Hemostasis Briefing

Sysmex Corporation
June 14, 2024

Together for a better
healthcare journey

Disclaimer

- This material contains forward-looking statements about the Sysmex Group. These forward-looking statements are based on the current judgments and assumptions of the Sysmex Group in light of the information currently available to it. Uncertainties inherent in such judgments and assumptions, the future course of our business operations and changes in operating environments may cause our actual results or performance to be materially different from any future results and performance either expressed or implied within these forward-looking statements.
- The product information contained in these materials is not intended as advertising or medical advice.

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1. The Hemostasis Environment
2. Strategies for Growth

Appendix

1. The Hemostasis Environment

- Internal Environment
- External Environment
- Competitive Environment

Story of Value Creation

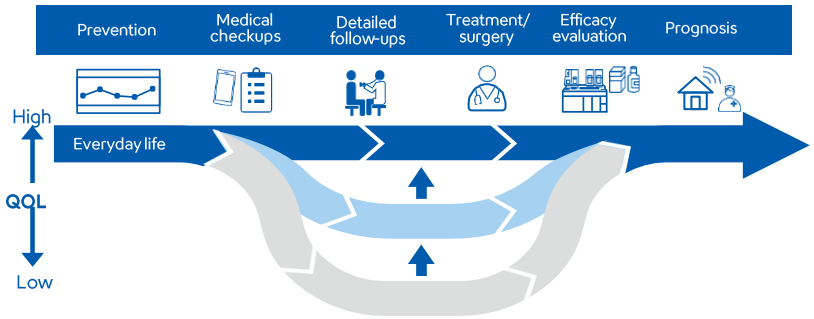
Our long-term vision: Together for a better healthcare journey

Input

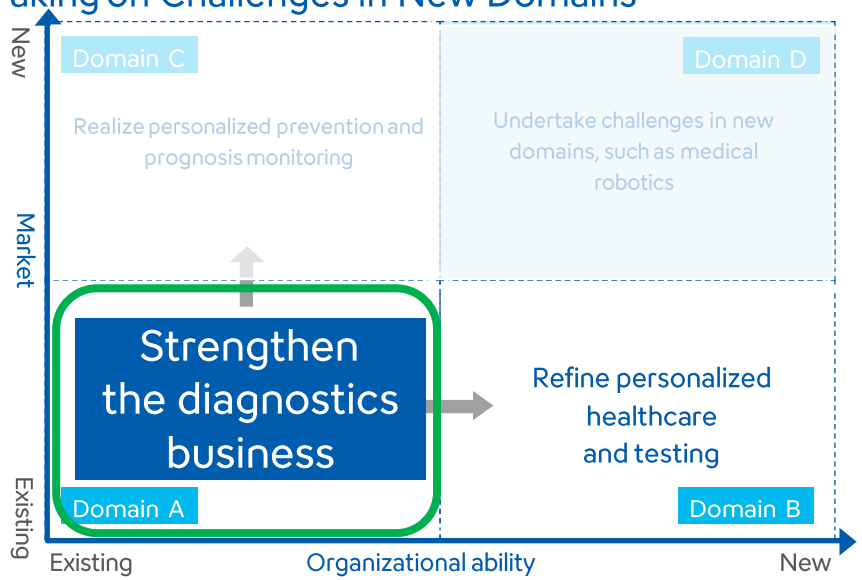
(Management Resources)

Business Domains

Domain Expansion
From "IVD" to "Healthcare Journey"



Growth in Existing Domains
+ Taking on Challenges in New Domains



Value Creation Strategies/ Outputs

(Materiality)

- Creating new value for a healthy society
- Providing responsible products, services, and solutions
- Reducing environmental impacts
- Creating an attractive workplace
- Strengthening governance

(Core Strategy)

Businesses and Technologies

Enhancing the Value of Testing, Developing Personalized Medicine and Prevention

Eco-social

Establishing a Business Model Adapted to a Circular Resource Society

Human Capital

Corporate Management

Outcomes

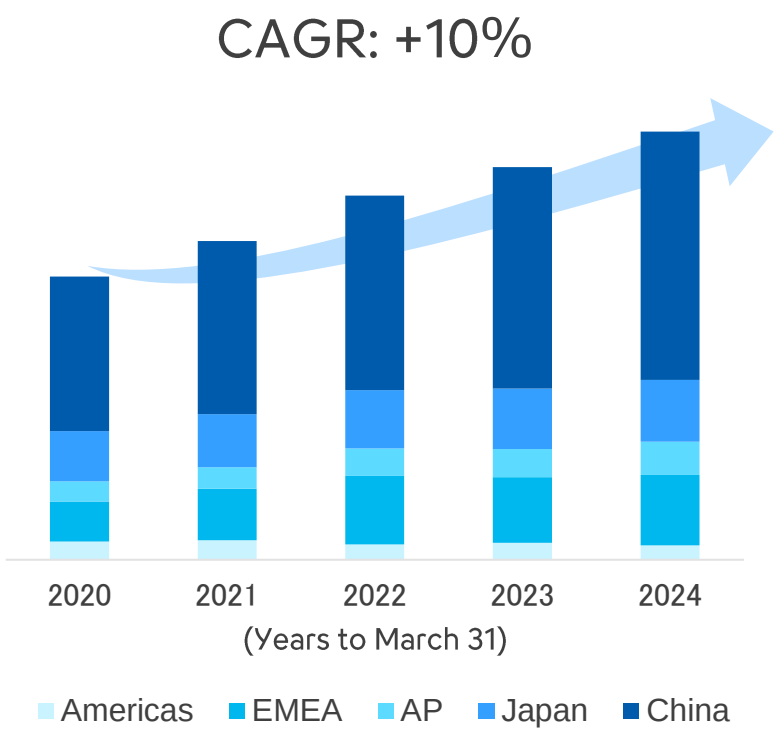
(Value Provided)

- **Extending Healthy Lifespans of People Around the World**
- **Realizing a Circular-oriented Society**
- **Creating Social Value**

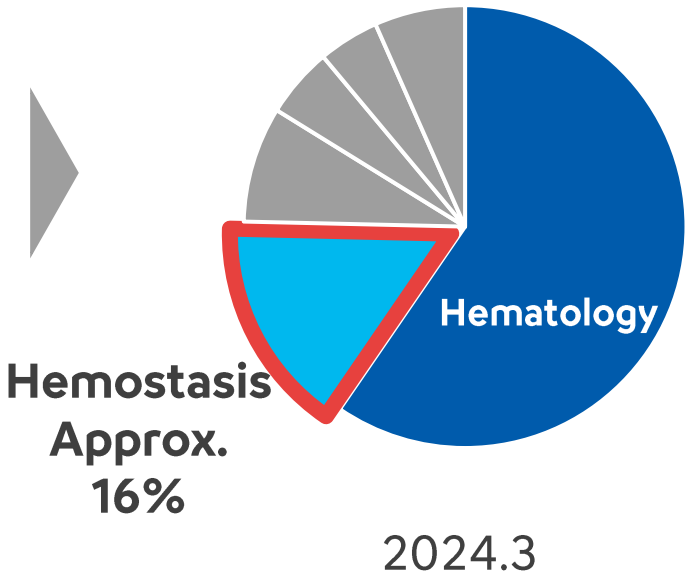
Internal Environment: Sales and Market Share in the Hemostasis Field

Second-highest percentage of Group sales, with a global market share of around 30%

