

# Outline and Strategies of Toray Life Science Businesses

Toray Industries, Inc.

Executive Vice President & Representative Director

Hiroaki Kobayashi

Managing Director, General Manager of Pharmaceuticals and  
Medical Products Division

Kouzo Nagai

Director, General Manager of R&D Division

Koichi Abe



◆ Summary

Executive Vice President & Representative Director

Hiroaki Kobayashi

◆ Outline and Strategies of Pharmaceuticals and Medical Products Businesses

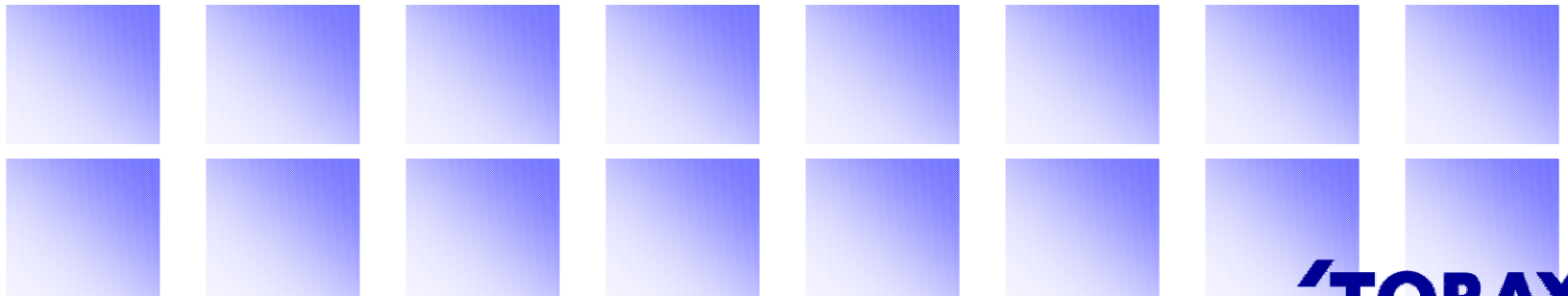
Managing Director, General Manager of  
Pharmaceuticals and Medical Products Division

Kouzo Nagai





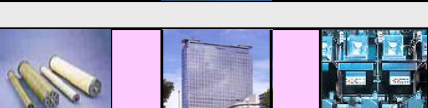

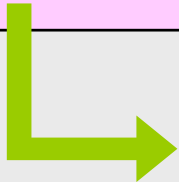
◆ R&D Strategies of Life Science Businesses

Director, General Manager of R&D Division

Koichi Abe



# Positioning of Life Science Businesses in Toray

<Business Segment>	<Major Products>	FY Mar/05 Net Sales	FY Mar/05 Operating Income
Fibers & Textiles		¥513.4 bill. (40%)	¥20.9 bill. (26%)
Plastics & Chemicals		¥300.4 bill. (23%)	¥15.7 bill. (19%)
IT-related Products		¥219.1 bill. (17%)	¥28.3 bill. (35%)
Carbon Fiber Composite Materials		¥44.7 bill. (3%)	¥5.6 bill. (7%)
Environment & Engineering		¥148.7 bill. (11%)	¥4.3 bill. (5%)
<b>Life Science</b> Other Businesses		¥72.3 bill. (6%)	¥6.5 bill. (8%)
		¥1,298.6 bill.	¥81.1 bill.
 <b>Life Science: Pharmaceuticals and Medical Products</b>		¥44.4 bill. (3%)	¥2.9 bill. (4%)

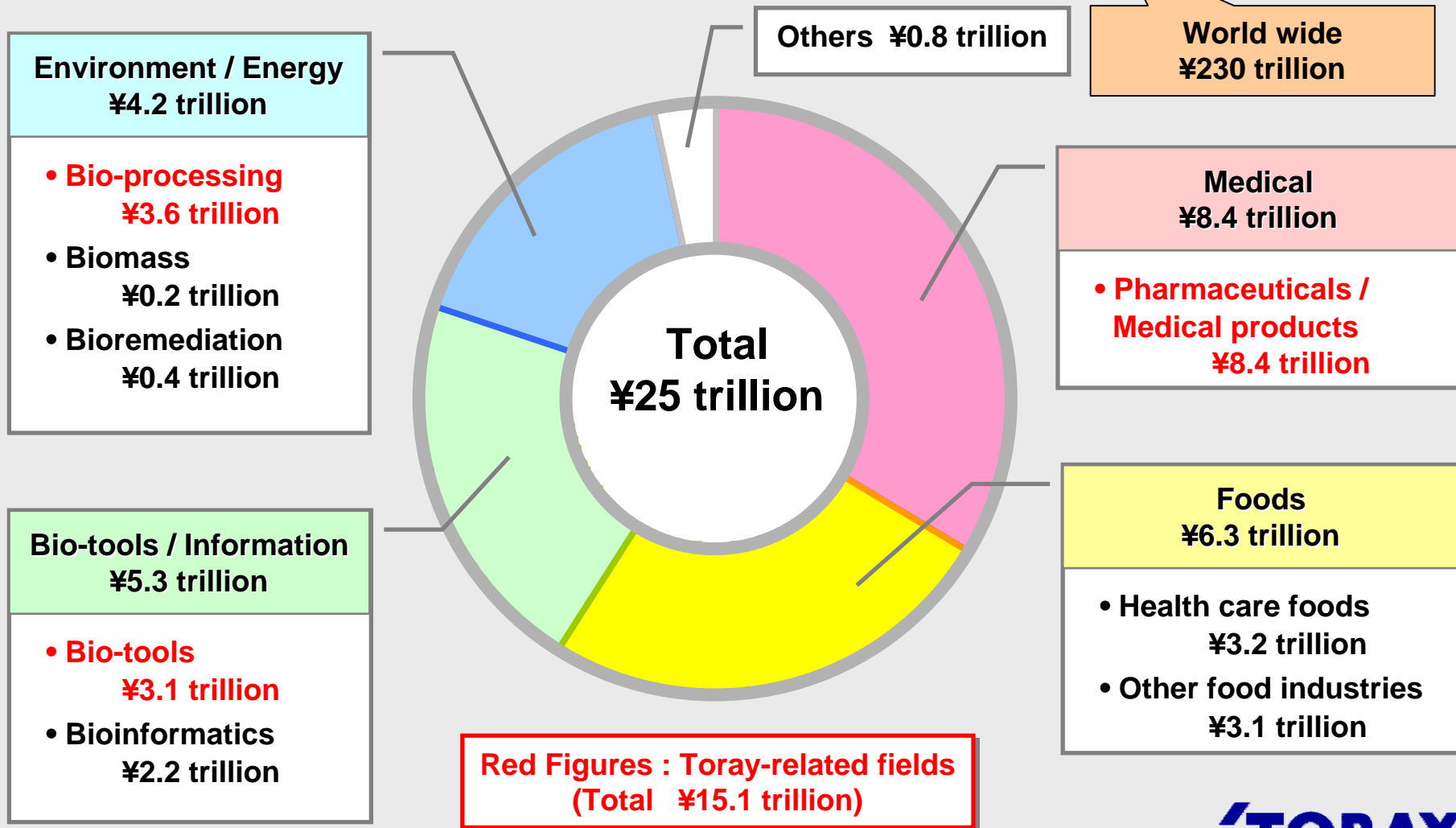
Strategically Expanding Businesses

★ Strategically Expanding Businesses (**Life Science**, IT-related Products, Environment, Safety, and Amenity)  
→ Candidates for next core businesses

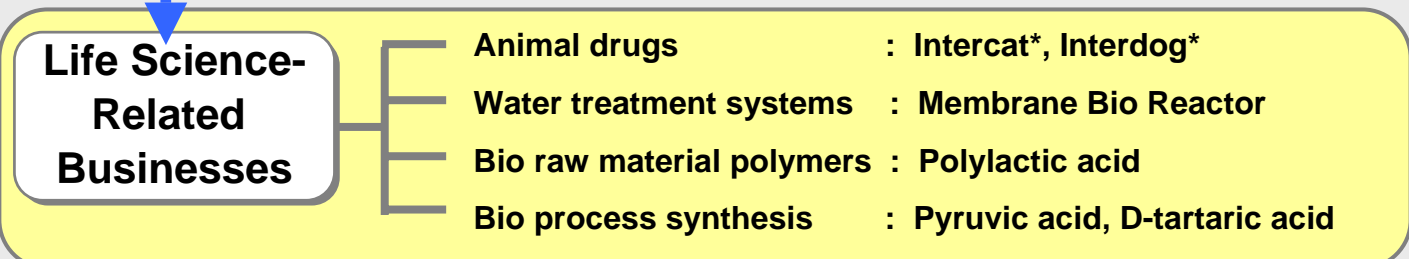
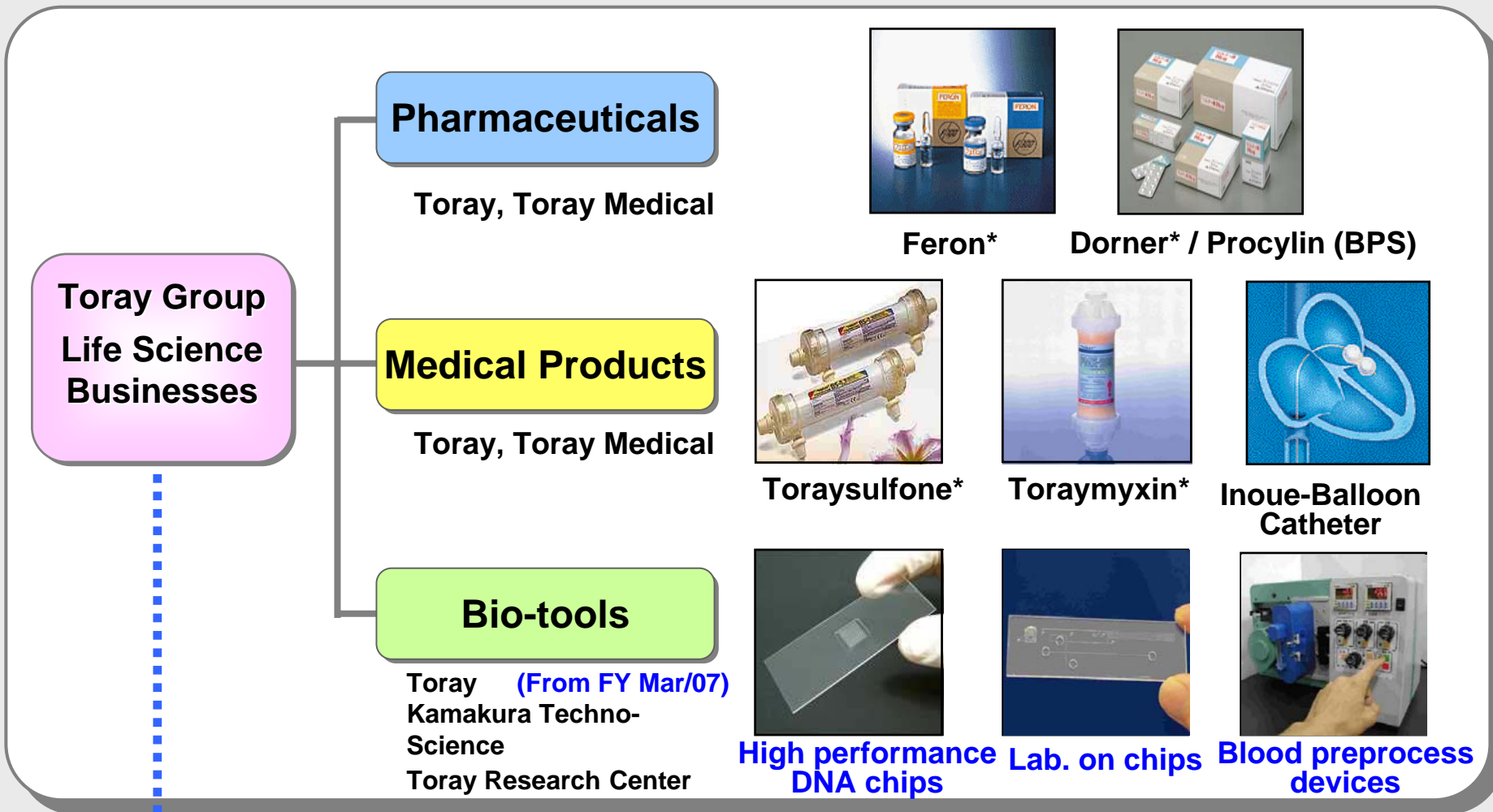
# Market Scale Forecast of Bio-related Industries Expected in 2010

