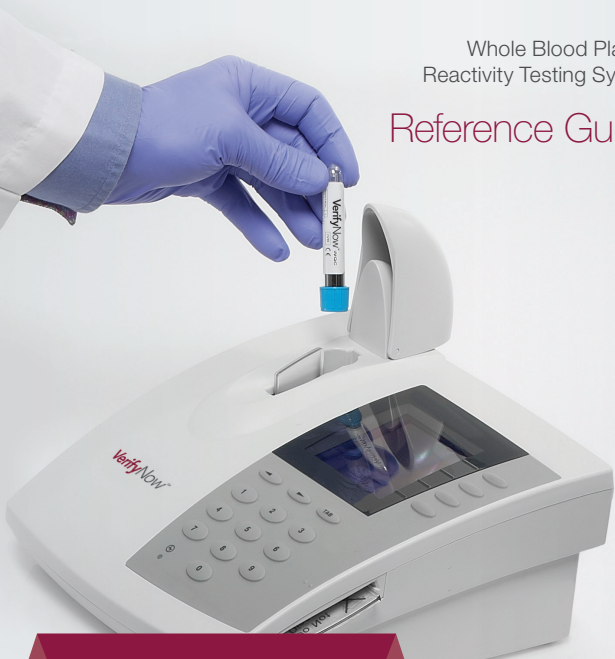


VerifyNow™

Whole Blood Platelet
Reactivity Testing System

Reference Guide



Acute Care Diagnostics



**Instrumentation
Laboratory**

A Werfen Company

Specific drug-receptor site activation

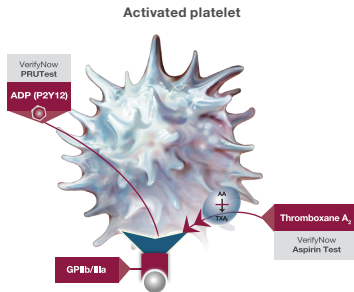
Receptor Blockade

VerifyNow PRUTest

Measures P2Y₁₂ platelet-receptor blockade to assess patient response to antiplatelet therapy

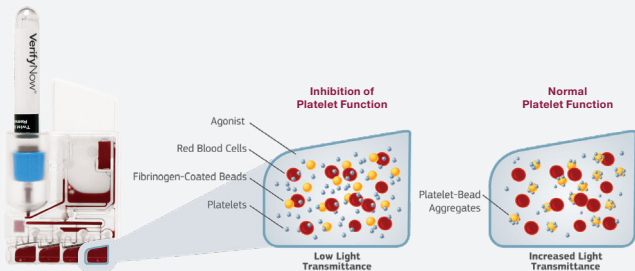
VerifyNow Aspirin Test

Measures platelet response to aspirin with an arachidonic acid



Correlated to Light Transmission Aggregometry (LTA)

The VerifyNow system uses patented, accurate and intuitive LTA-correlated technology.

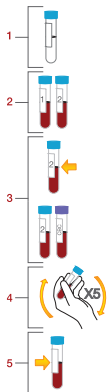


Sample Collection Procedure

Direct Venipuncture

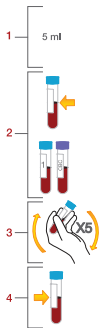
Sample collection directly into vacuum collection tubes.

1. Use 2 mL Greiner Bio-One partial-fill vacuette tubes with 3.2% sodium citrate (blue top, Greiner #454322).
2. Collect 2 tubes of whole blood using a 21-gauge or larger needle (Butterfly 21-gauge is acceptable). One is a discard tube (at least 2 mL). Ensure it does not contain platelet-inhibiting substances (e.g., EDTA).
3. Fill the sample tube to the black line (1/2 tube). Do not under-fill. Discard the first tube.
Note: If drawing blood for a CBC at the same time, fill the CBC tube last.
4. Gently invert the sample tube at least 5 times to ensure complete mixing. Do not shake. Samples with evidence of clotting should not be used.
5. Label tube with patient ID, date and time. Do not refrigerate. Do not put in pneumatic tube system.



Indwelling Catheter

1. Discard the first 5 mL from an indwelling catheter to clear the line. Ensure the catheter is free of clots.
2. Immediately transfer blood to a 2 mL Greiner Bio-One partial-fill vacuette tube with 3.2% sodium citrate (blue top, Greiner #454322). Fill to the black line (1/2 tube). Do not under-fill.
Note: If drawing blood for a CBC at the same time, fill the CBC tube last.
3. Gently invert the tube at least 5 times to ensure complete mixing. Do not shake. Samples with evidence of clotting should not be used.
4. Label tube with patient ID, date and time. Do not refrigerate. Do not put in pneumatic tube system.



