HEMOSIL® **HIT-Ab**$_{(PF4-H)}$ **ASSAY**

HIT Testing **in Minutes**

The on-demand solution that saves more than time.

HEMOSTASIS INNOVATION IS HERE.

Instrumentation Laboratory
A Werfen Company

The first on-demand, fully automated assay for HIT antibody detection on Hemostasis systems.

Simple to use, fast results

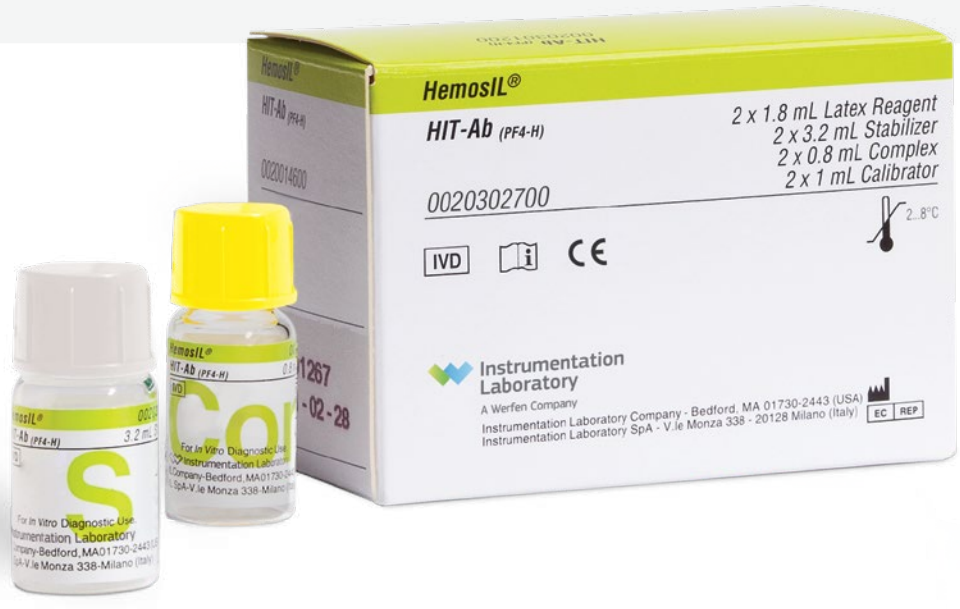
- Fully automated, liquid, ready-to-use
- Results available on-demand, 24 hours/day, 7 days/week
- Results in minutes; minimizes time to treatment decisions

Analytical excellence

- Detects anti-Platelet Factor 4-heparin (anti-PF4-H) antibodies
- Dedicated controls for complete quality management
- Excellent agreement with commercially available ELISA methods

Efficient

- Significantly reduces staff time
- Reduces costs



HemosIL®

Heparin-Induced Thrombocytopenia (HIT) overview

HIT is a severe adverse reaction to heparin

Causes

- HIT is associated with both unfractionated (UFH) and low molecular weight heparin (LMWH) administration
- HIT occurs when UFH or LMWH treatments cause an autoimmune reaction, triggering antibodies to activate platelets and initiate the formation of blood clots, resulting in venous and/or arterial thrombosis

Prevalence

- HIT is one of the most prevalent adverse drug effects, due to the number of patients receiving heparin therapy[1]
- 0.2–2.0% of patients treated with heparin (up to 12 million patients/year in the U.S. alone) develop HIT

Suspect HIT

When a patient treated with UFH or LMWH experiences:

- Platelet-count fall >50% vs. baseline
- Venous and/or arterial thrombosis
- Skin necrosis
- Anaphylactic reactions

Antibody detection

- Anti-PF4-H is the most critical antibody in patients with HIT
- PF4, a chemokine with very high affinity for heparin, forms a large immunocomplex with anti-PF4-H antibodies, leading to platelet activation
- The presence of anti-PF4-H antibodies does not always cause HIT
- A negative result for an anti-PF4-H antibody test can support the clinical decision to exclude HIT

