
WASHBUF	10X	8. Wash Buffer Concentrate (10X): Dilute 1 part concentrate + 9 parts deionized or distilled water. One, 100mL, clear-capped, bottle containing a 10X concentrated phosphate-buffered-saline and Tween-20 solution (blue solution). **NOTE: 1X solution will have a pH of 7.2 ± 0.2.**

NOTE: Test System also contains a Component Label containing lot specific information inside the Test System box.

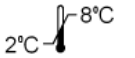
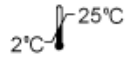
PRECAUTIONS

1. For *In Vitro* diagnostic use.
2. Follow normal precautions exercised in handling laboratory reagents. In case of contact with eyes, rinse immediately with plenty of water and seek medical advice. Wear suitable protective clothing, gloves, and eye/face protection. Do not breathe vapor. Dispose of waste observing all local, state, and federal laws.
3. Source material from which reagents of human origin were derived were found nonreactive for HBsAg and HIV-1 when tested with licensed reagents. No known test method can offer complete assurance that products derived from blood will not transmit hepatitis or other infectious agents. Reagents derived from animal sera have not been tested. **Handle these reagents as if they are potentially infectious.**
4. Household bleach should be used to wipe up spills and should be added to waste material prior to disposal.
5. Do not mix reagents from different lot numbers. The regents in this test system are formulated to be used as a kit for detection of HAMA. Dilution or adulteration of reagents other than directed will result in loss of sensitivity. Cross contamination of reagents and patient samples, or use of reagents other than those supplied in the kit may produce erroneous results.
6. Do not use components beyond the expiration date.
7. Do not reuse microtiter wells.
8. Stop Solution may cause severe irritation on contact with skin. Do not get in eyes, on skin, or on clothing. Do not ingest or inhale fumes. On contact, flush with copious amounts of water for at least 15 minutes.
9. Handle the TMB with care. Avoid contact with eyes, skin or clothing as TMB may cause irritation or an allergic skin reaction. The TMB is light sensitive. Keep vial **tightly** closed when not in use. Bring only the required amount to room temperature before use.
10. Do not allow the wells to dry during the test. Drying of wells may result in falsely high absorbance values.
11. Careful technique and use of properly calibrated pipetting devices are necessary to ensure reproducibility of the test.
12. Incubation times or temperatures other than those stated in this insert may affect the results.
13. Avoid air bubbles in microtiter wells as this could result in lower binding efficiency.
14. Washing procedures different than stated may adversely affect the results.
15. All liquid reagents should be mixed thoroughly prior to use. Avoid foaming.

MATERIALS REQUIRED BUT NOT PROVIDED

1. Dilution Plate.
2. 1 mL, 5 mL, and 10 mL serological pipettes.
3. 200 µL adjustable single channel micropipette.
4. 50 - 200 µL adjustable multichannel micropipette.
5. 50 - 200 µL disposable pipette tips (recommended by multichannel micropipette manufacturer).
6. Multichannel micropipette reservoir.
7. Disposable 12 x 75 mm or 13 x 100mm glass tubes.
8. Disposable plastic 25mL and 50mL tubes with caps.
9. ELISA multichannel wash bottle or automatic (semi-automatic) washing system.
10. Plastic microwell strip cover or polyethylene film.
11. Aliquot mixer.
12. 37°C incubator.
13. Microwell strip reader capable of reading at 450nm. **NOTE: Use of a single (450nm), or dual (450/620 - 650nm), wavelength reader is acceptable. Dual wavelength is preferred, as the additional reference filter has been determined to reduce potential interference from anomalies that may absorb light.**
14. Glass-distilled or deionized water.
15. 1 L volumetric glass container.
16. Bleach for disinfectant and disposal of waste.