Test	Therapy	Dose	Suggested Test Timing	Sample Incubation (mins)	Run Time (mins)
VerifyNow PRU Test	Clopidogrel (Plavix®)	75 mg	≥ 7 days on maintenance ¹	10	~3
		300 mg	≥ 8 hours post-bolus ¹⁰		
		600 mg	≥ 6 hours post-bolus ¹¹		
	Prasugrel (Effient®)	5 mg	≥ 5 days on maintenance ¹²		
		10 mg	≥ 5 days on maintenance ¹²		
		60 mg	≥ 45 minutes post-bolus ⁶		
	Ticagrelor (Brilinta®/ Brilique)	90 mg (BID)	≥ 1 day on maintenance ¹³ (within 8 hours of last dose)		
180 mg		≥ 2 hours post-bolus ¹³ (within 8 hours)			
VerifyNow Aspirin Test	Aspirin	81-325 mg	≥ 2 hours post-dose ^{9,14}	30	~5

References:

1. Stone GW, *et al.* Platelet reactivity and clinical outcomes after coronary artery implantation of drug-eluting stents (ADAPT-DES): a prospective multicentre registry study. *The Lancet*. 2013;382:614–23.
2. Price MJ, *et al.* Recovery of Platelet Function After Discontinuation of Prasugrel or Clopidogrel Maintenance Dosing in Aspirin-Treated Patients With Stable Coronary Disease: The Recovery Trial. *J Am Coll Cardiol*. 2012;59:2338–43.
3. Hochholzer W, *et al.* Time dependence of platelet inhibition after a 600-mg loading dose of clopidogrel in a large, unselected cohort of candidates for percutaneous coronary intervention. *Circulation*. 2005;111:2560–64.
4. Serebruany VL, *et al.* Variability in Platelet Responsiveness to Clopidogrel among 544 Individuals. *J Am Coll Cardiol*. 2005; 45(2):246–51.
5. Payne CD, *et al.* Increased Active Metabolite Formation Explains the Greater Platelet Inhibition With Prasugrel Compared to High dose Clopidogrel. *J Cardiovasc Pharmacol*. 2007;50:555–65.
6. Husted S, *et al.* Pharmacodynamics, pharmacokinetics, and safety of the oral reversible P2Y12 antagonist AZD6140 with aspirin in patients with atherosclerosis: a double-blind comparison to clopidogrel with aspirin. *Eur Heart J*. 2006;27:1038–47.
7. Ferraris V, *et al.* 2012 Update to The Society of Thoracic Surgeons Guideline on Use of Antiplatelet Drugs in Patients Having Cardiac and Noncardiac Operations. *Ann Thorac Surg*. 2012;94:1761–81.
8. VerifyNow PRU Test [package insert]. San Diego, CA; 2017.
9. VerifyNow Aspirin Test [package insert]. San Diego, CA, 2011.
10. Plavix [prescribing information]. Bridgewater, NJ: Bristol-Myers Squibb/Sanofi Pharmaceuticals Partnership; 2013.
11. Price MJ, *et al.* Onset and offset of platelet inhibition after high-dose clopidogrel loading and standard daily therapy measured by a point-of-care assay in healthy volunteers. *Am J Cardiol*. 2006;98:681–84.
12. Effient [prescribing information]. Indianapolis, IN: Daiichi Sankyo, Inc. and Lilly USA, LLC; 2015.
13. Brilinta [prescribing information]. Bridgewater, NJ: AstraZeneca group of companies; 2015.
14. Coleman J, *et al.* Determination of Individual Response to Aspirin Therapy Using the Accumetrics Ultegra RPPA-ASA System. *Point Care: The Journal of Near-Patient Testing and Technology*. 2004;3(2):77.

