

## HemosIL HIT-Ab<sub>(PF4-H)</sub> Assay

PRODUCT	PART NUMBER	KIT CONFIGURATION
HIT-Ab <sub>(PF4-H)</sub>	0020301200	<ul style="list-style-type: none"> <li>2 x 1.8 mL Latex Reagent (liq)</li> <li>2 x 0.8 mL Complex (liq)</li> <li>2 x 3.2 mL Stabilizer (liq)</li> <li>2 x 1 mL Calibrator (liq)</li> </ul>
HIT-Ab <sub>(PF4-H)</sub> Controls	0020013200	<ul style="list-style-type: none"> <li>3 x 3 mL Low HIT-Ab<sub>(PF4-H)</sub> Control (liq)</li> <li>3 x 3 mL High HIT-Ab<sub>(PF4-H)</sub> Control (liq)</li> </ul>

### References

- Greinacher A *et al*, Heparin-associated thrombocytopenia: isolation of the antibody and characterization of a molecular PF4-heparin complex as the major antigen. *Thromb. Haemost.* 1994, 71(2) 247-251.
- Warkentin TE *et al*, Heparin-induced thrombocytopenia in patients treated with low-molecular-weight-heparin or unfractionated heparin. *N Engl J Med.* 1995, 332(1):1330-1335.
- Amiral J *et al*, Pathogenicity of IgA and/or IgM antibodies to heparin-PF4 complexes in patients with heparin-induced thrombocytopenia. *British Journal of Haematology* 1996, 92(4): 954-9.
- Arepally GM, Ortel TL. Clinical practice. Heparin-induced thrombocytopenia. *N Engl J Med* 2006;355:809-17.
- Greinacher A. Heparin-Induced Thrombocytopenia. *J Thromb Haemost.* 2009, 7 (suppl. 1):9-12.

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NEW

HEMOSIL®

HIT-Ab<sub>(PF4-H)</sub>



## HIT TESTING IN MINUTES.

The on-demand solution that saves more than time.

Exclusively for use on the ACL TOP® Family of Hemostasis Testing Systems.



HEMOSTASIS INNOVATION IS HERE.

HEPARIN-INDUCED THROMBOCYTOPENIA

98089-98EU 08/10

# 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 total immunoglobulin against Platelet Factor 4-Heparin (PF4-H) complexes
- Dedicated controls for complete quality management
- Excellent agreement with commercially available ELISA methods

## EFFICIENT

- Significantly reduces staff time
- Reduces 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 (LMWH) Heparin administration.
- HIT occurs when UFH and 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

- One of the most common of all adverse drug effects, due to the sheer volume of patients receiving Heparin therapy.
- One of the most prevalent of all immune-mediated, drug-induced blood cell disorders.
- 1–2% of patients treated with Heparin develop HIT.

### When to suspect HIT

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

### Antibody detection

- Anti-Platelet Factor 4-Heparin (anti-PF4-H) is the most critical antibody in patients with HIT. PF4-H, a chemokine with very high affinity for Heparin, forms a large immunocomplex with anti-PF4-H, eventually leading to platelet activation.
- While platelet-activating antibodies cause HIT, the presence of PF4-H does not always cause HIT.
- A negative anti-PF4-H test can support the exclusion of HIT.

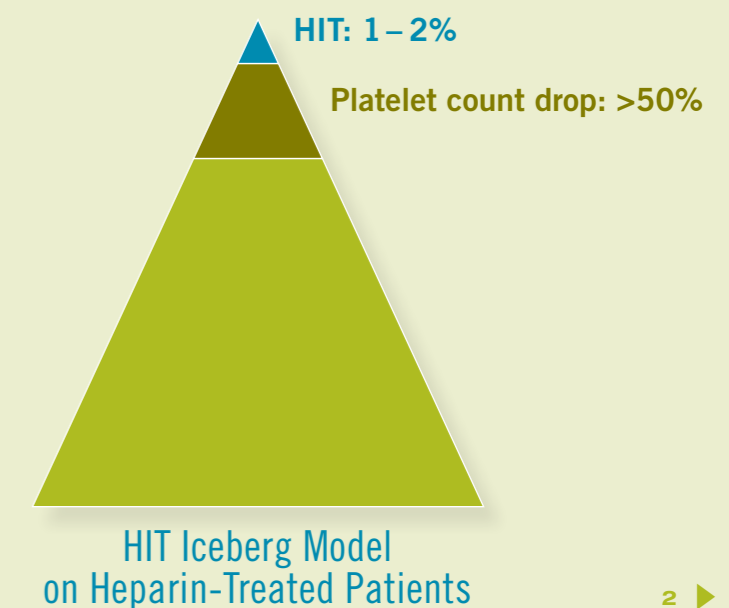
### Clinical events

- In 'typical-onset HIT,' platelet counts fall within 5–14 days after Heparin administration, while the risk of thrombosis and other adverse events significantly increases.
- 'Rapid-onset HIT' presents with an abrupt platelet count fall (generally within 24 hours), and typically follows recent Heparin administration.
- 'Delayed-onset HIT,' often the most clinically severe, occurs several days after Heparin discontinuation.
- If untreated, risk for thrombosis and subsequent morbidity and/or mortality increases significantly.