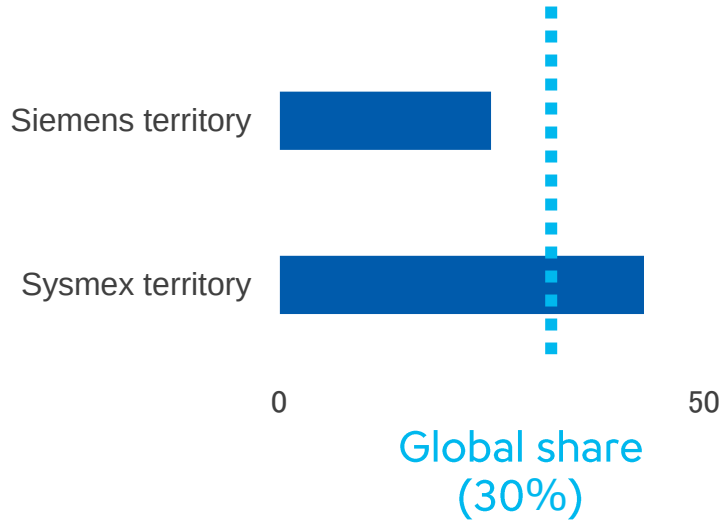
Net sales



Sales composition



Market share

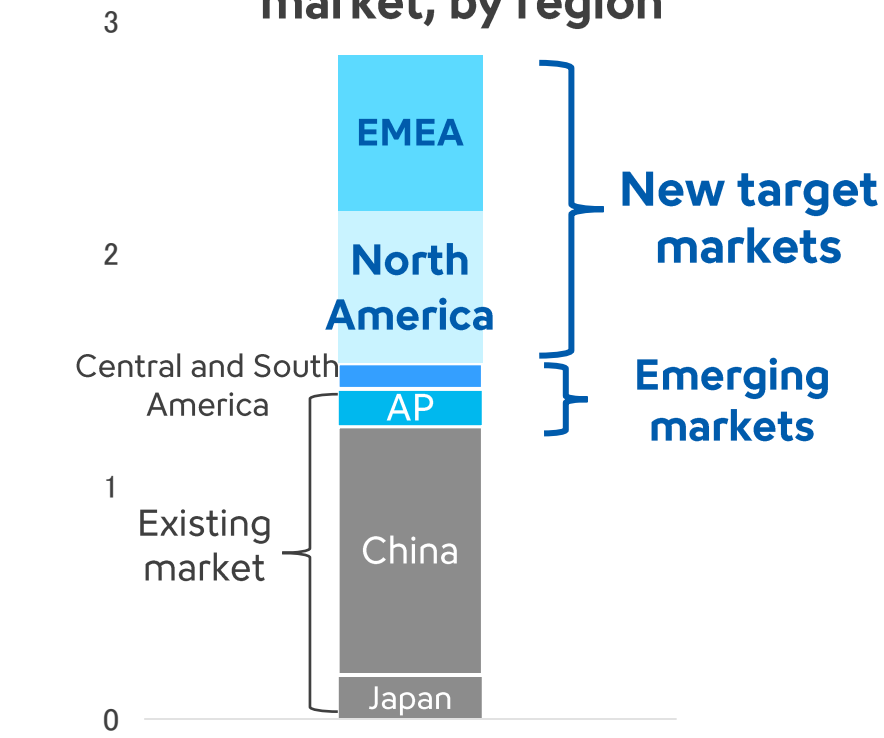


*Sysmex' s estimates based on information disclosed for 2022

External Environment: The Hemostasis Market

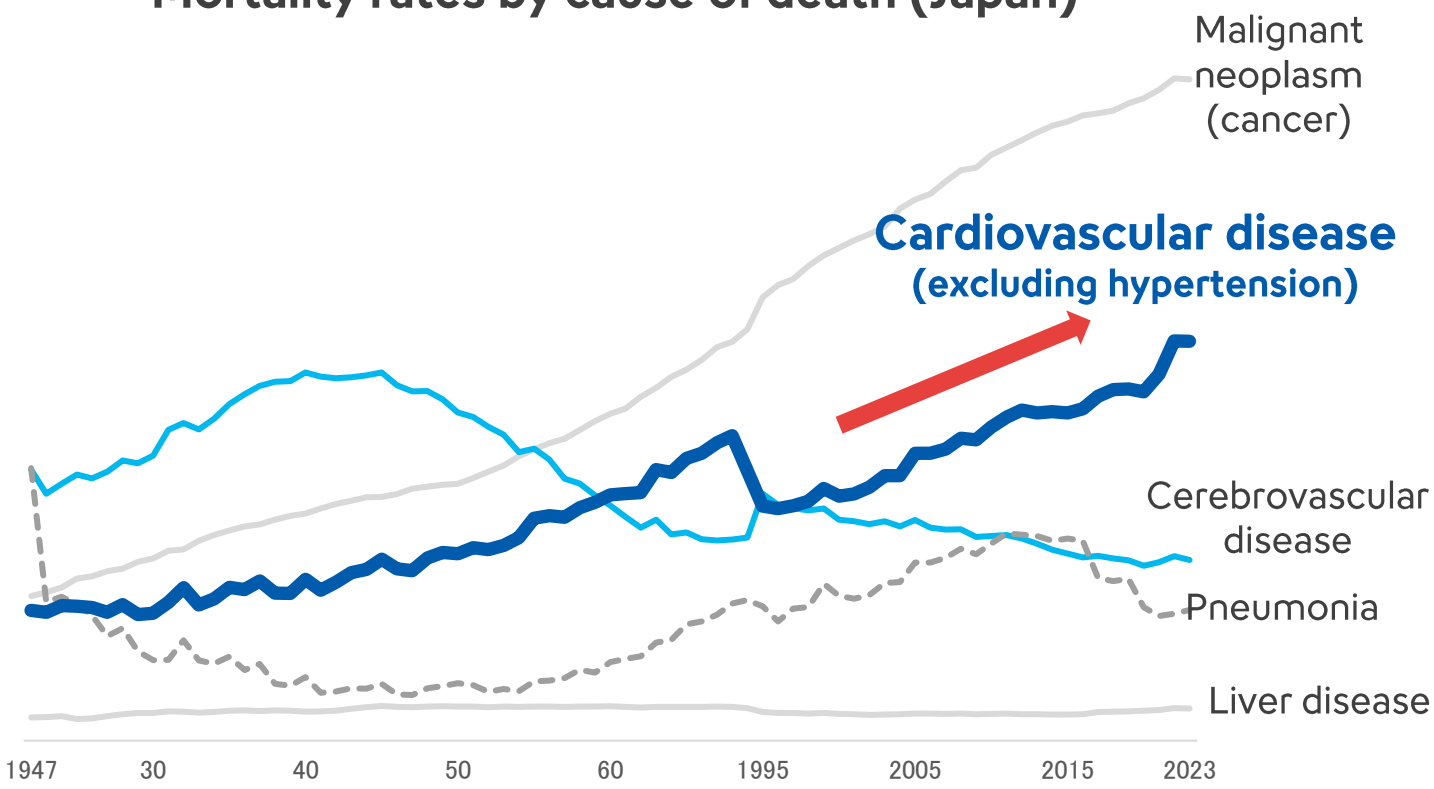
Market size of USD3 billion; cardiovascular and other target diseases on the rise
High growth potential, including expansion into European and U.S. markets and growth in emerging markets

Size of the hemostasis testing market, by region



Note: Based on research by Sysmex and Clearstate (2022)

Mortality rates by cause of death (Japan)



From Overview of the Annual Report on Monthly Demographic Statistics 2023, page 11, Jun.2024

External Environment: The Cost of Hematology Testing

The insurance reimbursement rate for hemostasis is more than ten times higher than that for hematology

	Hematology	Hemostasis testing
Test objective	Main screening tests - Differentiation of blood cells - Leukemia - Anemia, etc.	Identification of diseases and disease factors - Hemophilia, identification of deficiency factors - Myocardial infarction, cerebral infarction - Therapeutic drug efficacy, monitoring
insurance reimbursement rate (points)	Japan: 21 to 25 points United States: Around 8USD	Japan: **20 to 200 points** United States: **Approximately 30 to 200USD**

*Sysmex' s estimates based on information disclosed.

Changes in the Hemostasis Field (Instruments)

1980 to 1990

Automation of testing
Simultaneous development of test reagents to ensure testing quality

Equipping with world-first features such as random access to specimens, auto-sampling, etc.

CA-100 automated blood coagulation analyzer

Note: Recipient of the Good Design Award

CA-3000 automated blood coagulation analyzer

Pursuing products and services that exceed customers' expectations and capture the top share of the domestic market

Changes in the Hemostasis Field (Instruments)

1990 to 2000

Simultaneous and full automation of five basic test parameters (automated feeding of sample tubes)

IT-adapted products
(Bidirectional communication with host PCs)

Compatible with touch panels

Clotting, chromogenic substrate, and Immuno-turbidimetriry in a single instrument

Reflective function
(Automatically perform related tests for abnormal specimens)

Cap piercing function

CA-5000 automated blood coagulation analyzer

CA-6000 automated blood coagulation analyzer

Develop and deliver functions that contribute to increased laboratory productivity

Changes in the Hemostasis Field (Instruments)

Since 2000

World's fastest measurement speed
On-board platelet aggregation function
Multi-wave measurement

Space-saving
Equipped with immunochemistry modules

*Sysmex' s estimates based on information disclosed.

