

# Multiplate<sup>®</sup> analyzer

A reliable tool for platelet function testing



## Benefits of platelet function testing

Blood platelets or thrombocytes play a vital role in hemostasis, where they provide the initial primary hemostatic plug at the site of vessel injury to prevent bleeding. A variety of disorders of platelets, both inherited and acquired, can lead to a bleeding diathesis, which can be diagnosed using platelet function analysis<sup>1</sup>.

Platelets are also involved in thrombotic disorders and some rare inherited disorders, although the most common clinically are in cardiac disease (Myocardial Infarction) and thrombotic stroke. Development of arterial platelet thrombosis in myocardial infarcts is a leading cause of mortality in western society. To reduce the risk of thrombosis in these patients, antiplatelet medication like Aspirin and the P2Y12 platelet inhibitors clopidogrel, prasugrel and ticagrelor is administered to reduce platelet function. In some patients their response to these antiplatelet agents can be variable, with 30% of patients found as non-responders to clopidogrel<sup>2</sup>.

Platelet function testing can be used to monitor the efficacy of drugs and transition the change to other more effective antiplatelet drugs in non-responders or the de-escalation from one drug to another to reduce the bleeding risk<sup>3,4</sup>.

Platelet function testing can be performed in the following clinical scenarios; analysis of platelet function in patients who have been on antiplatelet medication before cardiac surgery as part of the anesthetic work up to reduce bleeding risk or allowing patients to go for surgery sooner<sup>5</sup>. Monitoring of platelet function antagonists like Aspirin, clopidogrel, prasugrel and ticagrelor in patients at high thrombotic risk or who require de-escalation from one antiplatelet agent to another to reduce bleeding risk<sup>2,3,5</sup>.

Heparin Induced Thrombocytopenia is another rare, but life-threatening thrombotic disorder, that can be diagnosed via platelet function testing and has been standardized by the ISTH SSC Platelet Immunology committee<sup>6</sup>.

Platelet function testing supports clinical decision making in:

- Percutaneous Coronary Interventions (PCI)<sup>3,4</sup>
- Pre-Cardiac surgery<sup>7</sup>
- De-escalation of antiplatelet treatment<sup>5</sup>
- Heparin Induced Thrombocytopenia<sup>6</sup>



## Product introduction

The Multiplate analyzer is an easy to use instrument to determine platelet function in small quantities of whole blood, in a highly standardized manner. Whole blood is the physiological environment where platelet function takes place in vivo. The use of whole blood for in vitro testing eliminates the need for time-consuming centrifugation steps.

The term “Multiplate” is derived from the phrase “multiple platelet function analyzer”. The testing method is called multiple electrode aggregometry (MEA). Impedance aggregometry was developed by Cardinal and Flower for the assessment of platelet function in whole blood.<sup>8</sup>

The 5 channel analyzer, with CE marked tests (ADPtest, ASPItest, TRAPtest, ADP HS)<sup>9</sup>, has been featured by almost 700 Medline-listed articles and has been reported by several groups to be useful in tailoring anti-platelet therapy, as well as improving the management of bleeding complications in surgical procedures.<sup>2,3</sup>

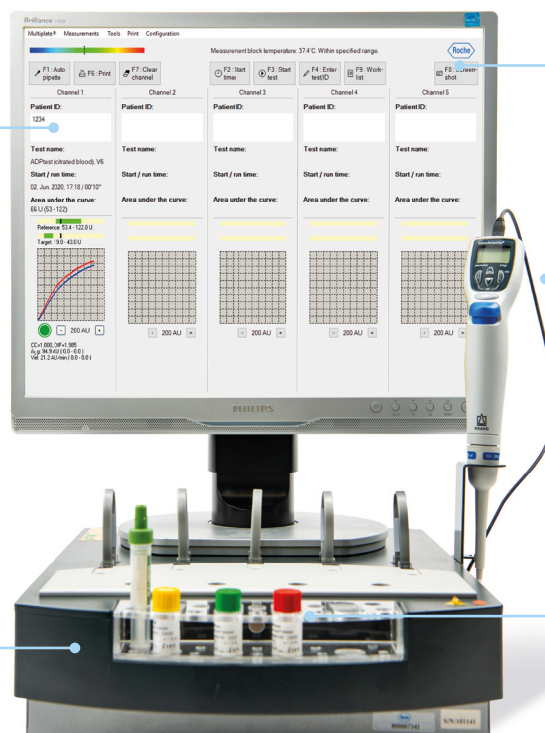
Graphical and parametric display of results

