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Reagent Red Blood Cells

IH-Cell A1&B / IH-Cell A2

0.6 ±0.1%

For In Vitro Diagnostic Use

Reagent Red Blood Cells for use with the IH-System

No U.S. Standard of Potency

U.S. LICENSE NUMBER: 1845

Rx only

Product-Identification:

IH-Cell A1&B	79000
IH-Cell A1	79100
IH-Cell B	79200
IH-Cell A2	79010

IH-Cell A1&B: VOL 2 x 10 mL vials

REF 814010100

IH-Cell A2: VOL 1 x 10 mL vial

REF 814020100

INTENDED USE

IH-Cell A1&B and IH-Cell A2 are intended for the detection of antibodies to ABO blood group antigens on human red blood cells.

SUMMARY

Between 1900 and 1902, Landsteiner and associates discovered the ABO system of red blood cell antigens. The importance of this discovery is the recognition that antibodies are present when the corresponding antigens are lacking. The ABO system is the only blood group system in which the reciprocal antibodies are consistently and predictably present in most people.

The IH-Cell A1&B and IH-Cell A2 are used to test for the presence or absence of the corresponding antibodies in plasma or serum grouping for the ABO system. Serum grouping should include at least A1 and B red blood cells.

PRINCIPLES OF THE TEST

Refer to the instructions for use for the specific IH-Card tested with the Reagent Red Blood Cells.

REAGENTS

IVD

OBSERVABLE INDICATIONS

Do not use if markedly hemolyzed or discolored.

Do not use damaged vials.

NOTE: INSPECT THE CONDITION OF THE REAGENT BEFORE USE (SEE PRECAUTIONS).

Each vial contains a 0.6 ± 0.1% suspension of pooled red cells prepared in a buffered (bovine albumin) preservative solution to retard hemolysis and/or loss of antigenicity during shelf life.

IH-Cell A1&B and IH-Cell A2 have the following antigen combinations:

- IH-Cell A1: A1 Rh negative (ccddee)
- IH-Cell B: B Rh negative (ccddee)
- IH-Cell A2: A2 Rh negative (ccddee)

The IH-Cell A1&B and IH-Cell A2 should be used directly from the vial without further modification. The contents of each vial should be re-suspended by gentle mixing.

Preservative: 32 µg/mL Trimethoprim and 160 µg/mL Sulfamethoxazol

STORAGE REQUIREMENTS

- Store at 2 to 8°C.
- Do not use reagents beyond their expiration date which is expressed as YYYY-MM-DD (year-month-day).
- Do not freeze or expose reagents to excessive heat.
- Store in an upright position.
- Do not store near any heat, air conditioning sources or ventilation outlets.

PRECAUTIONS

- All IH-System reagents and test samples must be brought to room temperature (18 to 25°C) prior to use.
- Use reagents as furnished.
- Once the IH-Card has been used for testing, it may contain infectious material and should therefore be handled and disposed of as biohazardous waste in accordance with local, state and national regulations.
- As with all Reagent Red Blood Cells, the reactivity of the cells may decrease during the dating period.
- Caution: The packaging of this product (dropper bulbs) contains natural rubber latex which may cause allergic reactions.
- Caution: ALL BLOOD PRODUCTS SHOULD BE TREATED AS POTENTIALLY INFECTIOUS. SOURCE MATERIAL FROM WHICH THIS PRODUCT WAS DERIVED WAS FOUND NEGATIVE WHEN TESTED WITH FDA LICENSED EIA/ELISA TESTS. NAT TESTING WAS NOT PERFORMED. NO KNOWN TEST METHOD CAN OFFER ASSURANCE THAT PRODUCTS DERIVED FROM HUMAN BLOOD WILL NOT TRANSMIT INFECTIOUS AGENTS.
- Consult downloads.bio-rad.com to download the valid version of this instruction for use.

SPECIMEN COLLECTION AND PREPARATION

No special preparation of the patient or donor is required prior to specimen collection. Blood samples should be collected following general blood sampling guidelines. Do not use grossly hemolyzed, lipemic or icteric samples.