CS-Series blood coagulation analyzers

CN-Series blood coagulation analyzers

Providing more value through IT-based external quality control, etc.

World's-First Functions Sysmex Has Realized

World's first functions	Value provided
Percentage detection method	Improved measurement capability (for low fibrin plasma)
Liquid level detection and aspiration of reagents and samples	Reduction of reagent loss, automation of specimen setting
Cap piercing	No need to open the caps, less burden on the user, improved safety
*World's-fastest processing (500 tests/hour)	High throughput, reduced inspection time, higher efficiency
Multi-wave random measurement	Higher sensitivity, reduction of re-tests

*Sysmex' s estimates based on information disclosed.

Reference: CN-3500/CN-6500 Automated Blood Coagulation Analyzers

Blue: continuation
Green: advances

High processing capacity, space saving

Establishment of a CLSI-compliant data assurance system

Network service using Caresphere™

Centralized testing workflow for hemostasis specimens

Potential to contribute to treatment through cross-mixing, platelet aggregation function, and CLEIA method measurement parameters

Cap piercing facilitates safe and secure operation

*Sales only in regions with regulatoly approval.

Changes in the Hemostasis Field (Reagents)

A robust portfolio of testing parameters with unique reagents

Thrombus screening (D-Dimer, FDP) → DOAC measurement, etc.

Bleeding screening →

Lyophilized reagents → Liquid reagents →

HYPHEN's reagents
Development and manufacture of state-of-the-art hemostasis parameters (from 2010)

Sysmex International Reagents'* reagents
Development and manufacture of reagents suitable for the domestic market (from 2001)
*now Sysmex Corporation

Siemens' reagents
*Largest manufacturer in the world, with an assortment of routine and specialized parameters (from 1995)

1995 2000 2005 2010 2015

*Sysmex' s estimates based on information disclosed.

Development advances on own reagents

+

Differentiation by Liquefaction

Six liquid reagents

(Including those under regulatory review)

PT, APTT, Fbg,
TT, AT, D-Dimer

Note: Other companies support two to four parameters

The Competitive Environment in Hemostasis

A unique competitive environment, unlike other fields of testing

Major competitors, competitors are Stago and Werfen

- ✓ Measurement and reagent development technologies involve a high degree of difficulty (complex reagents containing many animal-derived components)
- ✓ Interpretation of clinical results is difficult and requires a high level of expertise in scientific support

New models with improved functionality are more frequently available.

- ✓ Other companies : Between 12 to 18 years*
- ✓ **Sysmex: Between 5 to 7* years （Calculate including transport systems and peripheral modules）**

*Sysmex' s estimates based on information disclosed.

Our Resources in the Hemostasis Field

Hemostasis Assets

Research and development

R&D personnel: Approx. 100 people

R&D bases

- Technopark (product development)
- East Site (raw material development, production technologies)
- HYPHEN BioMed (development, production, sales)

Intellectual property rights owned*: Approx. 1,000

*including Patents, Trademark, Copyrights rights

Product portfolio

High-volume

CS-5100 (2011)

CN-3000/CN-6000 (2018)

CN-3500/CN-6500 (2020)

Middle- and low-volume

CA-620/CA-650 (2011)

CA-101/CA-104 (2013)
Note: Semi-automated

CS-2400/CS-2500 (2014)

CS-1600 (2015)

Sysmex reagents

2. Strategies for Growth

Positioning Hemostasis within Our Growth Strategies

Driving Sysmex's growth in the medium term

Three growth strategies

Reinforcement of existing businesses

Emerging market strategies

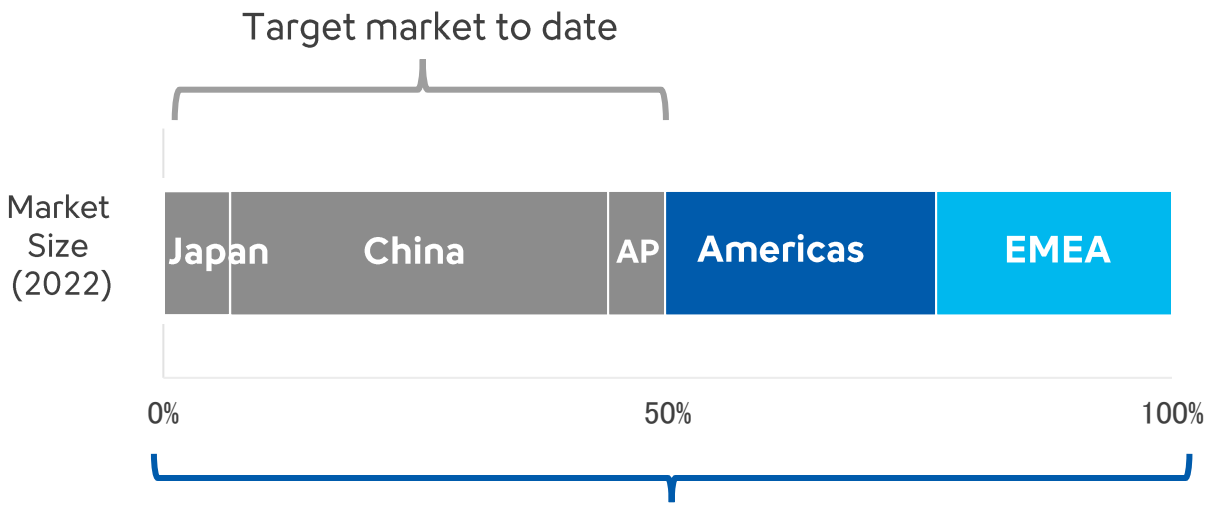
Expansion of new businesses

- ✓ Expansion of our target sales markets by initiating global OEM agreements (Europe and the United States)
- ✓ Cultivation of new markets, particularly in emerging markets

- Realization of initiatives in the hemostasis field
- Utilize resources developed in hematology

Growth Factor 1: Increase Sales by Expanding the Target Market

Potentially doubling the target market

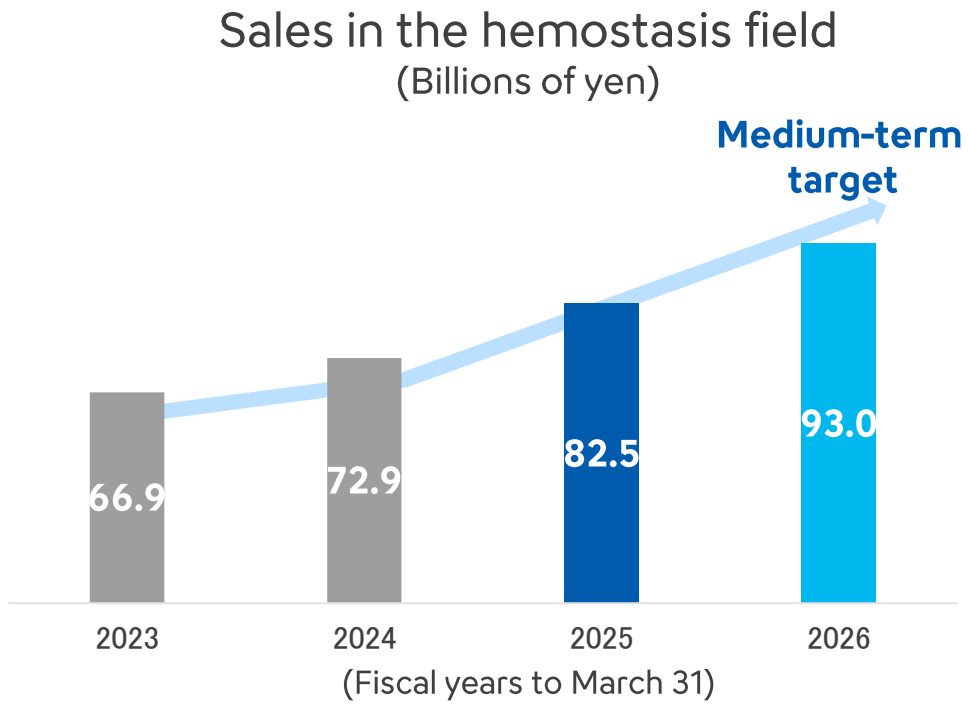


Size of market from the fiscal year ending March 31, 2025*

Approx. 3.0 billion USD*

*Sysmex' s estimates based on information disclosed.