STORAGE CONDITIONS

	Coated Microwell Strips: Immediately reseal extra strips with desiccant and return to proper storage. After opening - strips are stable for 60 days, as long as the indicator strips on the desiccant pouch remains blue.
	Conjugate – DO NOT FREEZE.
	Unopened Test System/Unused Opened Reagents.
	Stop Solution: 2 - 25°C Wash Buffer (1X): 20 - 25°C for up to 7 days, 2 - 8°C for 30 days. Wash Buffer (10X): 2 - 25°C

SPECIMEN COLLECTION

No special preparation of the individual is required prior to specimen collection. The whole-blood test specimen should be collected by accepted medical techniques. **The specimen must be allowed to clot for two hours at room temperature (15 - 30°C) before the serum is separated by centrifugation.** The serum should be separated from the clot within eight hours of collection and transferred to a glass test tube. The test specimen can be centrifuged at 850 – 1500 x g for 10 minutes at ambient temperature (15 - 30°C). Mechanical serum separating devices may be used. The resulting test specimen must be completely free of cellular debris. Once the serum has been separated from the clot, it may be stored at 2 - 8°C for up to 24 hours. If the serum specimen cannot be tested within one day of collection, the specimen should be stored at -70°C until tested. Serum samples are stable at -70°C for at least three months. Freeze and thaw only once. Specimens may be thawed either at room temperature or for up to 5 minutes at 37°C. Serum is required for the HAMA assay. Plasma or anticoagulated specimens collected as plasma and then clotted should not be used. Do not heat-inactivate serum specimens.

ASSAY PROCEDURE

1. Remove the individual components from storage and allow them to warm to room temperature (20 - 25°C).
2. Determine the number of microwells needed. Allow for twelve Control/Calibrator determinations (four Calibrators in duplicate and one Positive Control in duplicate) per run. Run a Blank (100µL of Specimen Diluent) in duplicate on each assay. Check software and reader requirements for the correct Controls/Calibrator configurations. Return unused strips to the resealable pouch with desiccant, seal, and return to storage between 2 - 8°C.

EXAMPLE PLATE SET-UP		
	1	2
A	BL	C4
B	BL	C4
C	C1	PC
D	C1	PC
E	C2	
F	C2	
G	C3	
H	C3	

3. Prepare the reagents as follows:
   a. Conjugate: Disposable glass or plastic ware must be used. The Conjugate Concentrate must be diluted with 1X Wash Buffer just prior to use. Dilute an aliquot of the conjugate concentrate 1:10. The diluted conjugate should be prepared just prior to use and should be used within 30 minutes. **For 96 tests (12 microwell strips):** Add 1mL conjugate concentrate to 9mL 1X Wash Buffer. A volume of 10mL is needed for 12 microwell strips.
   b. Test Samples: Prepare a 1:2 dilution of all patient samples with specimen diluent. Greater dilutions may be required for high positive samples.
   c. Positive Control: Prepare a 1:2 dilution of the Positive Control sample supplied in the kit, with Specimen Diluent.
   d. Calibrators: Using disposable glass tubes, prepare 1:2, 1:4, and 1:6 dilutions of the HAMA Calibrator in Specimen Diluent. To semi-quantitate positive samples, a calibrator curve is necessary. The curve should be prepared from the Calibrator supplied in the kit by diluting an aliquot with Specimen Diluent. **NOTE: The Blank can be used as a 0 ng/mL Calibrator.** Calibrator dilutions are prepared using the HAMA Calibrator (C1) as follows:

Calibrator	Antibody Concentration (ng/mL)	HAMA Calibrator (µL)	Specimen Diluent Volume (µL)	Test Dilution
(C1)	220	-	-	Undiluted
(C2)	110	200	200	1 : 2
(C3)	55	100	300	1 : 4
(C4)	37	100	500	1 : 6

4. Remove an appropriate number of microwell strips from their protective pouches.
5. Appropriately label all strips. All test samples, blanks, Calibrators and the PC should be run in duplicate.
6. Add 0.1 mL of diluted Conjugate to all wells to be used.
7. Add 0.1 mL of Specimen Diluent to the Blank wells.
8. Add 0.1 mL of each diluted Calibrator, the diluted PC, and each diluted test sample to the appropriate wells on the strips.
9. Cover the microwell strips and incubate at 37°C for 30 minutes.
10. After the 30 minute 37°C incubation, discard the contents of the microwell strips and wash the wells 3 times with 1X Wash Buffer. The washing procedure must be thorough. Washing may be performed using an automatic microtitration washing device or manually as follows:

a. **Manual Wash Procedure**:
   1. Vigorously shake out the liquid from the wells.
   2. Fill each microwell with Wash Buffer. Make sure no air bubbles are trapped in the wells.
   3. Repeat steps 1. and 2. for a total of 3 washes.
   4. Shake out the wash solution from all the wells. Invert the plate over a paper towel and tap firmly to remove any residual wash solution from the wells. Visually inspect the plate to ensure that no residual wash solution remains. Collect wash solution in a disposable basin and treat with disinfectant at the end of the day's run.

