Hemostasis Innovation is Here.

HEMOSIL® ACUSTAR
HIT-IgG(PF4-H) ASSAY

On-demand HIT detection

for better patient management



FOR USE ON THE
ACL AcuStar®
HEMOSTASIS TESTING SYSTEM

werfen

The first fully automated chemiluminescent assay for HIT antibody detection on a Hemostasis system

Simple to use, fast results

- Fully automated, pre-calibrated, ready-to-use reagent cartridge
- Results available on-demand, 24 hours/day, 7 days/week
- Results in minutes; minimizes time to treatment decisions
- Validated 1.00 U/mL cut-off value; facilitates result interpretation
- Uses serum or citrated plasma

Precise and accurate

- Detects IgG antibodies against Platelet Factor 4-heparin (PF4-H) complexes
- Chemiluminescent technology provides an expansive working range for high analytical sensitivity and precision
- Detects IgG-specific anti-PF4-H antibodies to optimize patient management
- Excellent agreement with commercially available ELISA methods

Efficient

- No batching required
- Extended three-month onboard stability and cartridge-based format accommodates variable testing volume
- Significantly reduces staff time and costs

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

Incidence

- HIT is one of the most prevalent of all adverse drug reactions[1]
- 0.2–5.0% of patients treated with heparin develop HIT[2]

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, potentially leading to platelet activation
- While platelet-activating antibodies cause HIT, the presence of anti-PF4-H antibodies does not always cause HIT
- A negative anti-PF4-H test can support the exclusion of HIT[8]

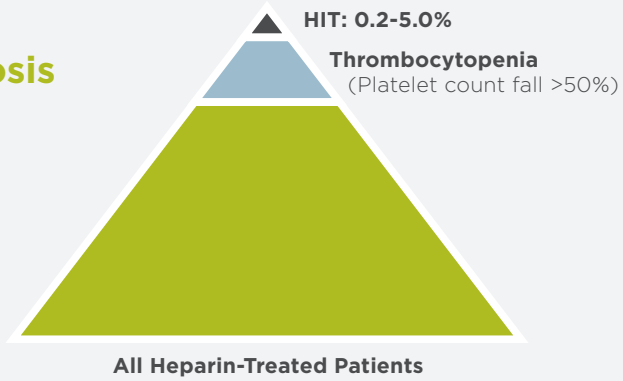
Clinical presentations of HIT

- ***Typical onset:*** platelet count fall within 5–10 days after heparin administration
- ***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.[3]

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

The iceberg model for HIT illustrates the concept that only a subset of patients receiving heparin develops thrombocytopenia, and only a subset of this population develops HIT.[4]



On-demand HIT antibody detection means better patient care

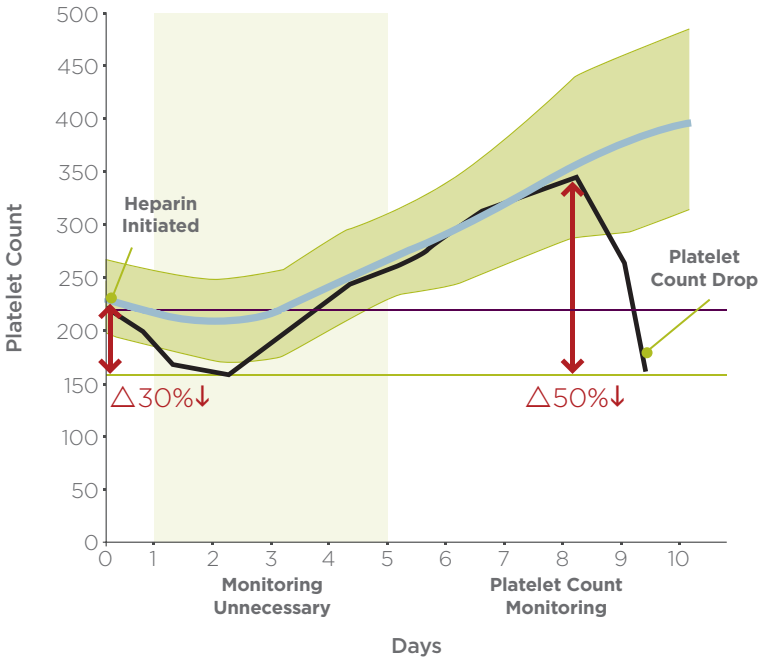
Assess for HIT at first clinical suspicion