Sales projected to grow by ¥20 billion over two years



Growth Factor 2-1: Leverage Our Strengths in Hematology

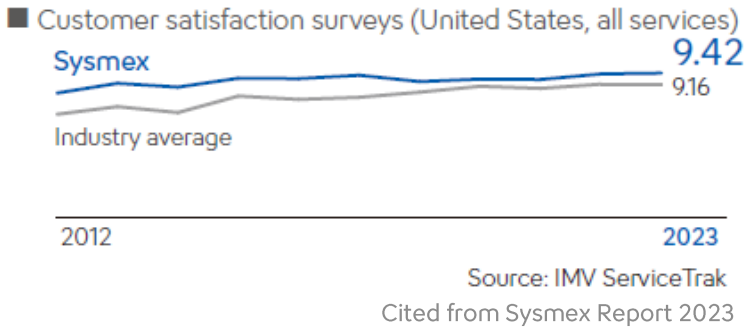
Leverage the brand strength in hematology

Global sales network and support

Leverage channels in the hematology field

High level of customer satisfaction

In the United States, our customer satisfaction in hematology has been No. 1 for 17 consecutive years.



Source: IMV ServiceTrak
Cited from Sysmex Report 2023

Provide our hemostasis customers with the same highly trusted products and services.

Growth Factor 2-2: Leverage Our Strengths in Hematology

Propose unique systems that offer connections with the hematology field

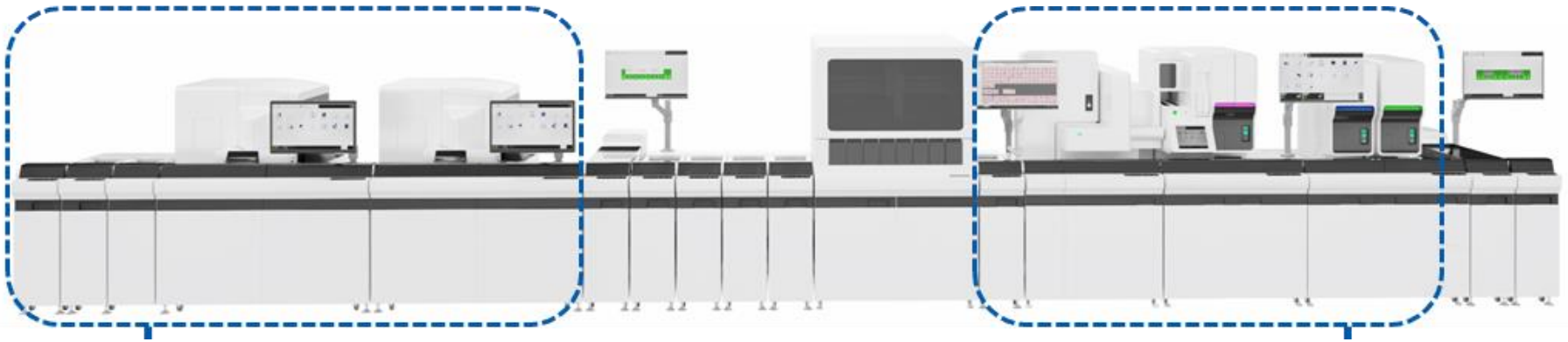
✓ Expand existing systems **in hematology, where we have the No. 1 market share*,** into hemostasis

*Sysmex' s estimates based on information disclosed.

✓ Improve laboratory workflow efficiencies

✓ Expand the range of value provided to users

Hemostasis **Hematology**



Growth Factor 3: Achieve Integration with Other Fields

Propose our own systems incorporating our immunoassay module

Equipped with an immunoassay module and possessing distinctive reagents

- Coagulation molecular markers (TAT, PIC)
- HIT antibody test, etc.*

*Sales only in regions with regulatory approval.

- ✓ Gain a more sophisticated understanding of patient status, promote the identification of causes to further **understanding of diagnosis**
- ✓ **Boost productivity** through integration of instruments

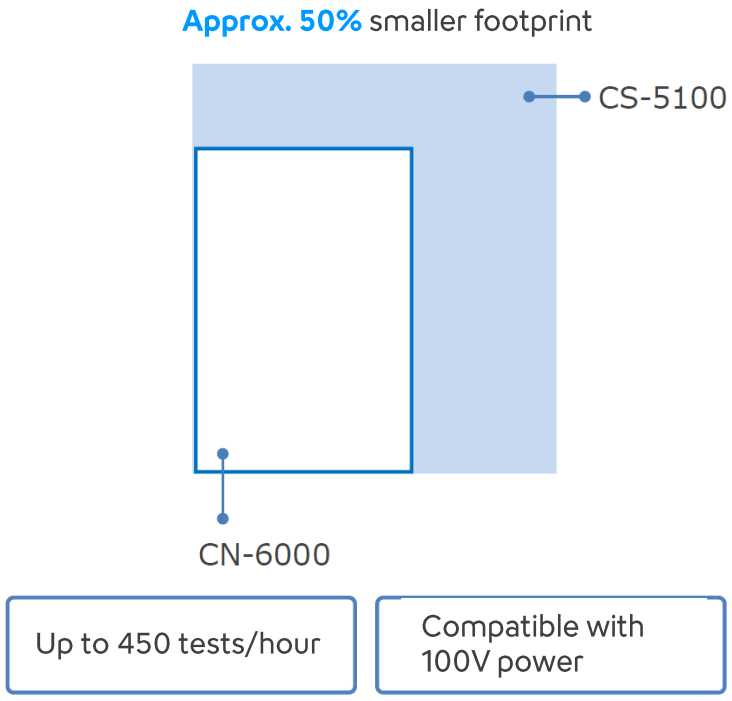
Automated blood coagulation analyzer
+ immunoassay module
CN-3500/CN-6500*

*Sales only in regions with regulatory approval.

Growth Factor 4-1: Eco-Social Strategy (Instruments)

Save energy and space, and gain a competitive advantage

- ✓ Save space through a smaller footprint (approx. 50% smaller)
- ✓ Achieve electricity savings



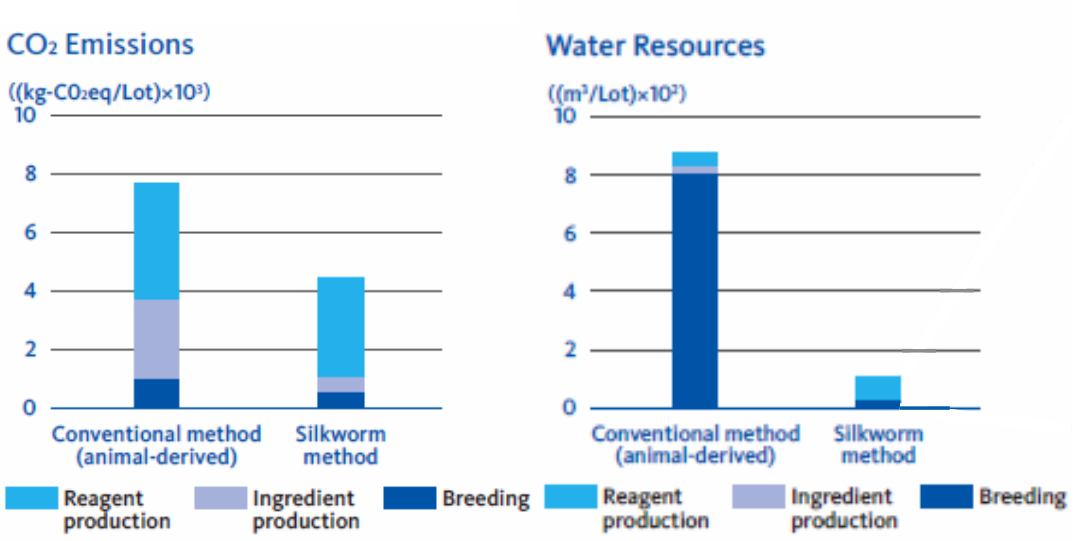
Achieving the world's fastest and most versatile performance* in limited testing spaces

*Sysmex' s estimates based on information disclosed.