b. **Automated Wash Procedure**:
   If using an automated microwell wash system, set the dispensing volume to 300 - 350µL/well. Set the wash cycle for 3 washes with no delay between washes. If necessary, the microwell plate may be removed from the washer, inverted over a paper towel and tapped firmly to remove any residual wash solution from the microwells.

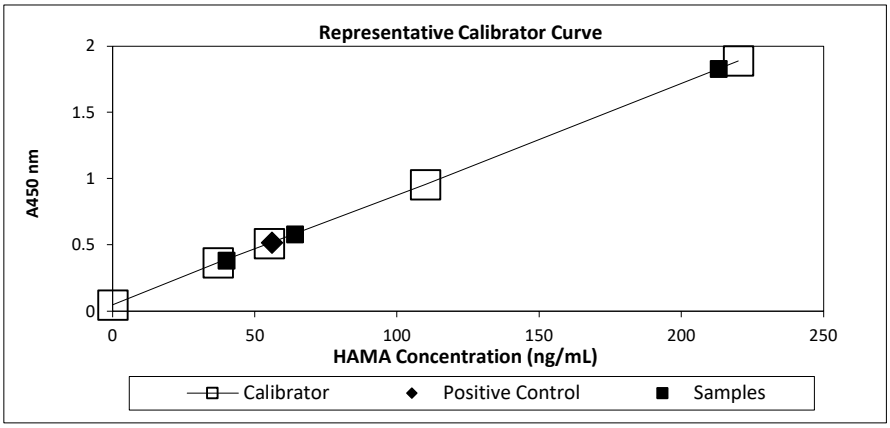
11. Add 0.2 mL of TMB to all wells, including the blank wells.
12. Place the strips in the dark at room temperature for 15 minutes.
13. Using a multichannel micropipette, forcibly eject 0.05 mL of Stop Solution into each well, including the blanks wells. It is important that the Stop Solution is spread quickly and uniformly throughout the wells to completely inactivate the enzyme.
14. Set the microwell strip reader at a wavelength of 450 nm and measure the color intensity in all microwells.

QUALITY CONTROL/INTERPRETATION OF RESULTS

1. Each time the assay is performed, the Blank, Calibrator dilutions, and PC must be run in duplicate.
2. **Control and Calibrators**
   a. Blank: Record the mean absorbance values of the blank wells. If the mean OD is ≥ 0.14, the test should be repeated.
   b. Calibrators: Calculate the mean absorbance value of the duplicate calibrators. For HAMA, the following values have been assigned.
      Cl 220 ng/mL
      C2 110 ng/mL
      C3 55 ng/mL
      C4 37 ng/mL
      BL 0 ng/mL
3. Preparation of the Calibrator Curve and Determination of HAMA Concentration (ng/mL) for the PC and each test sample.
   a. Calculation Method: Calculations can be made using a linear regression program. Follow the manufacturer's instructions for use of these programs to establish the calibrator curve and the HAMA concentration of the PC and each test sample. **NOTE: The PC contains 100 - 150 ng of precipitable antibody equivalents per mL.** In order for an assay to be valid, the following criteria must be met:
      i. Slope 0.005 - 0.015
      ii. Y-intercept ≤ 0.200
      iii. Correlation coefficient (r^2) ≥0.950
   b. Representative Calibrator Curve: A representative calibrator curve is shown in the table and graph presented below. This curve cannot be used to derive test results. Each laboratory must prepare a Calibrator Curve for each group of microwell strips assayed (up to 12).

