Multiplate® analyzer

Powerful analysis of platelet function
Multiplate® analyzer
Addressing unmet medical needs

Milestone in analysis, major asset to therapy
Roche’s stated aim is to combine true innovation with proven medical and diagnostic expertise. Multiplate® marks a milestone success in this ambitious endeavor.

The Multiplate® system addresses a significant unmet medical need by improving assessments of patients’ platelet function. It provides invaluable support for clinical decision-making in cardiology, surgery and intensive care. And that makes this analyzer a key asset for cardiologists, anesthetists and hematologists.

A potent force for platelet inhibition
Its best-in-class predictivity for thrombotic and bleeding risk is a potent force in anti-platelet therapy. It enables doctors to tailor treatment to the patient’s need and stratify patients who are at risk of bleeding.

Underpinned by highly standardized testing technology, Multiplate® is making powerful medical momentum in this important field of patient care. Here today, it is the analyzer destined to set tomorrow’s standards.
Predictive power

**Best predictivity – for tailored anti-platelet therapy**
- Approx. one in five patients responds inadequately to clopidogrel
- Risk of ischemic complications five to ten times greater in patients who respond poorly to clopidogrel.
- Other more potent drugs act more consistently but increase bleeding and cost up to 15 times as much as generic clopidogrel.
- Success with tailored, Multiplate®-assisted APT reported by several groups.

**Best predictivity – for stratification of bleeding risk**
- Patients on dual anti-platelet therapy with impaired platelet function are at greater risk of intra- and postoperative bleeding and transfusions.
- Patients stratified as high-responders to clopidogrel are at 2.6-times higher risk of major bleeding.
- Multiplate® helps improve hemostatic management in the bleeding patient after surgery, thereby contributing to a better outcome and lower costs.

**Medical momentum**
- Multiplate® features in > 400 Medline-listed publications.
- Consensus paper published by the Working Group on High On-Treatment Platelet Reactivity extols virtues of Multiplate®’s predictivity.
- Clinical guidelines recommend platelet function testing in CABG and PCI for patients treated with clopidogrel.

**Detection of platelet disorders**
- Platelet dysfunction can induce transient or permanent tendency to bleed.
- Multiplate® detects platelet dysfunction and disorders, and determines heparin-induced platelet aggregation in whole blood.
- It detects Glanzmann thrombasthenia, Bernard-Soulier syndrome, ADP receptor defects, and other platelet disorders associated with clinically relevant symptoms.

**Consistent results**
- Standardized test with low volume of whole blood.
- Wide range of CE marked tests for various applications.
- Fast five-channel, high-throughput analyzer.
- Great sensitivity and dynamic range.
- Dual-sensor design for enhanced quality control.
The challenge of adequate platelet inhibition
Clinical management of patients at high risk of arterial thrombosis, for example, after stent placement or in the event of acute coronary syndrome (ACS), presents a great challenge. In this case, it is imperative to achieve adequate platelet inhibition.

Multiplate® analyses have established that some 20 percent of patients do not respond adequately to clopidogrel after PCI.1 Patients who respond poorly to clopidogrel have been shown to have a fivefold to tenfold greater risk of ischemic complications.1-4 Conversely, the risk of major bleeding is 2.6 times greater in patients who are high responders to clopidogrel.5

More powerful but costly and risky
Novel P2Y12 receptor antagonists with more potent and consistent action than clopidogrel have been introduced. However, they cost up to 15 times as much as generic clopidogrel.6 The more effective action also comes at a human cost – a higher risk of major bleeding including fatal bleeding (prasugrel)7 and of non-CABG related major bleedings and dyspnea (ticagrelor).8

More effective treatment with Multiplate®
Real life studies with more than 2,000 PCI patients support the clinical benefit and cost-effectiveness of Multiplate®-guided anti-platelet therapy algorithms.9-12 It provides the guidance physicians need to tailor treatment. The ability to monitor and control anti-platelet therapy with Multiplate® is also a tremendous asset because it enables the treating physician to confirm patient compliance.

Citations from studies using the Multiplate® analyzer:
“Personalized antiplatelet treatment according to the platelet function testing with MEA (Multiple Electrode Aggregometry) resulted in an improved efficacy with an equal safety compared to the standard treatment (with clopidogrel)”. (Siller-Matula, J.M. et al. (2012)9)

“Routine platelet function testing [with Multiplate] is useful for guidance of tailored antiplatelet treatment and switching to prasugrel markedly reduces ST risk in HPR patients on clopidogrel” (Sibbing, D. et al. (2012))13

“ACS patients identified without HPR by the Multiplate assay had a remarkably low rate of thrombotic events on low–dose generic clopidogrel.” (Aradi, D. et al. (2013))10

1 Stented brain vessel. Sufficient anti-platelet therapy is key for the prevention of stent thrombosis.
Best predictivity – for stratification of bleeding risk

Mitigating complications, maximizing patient management
Platelet function plays a pivotal role in hemostasis during surgery and following traumatic injuries. Dysfunction can trigger complications that require increased blood transfusions and renewed exploratory surgery.