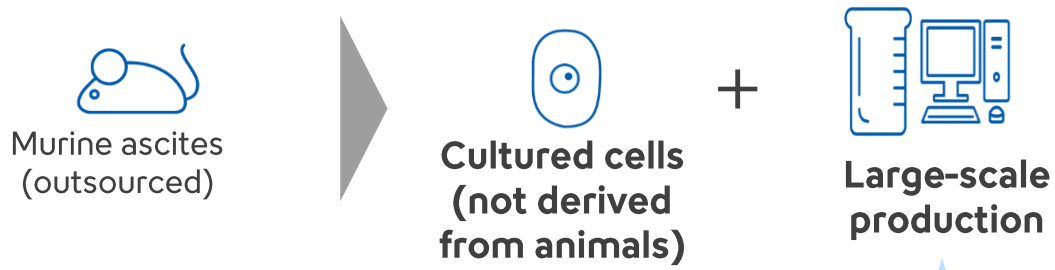
Growth Factor 4-2: Eco-Social Strategy (Reagents)

Move away from animal-based raw materials and gain a competitive advantage

- ✓ Switching to materials that are not animal-based
  - Utilize recombinant proteins from cultured cells and silkworms



- ✓ Stable provision of raw materials
  - Achieve mass production using cultured cells



Environmentally friendly and stable

Growth Strategy in Europe and the United States

Expanding market share in new our in-house sales area is a top priority.

Initiatives in Europe and the United States

- ✓ **Expand market share by leveraging existing hematology channels**
- ✓ **Launch the CN-Series**
  (launched in Europe already, planning to launch the CN-Series in the U.S.)
- ✓ **Strengthen competitive advantage through unique test parameters**
  (liquid reagents, chemiluminescent test parameters, etc.)
- ✓ **Introducing new reagents to the market**

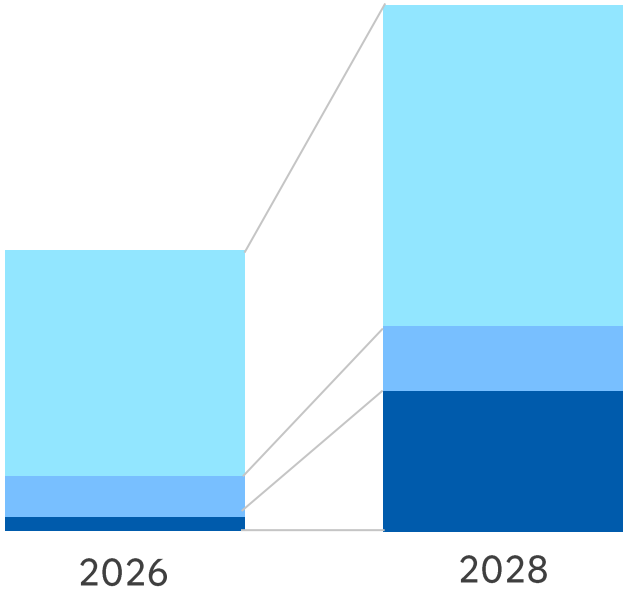
Center for Learning (United States)

Virtual training

Growth Strategy in Emerging Markets

In addition to high-volume markets, roll out products into low-volume and mid-volume markets.

Market growth forecast



High-volume markets

- Already enjoy a strong market share
- Expand our market share at core hospitals with the CN-Series and transport systems

Mid-volume markets

- Launch medium-sized models to take advantage of emerging testing needs

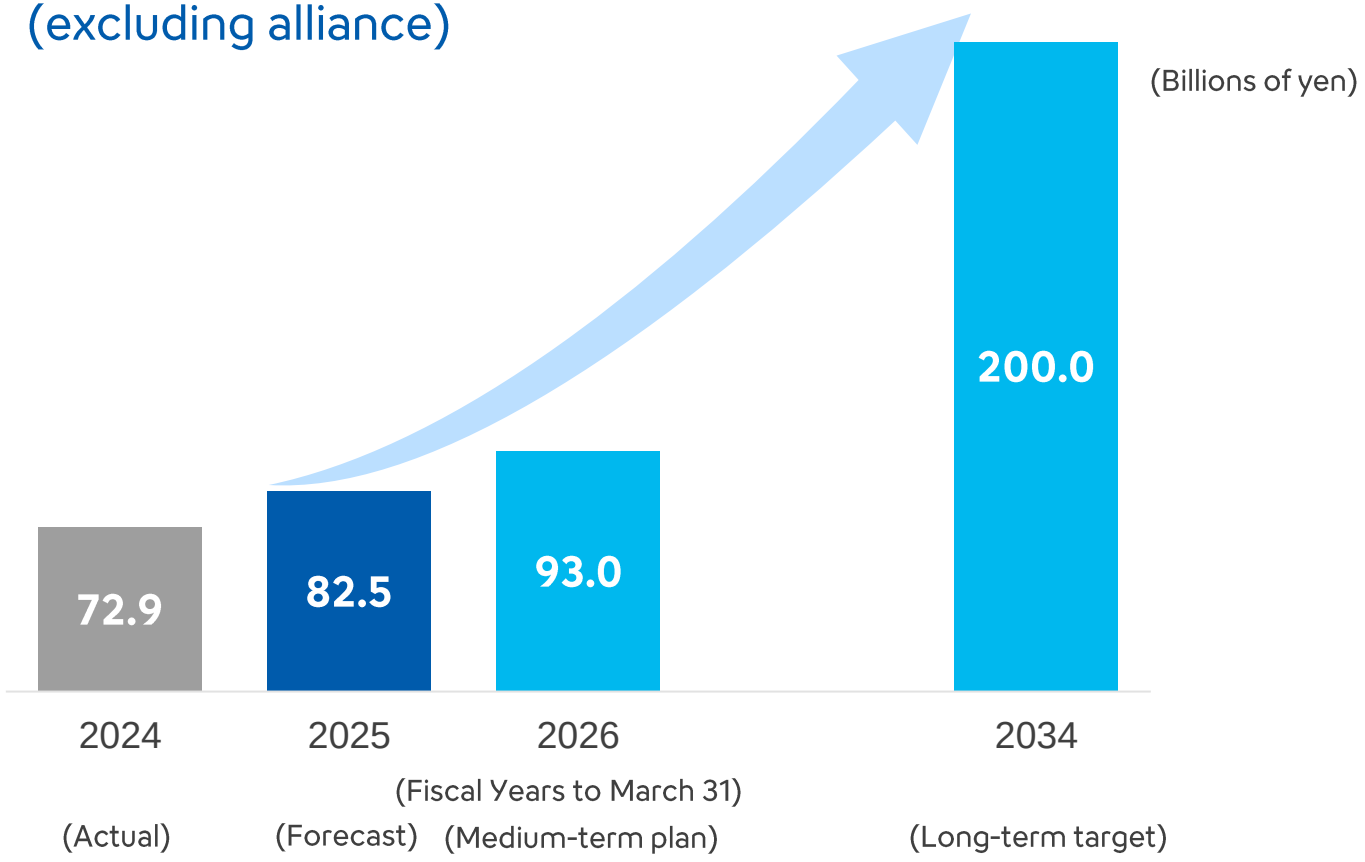
Low-volume markets

- Going forward, we aim to cultivate new markets by offering cross-sector solutions for emerging markets, which are expected to put hemostasis testing systems into place and where testing is slated to become more prolific.