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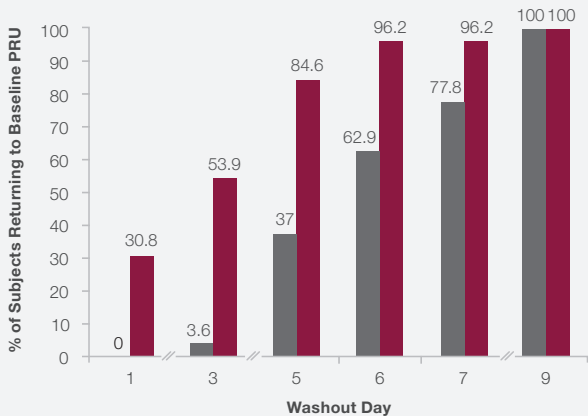
Antiplatelet Therapy Response

Up to 40% of patients taking antiplatelet medications may not receive the expected platelet-inhibiting effect.¹ Inadequate response to antiplatelet therapy may significantly increase risk of myocardial infarction, stent thrombosis and mortality. Conversely, hyper-response to antiplatelet medications may increase bleeding risk.^{2,3}

Factors contributing to inadequate response:⁴

- Drug Interactions (e.g., proton pump inhibitors)
- Genetic differences
- Pre-existing health conditions (e.g., diabetes)
- Non-compliance

Variability in Platelet Recovery When Antiplatelet Therapy Is Stopped²



■ Clopidogrel ■ Prasugrel

Decrease in Drug Effect Over Time

VerifyNow PRUtest™

Tests platelet response to P2Y12 inhibitors (e.g., clopidogrel, prasugrel, ticagrelor).

- Measures the on-treatment platelet reactivity of P2Y12 receptor

Measured in P2Y12 Reaction Units (PRU)

Extent of ADP-induced platelet aggregation in the presence of P2Y12 inhibitor

Pre-surgical application

- Patient response to P2Y12 inhibitors is variable.⁵
- Patients taking P2Y12 inhibitors are at risk of perioperative bleeding due to platelet dysfunction from drug effect.
- Husted *et al.*, recommend discontinuation of P2Y12 inhibitors for 5–7 days prior to surgery, allowing restoration of platelet function.⁶
- 2012 STS Guidelines⁷ recommend using platelet function testing to aid in timing of surgery, instead of arbitrarily waiting a pre-specified period of time.

Conditions that may affect test results:

- Exposure to GPIIb/IIIa inhibitors within 14 days of abciximab, or within 48 hours of eptifibatid or tirofiban
- Improper sample collection
- Interactions with other drugs that affect platelet aggregation

Sample Lab Report

PRU Test Results

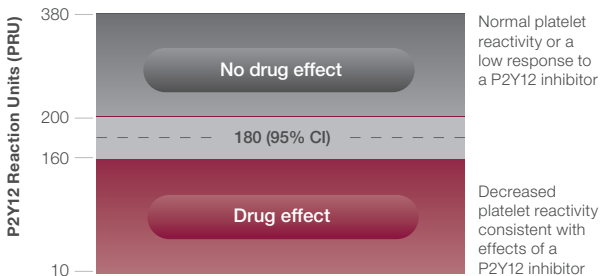
132 PRU

Reference Range

182–335 PRU

Values <180 PRU suggest a drug effect from a P2Y12 inhibitor, in patients with Acute Coronary Syndrome (ACS).

Patient Response to Antiplatelet Therapy^{8*}



* Based on patients with ACS not taking a P2Y12 inhibitor

VerifyNow Aspirin Test

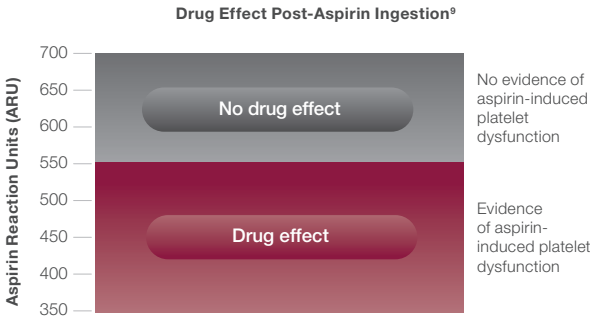
A qualitative test for platelet response to aspirin.

Measured in Aspirin Reaction Units (ARU)

- Arachidonic acid-induced aggregation

Result interpretation:

- > 550 ARU: No evidence of aspirin-induced platelet dysfunction
- ≤ 549 ARU: Evidence of aspirin-induced platelet dysfunction



Components

VerifyNow Instrument System

VerifyNow Aspirin Test, 25-Test Kit

VerifyNow PRUTest, 25-Test Kit

VerifyNow WQC Kit

VerifyNow Preventative Maintenance Kit

