IMPACT Ristocetin High – For Research Use Only

REF HB-2121-FG

Guide to Symbols

REF — Catalogue No.

Σ — Contains sufficient for <n> tests

Consult accompanying documents

Use By Date

8℃ / 2℃ — Store at 2-8ºC

RCNS 210µl Aqua — Reconstitute with 210µl De-ionised or Purified Water

LOT — Batch – Lot Code

HART BIOLOGICALS

IFU112-RUO Version 1

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IMPACT Ristocetin High – For Research Use Only

GB Handling Instructions

Section 1: Manufacturer
Hart Biologicals Ltd. 2 Rivergreen Business Centre, Queens Meadow, Hartlepool. UK. TS25 2DL.

Section 2: Identification of the Reagent
IMPACT Ristocetin High – For Research Use Only available as:
6 x 210µl – HB-2121-FG

Section 3: Intended use
Hart Biologicals IMPACT Ristocetin High – For Research Use Only, reagent is used to test platelet dysfunction, or normal platelet activity in whole blood, during testing on the IMPACT analyser. For use by trained professionals only.

The reagent contains a lyophilised preparation of 23.87mg/ml Ristocetin with added buffer.

Section 4: Principles of the examination method
IMPACT utilises whole blood impedance aggregometry (WBIA), an established technology for platelet function testing that has been widely used for many years. It is a rapid and standardised option for platelet function testing. [1,2,9,10] The method is impedance (electrical resistance) aggregometry and is non optical.[5] The analyser can be used to test platelet function and for antiplatelet studies.[3] Test principle is that platelets adhere to small wires suspended in the blood sample and the impedance between the wires as the platelets adhere and aggregate is measured and plotted.[8] In the IMPACT aggregation trace, the impedance is measured numerically in ohms and displayed graphically and numerically on the screen. Two measurements are performed in parallel in each test cell to provide internal verification and assurance.
Ristocetin can be used in an assay for the quantitative in vitro determination of von Willebrand Factor (VWF) by means of glycoprotein Ib (GpIb) receptors in the presence of Ristocetin. In vitro, Ristocetin forms complexes with VWF which bind to GpIb and trigger platelet activation and aggregation. Reduced or absent agglutination in the presence of ristocetin may be attributed to an absence of reduction of VWF or a lack of reduction in the number of GpIb receptors as may be encountered in Bernard-Soulier syndrome. Ristocetin High test normally induces a strong platelet aggregation response and an absence of aggregation in the Ristocetin High test can be based on a deficiency of GpIb receptors or vWF. In the Ristocetin Low test, a weak aggregation response is expected. If a higher than expected aggregation response is obtained, this may indicate an enhanced aggregation tendency of vWF (vWD type IIb).[5,6]

Section 5: Traceability of values assigned to calibrators and trueness-control material

No control material is currently available for platelet aggregation testing. However, IMPACT Control Set – For Research Use Only is provided for verification of the IMPACT analyser, with two level impedance quality control.

It is recommended that each laboratory establishes its own normal range parameters consisting of fresh whole blood samples collected from normal healthy donors.

IMPACT Ristocetin Low – For Research Use Only, can be used along side the Ristocetin High – For Research Use Only reagent, when testing samples.

Section 6: Components
IMPACT Ristocetin High – For Research Use Only is supplied as:
HB-2121-FG 6 x 210µl of lyophilised Ristocetin. Each kit is sufficient to perform 60 tests.

Section 7: Additional required equipment/information
IMPACT Operator's Manual - Research Use Only – IFU123-RUO
IMPACT Analyser – For Research Use Only (HB-2116-FG)
De-ionised or Purified Water
IMPACT Test Cells 5 x 12 For Research Use Only (HB-2117-FG)
IMPACT Diluent – For Research Use Only (HB-2129-FG)
IMPACT Diluent + Calcium – For Research Use Only (HB-2130-FG)
IMPACT Control Set – For Research Use Only (HB-2131-FG)
IMPACT Ristocetin Low – For Research Use Only (HB-2122-FG)

Section 8: Reagent preparation
Allow the IMPACT Ristocetin High – For Research Use Only vial to come to room temperature and then reconstitute using the reconstitution setting within the IMPACT software with automated pipette volume. IMPACT Operator's Manual - Research Use Only – IFU123-RUO should be referred to.
Use purified water as indicated on the vial label. Allow the IMPACT Ristocetin High – For Research Use Only vial to reconstitute at room temperature for 10 minutes. The IMPACT Ristocetin High – For Research Use Only reagent is then ready to use.