Forecast for Hemostasis

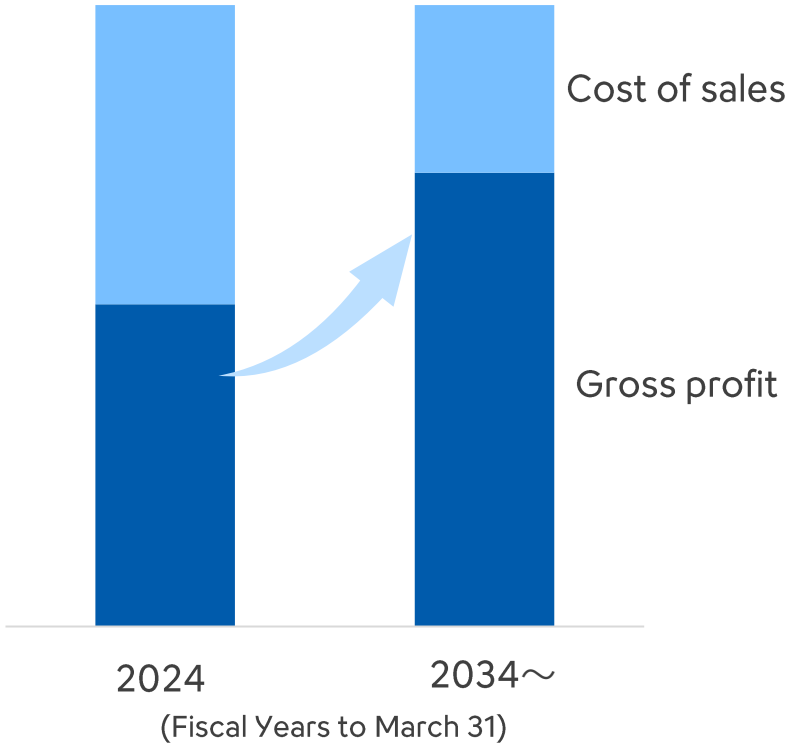
Sales, historical and forecast

Aiming for a global market share of 35% (excluding alliance)



A rising gross profit ratio

Increase of reagent sales and a shift to in-house production of reagents contribute to improve profitability.



(Appendix)

- This material describes general information and is not intended as medical advice.
- Some of the information is presented in simplified language.

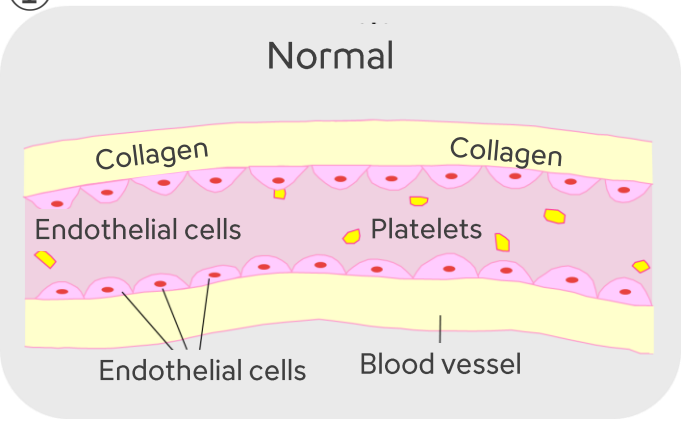
What Hemostasis Testing Tells Us

Whether there is a problem with the balance between coagulation and fibrinolysis

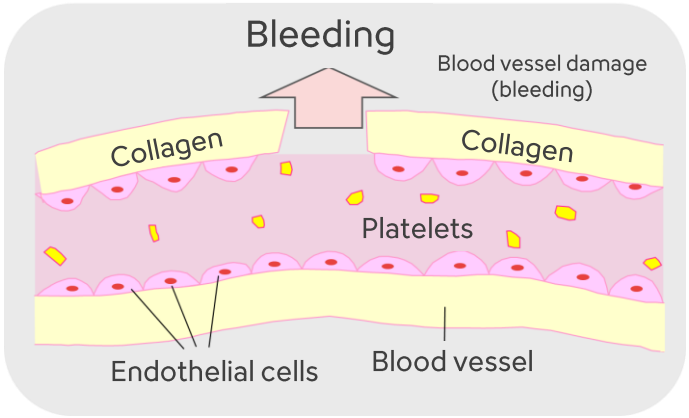
	Blood vessel interior	Blood	Blood vessel exterior
Normal	No coagulation		Coagulation
Abnormal	**Coagulation (clotting)** Cerebral infarction Myocardial infarction Pulmonary embolus Etc.		**No coagulation (abnormal bleeding)** Hemophilia Etc.

Process from the Formation to the Dissolution of a Blood Clot*

①

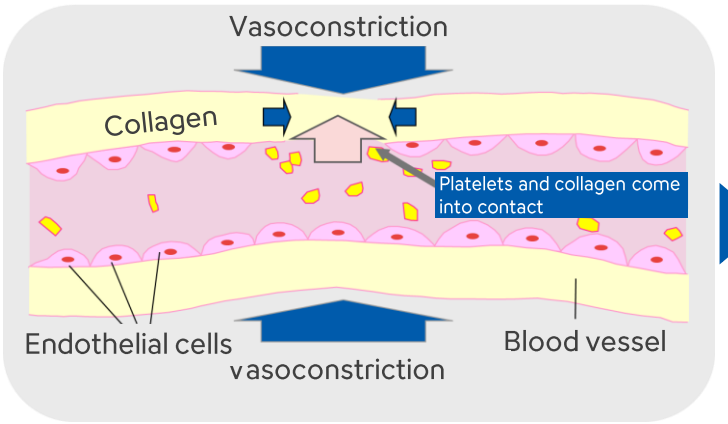


②



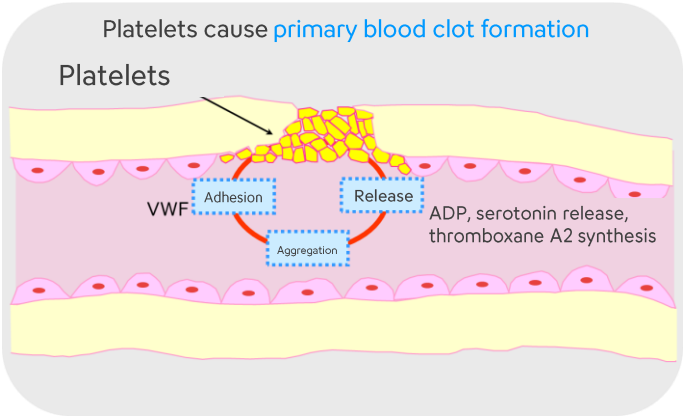
Collagen in blood vessels is exposed

③



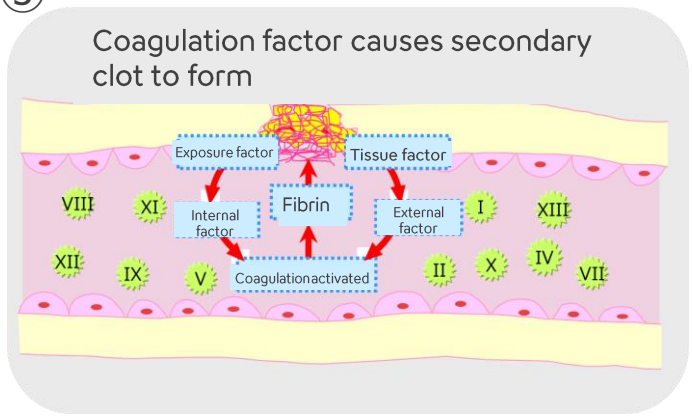
Vasoconstriction to reduce blood flow

④



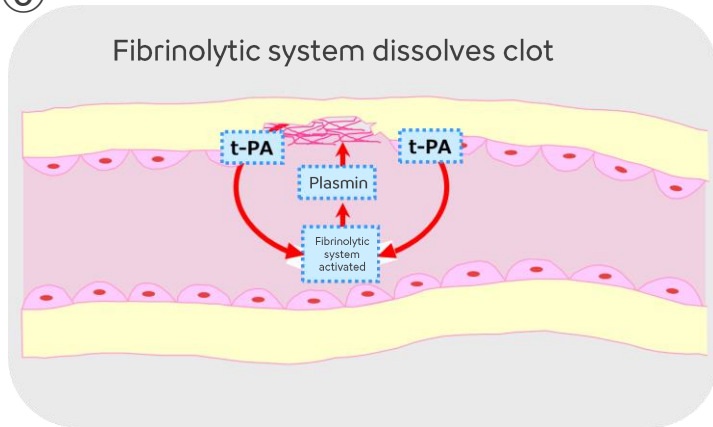
Platelets cause primary blood clot to form

⑤



Reaction with blood coagulation factors occurs, eventually forming fibrin and stronger clot

⑥



Blood clots are no longer needed as blood vessels repair, and the fibrinolytic system works to dissolve clots.