	Mean Absorbance Value	HAMA (ng/mL)
Calibrator 1	1.889	220
Calibrator 2	0.955	110
Calibrator 3	0.512	55
Calibrator 4	0.365	37
Blank	0.048	0
Positive Control	0.517	56 (2) = 112
Sample 1	1.828	213 (2) = 426
Sample 2	0.582	64 (2) = 128
Sample 3	0.382	40 (2) = 80
Slope	0.008	
Y-Intercept	0.049	
Correlation	0.999	

NOTE: The assay requires an initial 1:2 dilution of the positive control and test samples. HAMA values extrapolated from the calibrator curve must be multiplied by 2 for the final HAMA concentration. Some test samples may require a higher dilution factor. The value as ng/mL must be multiplied by the dilution factor of the test sample.



LIMITATIONS OF THE ASSAY

1. Heat-inactivated samples may result in false-negative results.
2. The presence of Rheumatoid Factor (RF) and/or heterophilic antibodies in the sample may interfere with the assay and could result in false-positive values (10, 11). If aberrant test results are obtained, it is recommended that the patient be tested for the presence of these interfering substances prior to therapy initiation. REFER TO SPECIFICITY/INTERFERING SUBSTANCES.
3. Lipemic serum samples may interfere with the assay and could result in false-positive values. REFER TO SPECIFICITY/INTERFERING SUBSTANCES.

4. Improper or insufficient washing at any stage of the procedure will result in either false-positive or false-negative results.
5. Adherence to the humidity, temperature and time periods for incubation is essential for accurate results.
6. Bacterial or fungal contamination of serum specimens or reagents, or cross contamination between reagents may cause erroneous results.
7. Water deionized with polyester resins may inactivate the horseradish peroxidase enzyme.

PERFORMANCE CHARACTERISTICS

1. **Reproducibility:**

a. Within run and between run assay reproducibility was evaluated by performing the ZEUS ELISA HAMA IgG Test System using low (50 ng/mL), medium (75 ng/mL) and high (200 ng/mL) control samples. The control samples were prepared by enriching normal human serum with purified HAMA. Between run CVs were calculated from assays performed on three different days. Each control sample was assayed in triplicate; the mean of the triplicates was reported. The coefficients of variations (CVs) for within run values were ≤ 10 %, and between run CVs were < 5%. Please refer to Table 1 below:

Table 1: Within Run and Between Run Assay Reproducibility

	Low Control (50 ng/mL) Within Run			Medium Control (75ng/mL) Within Run			High Control (200 ng/mL) Within Run		
Run Number	ng/mL	SD	CV(%)	ng/mL	SD	CV(%)	ng/mL	SD	CV (%)
1	53.4	±5.2	9.7	76.3	±2.1	2.8	187	±5.9	3.2
2	56.0	±2.5	4.5	72.5	±0.5	0.7	193	± 18	9.2
3	51.4	±1.8	3.5	71.5	±3.2	4.5	193	± 19	10.0
Between Run Mean	53.6	±2.3	4.3	73	±2.5	3.4	191	±3.7	1.9

b. Lot to lot reproducibility was performed by assaying six prepared serum controls with three lots of ZEUS ELISA HAMA IgG reagents. Six serum controls were prepared by enriching normal human serum with varying concentrations of purified HAMA. The range in HAMA concentration was 50 ng/mL to 400 ng/mL. The HAMA results were obtained from three calibrator curves prepared from the calibrator provided with each lot; all results are expressed as a mean of triplicate values. Please refer to Table 2 below:

Table 2: Lot to Lot Reproducibility for 6 Prepared Serum Controls

	HAMA (ng/mL)					
Serum (ng/mL)	Lot 1627	Lot 1628	Lot 1629	Average	SD	CV (%)
50	56.6	47.4	53.1	52.4	3.8	7.2
75	92	78.6	76.0	82.2	7.0	8.5
100	99	99.8	98.6	99.1	0.5	0.5
200	211	220	187	206	13.9	6.8
300	303	310	291	301	7.8	2.6
400	395	344	374	371	20.9	5.6

2. **Sensitivity:**

The sensitivity of the ZEUS ELISA HAMA IgG Test System is 37 ng of precipitable antibody equivalents/mL. The lowest concentration prepared from the calibrator (C1) is equal to 37 ng precipitable antibody equivalents/mL and is the labeled sensitivity of the assay. The recommended dilution of test sample is 1:2, therefore, a negative HAMA result has been defined as ≤74 ng precipitable antibody/mL, [37 X 2 (dilution factor)]. The following table summarizes the distribution of HAMA values in an apparently healthy population (expected values).