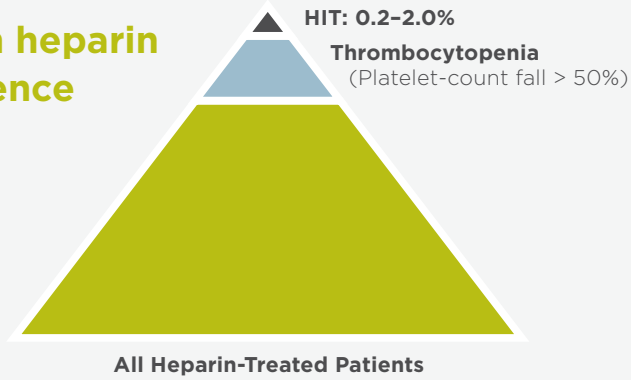
Clinical presentations of HIT

- ***Typical-onset:*** platelet-count fall within 5–10 days after heparin administration, significantly increasing risk of thrombosis and other adverse events
- ***Rapid-onset:*** abrupt platelet-count fall (generally within 24 hours), typically following recent heparin administration
- ***Delayed-onset:*** often the most clinically severe, occurs several days after heparin discontinuation. HIT is considered a transient autoimmune disease in this patient population

If untreated, risk for thrombosis and subsequent morbidity and/or mortality increases significantly.[2]

The HIT paradox: Patients treated with heparin may suffer a thrombosis as a consequence

The HIT Iceberg Model illustrates the concept that only a subset of patients on heparin develops thrombocytopenia, and only a subset of this population develops HIT.



On-demand HIT detection enhances patient care

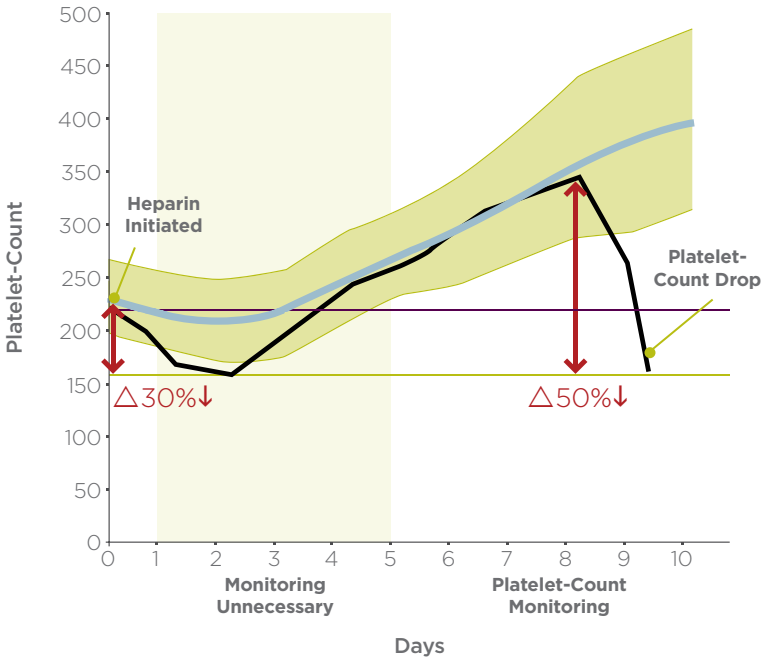
Assess for HIT at first clinical suspicion

The 4Ts HIT Assessment Point System[3]

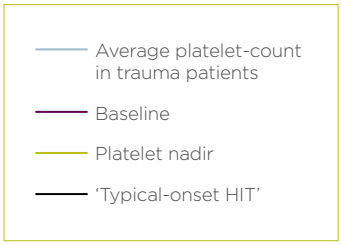
Points	2	1	0
Thrombocytopenia	Platelet-count fall >50% and platelet nadir >20 x 10^9/L	Platelet-count fall 30–50% or platelet nadir 10–19 x 10^9/L	Platelet-count fall <30% or platelet nadir <10 x 10^9/L
Timing of platelet-count fall	Clear onset between days 5–10 or platelet fall <1 day (prior heparin exposure within 30 days)	Consistent with days 5–10 fall, but not clear (*e.g.*, missing platelet-count); onset after day 10; or fall <1 day (prior heparin exposure 30–100 days ago)	Platelet-count fall <4 days without recent exposure
Thrombosis or other sequelae	New thrombosis (confirmed); skin necrosis; acute systemic reaction post-I.V. unfractionated heparin bolus	Progressive or recurrent thrombosis; non-necrotizing (erythematous) skin lesions; suspected thrombosis (not proven)	None
OTher causes for thrombocytopenia	None apparent	Possible	Definite

Assign a point value to each 'T' and then total to determine 4Ts score (maximum 8): High = 6–8, Intermediate = 4–5, Low = 0–3

Platelet-Count Monitoring in 'Typical-onset HIT'[1]



- Rapid results from on-demand testing can aid in the exclusion or confirmation of HIT and help inform appropriate therapeutic decisions.