Please refer to the instructions for use for the IH-Card used for testing and the IH-1000 or IH-500 User Manual U.S. for card and instrument specific specimen collection and preparation requirements, respectively.

TEST PROCEDURE FOR MANUAL AND AUTOMATED SYSTEMS

Materials provided

- IH-Cell A1&B
- IH-Cell A2

Materials recommended but not provided

- IH-Card ABO/Rh(DV1+) + Rev A1, B, or
- IH-Card ABO/Rh(DV1-) + Rev A1, B, or
- IH-Card Neutral (for A2 cells only)
- IH-LISS Rack and IH-LISS Solution
- Dispenser pipette capable of delivering 1 mL
- Pipettes: 10 µL, 50 µL and 1 mL
- Disposable pipette tips
- Glass or plastic test tubes

- IH-Centrifuge L or IH-Reader 24 to centrifuge the IH-Cards at 85g with pre-set time for manual working
- IH-1000 or IH-500 for full automation

Method

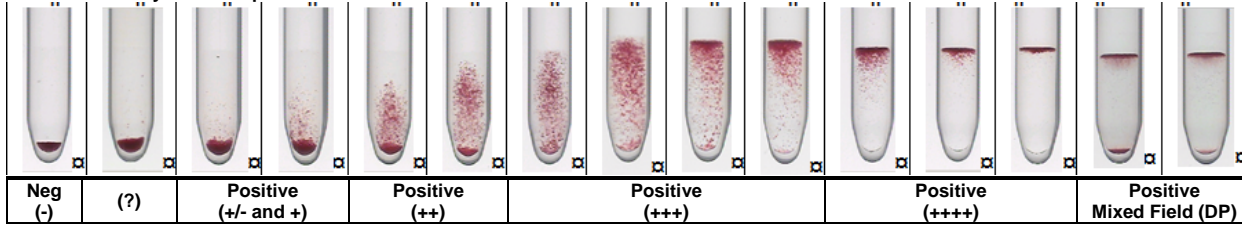
Please refer to the instructions for use for the specific IH-Card.

INTERPRETATION OF RESULTS

For visual interpretation

- **Positive result** - Agglutinates (on the surface of or dispersed through the gel) or hemolysis (in case of serum test) with very few or no red blood cells in the gel column. Report as a positive test result if hemolysis is present in the microtube but not in the sample column. Red blood cells may remain suspended on the top of the gel or are dispersed throughout the gel in varying degrees. A few cells may form a button in the microtube bottom in some positive reactions.
- **Negative result** - A compact button of red blood cells at the microtube bottom is a negative test result.