(from 2002 Cabinet Office BT Strategy Outline)

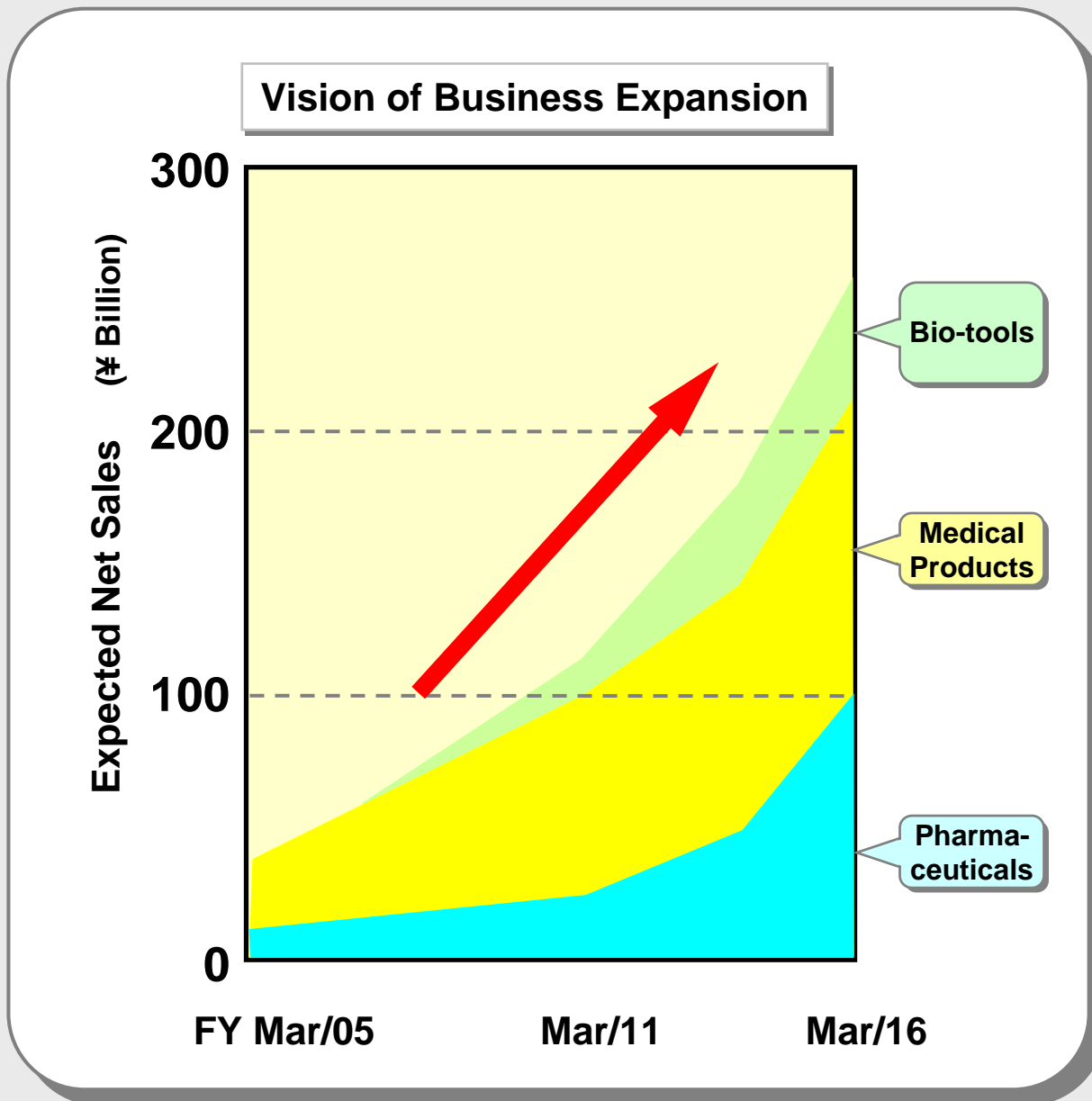
Bio-related industries in Japan : ¥1.3 trillion (2001) → ¥25 trillion (2010)



# Organization of Toray Life Science Businesses



# Expansion of Life Science Businesses



# Characteristics and Issues of Toray Life Science Businesses

## Life Science Businesses

### Pharmaceuticals



#### ◆ R&D for Drug Discovery

- New drugs for unmet medical needs
- New indications of Feron\* and Dorner\*

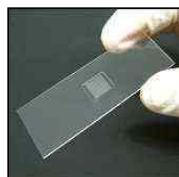
### Medical Products



#### ◆ R&D based on Extracorporeal Circulation

- Artificial kidney of the next generation under development
- Pipelines for novel medical devices

### Bio-tools



#### ◆ Integration of Biotechnology & Nanotechnology ⇒ Generation of Innovative Bio-tools

- Research tools & diagnosis businesses (business model by alliance)
- Contents business (joint R&D with medical institutes)

★ R&D Expenditures/Rate to Net Sales : over 20%  
(about 25% of total R&D Expenditures)

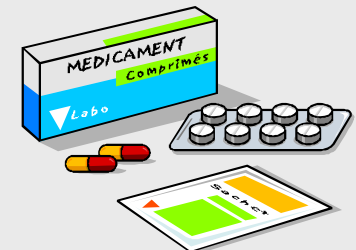
# Pipeline of Pharmaceuticals & Medical Products

## [ Pipeline of Pharmaceuticals ]

## [ Pipeline of Medical products ]

R&D Themes	R&D Stage
Antipruritic Agent (TRK-820) — Uremic Pruritis —	Phase III
Antipruritic Agent (TRK-820) — Itching of Atopic Dermatitis —	Phase I
Drug for Urinary Frequency (TRK-130)	Phase I
Analgesic for moderate to severe pains (TRK-091)	Phase II
Feron*(new indication) — Liver Cirrhosis —	Submitted
Feron*(new indication) — Combination Therapy with Ribavirin for Chronic Hepatitis C —	Phase III
Dorner*(slow released) — pulmonary hypertension —	Phase II/III
Dorner*(slow released) — chronic renal failure —	Phase II

R&D Themes	R&D Stage
Toraylite*(Dried product)	Preparing for Sale
Anti-thrombogenic PMMA membrane	Development
Oxidized LDL removal membrane	Development
Leukocyte removal column	Development
Catheter for atrial fibrillation	Development



P I :Phase I Clinical Study  
P II :Phase II Clinical Study  
P III:Phase III Clinical Study

**TORAY**



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◆ Outline and Strategies of Pharmaceuticals and Medical Products Businesses

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◆ R&D Strategies of Life Science Businesses

Director, General Manager of R&D Division

Koichi Abe

# History of Toray Development of Pharmaceuticals and Medical Products

Year	Highlights
1947 - 1953	Production and sales of penicillin
1970	Start in-house research for pharmaceuticals and medical products
1977	Launched Filtryzer* (kidney dialysis)
1978	Launched PGF2a (injectable solution, labor induction)
1983	Launched PGE2 (oral stabilization agent, labor induction)
1985	Launched Interferon-β (Feron*)
1986	Launched Anthron* (antithrombogenic catheter)
1988	Launched Inoue-Balloon Catheter (mitral stenosis) Established Pharmaceuticals & Medical Products Division
1992	Launched PGI <sub>2</sub> derivative BPS ( Dorner* / Procylin) New indication of Feron* to active hepatitis C
1993	Launched Toraymyxin* (blood purification device for treating severe septicemia)
1994	Launched Toraysulfone* (kidney dialysis)
1997	New indication of Feron* to inactive hepatitis C
1999	New indication of Dorner* / Procylin to pulmonary hypertension
2002	Filed MAA for TRK-820 (antipruritic drug) in Sweden

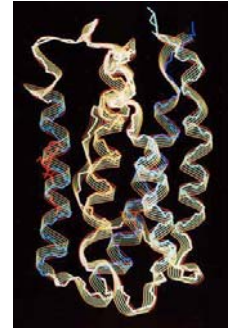
Green-letter : Pharmaceuticals  
Blue-letter : Medical Products

# Toray Products (Pharmaceuticals)

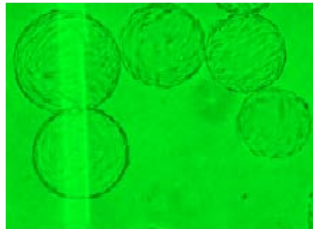
## Natural Human Interferon- $\beta$ : Feron\*

Establishment of large scale  
production technology  
(Beads culture)

The world first interferon product



World first structure elucidation of  
mouse interferon- $\beta$   
(Tokyo Univ. & Toray)



Fibroblast cells on the beads



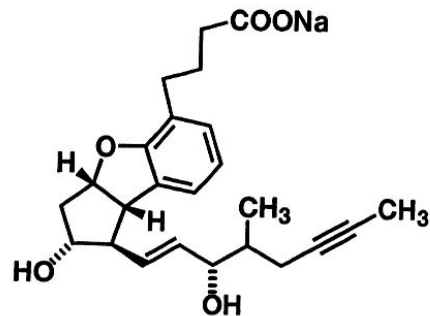
Launched in 1985 (Toray, Daiichi)

Indication: Hepatitis B & C  
Melanoma/Brain tumors

## Stable PGI<sub>2</sub> derivative (beraprost sodium): Dorner\*/Procylin

The world's first orally  
active PGI<sub>2</sub> derivative

Improvement in  
- efficacy  
- pharmacokinetics



Chemical structure of  
Dorner\*

Launched in 1992 (Toray/Astellas, Kaken)