Rapid detection of HIT antibodies optimizes therapeutic decisions

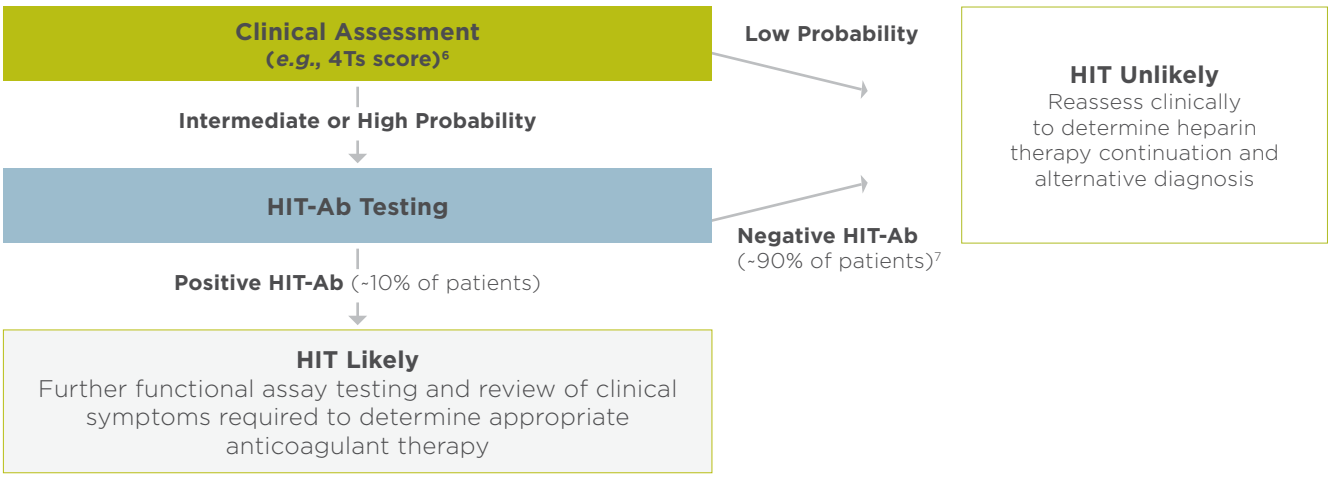
HIT management challenges

- In some cases, HIT is assumed without the confirmation of laboratory results, leading to unnecessary therapeutic changes
- Alternative anticoagulants may:
  - Pose a patient-management challenge
  - Increase bleeding risk
  - Represent a difficult transition to warfarin (direct thrombin inhibitors can prolong prothrombin time)
  - Increase treatment cost
  - Increase length of stay (increase hospital costs)[4]

Excluding HIT can prevent unnecessary and labor-intensive changes in anticoagulant therapy in the majority of HIT-suspected cases.

On-demand Model for Anti-PF4-H Antibody Testing[5]

- Approximately 90% of HIT-suspected patients do not have HIT antibodies and are unlikely to develop HIT
- On-demand HIT antibody testing can prevent unnecessary and costly anticoagulant therapy changes in the majority of HIT-suspected cases

