

and follow-up

D-Dimer clinical threshold

The use of a **unique clinical threshold** (cut-off) **usually found at 0.5 µg/mL FEU** has facilitated standardisation of the use of D-Dimer testing for the diagnosis of VTE. However, as a marker of fibrinolysis, D-Dimer may rise in a number of conditions. Because risk factors for VTE include a history of DVT, age over 60 years, surgery, obesity, prolonged travel, acute medical illness (including cancer) etc. the usefulness of using a unique cut-off for D-Dimer testing can be discussed. Adjusting the clinical threshold to the patients' condition has been assessed in different studies^{1, 2} and is still to be validated in a management study.

Diagnosis of Disseminated Intravascular Coagulation (DIC)

Because DIC is a **complication of an underlying disease** (infections, obstetric complications, trauma...) which involves a dynamic situation due to a dysregulation of coagulation, **its diagnosis is complex**. Among other existing clinical scores, the ISTH DIC diagnostic algorithm^{3,4} encompasses both clinical and laboratory information collected in emergency and involves repeated measurements of Fibrin Related Markers (FRM).

In a study performed on 241 patients, STA-Liatest D-Di showed excellent sensitivity and a very good negative predictive value in comparison with other components of the proposed ISTH DIC diagnostic algorithm.⁵

Assessment of the risk of recurrence

After a first idiopathic thrombotic event (DVT or PE), the **cumulative recurrence of VTE** (after 6 months) has been reported to reach **13% at 1 year**, 23% at 5 years, and 30% at 10 years¹.

In recent studies, it has been observed that elevated **D-Dimer levels**, either during or after discontinuation of anticoagulation may be correlated with an **increased risk of recurrence**^{1,6}.

Different methods to estimate the risk of recurrence or adjust the assays' cut-offs to patients' age, sex, and/or location of the thrombotic event have been evaluated in different studies² aiming to achieve a balance between an increased number of patients in whom anticoagulant therapy could be stopped and a minimal number of recurring events.



The Stago D-Dimer line

	Reagents		Controls		EQA
Name	STA-Liatest D-Di Plus*	STA-Liatest D-Di**	STA-D-Di Control*	STA-Liatest Control N+P	Qualiris QC D-Dimer***
Cat.Nr	00662	00515	00868	00526	01049
Format	Liquid	Liquid	Liquid	Lyophilised	Lyophilised
Stability on board	15 days	15 days	72h on STA-R and STA Compact	8 hours	-
Packaging	6 x 5 mL of reagent 1 (Buffer) 6 x 6 mL of reagent 2 (Latex)	6 x 5 mL of reagent 1 (Buffer) 6 x 6 mL of reagent 2 (Latex)	2 x 6 x 2 mL	2 x 12 x 1 mL	3 levels, 6 samples, 6 reports (per year)

*Not available in USA and Canada - **Commercial availability depending on the country - ***QC availability depending on the program subscription

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STA-Liatest D-Di, STA-Liatest D-Di Plus, Asserachrom D-Di, STA-D-Di Control, STA-R, STA Compact, STA-Liatest Control N+P, Qualiris QC D-Dimer are trademarks of the Stago Group. The rights of the trademarks and logos used in this document belong to the Stago Group. The use of these trademarks is not permitted without permission from the Stago Group.