Indications : Chronic Arterial Occlusion (ulcers, pain, chill)  
Pulmonary Hypertension

# Toray Products (Medical Products 1)

## Filtryzer\* • Toraysulfone\*

1977 Filtryzer\* Launched

Hemodializer made of PMMA hollow fibers with excellent absorption characteristics

1994 Toraysulfone\* Launched

Hemodializer of polysulfone hollow fiber with high performance



## Toraymyxin\*

1993 Launched

Only one blood purification device on which polymyxin B immobilized

- Severe septicemia
- Integration of in-house technology(Chemical-Fiber-Plastic-Bio)

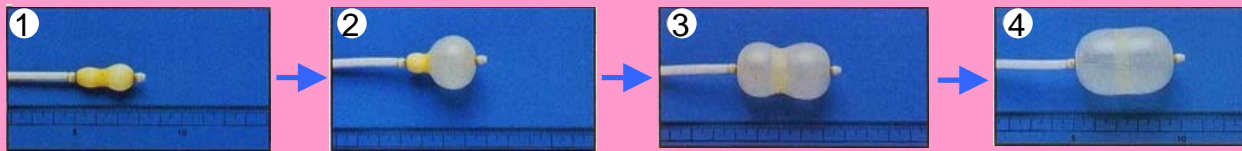


# Toray Products (Medical Products 2)

## Inoue- balloon Catheter

1988 Launched (Marketing in 80 countries world wide)

First catheter for treatment of mitral valve



Inflation of balloon

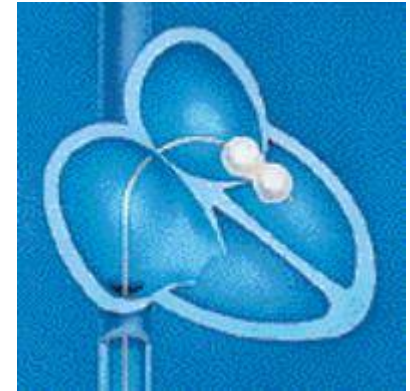


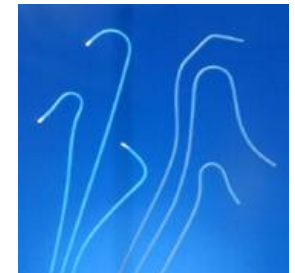
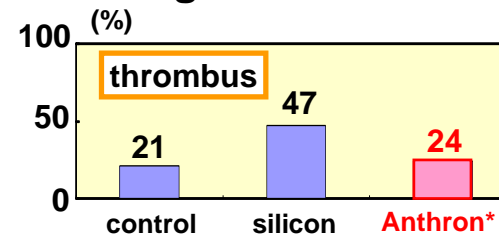
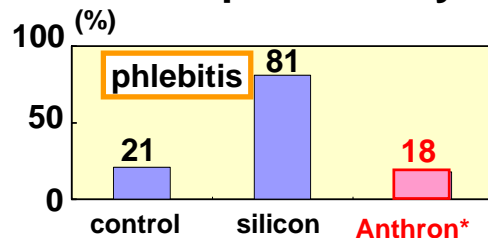
Image of treatment

## Anthron\*

1986 Launched \* Easy sliding in blood vessels and antithrombotic

Catheter coated with Anthron\*(heparinized hydrophilic material)

Prevention of complication by thrombus at diagnosis or treatment

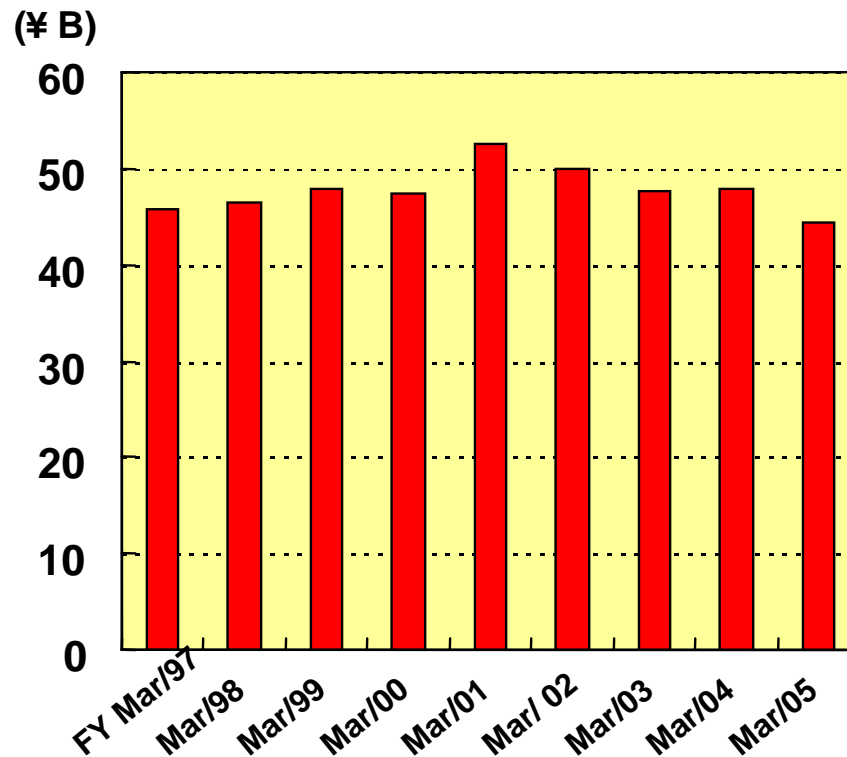


Appearance

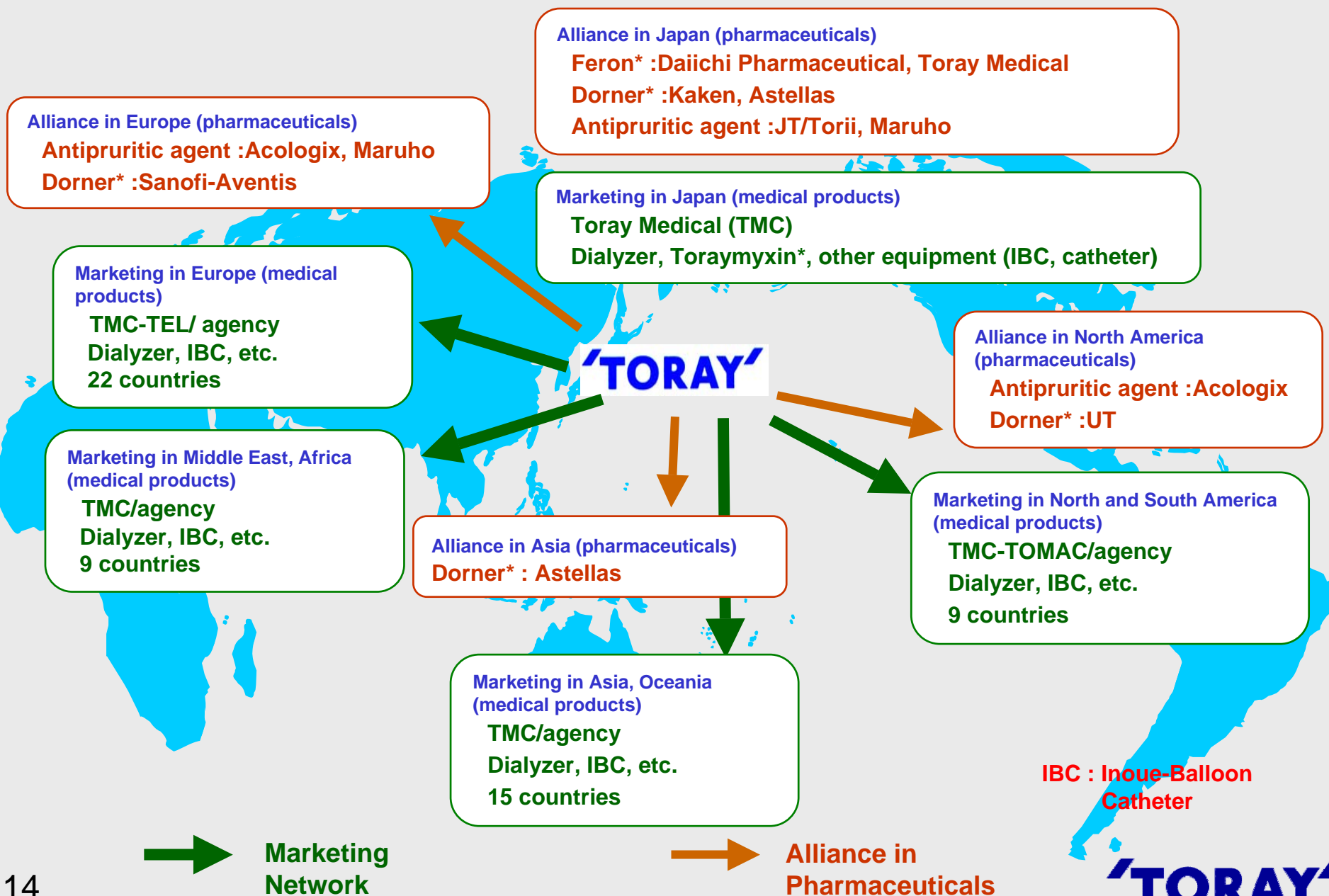
Outer  $\varnothing$  :ca.2mm  
Inner  $\varnothing$  :ca.1mm

