IMPACT

IMPACT ADP – For Research Use Only

REF HB-2118-FG

Guide to Symbols

REF	Catalogue No.	Σ	Contains sufficient for <n> tests
	Consult accompanying documents	BIO	Contains biological material of animal origin
2°C 8°C	Store at 2-8°C		Use By Date
LOT	Batch – Lot Code	RCNS 210µl Aqua	Reconstitute with 210µl De-ionised or Purified Water

HART BIOLOGICALS

IFU109-RUO Version 0

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IMPACT ADP – 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 ADP – For Research Use Only available as:
6 x 210µl – HB-2118-FG

Section 3: Intended use
Hart Biologicals IMPACT ADP – 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.
ADP (adenosine 5'-diphosphate) is an important mediator of platelet activation and aggregation. The reagent contains a lyophilised preparation of 200µM ADP with added buffer and stabilisers.

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] 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.[3,10] 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.
ADP is released from blood platelets in the vasculature upon activation by various agents, such as collagen and thrombin, and from damaged blood cells, endothelium or tissues. Activation by ADP results in the recruitment of more platelets and stabilisation of existing platelet aggregates. ADP binds to P2Y1 and P2Y12 receptors, leading to platelet shape change, activation, and aggregation. IMPACT ADP activates via P2Y12 receptors mediating aggregation and some of its derivatives and antagonised by ATP (adenosine 5'-triphosphate) and some of its derivatives[1,3,9].

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 P_2Y_{12} – For Research Use Only, is an inhibitor for the P_2Y_{12} activation pathway of human platelets and can be used together with IMPACT ADP – For Research Use Only.

Section 6: Components
IMPACT ADP – For Research Use Only is supplied as:
HB-2118-FG 6 x 210µl of lyophilised ADP. 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 P2Y12 - For Research Use Only (HB-2127-FG)

Section 8: Reagent preparation
Allow the IMPACT ADP – 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 Operators' Manual - Research Use Only – IFU123-RUO should be referred to.
Use purified water as indicated on the vial label. Allow the IMPACT ADP – For Research Use Only vial to reconstitute at room temperature for 10 minutes. The IMPACT ADP – For Research Use Only reagent is then ready to use.

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

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

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 animal derivatives:
Bovine Serum Albumin (BSA) (0.5%) used as a lyoprotectant within IMPACT ADP – For Research Use Only Reagent, was prepared from bovine plasma, which was tested for the absence of infectious agents and collected from animals free from VSE and BT Virus. However, no test may exclude fully the absence of infectious agents. As with any product of bovine origin, 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 ADP – For Research Use Only, product is not classifiable as hazardous.

IMPACT ADP – For Research Use Only, reagent vials, may be disposed of in accordance with laboratory procedures for hazardous waste. IMPACT ADP – 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 ADP test protocol are stated as follows:

- 300µl IMPACT Diluent / IMPACT Diluent + Calcium
- 300µl Whole Blood Sample
- Incubation
- 20µl IMPACT ADP – 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 ADP induced aggregation values are deemed 'normal' AUC >60 ohms*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 ADP testing were as follows over 20 normal healthy donors:

Citrate Sample:

AUC: 57 – 108 ohms*min.
Max Aggregation: 13 – 30 ohms.
Max Slope: 4 – 12 ohms/min.

Hirudin Sample:

AUC: 48 – 154 ohms*min.
Max Aggregation: 16 – 46 ohms.
Max Slope 5 – 15 ohmns/min.

These values are for reference only and each laboratory should establish its normal range values.

ii. Performance Characteristics

For Research Use Only. IMPACT ADP – For Research Use Only, may be used in platelet studies to test platelet dysfunction, or normal platelet activity in whole blood.

IMPACT ADP – For Research Use Only, induced aggregation would be sensitive to the following disorders/defects: Aspirin like defects, $P2Y_{12}$ and $P2Y_1$ Defects, Dense Granule Defects, Secretion Defects, Glanzmann Thrombasthenia and Storage Pool Defect.[6]

iii. Measuring Intervals

IMPACT ADP – For Research Use Only, when used according to semi-automated test protocol of the IMPACT analyser, the final ADP concentration is 6.5µM.

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

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2. Marcucci, Carlo; Schoettker, Patrick (17 September 2014). Perioperative Hemostasis: Coagulation for Anesthesiologists. Springer. pp. 54–56. ISBN 978-3-642-55004-1.3.
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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. 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
9. Sibbing D, Braun S, Jawansky S, et al. Assessment of ADP-induced platelet aggregation with light transmission aggregometry and multiple electrode platelet aggregometry before and after clopidogrel treatment. Thromb Haemost. 2007;98(4):784–9.
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.