Several studies attest to the Multiplate® analyzer’s ability to detect a higher risk of bleeding and the need for increased transfusions in patients during surgery.14-18

From insight to impact
The ability to assess platelet function before, during and after major surgical procedures helps improve hemostatic patient management. This insight is a positive force that can help reduce hospitalization time, exposure to allogenic blood products and, by extension, costs.19 The savings potential is considerable.

Citations from studies using the Multiplate® analyzer:
“The multiple electrode aggregometry ADP test in patients under thienopyridine treatment and undergoing cardiac surgery is associated with postoperative bleeding and platelet transfusion and provides an accurate preoperative prediction of postoperative bleeding risk.”
(Ranucci, M. et al. 2011)

“POC-guided therapy was associated with lower Fresh Frozen Plasma and Platelet Concentrates usage and costs as well as an improved clinical outcome in this prospective randomized single-center study.”
(Weber, C.F. et al. 2012)

1 The Multiplate® analyzer enables the assessment of platelet function in low volumes of whole blood.
Platelet dysfunction triggered by drugs, diseases or genetic factors may induce a transient or permanent tendency to bleed. The Multiplate® analyzer is able to detect platelet dysfunction. And that makes it an invaluable therapeutic asset for doctors who manage patients with platelet dysfunctions.

**Designed to determine and distinguish**
Sensitivity to platelet disorders is designed into Multiplate®. It detects Glanzmann thrombasthenia, Bernard-Soulier syndrome, ADP receptor defects and von Willebrand disease (comparable to optical aggregometry). It is also well-suited for the functional determination of heparin-induced thrombocytopenia in whole blood.

Citations from studies using the Multiplate® analyzer:
“Compared to LTA MEA is more standardized, easier and faster to perform and requires smaller blood volumes for the analysis and is therefore a suitable alternative for the assessment of platelet disorders”. (Stemberger, M. et al. (2012))

“MEA is capable of detecting defective platelet aggregation in Glanzmann thrombasthenia (GT) patients similar to LTA… we think that Multiplate can be used as the standard aggregometer to study platelet aggregation in patients with GT.” (Awidi, A. et al. (2009))

“…in our population of VWD patients, [Multiplate] was as sensitive as LTA in detecting VWD. …[Multiplate] correctly evidenced the challenging type 2B VWD subtype in 3/3 patients, among whom two were thrombocytopenic.” (Valarche, V. et al. (2011))

1. Hirudin anticoagulant enables platelet function analysis under physiological calcium conditions

2. Platelet aggregates and spreading on the Multiplate sensors
Speed paired with efficiency

Easy to use and compact, the Multiplate® system analyzes platelet function in whole blood. Designed for speed as well as accuracy, its turnaround time is just ten minutes per test. It is equipped with five channels, so it processes up to 30 tests per hour. Each analysis requires no more than 300 μL of blood.

The Multiplate® analyzer comes with a comprehensive menu featuring six CE marked and standardized PFT procedures (ADPtest, ASPItest, TRAPtest, COLtest, RISTOtest, ADPtest HS). The system’s underlying low-shear detection principle enables the specific activation of platelet receptors or transduction pathways.

Advanced detection with sophisticated sensors

The advanced detection principle and sophisticated sensors built into Multiplate® lend it a superior dynamic range, sensitivity and signal magnitude for detecting platelet function. Each test cell incorporates two pairs of sensors (multiple electrode aggregometry, or MEA for short) that serve as an on-board quality control feature.

Citations from studies using the Multiplate® analyzer:

“As a whole blood method, Multiplate® avoids the handling of blood samples, with the advantage that the cellular environment remains unchanged, and allows rapid evaluation of platelet aggregation by ready-to-use test cuvettes with two independent sensor units.”  
(Paniccia, R. et al. (2009) 25)

“The effect size by use of multiple electrode aggregometry (MEA) was consistently greater for clopidogrel and aspirin as compared to other methods.”  