Healthy Subjects	< 10 ng/mL	10-74 ng/mL	75-99 ng/mL	100-199ng/mL	200-299 ng/mL
300 Males	41.2	56.8	0.8	0.4	0.8
110 Females	49.1	50.9	0	0	0
104 Pregnant Females	35.6	60.5	1	1	2

The ZEUS ELISA HAMA IgG Test System defines a "negative" as ≤ 74 ng/mL. In this healthy population, 98% of the males, 100% of the non-pregnant females and 96.1% of the pregnant females were negative for HAMA. The presence of antibodies to mouse immunoglobulin in the serum of healthy individuals has been documented in several studies[10, 11, 16].

3. **Specificity/Interfering Substances:**

An evaluation of the specificity of ZEUS ELISA HAMA IgG was performed by assaying 57 serum samples having various concentrations of rheumatoid factor (RF). RF are autoantibodies directed to the Fc portion of human and other mammalian IgG molecules. In this study, serum RF concentrations, expressed in International Units (IU), varied in the range from negative (normal) to 3000 IU (high). All positive samples were from patients diagnosed with rheumatoid arthritis. All samples were assayed in duplicate, the mean of the duplicate values was reported. The patient population from which these samples had been collected either had no previous exposure to mouse protein or such exposure was unknown. Twenty-one (36.8%) of the RF serum samples resulted in falsely elevated HAMA test results (> 74 ng/mL). There was no apparent correlation between the level of RF in the sample and the severity of interference with the ZEUS ELISA HAMA IgG Test System. The following table lists the ZEUS ELISA HAMA IgG test results on serum samples containing other potentially interfering substances.

Number Tested	Interfering Substance	Amount of Interfering Substance in Sample	ZEUS ELISA HAMA IgG Test Result
38	Chemotherapeutic Serum Samples**	N/A*	37 Samples - Negative **1 Sample - Positive (85.3 ng/mL)
10	Hemolyzed Serum Samples	N/A*	10 Samples - Negative
10	Lipemic Serum Samples	Grossly Lipemic	9 samples -Negative ***1 sample - Positive (232 ng/mL)
2	Digoxin Serum Samples	1 - 2.7 ng/mL	2 Samples - Negative
10	Dilantin Serum Samples	5 - 10 µg/mL	10 Samples - Negative
2	Phenobarbital Serum Samples	22 - 30 µg/mL	2 Samples - Negative
3	Vancomycin Serum Samples	800.35 µg/mL	3 Samples - Negative
3	Theophylline Serum Samples	12.1 - 15.8 µg/mL	3 Samples - Negative
10	Protein Serum Samples	6.5 - 8.3 g/dl	10 Samples - Negative
5	Protein Serum Samples (Elevated)	8.9 - 9.5 g/dl	4 Samples - Negative ****1 Sample - Positive (100 ng/mL)
5	Protein Serum Samples (Low)	5.3 - 5.7 g/dl	5 Samples - Negative
9	Acetaminophen/ Aspirin Serum Samples	N/A*	9 Samples - Negative

*** N/A Not Applicable**

**Included serum samples from patients undergoing chemotherapy with the following agents: 5FU, Leucovorin, Cytoxan, Urokinase, Cysplatin, Taxol, Vinblastin, Carboplatinum, Levamisole, and Ondansetron. One sample tested slightly positive (85.3 ng/mL) with ZEUS ELISA HAMA IgG Test System; this result remains unexplained.

***One sample from the grossly lipemic serum group tested positive (232 ng/mL) with the ZEUS ELISA HAMA IgG Test System. Please refer to LIMITATIONS OF PROCEDURE.

****One sample from the elevated serum protein group tested positive with the ZEUS ELISA HAMA IgG Test System. This sample was further analyzed for the presence of Rheumatoid Factor, (see section (a) above) and was strongly positive (4+) with an RF latex assay.