Microsoft Windows® 10 based user interface

Simple, computer controlled pipetting

5 open channels for parallel tests

Standardized reagents



## Detection principle

- Platelets are non-thrombogenic in their resting state
- Activated platelets can attach on vascular injuries and artificial surfaces
- Activated platelets stick on the wire and enhance the electrical resistance (s. Fig. 1) (own illustration)

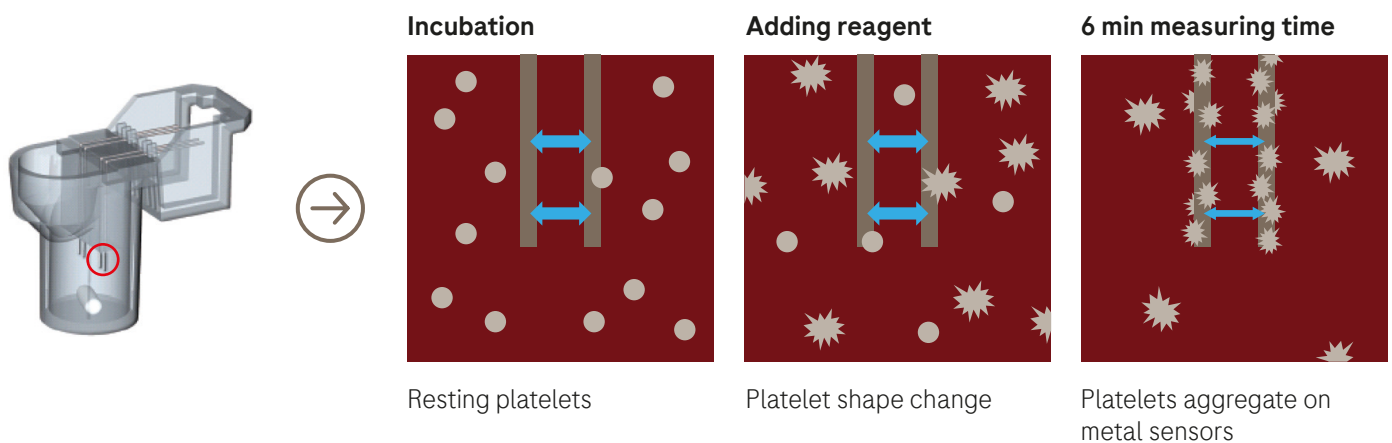


Figure 1. Multiplate detection principle: Activated platelets stick on the wire and enhance the electrical resistance

Every Multiplate test cell incorporates two independent sensor units, each consisting of 2 silver-coated highly conductive copper wires. The instrument detects the impedance change of each sensor separately. The impedance change is expressed in arbitrary “Aggregation Units (AU)” and plotted against time. The most important parameter is the area under the aggregation curve (AUC). It is affected by the total height of the aggregation curve as well as by its slope and is best suited to express the overall platelet activity. Two AUC units are used: U and AU\*min. The first unit (U) is the preferred one. Two more parameters are calculated: The aggregation (Agg) is the increase of impedance during analysis. The velocity (Vel) is the maximum slope of the aggregation curve (s. Fig. 2) (own illustration).<sup>10</sup>

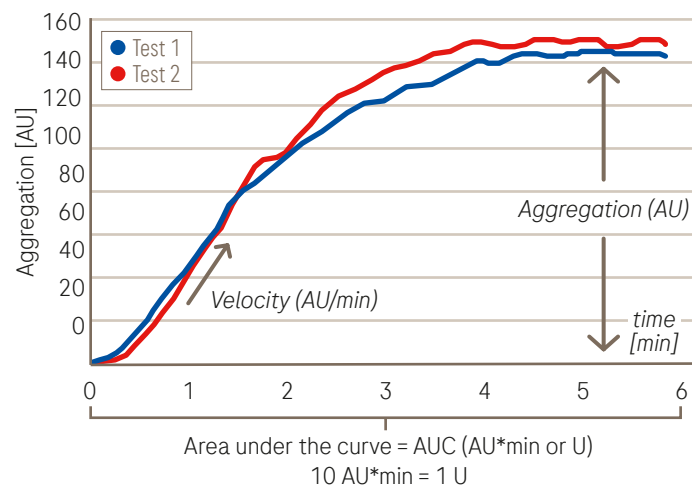


Figure 2. Multiplate parameters (Aggregation, Area under the curve, Velocity)

The analyzer automatically compares the signals of two sensors and gives an error message (Data alarm), if the difference is too high.