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

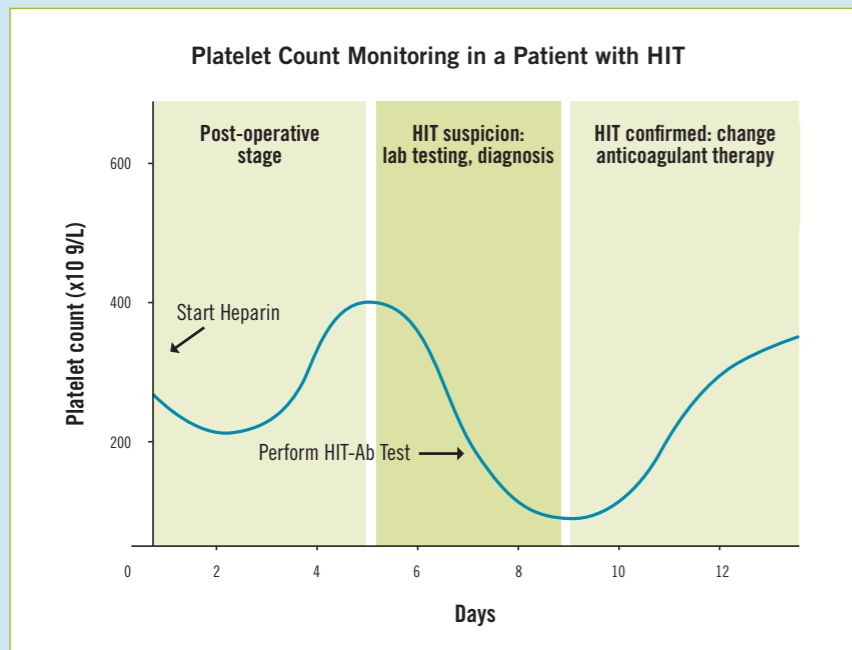
The iceberg model for HIT illustrates the concept that only a subset of patients on Heparin develop thrombocytopenia, and only a subset of this population develops HIT.



On-demand HIT detection means better patient care.

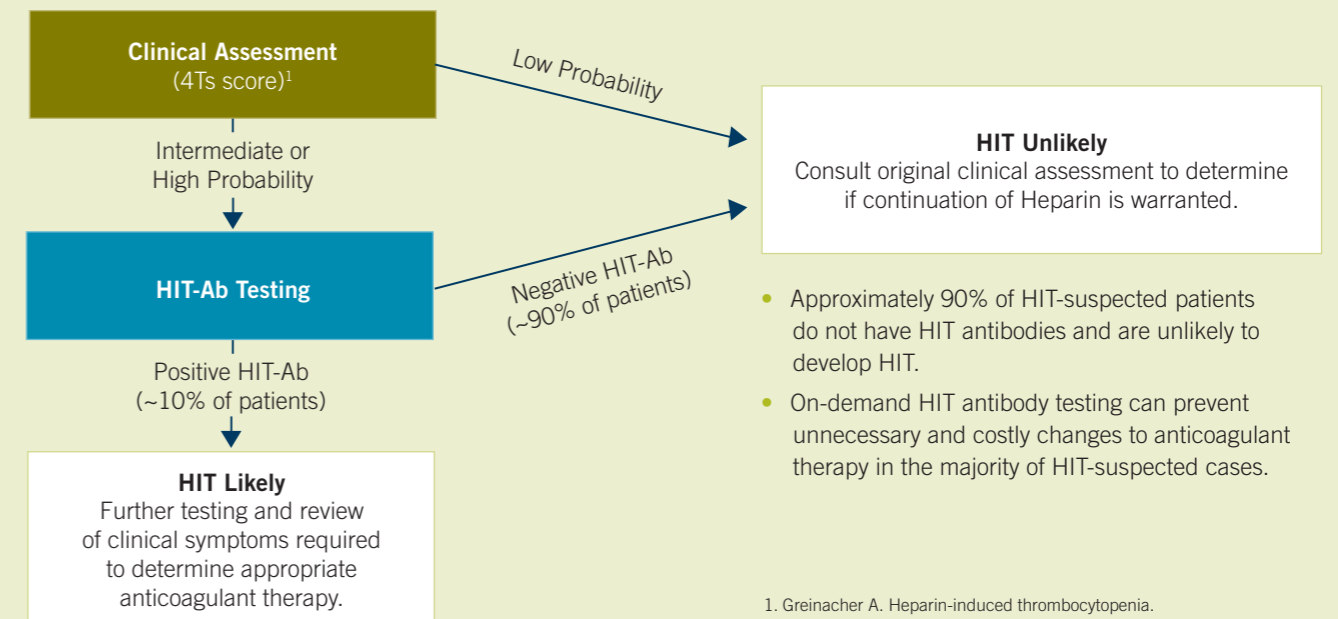
Rapid detection of HIT antibodies optimizes therapeutic decisions.