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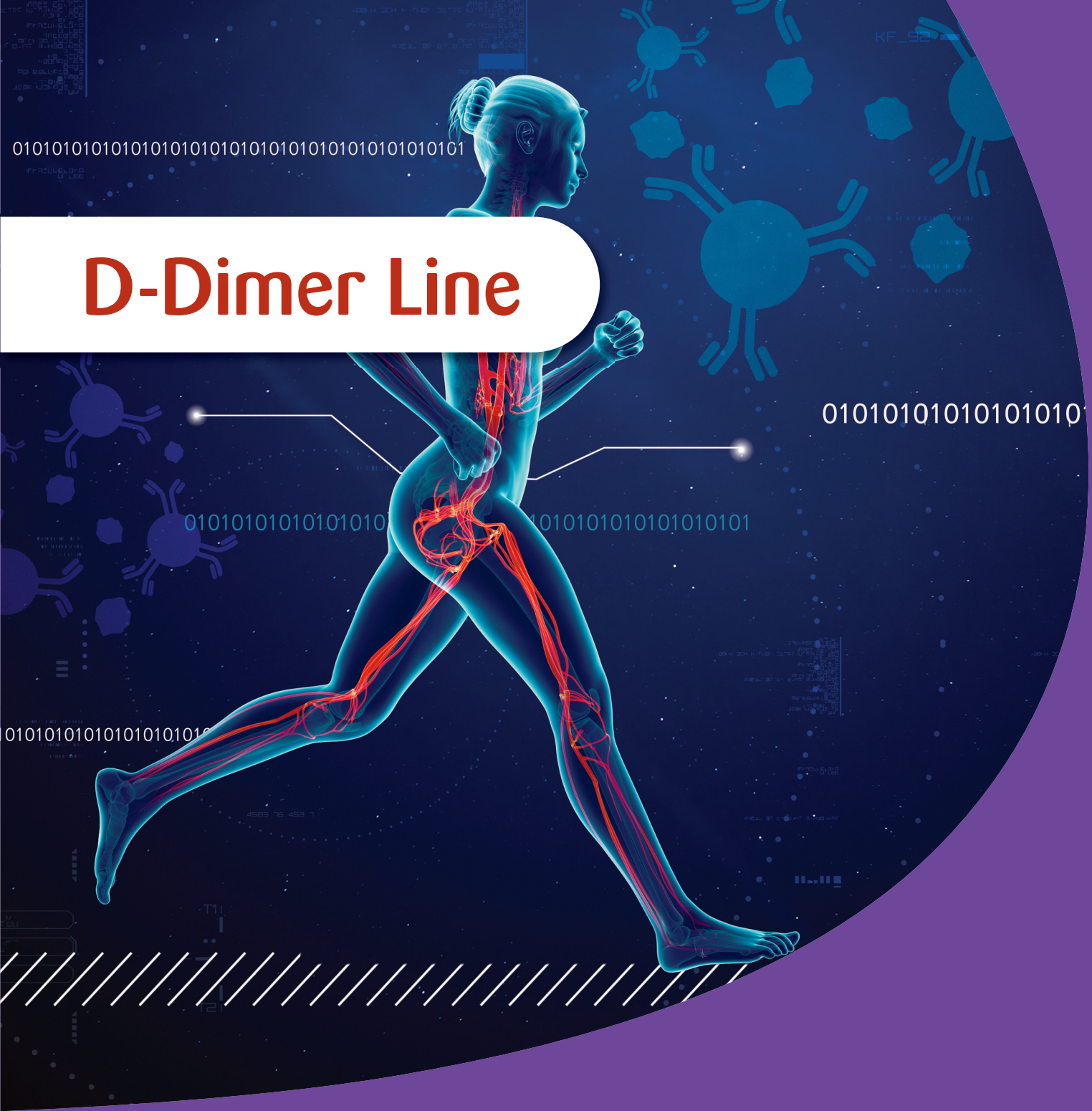
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D-Dimer Line



A reliable testing system for enhanced patient care

- Fully automated
- Easy-to-use
- Reliable
- Clinically Validated



A tool for diagnosis

Exclusion of Venous ThromboEmbolism (VTE), a clinical challenge

D-Dimer measurement, in conjunction with a standardized assessment of **Pre-test Probability (PTP)**, is successfully **used to exclude VTE without the need for an imaging study**, provided the threshold for the D-Dimer assay has been objectively established and validated for this purpose.

A safe D-Dimer test must show the appropriate balance between **sensitivity** and **specificity**⁸. Recommended D-Dimer assay clinical performances for safe exclusion of VTE:

- sensitivity >95%

Two types of assays could be distinguished:

- **Highly sensitive D-Dimer assays**⁹ (high sensitivity >95%, moderate specificity) such as some ELISA assays and some **automated latex immunoturbidimetric assays**
- **Moderately sensitive D-Dimer assays** (moderate sensitivity 85-90%, high specificity)

Because D-Dimer test is an exclusion test that is **performed in emergency situations**, an efficient test must be **rapid**, and show a **high Negative Predictive Value (NPV)**.