## Multiplate test cell

- Patented twin sensor test cell (s. Fig. 3)
- Testing in low volumes (300  $\mu$ l) of whole hirudinized or citrated blood
- Five measurement positions for simultaneous measurement of different patients or agonists
- Internal QC using duplicate detection of every measurement
- 10 minute time to result
- Sensitive signal detection with a large dynamic range

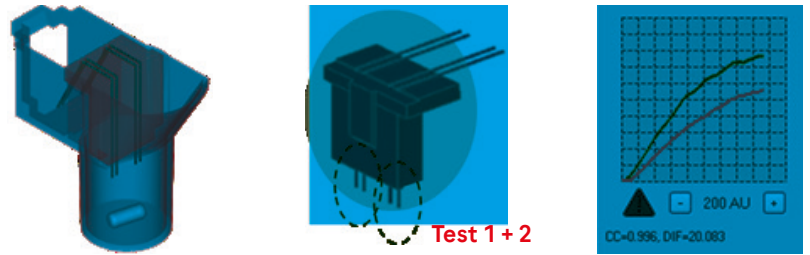
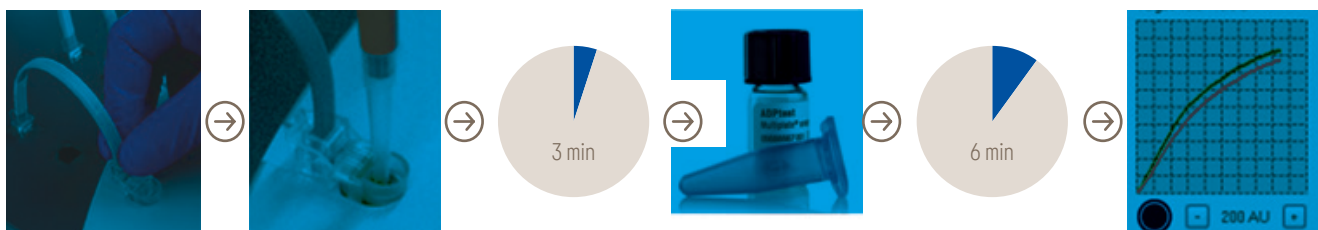


Figure 3. Two sensor test cell, for simultaneous determination of aggregation. The analyzer automatically compares signals and gives an error message if the difference is too high

## Test performance



Insert the test cell into Multiplate and attach the sensor cable

Pipette 300 $\mu$ l of saline and 300 $\mu$ l of whole blood

Warming & incubation phase

Add the reagent and start the test

Measuring time

Measurement is completed

Figure 4. Multiplate test performance<sup>11</sup>

## Electronic Pipette

- Predefined pipette programs for routine tests (s. Fig 5)
- Audiovisual user guidance
- One button operation for easy and safe pipetting
- Customizable setting for individual adaptation of different volumes

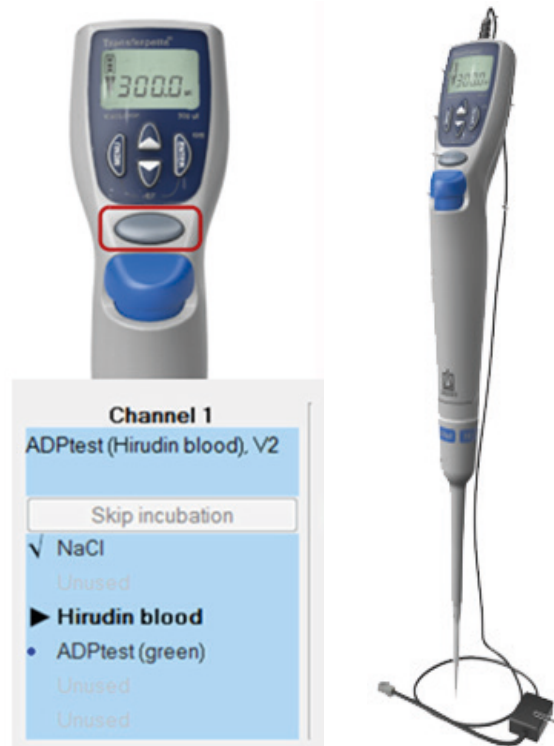


Figure 5. Multiplate Transferette. Easy-to-use one button operation, predefined programs, customizable settings<sup>11</sup>