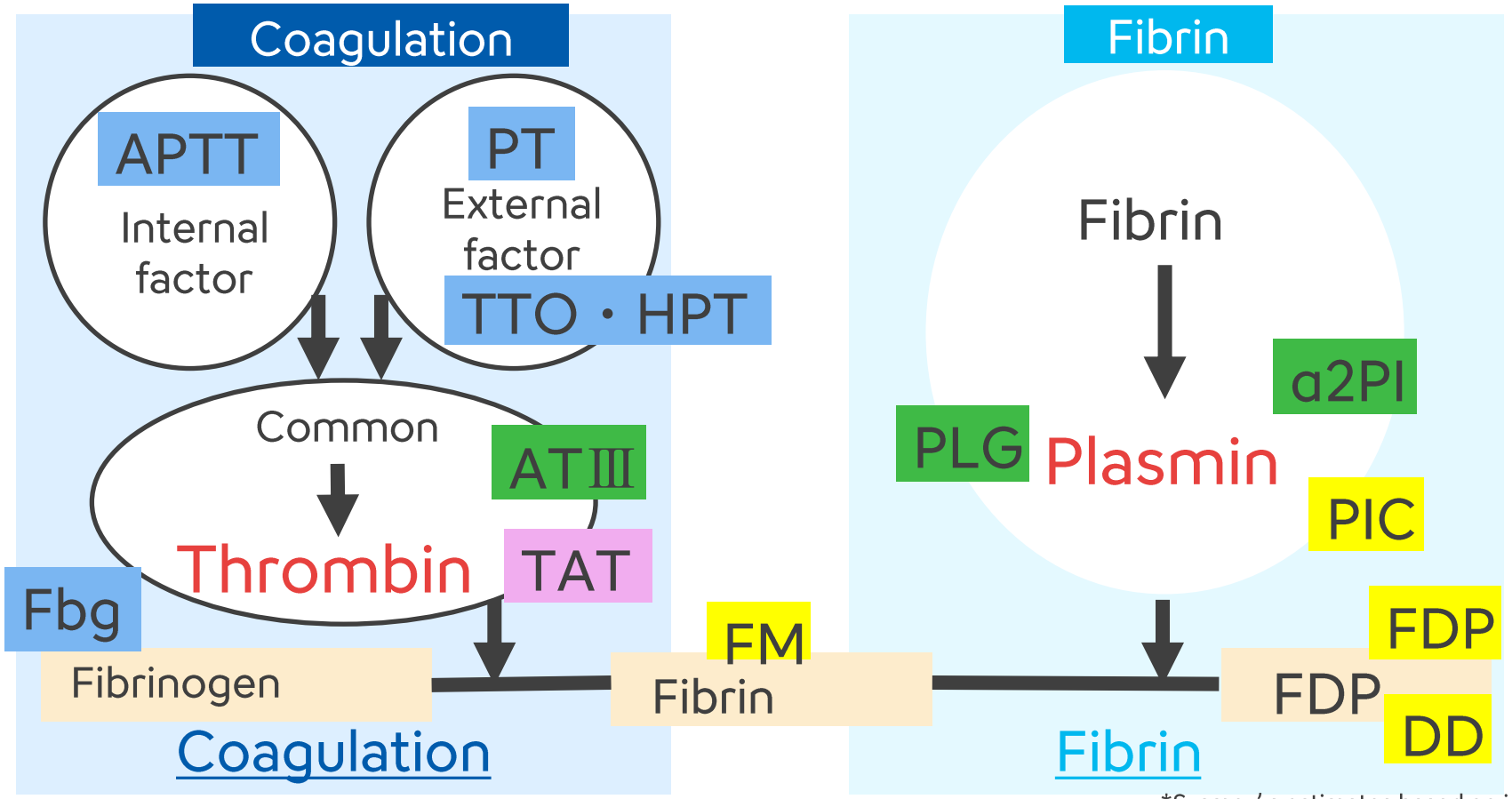
*Sysmex' s estimates based on information disclosed.

Coagulation Reaction*

Various coagulation factor reactions and actions work from bleeding → clot formation → clot dissolution

Coagulation: The system of action involving a series of molecules that allows blood in the body to clot in order to halt bleeding

Fibrin: The system of action that dissolves and breaks up clots that have hardened through the action of coagulation



*Sysmex' s estimates based on information disclosed.

What Hemostasis Testing Tells Us

Assists in diagnosing disease and understanding the ease of clotting, hemostasis, and dissolution

- Screening tests (PT, APTT, fibrinogen)
- Molecular markers (FDP, D-dimer, FM/SF, TAT, PIC, TM)

Understanding of blood concentrations and effects of anticoagulants, antiplatelet agents, and thrombolytic agents

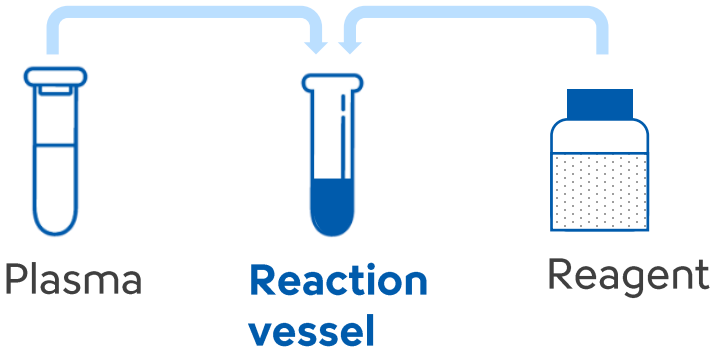
- Warfarin (PT), heparin (APTT), aspirin (platelet aggregation function test)
- Blood concentration measurement; antithrombin, FXIII, direct oral anticoagulants

Diagnosis and cause of disease (thrombosis/abnormal hemostasis)

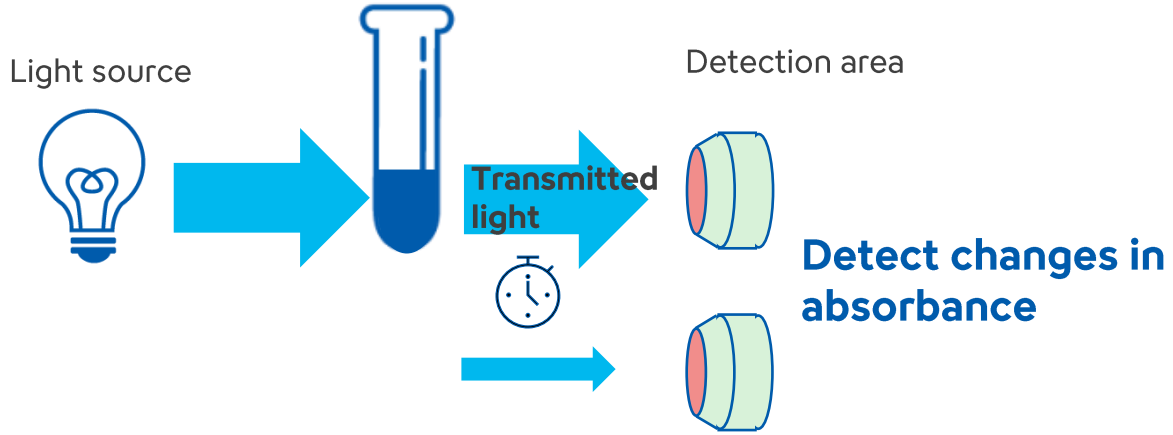
- Deficiency of coagulation regulation factors (antithrombin, protein C, protein S)
- Antiphospholipid antibody syndrome (APS), thrombotic thrombocytopenic purpura (TTP)
- Heparin-induced thrombocytopenia (HIT)
- Hemophilia A, B

Measurement Flow and Principles*

Step 1 Dispense specimens and reagents



Step 3 Transmitted light is irradiated and changes in absorbance are detected.