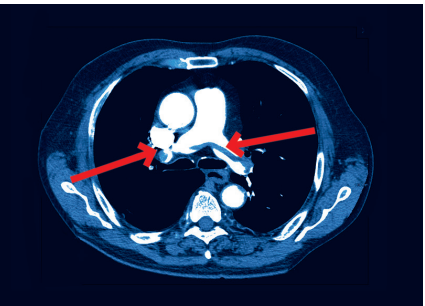
PTPA*	Recommended assay in first line ^{7,9}	Follow-up ^{7,9}
HIGH	D-Dimer assays should not be used to rule-out DVT or PE	
MODERATE	Only a highly sensitive D-Dimer assay	If D-Dimer result is negative, no further testing is required
LOW	Highly sensitive or moderately sensitive D-Dimer assay	If D-Dimer result is negative, no further testing is required

*PTPA: Pre-Test Probability Assessment according to a well validated score

The NPV should be as high as possible in considered patient population.

Clinically validated performances

The utility of D-Dimer testing for the **exclusion of Pulmonary Embolism (PE)** and **Deep Venous Thrombosis (DVT)** has long been established^{7,9,15}. Because this diagnosis is **critical**, recent guidelines from scientific societies or regulatory bodies have introduced performances to achieve a **safe exclusion of VTE diagnosis**.



Exclusion of Pulmonary Embolism (PE) and Deep Venous Thrombosis (DVT)

PE resulting from DVT is the most common preventable cause of hospital death:

- **If not treated, 10-30% of PEs are fatal.**
- If treated, 2-8% PEs are fatal.
- Many deaths from PE are undiagnosed¹⁰.
- **PE cannot be diagnosed solely on a clinical basis**, because of the **lack of sensitivity and specificity** of clinical signs and symptoms.
- Pulmonary imaging for PE diagnosis is resource demanding.

Because the prevalence of PE & DVT is relatively low (20% or less) amongst individuals who are clinically suspected of having the disease, **submitting all of them to imaging would not be cost-effective**.

Therefore, **diagnostic algorithms** have been developed that **include clinical probability assessment** and **D-Dimer measurement** to select the patients who require imaging¹¹.



DiET study

The DiET study is a huge multi-centre clinical trial, performed in compliance with the very high and strong requirements of **CLSI guideline H59-A¹⁶**, involving the inclusion of more than **2000 patients** with a suspicion of PE or DVT in 16 sites throughout the world: United States (10), Canada (1), France (2), Italy (2) and Spain (2).



STA-Liatest D-Di				CLSI Recommendation	
PE Exclusion ¹⁶	Performances*	Lower Limit of CI*	Upper Limit of CI*	Performances	Lower limit of CI
NPV	99.7%	99.2%	100.0%	≥98%	≥95%
Sensitivity	97%	91.6%	99.4%	≥97%	≥90%
Specificity	75.5%	72.8%	78.1%	None	None