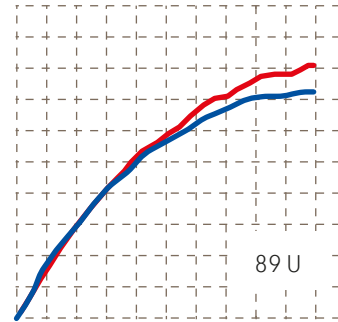
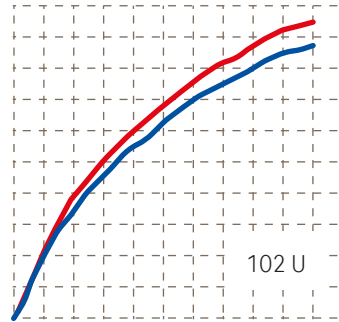
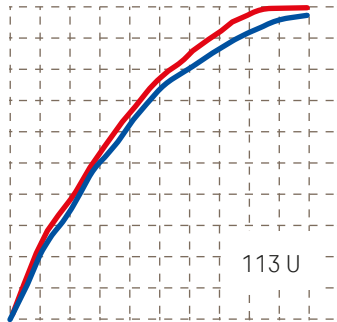


# Test examples

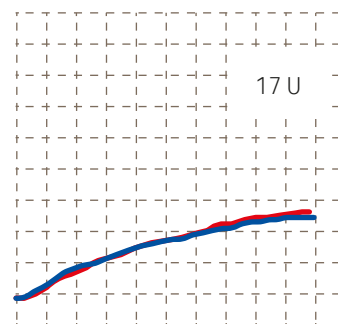
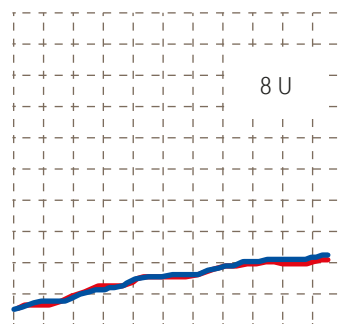
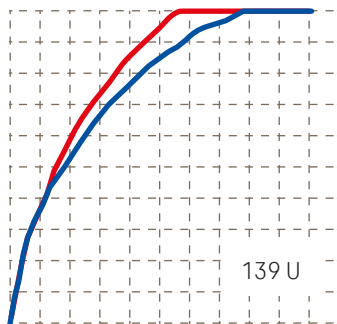
TRAPtest

ASPItest

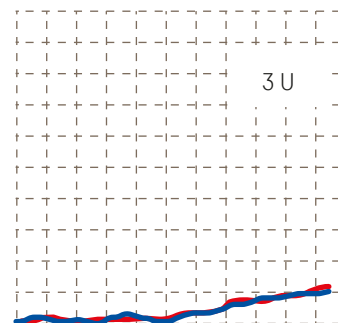
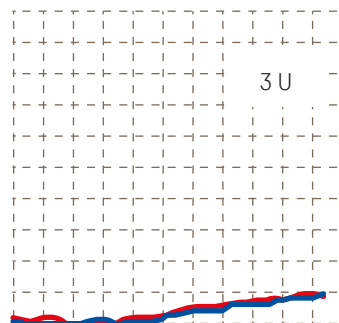
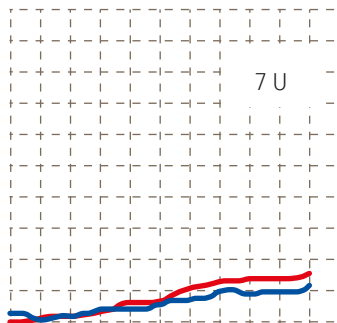
ADPtest



No platelet inhibition



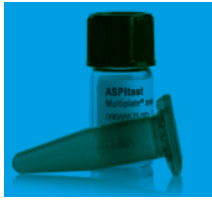
100 mg Aspirin +  
75 mg Clopidogrel



Tirofiban i.v.