Refer to the IH-System Interpretation Guide for additional information



Well Reaction Grade	Result Interpretation	Reaction Description
-	Negative	A compact, pellet of RBCs* with a smooth surface at the bottom of the well with no visible agglutination.
+/-	Blood Grouping ◀ and Phenotyping including Anti-D Blend = Not interpretable For Reverse (serum) ABO Testing = Positive Direct Antiglobulin Test, Antibody Detection, Autocontrol = Positive Antibody Identification = no overall result interpretation, only well result shown as +/- For Crossmatching = Incompatible	A pellet of RBCs at the bottom of the well with a very few agglutinated RBCs visible above the pellet or an irregular pellet.
+	For Blood Grouping ◀ and Phenotyping including Anti-D Blend = Not interpretable For Reverse (serum) ABO Testing = Positive For Antibody Detection and DAT = Positive For Antibody Identification = no overall result interpretation, only well result shown as positive For Crossmatching = Incompatible	A pellet of RBCs at the bottom of the well with agglutinated RBCs visible in the lower half of the gel column.
++	For Blood Grouping ◀ and Phenotyping including Anti-D Blend = Positive For Reverse (serum) ABO Testing = Positive For Antibody Detection and DAT = Positive For Antibody Identification = no overall result interpretation, only well result shown as positive For Crossmatching = Incompatible	Agglutinated RBCs distributed throughout the entire length of the gel column, with no line of RBCs on the top of the well.
+++	For Blood Grouping ◀ and Phenotyping including Anti-D Blend = Positive For Reverse (serum) ABO Testing = Positive For Antibody Detection and DAT = Positive For Antibody Identification = no overall result interpretation, only well result shown as positive For Crossmatching = Incompatible	Most agglutinated RBCs concentrated at the top of the gel or upper half of the gel column.
++++	For Blood Grouping ◀ and Phenotyping including Anti-D Blend = Positive For Reverse (serum) ABO Testing = Positive For Antibody Detection and DAT = Positive For Antibody Identification = no overall result interpretation, only well result shown as positive For Crossmatching = Incompatible	Agglutinated RBCs concentrated as a line at the top of the gel column with a few agglutinated RBCs just underneath the gel surface.
Mixed Field (DP)	Blood Grouping ◀ and Phenotyping including Anti-D Blend = Not interpretable For Reverse (serum) ABO Testing = Positive Direct Antiglobulin Test, Antibody Detection, Autocontrol = Positive Antibody Identification = no overall result interpretation, only well result shown as DP For Crossmatching = Incompatible	Agglutinated RBCs as a line at the top of the gel or dispersed in upper part of the gel and non-agglutinated RBCs forming a pellet at the bottom of the well. The instrument interpretation software displays "DP" (double population) for a mixed field result.
?	For Blood Grouping including Reverse ABO Testing ◀ and Phenotyping including Anti-D Blend, Antibody Detection and Identification, Direct Antiglobulin Testing = Not interpretable For Crossmatching = Incompatible	Ambiguous result.

For automated reading

Below is a description of the various reaction grades and how the software uses that well reaction to determine the result interpretation. Please refer to the IH-Reader 24 User Manual, IH-1000, IH-500 and IH-Com User Manual U.S. for further information.

Well Reaction Grade	Result Interpretation	Reaction Description
-	Negative	A compact, pellet of RBCs* with a smooth surface at the bottom of the well with no visible agglutination.
+/-	Blood Grouping ◀ and Phenotyping including Anti-D Blend = Not interpretable For Reverse (serum) ABO Testing = Positive Direct Antiglobulin Test, Antibody Detection, Autocontrol = Positive Antibody Identification = no overall result interpretation, only well result shown as +/- For Crossmatching = Incompatible	A pellet of RBCs at the bottom of the well with a very few agglutinated RBCs visible above the pellet or an irregular pellet.
+	For Blood Grouping ◀ and Phenotyping including Anti-D Blend = Not interpretable For Reverse (serum) ABO Testing = Positive For Antibody Detection and DAT = Positive For Antibody Identification = no overall result interpretation, only well result shown as positive For Crossmatching = Incompatible	A pellet of RBCs at the bottom of the well with agglutinated RBCs visible in the lower half of the gel column.
++	For Blood Grouping ◀ and Phenotyping including Anti-D Blend = Positive For Reverse (serum) ABO Testing = Positive For Antibody Detection and DAT = Positive For Antibody Identification = no overall result interpretation, only well result shown as positive For Crossmatching = Incompatible	Agglutinated RBCs distributed throughout the entire length of the gel column, with no line of RBCs on the top of the well.