Step 2 React them (heat, agitate)

Heat and agitate the reaction vessel

Detect changes in absorbance utilizing each measurement principle

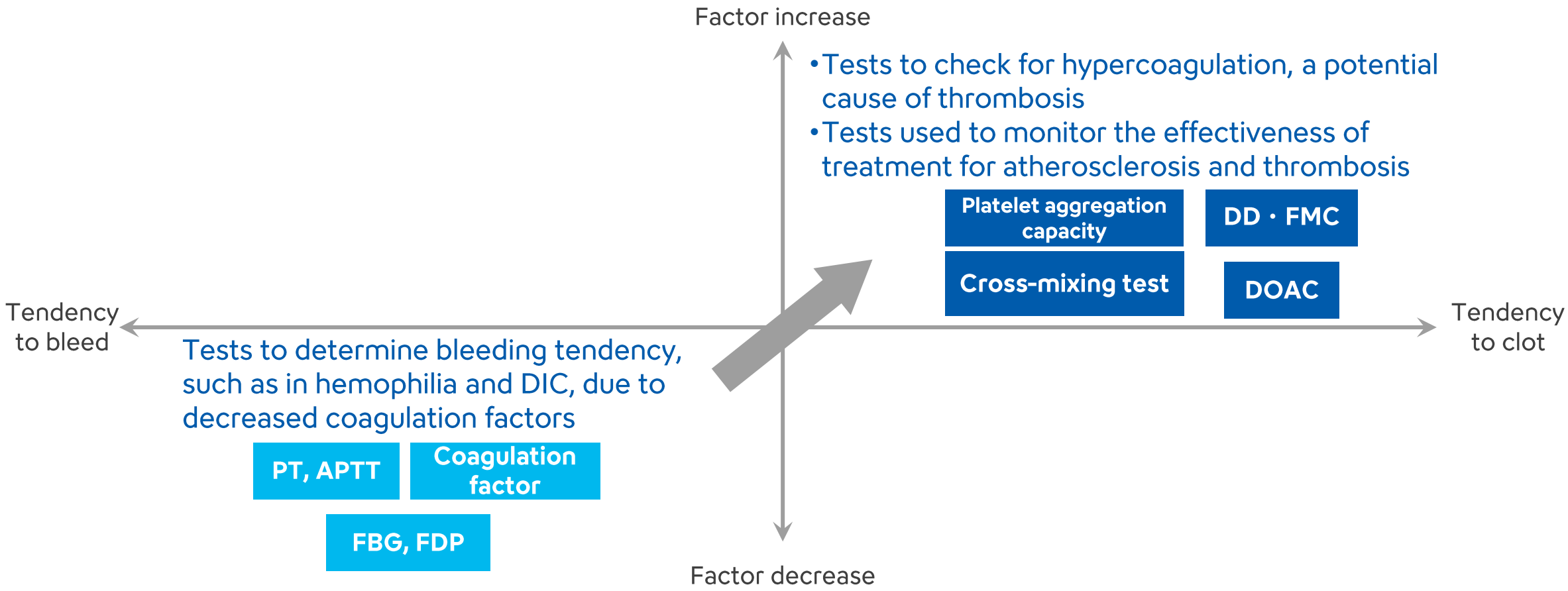
- Clotting principle: Detects the process of blood coagulation
- Chromogenic substrate principle: Detects the process by which chromogenic synthetic substrates develop color
- Immuno-Turbidimetry principle: Detects the process of increasing turbidity due to antigen-antibody reactions
- Aggregation: Detects the platelet aggregation process

*Sysmex' s estimates based on information disclosed.

Changes in Hemostasis Testing

More tests are being used* to measure thrombotic tendencies as the number of thrombotic diseases increases, compared to hemorrhagic diseases

*Sysmex' s estimates based on information disclosed.



Hemostasis testing and related diseases

Tests mainly related to hemorrhage	Tests related to hemorrhage and thrombosis		Tests mainly related to thrombosis	
α2-AP	PT	vWF:Rco	AT	FDP
	APPT	vWF Ag	PC	D-dimer
ADP	Fbg		PS	FM
Collagen			LA	
Epinephrine	Factor II	Factor IX		TAT
Arachidonic acid	Factor V	Factor X	Plg	PIC
Ristocetin	Factor VII	Factor XI	C1-INA	tPAI-C
	Factor VIII	Factor XII		TM

History of Hemostasis Instruments

1985 1990 1995 2000 2005 2010 2015 2020

High

function

Low

- Clotting/Chromogenic/Immuno-turbidimetry/Aggregometry
- Clotting/Chromogenic/Immuno-turbidimetry
- Clotting/Chromogenic
- Clotting

Fully automated analyzer



CA-3000 (1985) — CA-4000 (1986) — CA-5000 (1990) — CA-1000 (1992)

CA-1000 → CA-6000 (1995) → CA-7000 (1999) → CA-8000 (2010) → CS-5100 (2011) → CN-3000 /CN-6000 (2018) → CN-3500 /CN-6500 (2020)





CA-1000 → CA-1500 (1998) → CS-2000i /CS-2100i (2006) → CS-2400i /CS-2500i (2014)



CA-1500 → CS-1600 (2015)

CA-1000 → CA-540 /CA-530 / CA-520 /CA-510 (1997) → CA-560/ CA-550 (2002) → CA-660/ CA-650

CA-540 /CA-530 / CA-520 /CA-510 → CA-610/620 (2011)


Semi-automated analyzer

CA-100 (1984) → CA-50 (1999) → CA-101 /CA104 (2013)

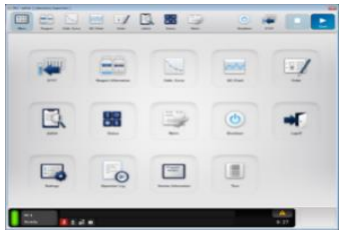


Compatibility with Hematology Products

An interface compatible with the operating screens on hematology systems helps improve operability and reduce uncertainty

Hemostasis

CS-Series　　CN-Series



Operating screen uses a compatible interface

Hematology

XR™-Series

XN™-Series

Glossary

Glossary

Anticoagulant agent	A drug that makes blood less likely to clot and prevents the formation of blood clots.
Antiplatelet agent	A drug used to prevent platelet thrombus owing to atherosclerosis or other causes.
CLEIA method	Refers to the chemiluminescent enzyme immunoassay method. Chemiluminescent substrates are bound to antigen-antibody reactants, which are degraded by enzyme catalysis. This method measures the amount of luminescence emitted at this time and quantifies the target substance.
CLSI	Guidelines of the U.S. Clinical and Laboratory Standard Institution, which are used as global standards.
Cross-mixing test	When the coagulation time (APTT, etc.) is prolonged, this test is performed to screen whether the prolonged coagulation time is due to a deficiency coagulation factor, coagulation factor inhibitor (which interferes with its function), or a lupus anticoagulant (an acquired antibody produced by the body that is a risk factor for thrombosis). This useful test should be performed as the first step in determining the cause of prolonged clotting time.
Cultured cells	Cells that are cultured artificially, *ex vivo*.
Deficiency factor	A factor that is deficient or missing from the factors used to clot the blood.
DIC	Short for “disseminated intravascular coagulation.” In this condition, some mechanism from an underlying disease causes Intravascular coagulation, consuming platelets and coagulation factors, which, combined with increased fibrinolysis, leads to severe bleeding tendency and organ damage.
DOAC	Short for “direct oral anticoagulant,” DOACs are easier to administer than warfarin, have the same or better stroke prevention effect, a similar or lower incidence of major bleeding, and a significant reduction in intracranial hemorrhage.
HIT	Short for “heparin-induced thrombocytopenia.” Measuring HIT antibodies facilitates the diagnosis of HIT and aids in pursuit of the causes of thrombocytopenia.
Multi-wave measurement	Measurement using the multi-wavelength transmitted light detection method. Highly reliable test results can be reported by wavelength switching, abnormal specimen detection and analysis functions.
PIC	A test parameter indicating that fibrinolysis is occurring *in vivo*. Values increase as a result of disseminated intravascular coagulation syndrome (DIC), subclinical DIC, thrombosis (especially venous thrombosis and pulmonary infarction with high thrombus volume), fibrinolytic therapy, etc.
Platelet aggregation function test	A test to examine the function of platelets, which play a central role in hemostasis. In addition to the diagnosis of congenital diseases such as thrombasthenia, it is expected that this test may be utilized in antiplatelet therapy, one of the treatment methods for thrombotic diseases of the arterial system.
TAT	A test parameter indicating that coagulation is occurring *in vivo*. This parameter is used to diagnose various thrombotic diseases, such as disseminated intravascular coagulation syndrome (DIC), and to determine the efficacy of treatment.
Thrombolytic agent	Drug that dissolves the blood clots that cause myocardial infarction, cerebral infarction, etc.

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