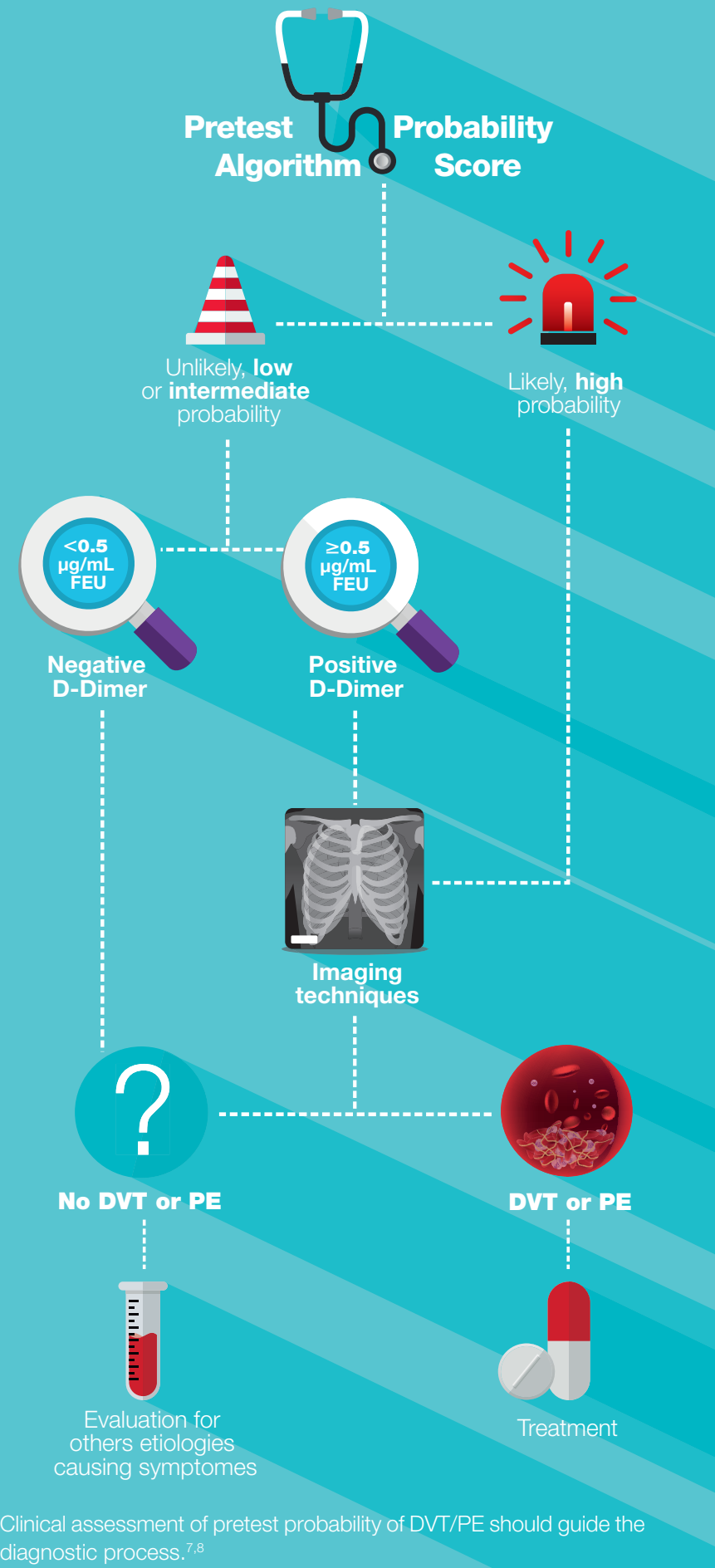


STA-Liatest D-Di				CLSI Recommendation	
DVT Exclusion	Performances*	Lower Limit of CI*	Upper Limit of CI*	Performances	Lower limit of CI
NPV	100.0%	99.3%	100.0%	≥98%	≥95%
Sensitivity	100.0%	95.8%	100.0%	≥97%	≥90%
Specificity	55.2%	51.9%	58.5%	None	None

* 95% Confidence Interval (CI)

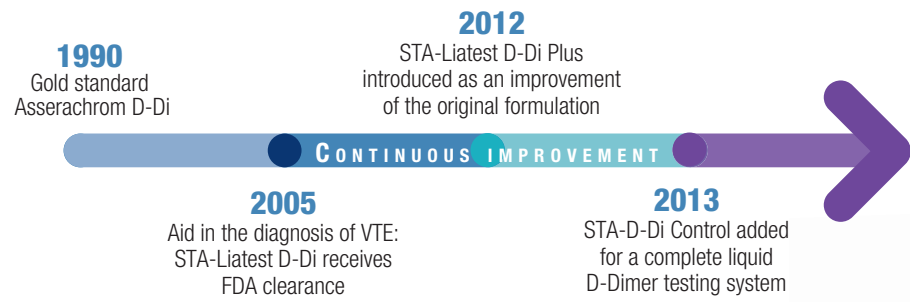
Results exceed the CLSI performance goals required on sensitivity and Negative Predictive Value (NPV), the two relevant criteria **allowing the exclusion of PE & DVT on patients with a low or moderate risk** as stated in the CLSI guideline H59-A.