The 4Ts HIT Assessment Point System[5]

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	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; skin necrosis; acute systemic reaction post-IV UFH bolus	Progressive or recurrent thrombosis; non-necrotizing (erythematous) skin lesions; suspected thrombosis	None
O**T**her 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 determining the risk of HIT and aid therapeutic decisions

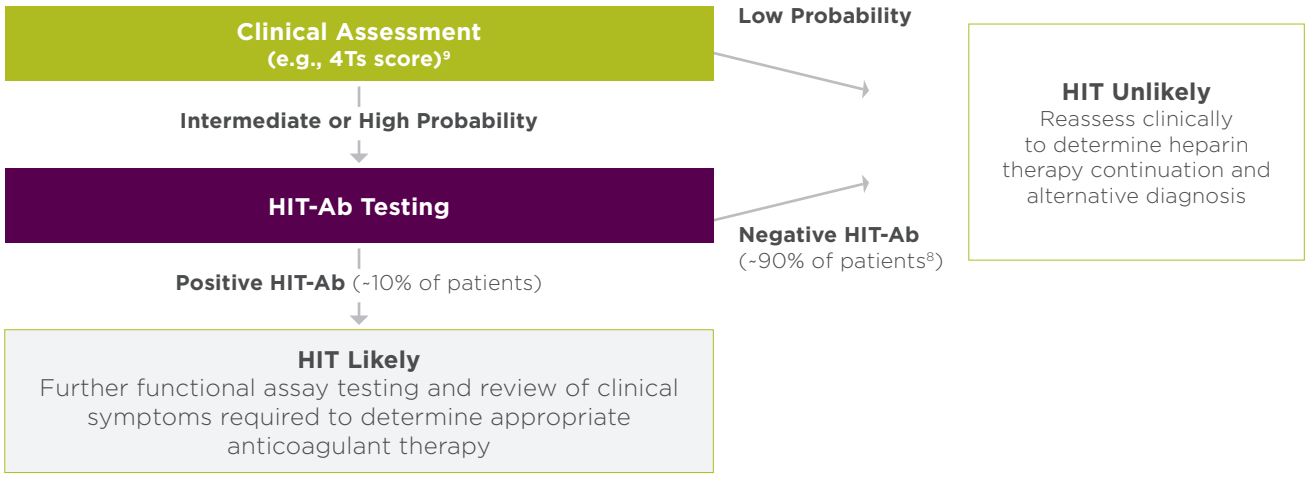
Rapid detection of HIT antibodies optimizes therapeutic decisions

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)[6]

Determining the risk of HIT can prevent unnecessary changes in anticoagulant therapy in the majority of HIT-suspected cases.

On-Demand Model for Anti-PF4-H Antibody Testing[7]



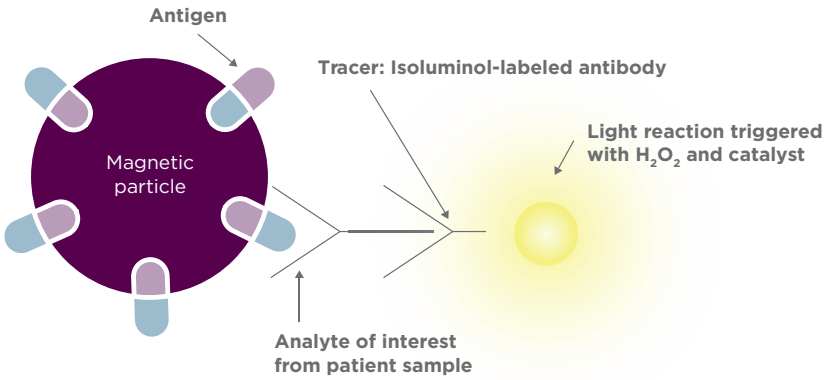
- Approximately 90% of HIT-suspected patients do not have HIT antibodies and are unlikely to develop HIT
- On-demand HIT antibody testing can prevent unnecessary and costly anticoagulant therapy changes in the majority of HIT-suspected cases