# Net Sales of Pharmaceuticals and Medical Products Businesses

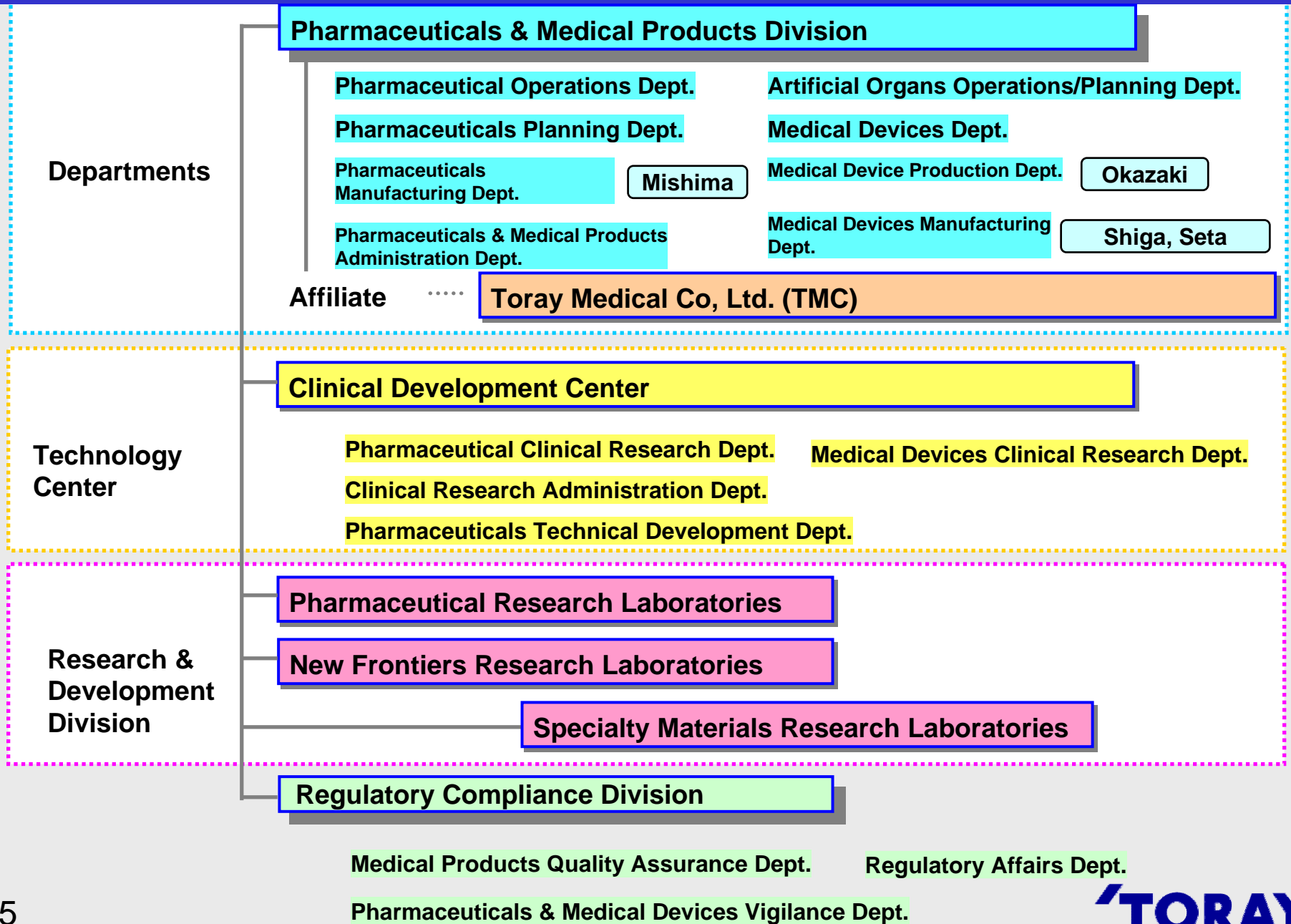
## Consolidated Net Sales



# Strategic Alliance in Pharmaceuticals Businesses and Marketing Network of Medical Products Businesses



# Organization of Pharmaceuticals & Medical Products





# Characteristics and Basic Objectives of Pharmaceuticals Businesses

## Characteristics of Pharmaceuticals Businesses

- ◆ **Centralize resources in research oriented drug discovery and line extension of existing products**  
Characteristics : Development of bio-active substances (interferon, prostaglandin, opioid, etc.)  
Creation of innovative drugs
- ◆ **Clinical development : Mainly Toray in Japan, through alliance outside Japan**
- ◆ **Marketing : Consign marketing to appropriate business partner (new business model)**  
Partial sales of Feron\* at Toray Medical (TMC)
- ◆ **Licensing to be one of business pillar**

## Basic Objectives

**R&D for Drug Discovery : Focusing on innovative drug discovery in areas of unmet medical need**

**Line extension of existing products**

- ◆ **Strengthen profit-structure through sales expansion of existing product line and corporate-structure reinforcement**
- ◆ **Marketing will be done mainly through alliance for the near-term**
- ◆ **M & A is in vision as a constructive alternative**

# Antipruritic Drug (TRK-820)

New (antipruritic) drug for treatment of pruritus uncontrolled by current medication

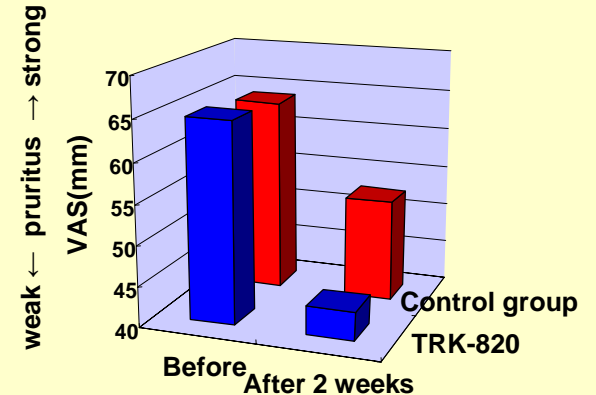
**Mechanism of Action:** opioid kappa agonist (Basic Patent)

**Characteristics:**

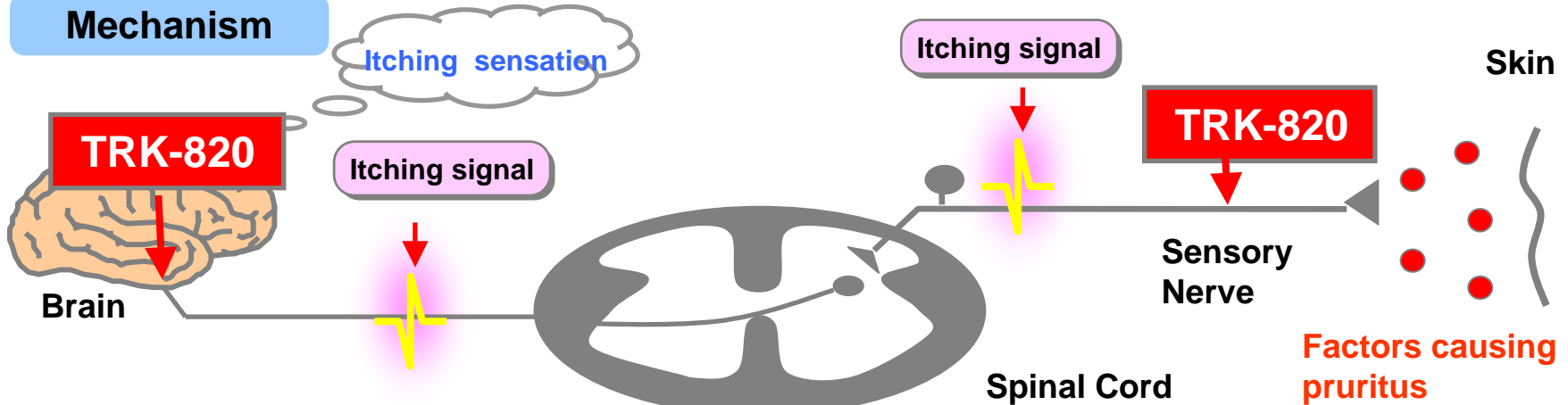
- (1) Inhibition of pruritus in humans (5 $\mu$  g/body) <right figure>
- (2) No potential to induce dependency

**Indication:**

Intractable pruritus in hemodialysis patients, pruritus associated with liver injuries and skin diseases (atopy, pruritus senilis, etc.)



## Mechanism



# Drug for Urinary Frequency (TRK-130)

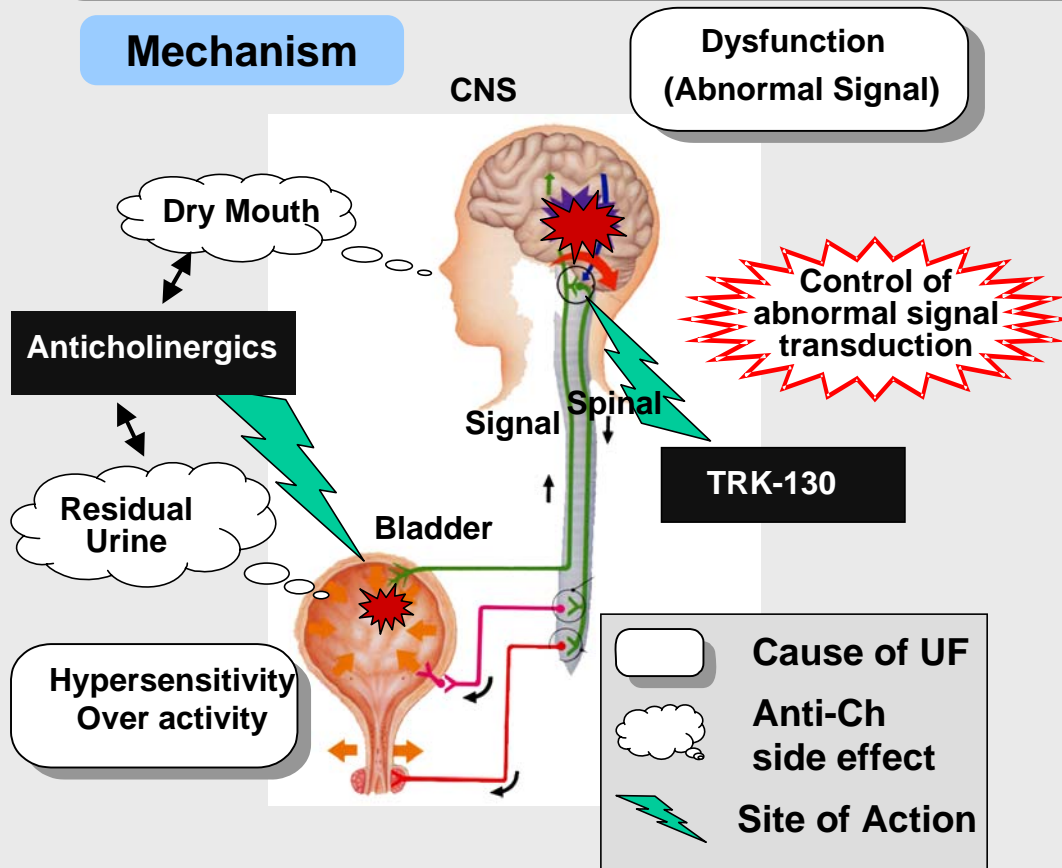
Non Anticholinergic Mechanism : Control of Neuronal Signal Transduction

**Mechanism:** Inhibit the abnormal signal transduction on overactive bladder (**Basic Patent**)

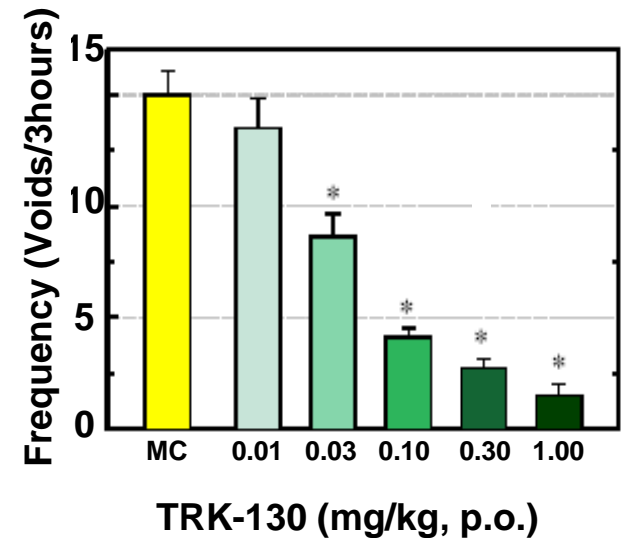
**Characteristics:** Free from Anticholinergic side effects (e.g. dry mouth, residual urine)