## Multiplate tests and reagents



### ASPItest<sup>9</sup>

Activation by arachidonic acid, the substrate of the cyclooxygenase (COX). COX forms Thromboxane A<sub>2</sub> (TXA<sub>2</sub>) which is a potent platelet agonist.



### ADPtest<sup>9</sup>

ADP stimulates platelet activation by the ADP receptors. The most important ADP receptor (P2Y<sub>12</sub>) is blocked by clopidogrel, prasugrel and ticlopidine



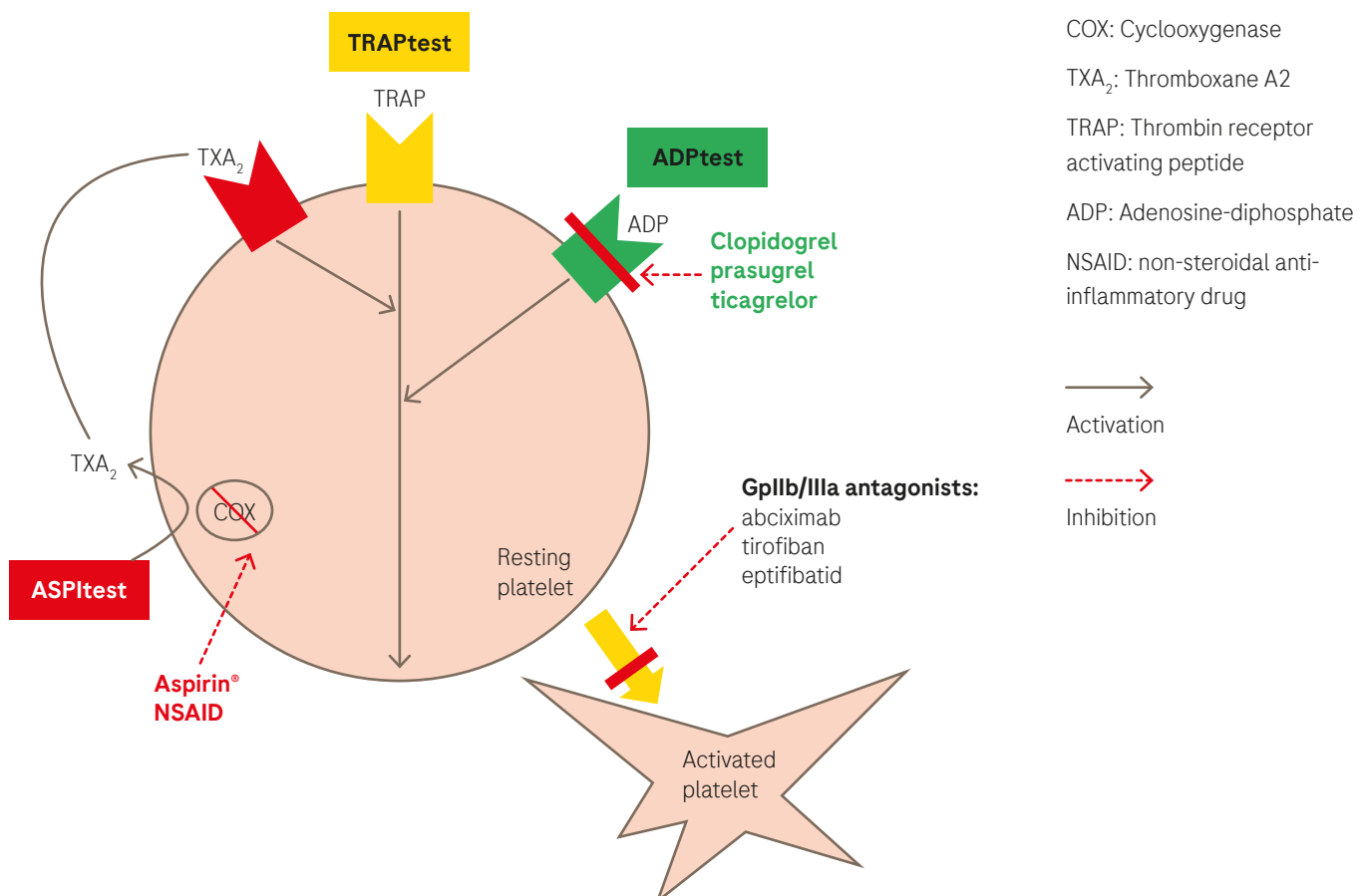
### TRAPtest<sup>9</sup>

TRAP-6 stimulates the thrombin receptor on the platelet surface. Thrombin is a very potent platelet activator. Its action is not blocked by Aspirin or clopidogrel. TRAPtest allows detection of GpIIb/IIIa antagonists even in samples treated by Aspirin or clopidogrel.



### ADPtest HS<sup>9</sup>

The addition of the endogenous inhibitor Prostaglandin E 1 makes ADPtest HS more sensitive towards the effects of clopidogrel and related drugs compared to ADPtest.



## Blood collection tubes

Multiplate system uses two different blood collection systems: hirudinized blood and citrated blood.

The preferred sample collection tube is one containing hirudin, thereby retaining the platelet's intracellular calcium stores.<sup>2</sup>

Free calcium is an important second messenger for platelet aggregation. Therefore, the use of commercial hirudin blood collection tubes is recommended.

## Test procedure for hirudinized blood



**TRAP test**  
**ADP test**  
**ASPI test**



**ADPtest HS**

### 1 | Pipette

300µL saline 0.9% (37 °C) + 300µL hirudinized blood



### 2 | Incubation

3 minutes



### 3 | Pipette

20µL TRAPtest

20µL ADPtest

20µL ASPItest



### 4 | Measuring

6 minutes

For ADPtest HS (high sensitivity)



### 3a | Pipette

20µL Prostaglandin E1



### 3b | Pipette

20µL ADPtest



## Test procedure for citrated blood<sup>5</sup>



### TRAP test ADP test

- 1 **Pipette**  