REFERENCES

1. La Fontaine GS, Hansen HJ, Weiss BF, et al. Enzyme immunoassay for the detection of circulating immunoglobulins in human to mouse monoclonal antibody (HAMA). Presented at the Third International Conference of Monoclonal Antibody Immunoconjugates for Cancer, San Diego, February 4-6, 1988.
2. Courtenay-Luck NS, Epenetos AA, Moore R, et al. Development of primary and secondary immune responses to mouse monoclonal antibodies used in the diagnosis and therapy of malignant neoplasms. *Cancer Res 1986;* 46:6489-6493.
3. Davies AG, Bourne SP, Richardson RB, et al. Pre-existing anti-mouse immunoglobulin in a patient receiving ^{131}I-murine monoclonal antibody for radioimmunolocalization. *Br J Cancer 1986;* 53:289-292.
4. Klein JL, Sandoz JW, Kopher MS, et al. Detection of specific anti-antibodies in patients treated with radiolabeled antibody. *Int J Radiat Oncol Biol Phys 1986;* 12:939-943.
5. Pimm MV, Perkins AC, Armitage NC, et al. The characteristics of blood-borne radiolabels and the effect of anti-mouse IgG antibodies on localization of radiolabeled monoclonal antibody in cancer patients. *J Nucl Med 1985;* 26:1011-1023.
6. Schroff RW, Foon KA, Beatty SM, et al. Human anti-murine immunoglobulin responses in patients receiving monoclonal antibody therapy. *Cancer Res 1985;* 45:879-885.
7. Bock JL, Forgiuele J, Wenz B. False positive immunometric assays caused by anti-immunoglobulin antibodies: a case report. *Clin Chim Acta 1985; 147:241-246*.
8. Boscato LM, Egan G, Stuart MC. Covert cross reactants in a two-site immunoassay studied with monoclonal antibodies. *Anal Biochem 1985; 146:393-401*.
9. Boscato LM, Stuart MC. Incidence and specificity of interference in two-site immunoassays. *Clin Chem 1986; 32:1491-1495.*
10. Boscato LM, Stuart MC. Heterophilic antibodies: a problem for all immonoassays. *Clin Chem 1988; 34(1):27-33.*
11. Courtenay-Luck NS, Epenetos AA, Winearls CG, et al. Pre-existing human anti-murine immunoglobulin reactivity due to polyclonal rheumatoid factors. *Cancer Res 1987; 47:4520-4525.*
12. Cusick CF, Mistry K, Addison GM. Interference in a two-site immunoradiometric assay for thyrotropin in a child. *Clin Chem 1985; 31:348-349.*
13. Hansen HJ, LaFontaine G, Newman E. Solving the problem of antibody interference in commercial "sandwich"-type immunoassays of carcinoembryonic antigen. *Clin Chem 1989; 35:146-150.*
14. McCarthy RC, Ryan FJ. Interference in immunoenzymometric assays (IEMA) using mouse monoclonal antibodies (MCAB) caused by human IgM antibody to mouse IgG (Abstract). *Clin Chem 1987; 33:918.*
15. Primus JF, 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*.
16. Thompson RJ, Jackson AP, Langiois N. Circulating antibodies to mouse monoclonal immunoglobulins in normal subjects—incidence, species specificity, and effects on a two-site assay for creatine kinase-MB isoenzyme. *Clin Chem 1986; 32:476-481.*
17. Vladutiu A, Sulewski JM, Pudlak KA, et al. Heterophilic antibodies interfering with radioimmunoassay: a false positive pregnancy test. *JAMA 1982; 248:2489-2490.*
18. Zweig MH, Csako G, Benson CC, et al. Interference by anti-immunoglobulin G antibodies in immunoradiometric assays for thyrotropin involving mouse monoclonal antibodies. *Clin Chem 1987; 33:840-844.*
19. Price T, Beatty BG, Beatty JD, McNally AJ. Human anti-murine antibody interference in measurement of carcinoembryonic antigen assessed with a double-antibody enzyme immunoassay. *Clin Chem 1991;* 37/1:51-57.
20. Kaladas PM, et al. Detection of human anti-murine antibody (HAMA) following infusion of OncoScint® CR103. Comparison of ZEUS ELISA with a double antigen radiometric assay. *Antib Immunoconj Radiopharm 1993;* 4:309-317.
21. Hansen HJ, Sharkey RM, Sullivan CL, Goldenberg DM. HAMA interference with murine monoclonal antibody-based immunoassays. *J Clin Immunoassay 1993; 16(4):294-299.*

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