“MEA is a fast and standardized method to individually assess platelet function prior to and after clopidogrel treatment.”  
(Sibbing, D. et al. (2006) 27)
The Multiplate® analyzer already figures prominently in more than 400 Medline-listed publications. For example, the consensus paper published by the Working Group on High On-Treatment Platelet Reactivity extolled the virtues of Multiplate®’s peerless clinical predictivity.28

**Proven and recommended**

Multiplate®’s ability to predict thrombotic and bleeding risk is documented. Three studies with more than 2,000 PCI patients have independently confirmed the improved patient outcomes that come as a result of anti-platelet therapy tailored with the benefit of Multiplate®.9-11 A health economic study supports a Multiplate®-guided therapy to may be more cost-effective than prasugrel or ticagrelor treatment in ACS patients undergoing PCI.12

Clinical practice guidelines now recommend platelet function testing in patients treated with anti-platelet therapies in major surgical procedures29-30 and in coronary interventions with stenting in ACS patients and stable patients31-34 in case of high risk situations and if results may change the treatment strategy. Two position papers on the current role of platelet function testing in patients undergoing PCI35-36 advocate a role for routine testing in patients at high risk for stent thrombosis.

The recommendations set out in such guidelines and consensus opinions are sure to become stronger as more evidence attesting to the benefits of Multiplate®-assisted anti-platelet therapy is gathered. The TROPICAL-ACS trial (NCT01959451)37, a large investigator initiated multi-center study on Multiplate®-guided anti-platelet therapy in ACS patients investigates the clinical and health-economic impact of tailored anti-platelet therapies in PCI.
References


Multiplate® analyzer
Supporting clinicians with consistent results

1 Measurement position
- Patented twin sensor test cell
- Testing in low volumes (300 µL) of whole blood
- 5 measurement positions for simultaneous measurement of different samples/agonists
- Internal QC using duplicate detection of every measurement
- 10 minute time to result
- Sensitive signal detection with a large dynamic range

2 Reagent and sample compartment
- 4 reagent vial positions
- 1 sample position
- 9 positions for reagent
- Removable for cold storage

3 Electronic pipette
- Predefined pipette programs for routine tests
- Customizable settings for individual adaptation
- Audiovisual user guidance
- One button operation for easy and safe pipetting

4 Software
- Windows® XP-based user interface
- Pre-programmed test settings
- Automatic analysis and documentation of measurements
- Parameterization of dynamic signal
## Multiplate® analyzer

### Product specifications

<table>
<thead>
<tr>
<th><strong>Hardware specifications</strong></th>
<th><strong>PC</strong></th>
<th><strong>Processor</strong></th>
<th>Intel Atom (1.6 GHz)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RAM</strong></td>
<td></td>
<td>2 GB</td>
<td></td>
</tr>
<tr>
<td><strong>Hard drive</strong></td>
<td></td>
<td>min. 60 GB</td>
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</tr>
<tr>
<td><strong>Ports</strong></td>
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<td>USB 2.0/RS 232</td>
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</tr>
<tr>
<td><strong>Network</strong></td>
<td></td>
<td>100/1000 Mbit</td>
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</tr>
<tr>
<td><strong>Monitor</strong></td>
<td></td>
<td>min. 15” TFT</td>
<td></td>
</tr>
<tr>
<td><strong>Printer</strong></td>
<td></td>
<td>Laser printer (optional)</td>
<td></td>
</tr>
<tr>
<td><strong>Input devices</strong></td>
<td></td>
<td>Keyboard in various languages; mouse</td>
<td></td>
</tr>
<tr>
<td><strong>Software</strong></td>
<td></td>
<td>Windows® XP Professional (Multi User Interface)</td>
<td></td>
</tr>
</tbody>
</table>

| **Dimensions of the Multiplate analyzer** | **Height** | 11 cm |
|**Width**                                  | 32 cm  |
|**Depth**                                  | 45 cm  |
|**Weight**                                 | 11 kg  |

| **Electrical specifications** | **Device** | 100–240 V, 50–60 Hz |
|**Monitor**                    | See operator manual |
|**Printer**                    | See operator manual |

| **Electronic pipette** | **10-300 µL pipette volume** |
|**Programmable rate for aspiration and dispersal of liquids** | |
|**Pipette holder attached to housing** | |

| **Test** | **Sample volume** | 300 µL whole blood per test |
|**Key reagents** | **ASPiTest** |
|               | **ADPTest** |
|               | **TRAPTest** |
|               | **COLTest** |
|               | **RISTOTest** |
|               | **Prostaglandin E1 Reagent** |
|               | **GPIIb/IIIa Antagonist Reagent** |
|               | **ASA Reagent** |
The Multiplate® test principle is based on an advancement of Cardinal and Flower’s 1979 impedance aggregometry method.

- Unlike earlier applied systems, the Multiplate® analyzer provides a disposable test cuvette featuring a duplicate sensor.
- Patented twin sensor technology (Multiple Electrode Aggregometry, MEA) for optimal results and quality control.
- Whole blood testing eliminates the need for time-consuming sample preparation while maintaining the natural physiological matrix for platelet function.