### Test for HIT at first clinical suspicion



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

### On-demand model for HIT antibody (HIT-Ab) testing



1. Greinacher A. Heparin-induced thrombocytopenia. *J. Thromb Haemost* 2009; 7 (Suppl. 1): 9-12.

### Excluding HIT in suspected patients may prevent unnecessary alternative anticoagulant treatment

- 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
  - Increase drug cost

### The '4 Ts' HIT Assessment Point System

POINTS	2	1	0
Thrombocytopenia	>50% fall or platelet nadir 20–100 x 10 <sup>9</sup> /l	30–50% fall or platelet nadir 10–19 x 10 <sup>9</sup> /l	Fall <30% or platelet nadir <10 x 10 <sup>9</sup> /l
Timing* of platelet count fall or other sequelae	Clear onset on days: 5–10 or <1 day (if Heparin exposure within past 100 days)	Consistent with immunization, but not clear (e.g., missing platelet counts) or onset of thrombocytopenia >10 days	Platelet count falls too early (without recent Heparin exposure)
Thrombosis or other sequelae (e.g., skin lesions)	New thrombosis; skin necrosis; post-Heparin bolus acute systemic reaction	Progressive or recurrent thrombosis; erythematous skin lesions; suspected thrombosis not yet proven	None
Other causes for thrombocytopenia are not evident	No other cause for platelet count fall is evident	Possible other cause is evident	Definite other cause is present

► Assign a point value to each "T" and then total (maximum 8) to determine HIT score. Probability of HIT score: 6–8 = high; 4–5 = intermediate; 0–3 = low.

\*First day of immunizing Heparin exposure considered day 0; the day the platelet count begins to fall is considered the day of onset of thrombocytopenia (it generally takes 1–3 days more until an arbitrary threshold that defines thrombocytopenia is passed).

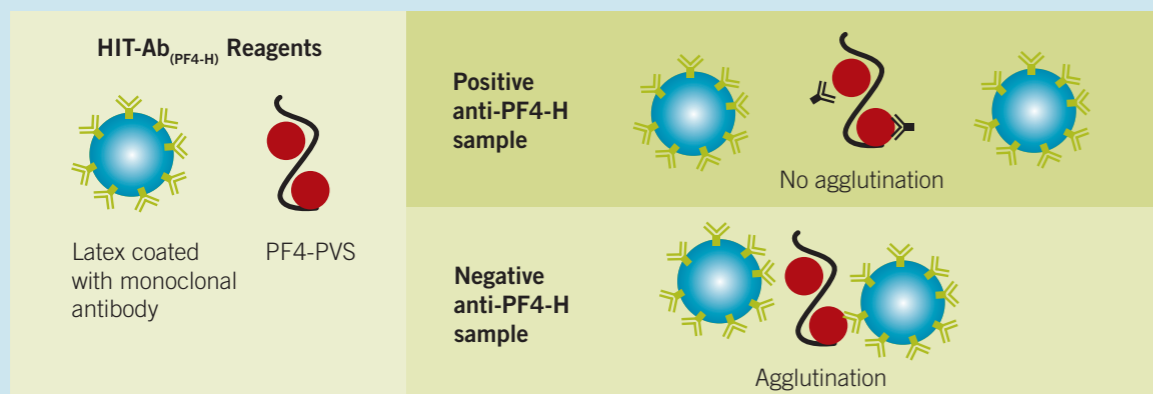
Adapted from Warkentin TE. *British Journal of Haematology* 2003; 121: Date of Preparation: July 2010