**Indication:** Overactive Bladder (Urinary Frequency (UF), Urinary Incontinence (UI))

## Mechanism



## Anti-UF effect



# Analgesic for Moderate to Severe Pains (TRK-091)

Sustained-release tablets containing Tramadol Hydrochloride as an active ingredient  
(once-daily oral dose)

## Analgesic Mechanism:

Weak opioid-receptor agonist having norepinephrin- and serotonin-reuptake inhibitory activity

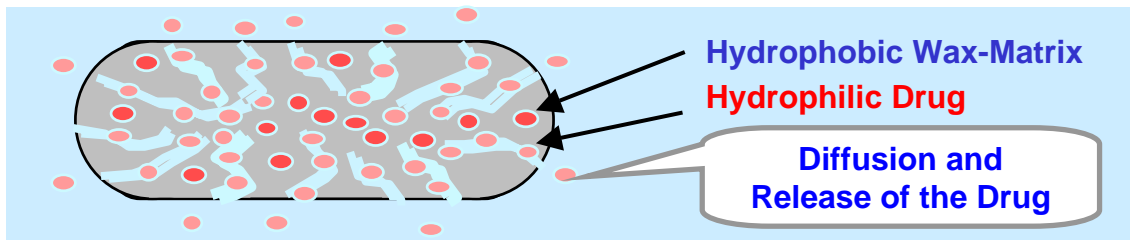
## Characteristics:

- (1) Analgesic activity considered intermediate between nonsteroidal anti-inflammatory drugs (NSAIDs) and potent analgesics (morphine etc.)
- (2) Reduction of the side effects observed in NSAIDs (gastrointestinal ulcer/hemorrhage, hepatopathy, nephropathy, etc.)

## Indication:

Chronic pain (upper or lower back pain, osteoarthritis), cancer pain, post-operative pain

Release mechanism of Tramadol Hydrochloride in the matrix-type sustained-release tablets



Licensed from  
Mundi Pharma

# Feron\* / Dorner\* slow released

## Feron\* : Liver cirrhosis / Combination therapy with Ribavirin for chronic hepatitis C

**Characteristics :** Antiviral and antifibrotic effects of Feron\* delay the progress of liver cirrhosis and hepatocellular carcinoma in Chronic Hepatitis C patients

**Background :** Chronic Hepatitis C patients

World wide : 170 million patients (about 4 million people are newly infected with Hepatitis C virus each year in the world)

Japan : 2 million patients (WHO report 1999)

Many of Hepatitis C patients progress to cirrhosis and the cancer of liver

If progress to cirrhosis and the cancer of liver can be delayed, **the meaning in the medical treatment is high**

## Dorner\* slow released : Chronic renal failure / Pulmonary hypertension

**Characteristics :** Prevention of progression for chronic renal failure preceding ESRD for which existent drugs are insufficient

1. The concept was proved in pilot clinical studies in human and cat

(1) increase of renal blood flow, (2) protection of blood endothelial cell,  
(3) prevention of inflammatory cytokine production

2. Sustained release formulation

### Chronic renal failure :

- Existent drugs are insufficient
- 30,000 CRF patients enter ESRD a year in Japan
- Total number of ESRD patients : 250,000 (Japan)

### Effect of Dorner\* on renal blood flow in rats

Normal



Renal failure



Dorner\* treated



# Basic Objectives of Medical Products

## Characteristics of Medical Devices

- ◆ R&D by in-house polymer technology and establishment of business in 3 areas
  - Dialysis : PMMA membrane, polysulfone membrane, machine
  - ER • ICU : Toraymyxin\*
  - Catheters : Inoue-balloon catheter, PU-Celsite, Anti-thrombotic catheter, Protect, etc.
- ◆ Integration of manufacturing & marketing (Toray • TMC)
- ◆ Ensuring business base through global expansion by TMC

## Basic Objectives

- ◆ To create new products by frontier material technology
  - Business development by innovative devices for extracorporeal circulation and catheter for treatment of atrial fibrillation
- ◆ Secure profit by efficient manufacturing and sales

# Development Pipeline of Medical Products

## Dialyzer: Toraylite\*

Plan for launch in 2006

- Dried Toraysulfone\*
- Characteristics: light, easy priming
- Patient No.(EU/US 500,000:Japan 250,000)



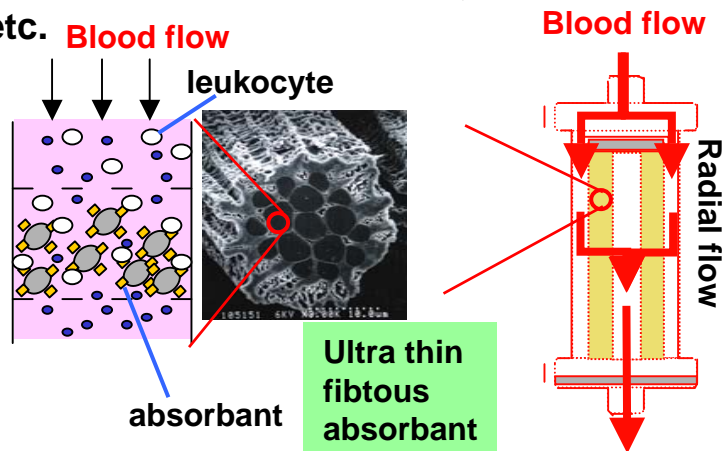
## EU • ICU

### Leukocyte removal column

Plan for launch in 2008

Removal of activated leukocyte

Indication: Crohn's disease, Ulcerative colitis etc.



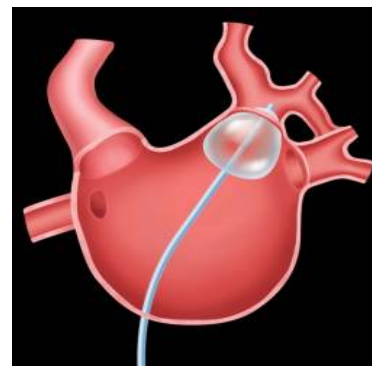
## Catheter

### Balloon for atrial fibrillation

Plan for launch in 2008

First balloon type ablation catheter in the world

Circular ablation: reduction of operation time



Balloon by X ray

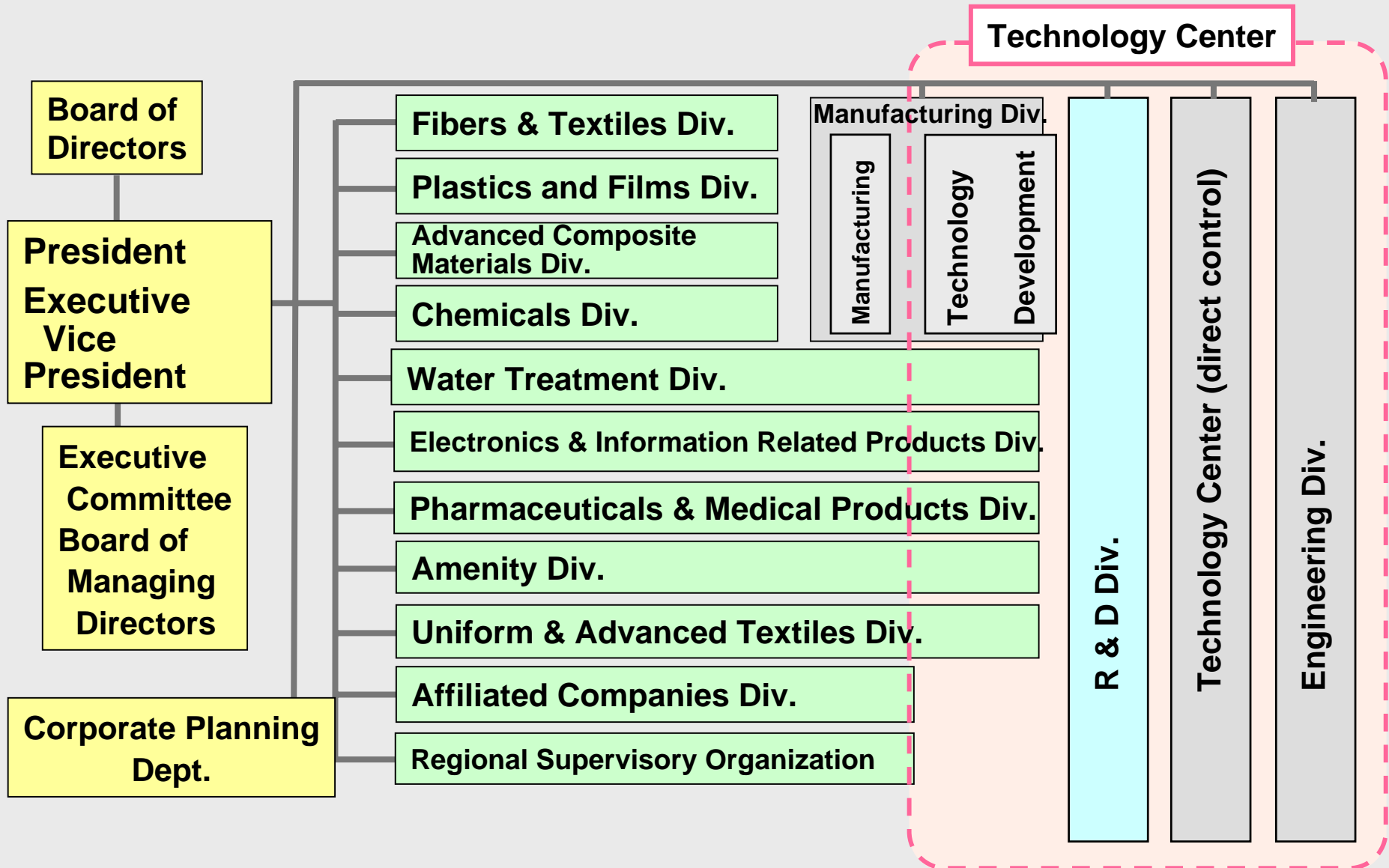
# Summary : Expansion of Pharmaceuticals and Medical Products Businesses

- **Promote development of existing products to ensure business expansion in or around 2010**
- **Promote R & D of new pharmaceuticals and medical products for further business development in or around 2015**
- **Strengthen profit-structure through sales expansion of existing product line and corporate-structure reinforcement**