- Small quantity (300 µL) of whole blood required per test, permitting up to 9 tests per blood tube draw.
- Upon activation platelets aggregate on metal sensors and increase the electrical resistance.

1. Disposable test cell with incorporated sensor and teflon coated stirring bar.
2. Duplicate sensor electrodes serve as an integrated quality control for each analysis.
3. The electronic detection of platelet function is not affected by optical variables within the sample.
Multiplate® test principle
Supporting best predictivity

Easy four-step process with results available in 10 minutes, a throughput of up to 30 tests per hour, and a superior dynamic range.

1. Place the test cell into the measurement position
2. Attach the sensor cable
3. Pipette 300 µL of saline + 300 µL of hirudin blood
4. Warming and equilibration
5. Pipette reagent
6. Results after 10 minutes
Multiplate® analyzer

Comprehensive reagent menu

<table>
<thead>
<tr>
<th>Material number</th>
<th>Product</th>
<th>Size</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>06675786190</td>
<td>ADPtest</td>
<td>1 x 1 mL</td>
<td>ADP induced platelet activation sensitive to clopidogrel, prasugrel and other ADP receptor antagonists</td>
</tr>
<tr>
<td>06675794190</td>
<td>ADPtest</td>
<td>3 x 1 mL</td>
<td>Cyclooxygenase dependent aggregation (using arachidonic acid) sensitive to Aspirin®, NSAIDs and other inhibitors of platelet cyclooxygenase</td>
</tr>
<tr>
<td>06675808190</td>
<td>ASPtest</td>
<td>1 x 1 mL</td>
<td>Collagen induced aggregation</td>
</tr>
<tr>
<td>06675816190</td>
<td>ASPtest</td>
<td>3 x 1 mL</td>
<td></td>
</tr>
<tr>
<td>06675824190</td>
<td>COLtest</td>
<td>1 x 1 mL</td>
<td></td>
</tr>
<tr>
<td>06675832190</td>
<td>COLtest</td>
<td>3 x 1 mL</td>
<td>vWF and GpIIb/IIIa dependent aggregation (using ristocetin)</td>
</tr>
<tr>
<td>06675859190</td>
<td>RISTOtest</td>
<td>1 x 1 mL</td>
<td></td>
</tr>
<tr>
<td>06675867190</td>
<td>RISTOtest</td>
<td>3 x 1 mL</td>
<td></td>
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<tr>
<td>06675875190</td>
<td>TRAPtest</td>
<td>1 x 1 mL</td>
<td>Platelet stimulation via the thrombin receptor (using TRAP-6), sensitive to IIb/IIIa receptor antagonists</td>
</tr>
<tr>
<td>06675883190</td>
<td>TRAPtest</td>
<td>3 x 1 mL</td>
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<tr>
<td>06675891190</td>
<td>Prostaglandin E1 Reagent</td>
<td>1 x 1 mL</td>
<td>For the assessment of ADPtest HS (high sensitivity). For the assessment of positive (i.e. abnormal) controls of the ADPtest</td>
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<td>06675905190</td>
<td>Prostaglandin E1 Reagent</td>
<td>3 x 1 mL</td>
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<tr>
<td>06675913190</td>
<td>ASA Reagent</td>
<td>1 x 1 mL</td>
<td>Inhibitor of cyclooxygenase. Addition of ASA reagent to the blood sample leads to reduced aggregation responses in ASPtest and COLtest</td>
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<tr>
<td>06675921190</td>
<td>ASA Reagent</td>
<td>3 x 1 mL</td>
<td></td>
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<tr>
<td>06675930190</td>
<td>GpIIb/IIIa Antagonist Reagent</td>
<td>1 x 0.5 mL</td>
<td>Inhibitor of the platelet GpIIb/IIIa receptor. Addition to a blood sample leads to strongly reduced aggregation in the TRAPtest</td>
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<tr>
<td>06675948190</td>
<td>GpIIb/IIIa Antagonist Reagent</td>
<td>3 x 0.5 mL</td>
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<tr>
<td>06675972190</td>
<td>NaCl/CaCl₂ Diluent Solution</td>
<td>10 x 5 mL</td>
<td>Sample diluent for platelet function testing with the Multiplate® analyzer under reduced calcium concentrations associated with the use of citrated blood samples</td>
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<td>06675975190</td>
<td>Hirudin Blood Tubes</td>
<td>50 x 3 mL</td>
<td>Anticoagulant for platelet function analysis under physiological calcium concentrations</td>
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<tr>
<td>06675960001</td>
<td>Hirudin Blood Tubes</td>
<td>10 x 3 mL</td>
<td>Quality control for electrical signal in impedance aggregometry based on the analysis of an artificial liquid control material</td>
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<tr>
<td>06675999190</td>
<td>Liquid Control Set</td>
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