Well Reaction Grade	Result Interpretation	Reaction Description
+++	For Blood Grouping ◀ and Phenotyping including Anti-D Blend = Positive For Reverse (serum) ABO Testing = Positive For Antibody Detection and DAT = Positive For Antibody Identification= no overall result interpretation, only well result shown as positive For Crossmatching = Incompatible	Most agglutinated RBCs concentrated at the top of the gel or upper half of the gel column.
++++	For Blood Grouping ◀ and Phenotyping including Anti-D Blend = Positive For Reverse (serum) ABO Testing = Positive For Antibody Detection and DAT = Positive For Antibody Identification = no overall result interpretation, only well result shown as positive For Crossmatching = Incompatible	Agglutinated RBCs concentrated as a line on the top of the gel column with a few agglutinated RBCs just underneath the gel surface.
Mixed Field (DP)	Blood Grouping ◀ and Phenotyping including Anti-D Blend = Not interpretable For Reverse (serum) ABO Testing = Positive Direct Antiglobulin Test, Antibody Detection, Autocontrol = Positive Antibody Identification = no overall result interpretation, only well result shown as DP For Crossmatching = Incompatible	Agglutinated RBCs as a line at the top of the gel or dispersed in upper part of the gel and non-agglutinated RBCs forming a pellet at the bottom of the well. The instrument interpretation software displays "DP" (double population) for a mixed field result.
?	For Blood Grouping including Reverse ABO Testing ◀ and Phenotyping including Anti-D Blend, Antibody Detection and Identification, Direct Antiglobulin Testing = Not interpretable For Crossmatching = Incompatible	Ambiguous result.

* RBCs = Red Blood Cells

STABILITY OF REACTIONS

For visual reading of reactions, best results are obtained within six (6) hours of centrifugation. Interpretation may be affected by drying of the gel, hemolysis of red blood cells and slanting of reaction patterns due to storage in a non-upright position. Processed cards that are stored in the refrigerator (2 to 8 °C) and properly sealed to protect from evaporation may be interpreted for up to one (1) day. Gel cards should not be interpreted after the first sign of drying, or if hemolysis is observed. The age and condition of red blood cells, as well as the temperature at which the card is stored, will affect how long cards can be stored. The presence of sodium azide in the gel may cause the red blood cells to become dark in color over time. This darkening does not interfere with the test result.

QUALITY CONTROL

On each day of use, the IH-Cells should be tested with antibody positive and negative samples. Each IH-Cell is satisfactory for use if positive and negative samples react as expected.

LIMITATIONS

- Erroneous and abnormal results may be caused by:
 - Bacterial or chemical contamination of the serum, plasma, red blood cells or equipment.
 - Patient medication or disease yielding a cross-reaction.
 - Presenting panagglutinins in the blood specimen.
 - Cold agglutinins in the blood specimen.
 - Autoantibodies treatment of specimen red blood cells.
 - A red blood cell concentration or suspension medium different from that recommended.
 - Incomplete resuspension of the red blood cells.
 - Sample or Reagent Red Blood Cells hemolysis.
 - Contamination between microtubes through pipetting errors.
- Grossly icteric, hemolytic or lipemic blood samples, blood samples with abnormally high concentrations of protein or blood samples from patients who have received plasma expanders of high molecular weight may give false positive or questionable results. Icteric blood samples may cause difficulty in interpretation and test results should be used with caution.
- Fibrin, clots, particulates or other artifacts may cause some red blood cells to be trapped at the top of the gel and cause an anomalous result. They may appear as a pinkish layer. In a negative reaction the false appearance of a mixed field could lead to misinterpretation.
- If red blood cells (pellet at the bottom of the microtube) are too low in concentration they become difficult to visualize, and, in certain cases, a weak positive reaction can fail to be detected.
- Weak reactions may be obtained in ABO serum/plasma blood grouping and is a valid result.
- Decreased ABO antibody reactivity may be seen with low titer isoagglutinin antibodies may be caused by disease states, the elderly or infants resulting in false negative reactions. Generally, newborns and young babies do not show test reaction due to missing isoagglutinins.
- Weak isoagglutinins may not be detectable by IH-Cell A2.
- Testing cord blood samples for ABO antibodies may give incorrect results.
- The reactivity of the product may decrease during the dating period and should not be used after the expiration date. The rate of decrease in reactivity is partially dependent on individual donor characteristics that are neither controlled nor predicted by the manufacturer
- The A2 Reagent Red Blood Cells may not be agglutinated by low-titered anti-A found in the sera of infants and elderly individuals who are group O and group B.
- If testing is only performed with IH-Cell A1&B and/or IH-Cell A2, blood group Bombay will not be detected. To detect blood group Bombay, additional testing with Red blood cells of blood group O is recommended.