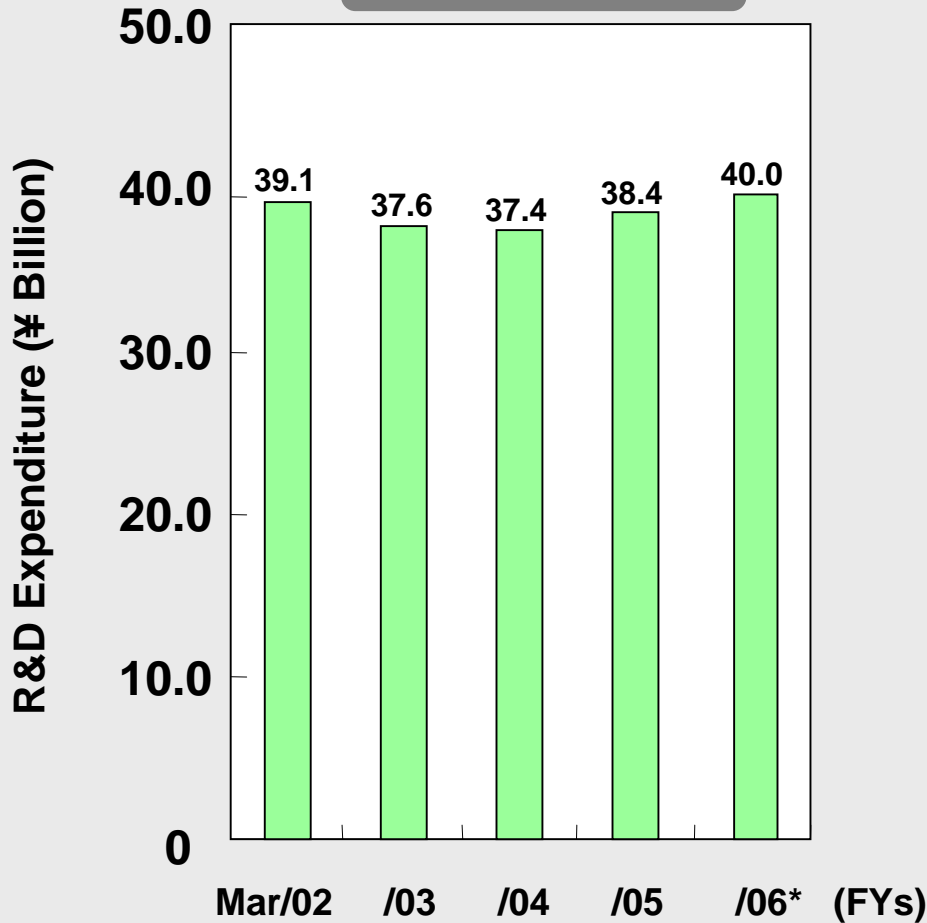
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# Organization of Toray Industries, Inc.

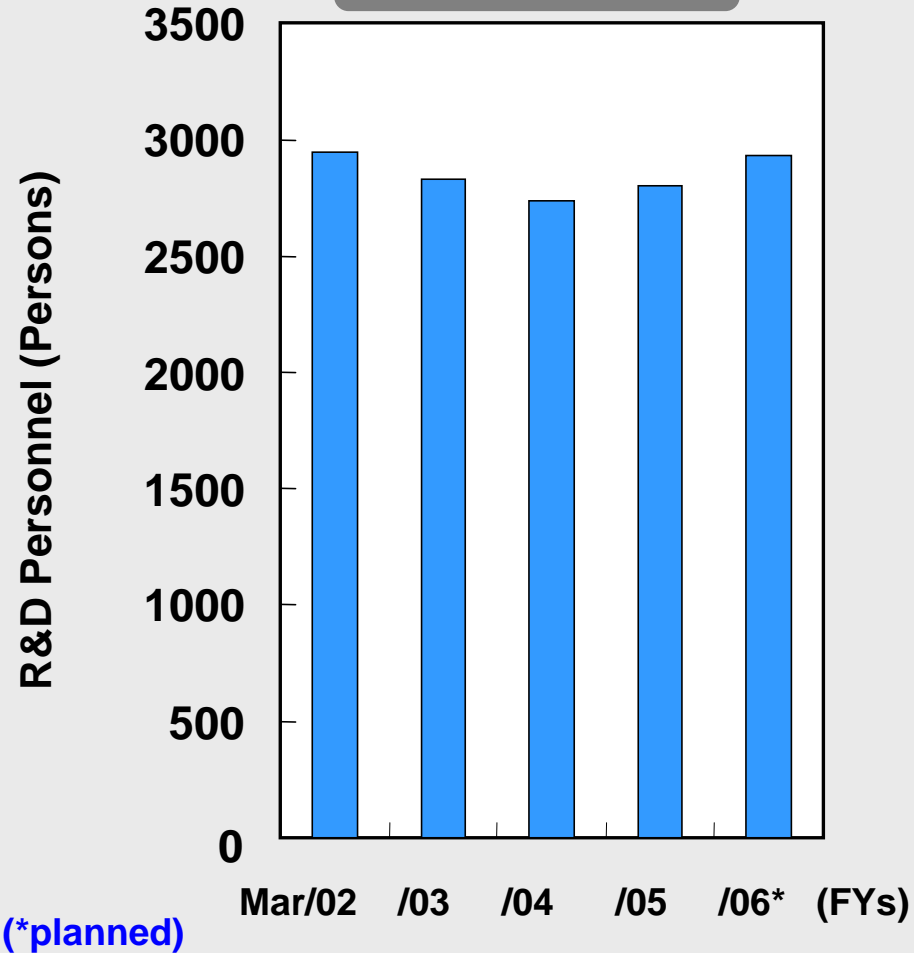


# R&D Expenditure and Personnel

Approx. ¥ 40 billion

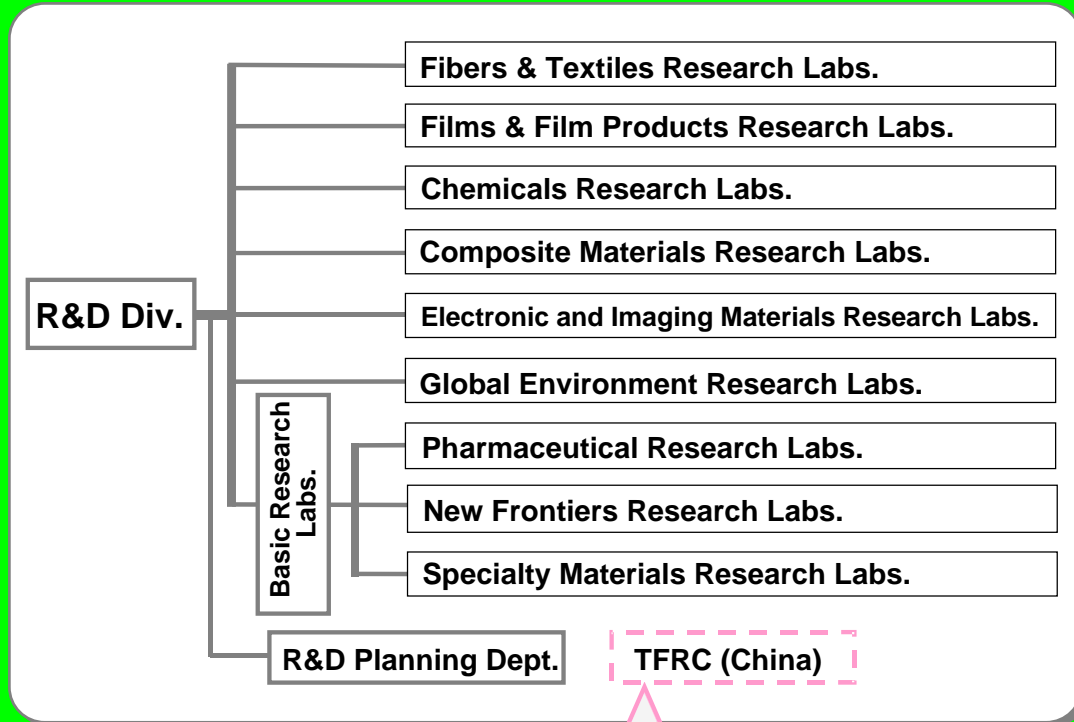


Approx. 2,900



**R&D Expenditures / Net Sales (excluding affiliated trading companies) ≙ 4.5%**  
**(life sciences ≙ over 20%)**

# Organization of R & D Division



## Shiga Plant

- Films & Film Products Research Labs.
- Electronic & Imaging Materials Research Labs.
- Global Environment Research Labs.
- [Basic Research Labs.] Specialty Materials Research Labs. / Medical System Research Lab.
- R&D Planning Dept.

## Tokyo Head Office

- R&D Planning Dept.
- Corporate Planning Dept.

## Kamakura Plant

- [Basic Research Labs.] Pharmaceuticals & Medical Products Research Labs.
- New Frontiers Research Labs.

## Mishima Plant

- Fibers & Textiles Research Labs.

## Ehime Plant

- Composite Materials Research Labs.

## Nagoya Plant

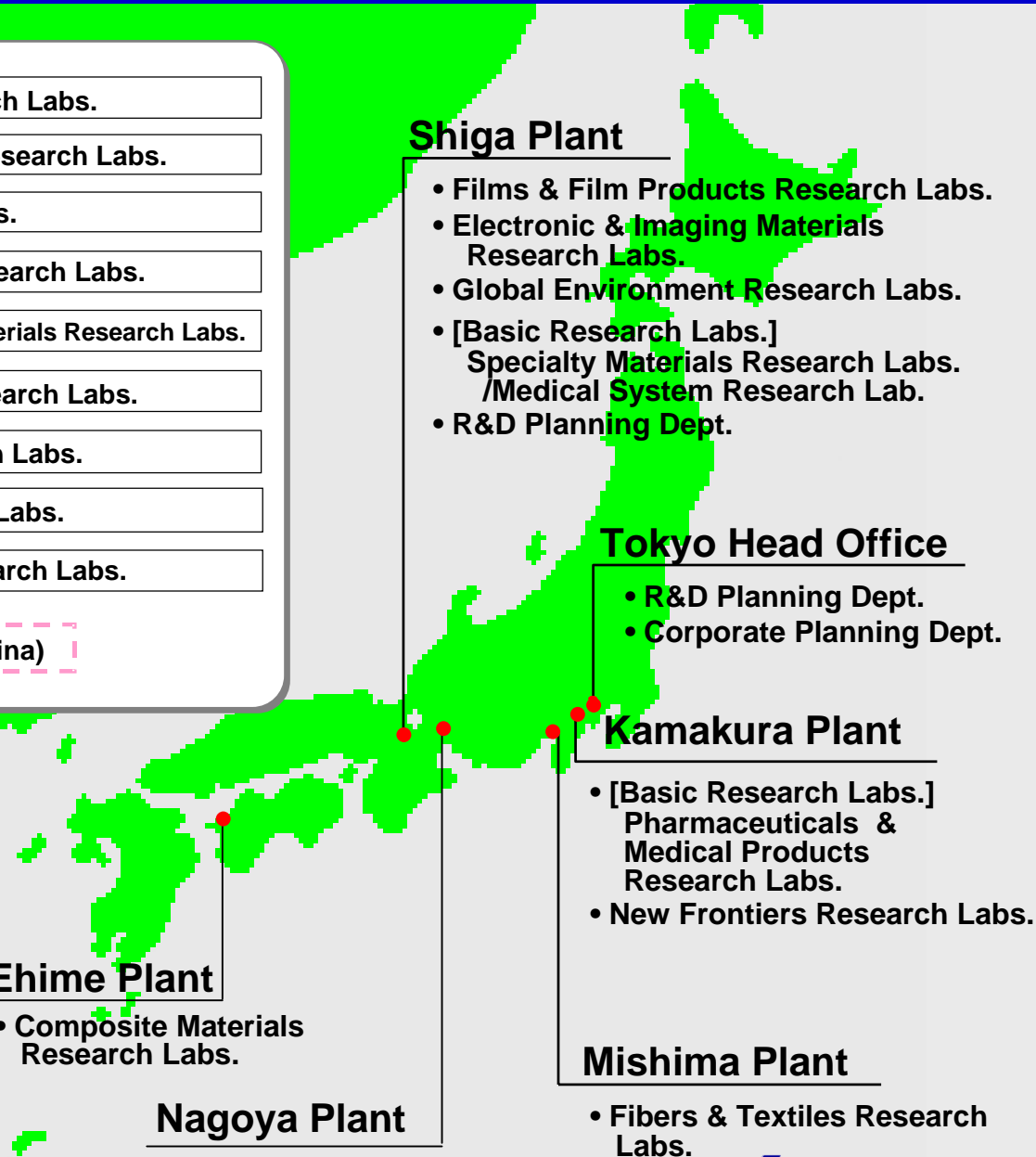
- Chemicals Research Labs.