# HemosIL HIT-Ab<sub>(PF4-H)</sub>

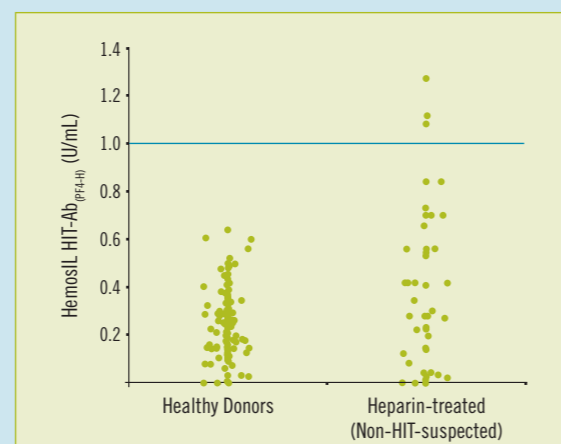
## Principle

HemosIL HIT-Ab<sub>(PF4-H)</sub> is a latex-enhanced immunoturbidimetric assay for the detection of anti-PF4-H, 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, thereby inhibiting agglutination, while the absence of anti-PF4-H will allow the complex to bind to the latex, thereby allowing agglutination.



## Expected Values

An Expected Values study was performed to evaluate 95% reference intervals in 131 healthy donors and 51 Heparin-treated (non-HIT-suspected) patient samples. Healthy donors 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<sub>(PF4-H)</sub> results, equal or higher than 1.0 U/mL, may indicate the presence of HIT antibodies.



## Excellent Correlation vs. ELISA

A multi-center study was performed using HemosIL HIT-Ab<sub>(PF4-H)</sub> assay on the ACL TOP vs. a commercially available ELISA method. Using a population of 414 HIT-suspected patients, HIT-Ab<sub>(PF4-H)</sub> demonstrated a high degree of agreement between the two methods.

HIT-Ab <sub>(PF4-H)</sub>	ELISA
<b>Co-positivity</b>	60.2% (48.9 – 70.8)
<b>Co-negativity</b>	94.6% (91.5 – 96.7)
<b>Agreement</b>	87.7% (84.1 – 90.7)

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

<b>TEST RANGE</b>	0–5.7 U/mL without rerun 0–16 U/mL with rerun		
<b>PRECISION</b>		<b>Mean (U/mL)</b>	<b>CV% (Total)</b>
	Low HIT-Ab <sub>(PF4-H)</sub> Control	0.7	0.11 (SD)
	Weakly Positive HIT-Ab sample	1.6	8.1
	High HIT-Ab <sub>(PF4-H)</sub> Control	3.5	6.1
	High HIT-Ab sample	5.2	3.5
	Very High HIT-Ab sample	10.0	9.5
<b>INTERFERENCES</b>		<b>None up to:</b>	
	Hemoglobin	495 mg/dL	
	Bilirubin	18 mg/dL	
	Triglycerides	250 mg/dL	
	Rheumatoid Factor	1,000 IU/mL	
	Human Anti-Mouse Antibody (HAMA)	1 µg/mL	
	Antiphospholipid Antibodies	None	
<b>ONBOARD STABILITY</b> <i>(of latex reagent, complex, stabilizer)</i>	Continuous	36 hrs at 15°C	
	Cumulative (2 hrs/day, then 2°C–8°C)	16 hrs over 15 days	
	Cumulative (4 hrs/day, then 2°C–8°C)	20 hrs over 9 days	

## Automated HIT detection for the ACL TOP Family.

### A Revolution in Standardization

**ACL TOP 700 • ACL TOP 700 CTS • ACL TOP 700 LAS • ACL TOP 500 CTS**

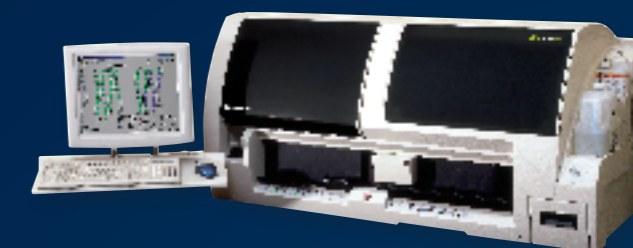
The ACL TOP Family of Hemostasis Testing Systems combines speed, simplicity and intelligence to meet varied needs of hospitals and specialty labs. Take advantage of *Testing-Process Automation*—reducing workload while expanding productivity, and enabling true standardization throughout the lab and hospital.



ACL TOP 500 CTS

### All ACL TOP systems offer:

- Same accurate results
- Same reagents and consumables
- Same broad test menu features and usability
- Same powerful and intuitive software



ACL TOP 700