Example of DVT/PE algorithm



The optimised complete testing system

As part of Stago's continuous improvement commitment, STA-Liatest D-Di Plus has been developed as an enhancement of **STA-Liatest D-Di**. By minimizing the interferences from heterophilic antibodies (incl. HAMA) and Rheumatoid Factor (RF), **STA-Liatest D-Di Plus** has been designed to show improved analytical specificity **for even better efficacy with the same excellent clinical performances**.



Less interference for even more efficiency

- **Validated:** STA-Liatest D-Di Plus is intended for use as exclusion of the diagnosis of DVT and PE^{8, 12, 13, 14}.
- **Adapted to STAT (available 24/7):** Stable for 15 days on board, short time-to-result (7 min).
- **Easy-to-use:** Precalibrated, automated assay. Ready-to-use reagent with standardised results across Stago analysers.
- **Reliable:** Low coefficients of variations (CV) across international proficiency testing programme reports.

Diagnostic Performances	PE exclusion	DVT Exclusion
NPV	99.7%	100%
Sensitivity	97%	100%
Specificity	75.5%	55.2%

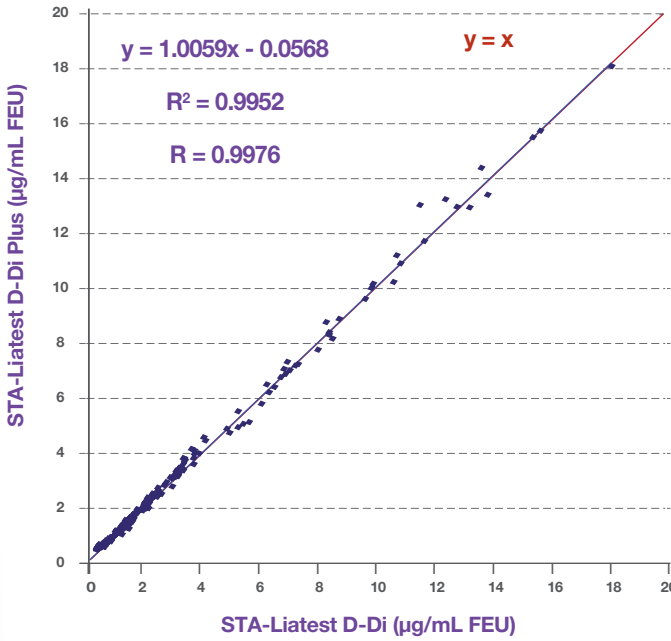
Adapted to your Day-to-Day D-Dimer testing

With **Liquid, ready-to-use** STA-D-Di Control

- **Located at ideal levels**
 - Control 1: Low positive
 - Control 2: Pathological
- **Extended stability**
 - **72h on board STA-R and STA Compact**
 - **Stable for 15 days** after opening when stored at 2-8°C
- **2 mL vials:** allows several QC runs per day



Method comparison STA-Liatest D-Di / STA-Liatest D-Di Plus on STA-R (N=200)



Assay Key features	
Reporting unit	µg/mL FEU
Assay range	0.27-20 µg/mL FEU
Cut-off value	0.5 µg/mL FEU
Repeatability	6.6% (at 0.69 µg/mL FEU) 2.4% (at 2.30 µg/mL FEU)
Within-Lab precision	7.6% (at 0.69 µg/mL FEU) 3.2% (at 2.30 µg/mL FEU)
Calibration	Unique precalibration on STA line analyzers
Time-to-result	<7 min
Interferences to RF	Eliminated up to 1000 IU/mL
Interferences to HAMA	Minimized

A comprehensive testing system

Stago offers a reliable, fully automated, ready-to use testing system:

- **Reagents**
 - STA-Liatest D-Di Plus*
 - STA-Liatest D-Di**
- **Controls**
 - STA-D-Di Control*
 - STA-Liatest Control N+P
- **EQA**
 - Qualiris QC D-Dimer***

* Not available in USA and Canada

** Commercial availability depending on the country

*** QC availability depending on the programme subscription