## Nantong

- Polymers and fiber R&D Dept.
- Water Treatment Research Labs.

## Shanghai

- Polymer Materials Research Labs.
- Water Treatment Research Labs.

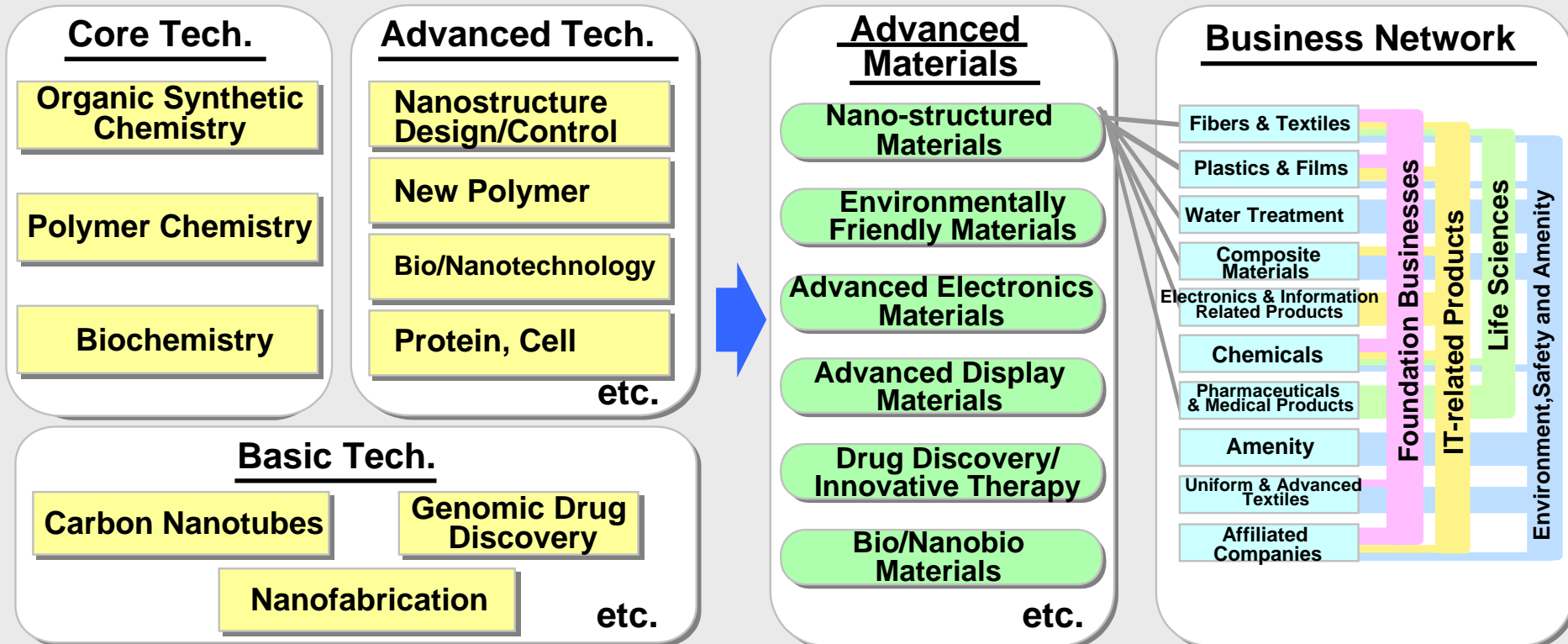
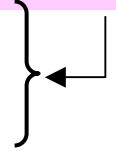


# Features of Toray's R&D

## Advantages

1. Culture and history that create innovative technologies
2. Various kinds of specialists groups in many fields
3. Unified R&D structure
4. Leading company in academia/industry / government collaboration
5. Advanced analytical capabilities : TRC

Technology Integration

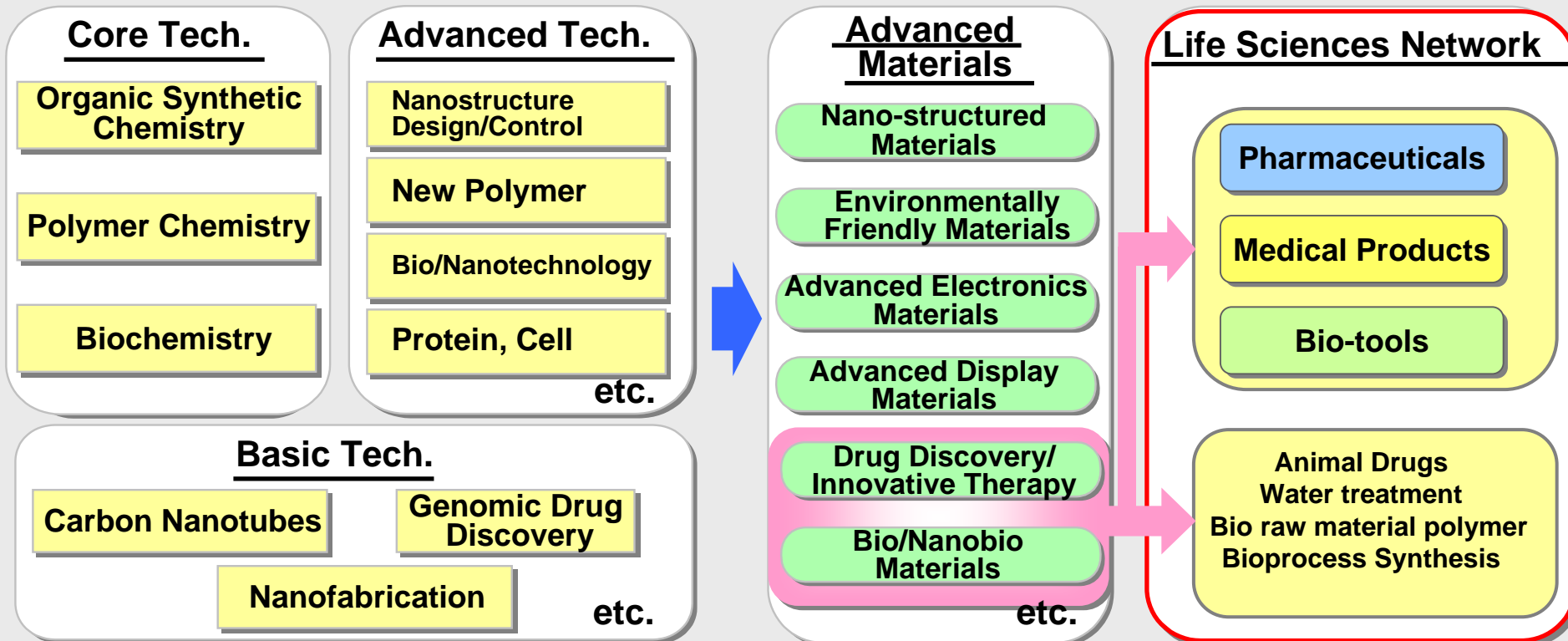
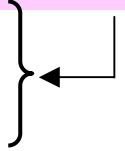


# Features of Toray's R&D

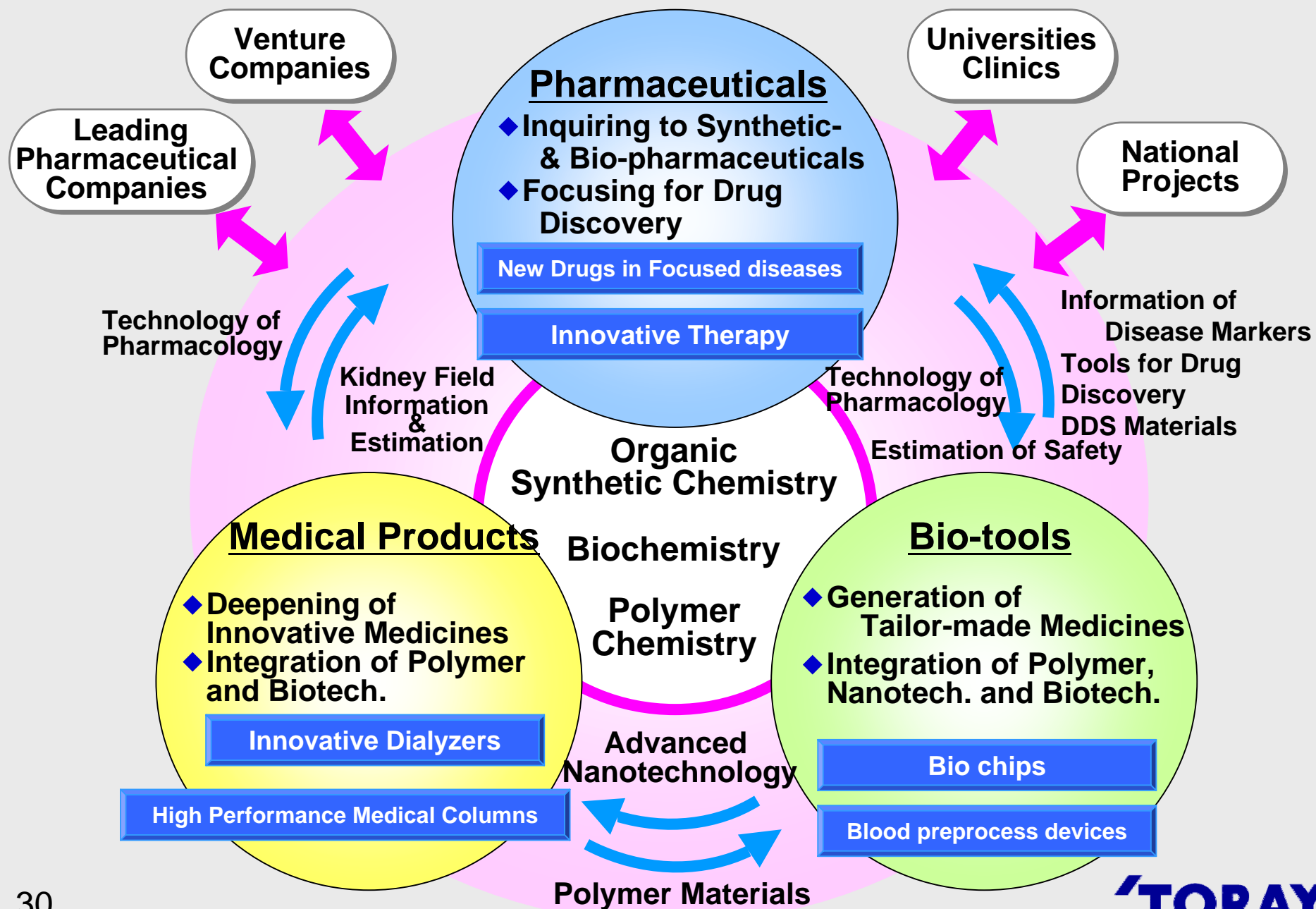
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5. Advanced analytical capabilities : TRC