HemosIL AcuStar HIT-IgG$_{(PF4-H)}$ assay

Principle

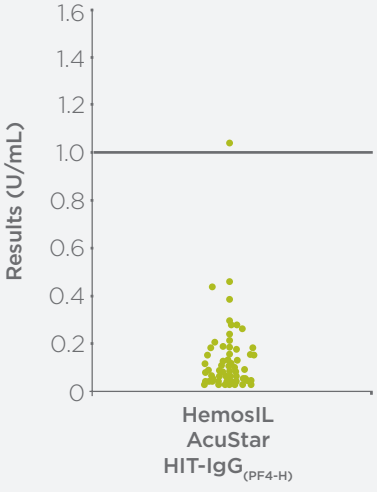
HemosIL AcuStar HIT-IgG$_{(PF4-H)}$ assay is a fully automated chemiluminescent immunoassay for the detection of anti-PF4-H IgG antibodies, commonly associated with HIT. The reagent mechanism consists of magnetic particles coated with a PF4 and PVS (polyvinyl sulfonate, a compound similar to heparin) complex, which have the ability to capture PF4-H IgG antibodies commonly associated with HIT. The antigen-coated magnetic particles capture the anti-PF4-H antibodies, if present in the sample. An isoluminol-labeled secondary antibody in the tracer binds to the captured antibodies, resulting in an emission of light proportionate to the concentration of the antibodies.

HemosIL AcuStar assay reaction mechanism



Standardization

150 citrated plasma samples from healthy donors and 91 heparin-treated samples using HemosIL AcuStar HIT-IgG$_{(PF4-H)}$ were analyzed to determine cut-off. The assay was standardized to a cut-off value of 1.00 U/mL. Based on these studies, HemosIL AcuStar HIT-IgG$_{(PF4-H)}$ assay results ≥1.00 U/mL may indicate the presence of HIT IgG antibodies.





Excellent analytical performance on the ACL AcuStar system

	HIT-IgG$_{(PF4-H)}$	
Precision (%CV)	**Within Run**	**Total**
Below cut-off	5.0	6.3
Medium titer	4.9	6.9
High titer	4.3	5.9
Test Range (U/mL)	0.00–128.00	
Cut-off (U/mL)	1.00	
Interferences	Hemoglobin Bilirubin Triglycerides Heparin (LMWH and UFH) Rheumatoid Factor Antiphospholipid Syndrome Prozone Effect Note: Positive Rheumatoid Factor samples may increase the value of an already positive HIT sample.	

Excellent correlation vs. ELISA

A method comparison study was performed using HemosIL AcuStar HIT-IgG$_{(PF4-H)}$ assay and commercially available ELISA methods on HIT-suspected samples. In approximately 400 samples, the HemosIL AcuStar HIT-IgG$_{(PF4-H)}$ assay demonstrated a high degree of agreement. In addition, the HemosIL AcuStar HIT-IgG$_{(PF4-H)}$ assay demonstrated excellent agreement (91%) with a functional serotonin release assay (SRA).

HIT-IgG$_{(PF4-H)}$ vs. ELISA		
Sample Type	**Plasma**	**Serum**
Samples (n)	266	125
Co-positivity (%)	61.4	92.3
Co-negativity (%)	97.0	97.7
Overall (%)	83.5	96.0

Fully automated ACL AcuStar system ensures quality, efficiency and accuracy.

HemosIL AcuStar HIT Assay Panel*

Product	Part Number	Kit Configuration
HemosIL AcuStar HIT-IgG$_{(PF4-H)}$*	0009802028	1 Cartridge (25 tests) Calibrator 1, 1 x 1 mL Calibrator 2, 1 x 1 mL
HemosIL AcuStar HIT Controls*	0009802122	Low HIT Control, 3 x 1 mL (liq) High HIT Control, 3 x 1 mL (liq)
HemosIL AcuStar Multi-Ab Controls**	00009800003	Low Multi-Ab Control, 3 x 2 mL (liq) High Multi-Ab Control, 3 x 2 mL (liq)

*Not FDA 510(k)-cleared. Not saleable in US.
**Not available in all countries.

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4. Warkentin TE. Heparin-induced thrombocytopenia: pathogenesis and management. *Br J Haematol*. 2003;121(4):535–555.
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Additional Literature

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