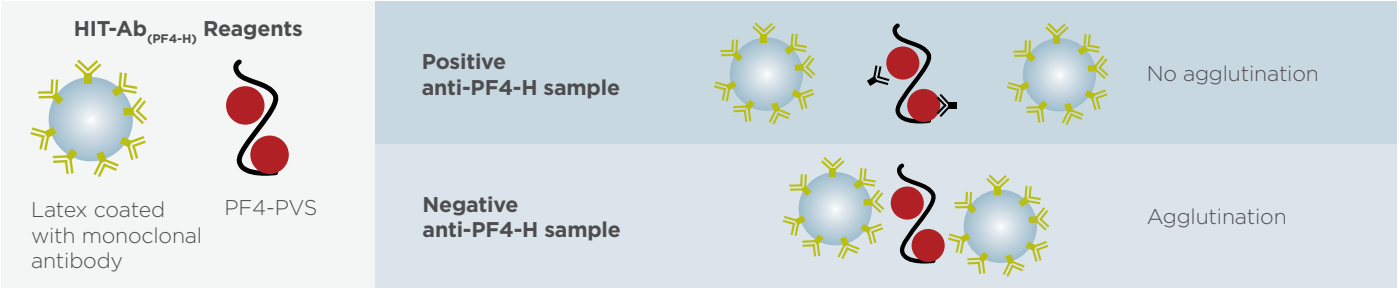


HEMOSIL

HIT-Ab$_{(PF4-H)}$ assay

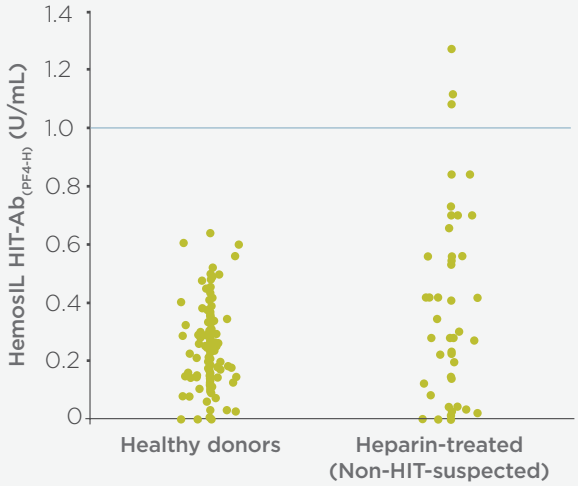
Principle

HemosIL HIT-Ab$_{(PF4-H)}$ is a latex-enhanced immunoturbidimetric assay for the semi-quantitative detection of anti-PF4-H antibodies, commonly associated with HIT. The latex reagent is a suspension of polystyrene particles, coated with a monoclonal antibody against PF4-H. The competitive agglutination reaction occurs when a complex of PF4 and PVS (polyvinyl sulfonate, a compound similar to heparin) is mixed with the latex and patient sample. Anti-PF4-H in a positive sample will bind to the complex, inhibiting agglutination, while the absence of anti-PF4-H will allow the complex to bind to the latex, allowing agglutination.



Expected Values

An expected values study evaluated 95% reference intervals in 131 healthy donors and 51 heparin-treated (non-HIT-suspected) patient samples. Healthy donor samples demonstrated a reference interval of 0–0.6 U/mL, and heparin-treated samples demonstrated a reference interval of 0–1.2 U/mL. Additionally, a comparison with the Serotonin Release assay (SRA) on 66 HIT-suspected patient samples indicated that the optimal cut-off (blue line), determined by receiver operating characteristic (ROC) analysis, was 1.0 U/mL (92.4% agreement). Based on these studies, HemosIL HIT-Ab$_{(PF4-H)}$ results ≥ 1.0 U/mL may indicate the presence of HIT antibodies.



Excellent Correlation vs. ELISA

A multi-center study compared the HemosIL HIT-Ab$_{(PF4-H)}$ assay on the ACL TOP system versus a commercially available ELISA method. In 414 HIT-suspected samples, HIT-Ab$_{(PF4-H)}$ demonstrated a high degree of agreement with ELISA.

HemosIL HIT-Ab$_{(PF4-H)}$ vs. ELISA	
Co-negativity %	94.6 (91.5–96.7)
Co-positivity %	60.2 (48.9–70.8)
Overall %	87.7 (84.1–90.7)

Analytical performance on the ACL TOP® Family of Hemostasis Testing Systems

		Mean (U/mL)	CV% (Within run)	CV% (Total)
Precision	Low HIT-Ab Control	0.8	7.1	9.0
	High HIT-Ab Control	2.95	4.4	6.4
	Weakly Positive HIT-Ab Sample	1.6	4.9	8.1
	High HIT-Ab Sample	5.2	2.8	3.5
	Very High HIT-Ab Sample	10.0	5.5	9.5
Interferences	Hemoglobin		495 mg/dL	
	Bilirubin		18 mg/dL	
	Triglycerides		375 mg/dL	
	Rheumatoid Factor		1,000 IU/mL	
	Human Anti-Mouse Antibody		1 µg/mL	
	Antiphospholipid Antibodies		None	
Test Range	0–5.7 U/mL without rerun 0–16 U/mL with rerun			
Linearity	0.7–5.7 U/mL without rerun 2.1–16.0 U/mL with rerun			
Onboard Stability (of latex reagent, complex, stabilizer)	Continuous		36 hrs at 15°C	
	Cumulative (1 hr/day, then 2–8°C)		4 hrs over 120 days	
	Cumulative (2 hrs/day, then 2–8°C)		16 hrs over 15 days	
	Cumulative (4 hrs/day, then 2–8°C)		20 hrs over 9 days	

Automated HIT detection with ACL TOP Family 50 Series systems

A Breakthrough in Hemostasis Testing

ACL TOP 750/750 CTS/750 LAS

New ACL TOP Family 50 Series* systems deliver advanced automation and quality management for routine-to-specialty Hemostasis testing. Minimizing errors and enhancing quality, all models are standardized and offer automated pre-analytical sample integrity checks. Plus, all ACL TOP 50 Series systems are optimized for the comprehensive panel of HemosIL assays—offering complete disease-state management solutions.