SPECIFIC PERFORMANCE CHARACTERISTICS

The final release testing is performed according to the product specific Standard Operating Procedures. As part of the lot release process, each lot of Bio-Rad Reagent is tested against antigen positive and negative samples to ensure suitable reactivity and specificity.

Performance characteristics using the IH-1000

Testing to determine the performance characteristics of the Bio-Rad IH-Cell A1&B and IH-Cell A2 was performed at four different US clinical sites and included patient, and donor samples. The positive and negative percent agreements were calculated for the Bio-Rad IH-Reagent Red Blood Cells in comparison to the FDA licensed reference reagents.

Results of the positive percent agreement and negative percent agreement, with the one-sided Exact 95% Lower Confidence Limit (LCL) are listed in the data table below. Note: See the IH-1000 User Manual U.S. and IH-Com User Manual U.S. for more information on verification of results.

Results from Clinical Trials

Test	Negative Agreement N	Negative Agreement (one-sided Exact 95% LCL)	Positive Agreement N	Positive Agreement (one-sided Exact 95% LCL)
A1	2,525	99.80% (99.58%)	3,805	99.89% (99.76%)
B	1,007	99.21% (98.57%)	5,312	99.85% (99.73%)
A2	443	97.52% (95.92%)	607	98.85% (97.84%)

Agreement between the methods does not imply which method obtained the correct result. The above results do not reflect any discrepancy resolution between the methods.

Reproducibility was evaluated at two external sites and one internal site by testing a reproducibility panel according to the following scheme: one lot of reagent x 3 sites x 1 operator x 5 non-consecutive days x 2 runs x 2 replicates over a period of 20 days using the IH-1000 Analyzer. Reproducibility was demonstrated for the IH-Cell A1&B and IH-Cell A2 within run, between runs and between sites.

A precision study was conducted internally using three reagent lots x 5 non-consecutive days x 2 runs x 2 replicates over a period of 20 days using the IH-1000 Analyzer. Precision was demonstrated with all three lots of IH-Cell A1&B and IH-Cell A2.

Performance characteristics using the IH-500

Testing to determine the performance characteristics of the Bio-Rad IH-Cell A1&B and IH-Cell A2 was performed at three different US clinical sites and included patient, and donor samples. The positive and negative percent agreements were calculated for the Bio-Rad IH-Reagent Red Blood Cells in comparison to the FDA licensed reference reagents.

Results of the positive percent agreement and negative percent agreement, with the one-sided Exact 95% Lower Confidence Limit (LCL) are listed in the data table below. Note: See the IH-500 User Manual U.S. and IH-Com User Manual U.S. for more information on verification of results.

Results from Clinical Trials

Test	Sample type	Negative Agreement N	Negative Agreement (one-sided Exact 95% LCL)	Positive Agreement N	Positive Agreement (one-sided Exact 95% LCL)
A1	Random samples	553	99.82% (99.15%)	631	100% (99.53%)
A1	Known group B	NA	NA	255	100% (98.83%)
A1	All samples	553	99.82% (99.15%)	886	100% (99.66%)
B	Random samples	166	94.58% (90.73%)	1,018	100% (99.71%)
B	Known group B	255	100% (98.83%)	NA	NA
B	All samples	421	97.86% (96.30%)	1,018	100% (99.71%)
A2	Random samples	577	97.92% (96.65%)	608	100% (99.51%)
A2	Known group B	23 ¹	34.78% (18.63%)	232	100% (98.72%)
A2	All samples	600	95.50% (93.85%)	840	100% (99.64%)

¹Eight (8) samples enrolled in the study as known blood group B were negative in testing with IH-Cell A2 by both the investigational and reference method. The samples were not tested with A2 RRBCs prior to enrollment in the study so an expected positive result with the IH-Cell A2 RRBCs is only inferred from the known blood group. Agreement between the methods does not imply which method obtained the correct result. The above results do not reflect any discrepancy resolution between the methods.