Section 9: Storage and shelf life after first opening
Unopened vials (lyophilised):
- 3 years @ 2-8ºC

Opened vials (after reconstitution):
- 7 Days @ 2-8ºC
-24 Hours On Board @ Room Temperature (18-25ºC)

The vial label carries the expiry date of the reagent from the date of manufacture.

Section 10: Warnings and precautions
For Research Use Only.
Contains microbiological derivatives:
IMPACT Ristocetin High comprises of Ristocetin Sulphate, which is free from pathogenic agents that could be transmitted to humans. However, it must be used with all cautions required for handling potentially hazardous material.

According to REACH (EC) No. 1907/2006 and CLP Regulation (EC) No. 1272/2008, IMPACT Ristocetin High – For Research Use Only, product is not classifiable as hazardous.

IMPACT Ristocetin High – For Research Use Only, reagent vials, may be disposed of in accordance with laboratory procedures for hazardous waste. IMPACT Ristocetin High – For Research Use Only Kit Packaging may be recycled in line with local regulatory requirements.

Section 11: Primary sample collection, handling and storage
The recommended sample collection for impedance aggregometry using whole blood is stated as follows: Citrated tubes (3.2 % Citrate) or Hirudin (25µg/ml) as anticoagulant may be used.[4,5,7]
Guidelines for blood draw of Platelet Function Testing (PFT) should be followed with needle gauge of 19-21G.[4] It is only possible to compare the results of an individual sample with reference ranges when the same sample anticoagulant (i.e. Citrate or Hirudin) is used.
Samples should be analysed within the period of 0.5-3 hours after blood collection. [5,7] Prior to immediate testing the sample, the blood tube should be gently inverted by hand. [5,6]

Section 12: Examination procedure
The IMPACT analyser is designed to ensure easy, efficient, and safe user handling. The Software User Interface is developed for the use of a touchscreen and semi-automated test programme with step by step protocol. IMPACT Operator's Manual - Research Use Only – IFU123-RUO, should be referred to.
Data entry can be performed via the integrated label scanner on the front of the IMPACT analyser or manually via an integrated keyboard.) Test volumes used during the IMPACT Ristocetin High test protocol are stated as follows:

- 300µl IMPACT Diluent / IMPACT Diluent + Calcium
- 300µl Whole Blood Sample
- Incubation
- 20µl IMPACT Ristocetin High – to start the test
- Measuring Time – 6 Minutes

Section 13: Control Procedure
For Research Use Only. The results of platelet aggregation studies should be interpreted against the results of aggregation profiles of a normal sample tested at the same time. The normal donor should not have taken acetylsalicylic acid or acetylsalicylic acid containing compounds COX inhibitors, or other platelet aggregation inhibitors within 10 days.
Each laboratory should define its acceptable ranges and verify the expected performance characteristics.
IMPACT Control Set – For Research Use Only, should be used to verify performance of the IMPACT analyser prior to testing samples.

Section 14: Calculation of examination results
During the IMPACT testing, results are expressed within the software interface as Area Under Curve (AUC) value, this is the measured impedance in ohms*minute. Additionally, the Maximum Slope in ohms/minute and the Maximum Aggregation in ohms are also displayed. These values should be recorded as well as the aggregation trace and considered alongside a normal whole blood sample control and inhibited control sample where applicable. Normal IMPACT Ristocetin High induced aggregation values are deemed 'normal' AUC >70ohms*min. However, each laboratory should establish the normal range.