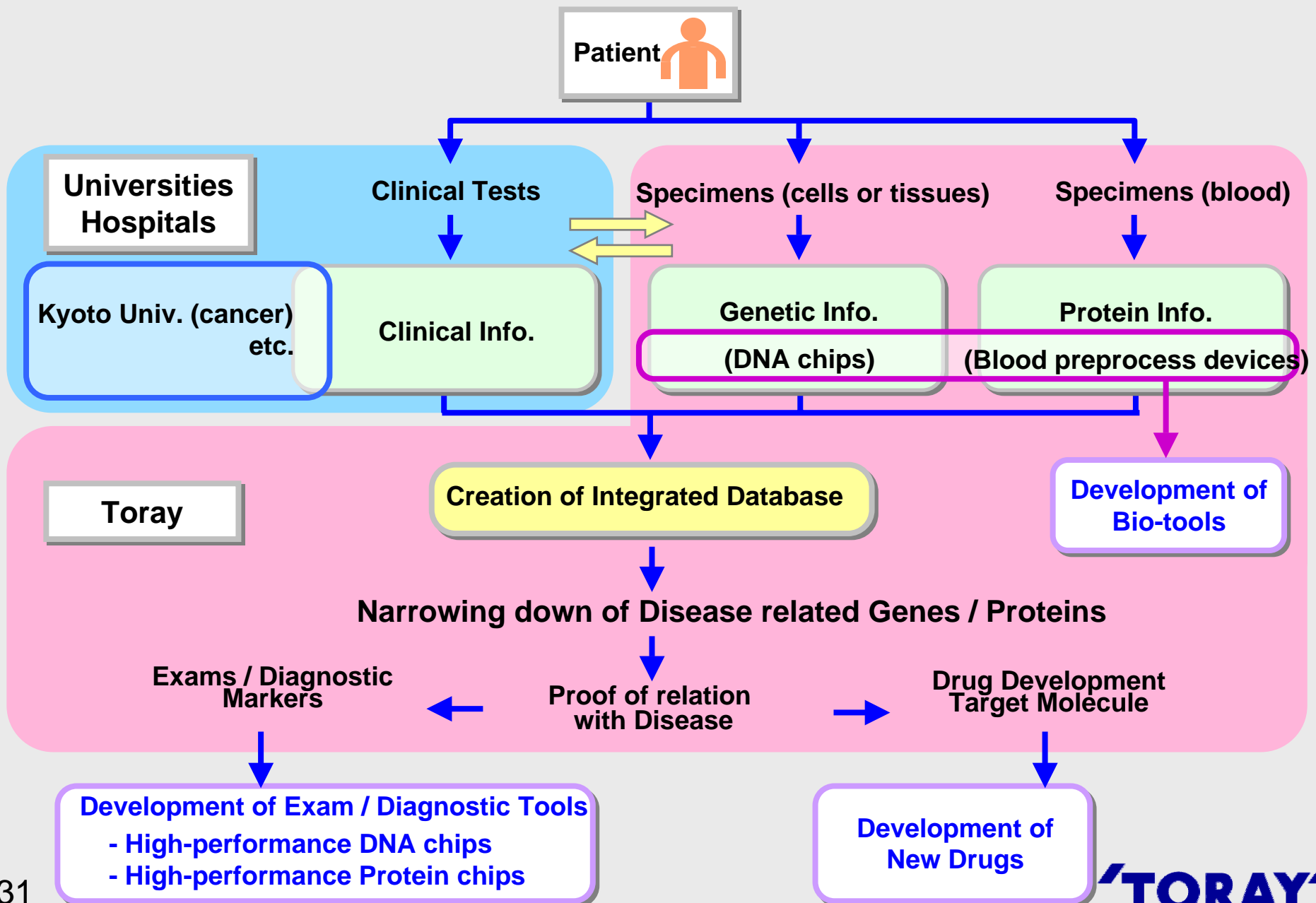
Technology Integration



# R&D Policy in Life Science Fields



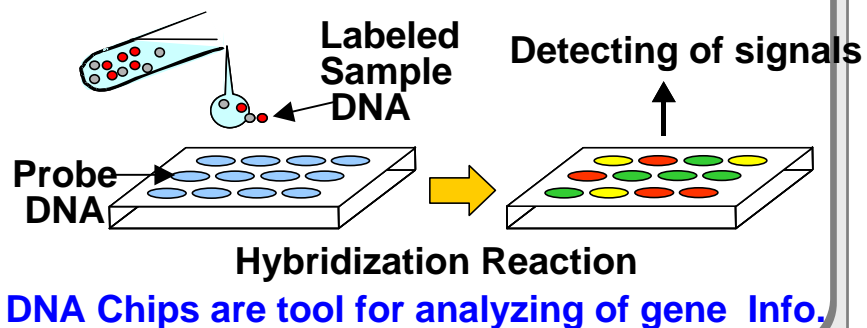
# R&D Strategy of Bio-tools





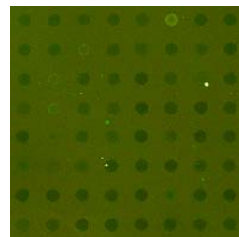
# High Performance DNA Chips

## What is DNA Chip?



## Assignments of Conventional DNA Chip

(Glass substrate / Plane structure)

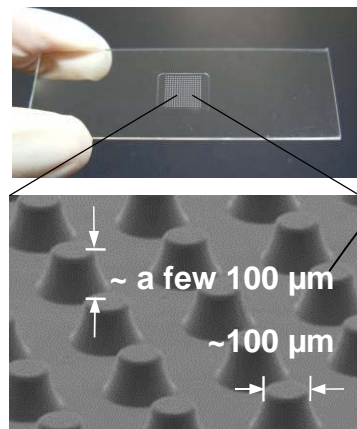


Sample amount of biopsy: 1mg

- Signal < Noise
- Irregular for detecting
  - : Low signal strength and stability

**Low sensitivity**  
**Low quantitiveness**  
**Low reproducibility**

## High Performance DNA Chips

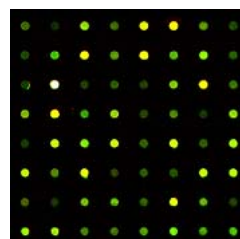


Original Resin

Probe DNA

Unique structure by micro fabrication

- High Signal
- Low noise



Sample amount of biopsy: 1mg

High sensitivity  
(Approx. 100-fold higher than conventional type)

High quantitiveness

High reproducibility

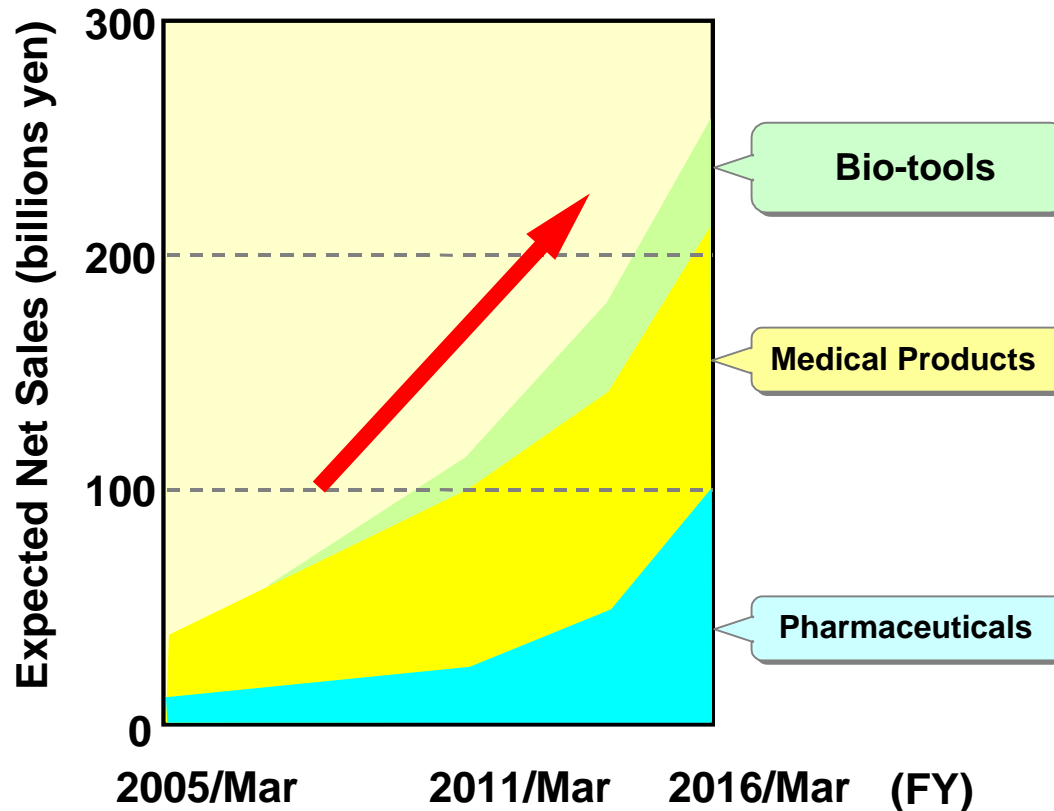
Short reaction time  
(Approx. one-tenth of conventional type)

★ Development of DNA chip with unique structure by micro fabrication of original resin.

★ Realization of high sensitivity, high quantitiveness, high reproducibility and high speed detecting.

# Summary : Strategies for Business Expansion

## Framework of Business Expansion



- ★ Continuous introduction of new products strengthened by Toray's advanced materials and technologies
- ★ Accelerating speed of R&D by effective alliance formation

Descriptions of predicted business results, projections and business plans contained in this material are based on assumptions and forecasts regarding the future business environment, made at the present time.

The material in this presentation is not a guarantee of the Company's future business performance.