Reproducibility was evaluated at three external sites by testing a reproducibility panel according to the following scheme: one lot of reagent x 3 sites x 1 operator x 5 non-consecutive days x 2 runs x 2 replicates over a period of 20 days. Reproducibility for the Reagent Red Blood Cells IH-Cell A1&B and IH-Cell A2 using the IH-500 was demonstrated within run, between runs and between sites.

Performance characteristics for manual testing

Testing to determine the performance characteristics of the Bio-Rad IH-Cell A1&B and IH-Cell A2 was performed at five different US clinical sites and one internal site and included patient, and donor samples. The positive and negative percent agreements were calculated for the Bio-Rad IH-Reagent Red Blood Cells in comparison to the FDA licensed reference reagents.

Results of the positive percent agreement and negative percent agreement, with the one-sided Exact 95% Lower Confidence Limit (LCL), are listed in the data table below.

Results from Clinical Trials

Test	Negative Agreement N	Negative Agreement (one-sided Exact 95% LCL)	Positive Agreement N	Positive Agreement (one-sided Exact 95% LCL)
A1	437	99.77% (98.92%)	781	99.74% (99.20%)
B	313	100% (99.05%)	904	99.78% (99.31%)
A2	382	97.64% (95.92%)	688	96.22% (94.79%)

Agreement between the methods does not imply which method obtained the correct result. The above results do not reflect any discrepancy resolution between the methods.

Reproducibility was evaluated at three external sites by testing a reproducibility panel according to the following scheme: one lot of reagent x 3 sites x 2 operators x 5 non-consecutive days x 2 runs x 2 replicates over a period of 20 days. Reproducibility for the IH-Cell A1&B and IH-Cell A2 using the IH-Centrifuge L was demonstrated within runs, between runs and between sites.

Performance characteristics using the IH-Reader 24

Testing to determine the performance characteristics of the Bio-Rad IH-Cell A1&B and IH-Cell A2 was performed at five different US clinical sites and one internal site and included patient and donor samples. The positive and negative percent agreements were calculated for the Bio-Rad IH Blood Grouping Reagents in comparison to the FDA licensed reference reagents. Microtube results for a given reagent were combined across applicable IH-Cards.

Results of the positive percent agreement and negative percent agreement, with the one-sided Exact 95% Lower Confidence Limit (LCL) are listed in the data table below. Note: See the IH-Reader 24 User Manual and IH-COM User Manual U.S. for more information on verification of results.

Results from Clinical Trials

Test	Negative Agreement N	Negative Agreement (one-sided Exact 95% LCL)	Positive Agreement N	Positive Agreement (one-sided Exact 95% LCL)
A1 RRBCs	434	99.77% (98.91%)	784	99.87% (99.40%)
B RRBCs	313	100% (99.05%)	904	99.89% (99.48%)
A2 RRBCs	365	97.53% (95.74%)	610	97.21% (95.85%)

Agreement between the methods does not imply which method obtained the correct result. The above results do not reflect any discrepancy resolution between the methods.

Reproducibility was evaluated at three external sites by testing a reproducibility panel according to the following scheme: one lot of reagent x 3 sites x 2 operators x 5 non-consecutive days x 2 runs x 2 replicates over a period of 20 days. Reproducibility for the IH-Cell A1&B and IH-Cell A2 using the IH-Reader 24 was demonstrated within run, between runs and between sites.

For technical support or further product information, contact Bio-Rad Laboratories, Inc at 800-224-6723.

GLOSSARY OF SYMBOLS

Symbol	Definition	Symbol	Definition
	Batch Code		<i>In vitro</i> diagnostic medical device
	Consult the instructions for use for important cautionary information such as warnings and precautions		Consult instructions for use
	Manufacturer		Use by YYYY-MM-DD
	Contains sufficient quantity for <n> tests		Catalog number
	Temperature limitation		Volume

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Key: Underline = Addition of changes ◀ = Deletion of text