Section 15: Interpretation of results
For Research Use Only. Substances such as caffeine, tobacco, alcohol and vitamin C may also affect the result. [6,8]

Section 16: Performance characteristics

i. Analytical Performance Characteristics
From testing at Hart site, normal aggregation response for IMPACT Ristocetin High testing were as follows over 20 normal healthy donors:
Citrate Sample:
AUC: 54 – 133 ohms*min.
Max Aggregation: 16 – 38 ohms.
Max Slope: 6 – 20 ohms/min.
Hirudin Sample:
AUC: 73 – 175 ohms*min.
Max Aggregation: 26 – 58 ohms.
Max Slope 10 – 24 ohms/min.
These values are for reference only and each laboratory should establish its normal range values.

ii. Performance Characteristics
For Research Use Only. IMPACT Ristocetin High – For Research Use Only, may be used in platelet studies to test platelet dysfunction, or normal platelet activity in whole blood.
IMPACT Ristocetin High – For Research Use Only, induced aggregation would be sensitive to the following disorders/defects: von Willebrand Disease, Bernard-Soulier-Syndrome, or Glanzmann thrombasthenia. Where von Willebrand factor is absent or defective, abnormal agglutination occurs.[6]

iii. Measuring Intervals
IMPACT Ristocetin High – For Research Use Only, when used according to semi-automated test protocol of the IMPACT analyser, the final Ristocetin concentration is 0.77mg/ml.

Section 17: Biological reference intervals
For Research Use Only. Each laboratory should define its acceptable normal aggregation ranges with use of normal healthy donors and verify the expected performance characteristics.

Section 18: Limitations of the examination procedure
For Research Use Only.
For use by trained professionals only.
Impaired platelet function has been reported after the ingestion of several drugs and herbal medicines. Aggregation can be abnormal in thrombocytopenia samples.

Section 19: Literature references

1. Ranucci, Marco; Simioni, Paolo (20 January 2016). Point-of-Care Tests for Severe Hemorrhage: A Manual for Diagnosis and Treatment. Springer. pp. 40–42. ISBN 978-3-319-24795-3
2. Marcucci, Carlo; Schoettker, Patrick (17 September 2014). Perioperative Hemostasis: Coagulation for Anesthesiologists. Springer. pp. 54–56. ISBN 978-3-642-55004-1.3.
3. Dacie & Lewis, 'Practical Haematology', Lewis, S.M., Bain, B.J. and Bates, I. (Editors); 9th Edition, Elsevier Science Ltd., 2002, pages 380-385.
4. WHO Guidelines on Drawing Blood: Best Practices in Phlebotomy', World Health Organisation, 2010, ISBN 978 92 4 159922
5. CLSI. Platelet Function Testing by Aggregometry; Approved Guideline. CLSI document H58-A. Wayne, PA: Clinical and Laboratory Standards Institute; 2008.
6. BSCH Guideline Harrison P. Et al. Guidelines for the laboratory investigation of heritable disorders of platelet function.
7. Kaiser AF, Neubauer H, Franken CC, et al. Which is the best anticoagulant for whole blood aggregometry platelet function testing? Comparison of six anticoagulants and diverse storage conditions. Platelets. 2011 Oct 14.
8. Jambor C, Weber CF, Gerhardt K, et al. Whole Blood Multiple Electrode Aggregometry Is a Reliable Point-of-Care Test of acetylsalicylic acid-Induced Platelet Dysfunction. Anesth Analg 2009;109:25-31.
9. Tóth O., Calatzis A., Penz S., Losonczy H, Siess W.: Multiple electrode aggregometry: A new device to measure platelet aggregation in whole blood; Thromb Haemost 2006; 96: 781-8
10. Aradi D, Komócsi A, Price MJ, et al. Efficacy and safety of intensified antiplatelet therapy on the basis of platelet reactivity testing in patients after percutaneous coronary intervention: systematic review and meta-analysis. Int J Cardiol. 2013;167(5):2140–8.