300µL saline 0.9%/3mM CaCl<sub>2</sub> (37 °C)  
+ 300µL citrated blood
- ↓
- 2 **Incubation**  
3 minutes
- ↓
- 3 **Pipette**  
20µL TRAPtest  
20µL ADPtest
- ↓
- 4 **Measuring**  
6 minutes



### ASPI test

- 1 **Pipette**  
300µL saline 0.9% (37 °C)  
+ 300µL citrated blood
- ↓
- 2 **Incubation**  
3 minutes
- ↓
- 3 **Pipette**  
20µL ASPItest
- ↓
- 4 **Measuring**  
6 minutes

## Quality controls<sup>10</sup>

- Twin sensor/duplicate analysis in one test cell
- Electronic Control (EQC)
- Liquid Control: Level 1 and Level 2



## Summary



Multiplate is a common platelet function analyzer which may be used in critical clinical settings and also in general laboratories<sup>12</sup>



No time consuming centrifugation steps, due to the use of whole blood



Easy to use instrument



Use of standardized lyophilized reagents



Computer guided electronic pipette



High throughput of 25 measurements per hour



Customizable settings for user defined test



Connection to LIS (Laboratory Information System)



Patented twin sensor/duplicate analysis in one test cell for internal quality control<sup>13</sup>

## Product specification<sup>10</sup>

### Physical dimensions

<b>Width</b>	45cm
<b>Depth</b>	32cm
<b>Height</b>	10cm
<b>Weight</b>	9.5kg

### Power requirements

<b>Line voltage</b>	100-240 V
<b>Line frequency</b>	50/60 Hz
<b>Power consumption</b>	180 W

### Data output

<b>Monitor</b>	See operators manual
<b>Printer</b>	See operators manual
<b>LAN-Network</b>	Data transfer
<b>USB flash drive</b>	Data transfer

### Environmental conditions

<b>Temperature</b>	+ 18 to 30 °C
<b>Humidity</b>	20-80%
<b>Altitude</b>	0-2000 m

### Technical features

<b>LIS</b>	Support of HL7 v2.5.1 with IHE profiles LAB27, LAB28 and LAB29
	Request orders
	Result Transfers also without orders
<b>System pipette</b>	Electronic pipette with cable

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