All ACL TOP Family 50 systems offer:

- ***Same*** assay-specific pre-analytical sample checks
- ***Same*** advanced lab accreditation support
- ***Same*** advanced quality management

Plus the *same* standardized features of all ACL TOP systems:

- ***Same*** quality results
- ***Same*** comprehensive assay portfolio
- ***Same*** powerful and intuitive software
- ***Same*** features and usability

Advanced automation and quality for lab efficiency and better patient care.

*Not available in all countries.

Product	Part Number	Kit Configuration
HIT-Ab$_{(PF4-H)}$	0020302700	2 x 1.8 mL Latex Reagent (liq) 2 x 0.8 mL Complex (liq) 2 x 3.2 mL Stabilizer (liq) 2 x 1 mL Calibrator (lyo)
HIT-Ab$_{(PF4-H)}$ Controls	0020013300	3 x 1 mL Low HIT-Ab$_{(PF4-H)}$ Control (liq) 3 x 1 mL High HIT-Ab$_{(PF4-H)}$ Control (liq)

References

1. Greinacher A, Althaus K, Krauel K, *et al*. Heparin-induced thrombocytopenia. *Hämostaseologie*. 2010;1(Review):17–28.
2. Linkins L, *et al.* Treatment and Prevention of Heparin-Induced Thrombocytopenia: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141(2):495S–530S.
3. Lo GK, Juhl D, Warkentin TE, *et al.* Evaluation of pretest clinical score (4Ts) for the diagnosis of heparin-induced thrombocytopenia in two clinical settings. *J Thromb Haemost*. 2006;4:759.
4. Smythe MA, *et al*. The financial impact of heparin-induced thrombocytopenia. *Chest*. 2008;134(3):568–73.
5. Cuker A, Crowther M. 2013 Clinical practice guideline on the evaluation and management of adults with suspected heparin-induced thrombocytopenia (HIT). *Washington, DC: ASH (American Society of Hematology);*2013;4.
6. Greinacher A. Heparin-induced thrombocytopenia. *J Thromb Haemost*. 2009;7(Suppl. 1):9–12.
7. Greinacher A, *et al*. Heparin-induced thrombocytopenia: a prospective study on the incidence, platelet-activating capacity and clinical significance of antiplatelet factor 4/heparin antibodies of the IgG, IgM, and IgA classes. *J Thromb Haemost*. 2007;5:1666–73.

Additional literature

- Amiral J, *et al.* Pathogenicity of IgA and/or IgM antibodies to heparin-PF4 complexes in patients with heparin-induced thrombocytopenia. *Br J Haematol.* 1996;92(4):954–9.
- Althaus K, Hron G, Strobel U, *et al*. Evaluation of automated immunoassays in the diagnosis of heparin induced thrombocytopenia. *Thromb Res.* 2013;131(3):e85–90.
- Davidson SJ, Ortel TL, Smith LJ. Performance of a new, rapid, automated immunoassay for the detection of anti-platelet factor 4/heparin complex antibodies. *Blood Coagul Fibrinolysis.* 2011;22(4):340–4.
- Greinacher A, *et al*. Heparin-associated thrombocytopenia: isolation of the antibody and characterization of a molecular PF4-heparin complex as the major antigen. *J Thromb Haemost.* 1994;71(2):247–51.
- Morelli B, Novelli C, Grassi C, *et al*. Preliminary assessment of a new kit (HemosIL HIT-Ab$_{(PF4-H)}$) manufactured by Instrumentation Laboratory for the determination of anti-PF4/heparin antibodies. *Clin Chem Lab Med.* 2010;49(9):A183–A203.
- Warkentin TE, *et al.* Heparin-induced thrombocytopenia in patients treated with low-molecular-weight heparin or unfractionated heparin. *N Eng J Med.* 1995;332(1):1330–5.
- Warkentin TE, *et al*. Performance characteristics of an automated latex immunoturbidimetric assay [HemosIL® HIT-Ab(PF4-H)] for the diagnosis of immune heparin-induced thrombocytopenia. *Thromb Res.* 2017;153:108–17.

IL is passionate about bringing the most innovative solutions to Hemostasis testing. Offering a broad range of the highest quality instruments, data management solutions and a full panel of HemosIL® assays—supported by a world-class technical team—IL is committed to enhancing patient care through continuous innovation.

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