Industries' Activities related to Medical Device Regulation and Expectation on Bilateral Cooperation

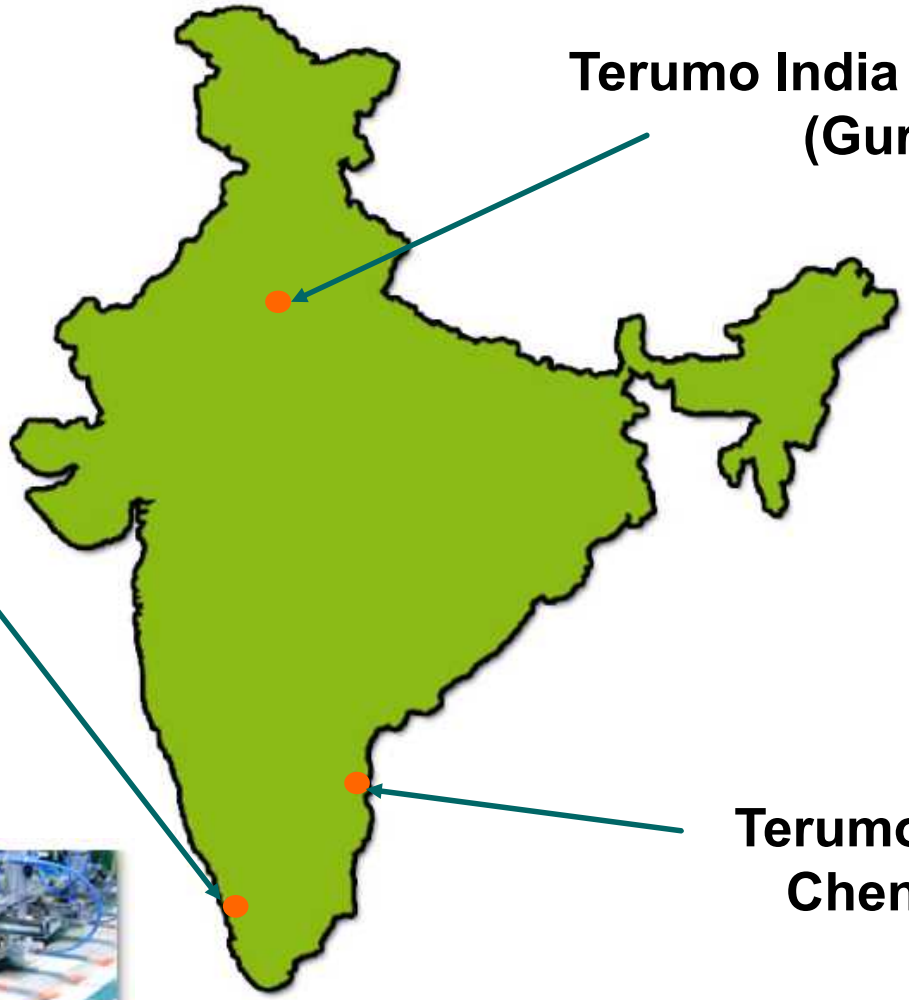
Kuniko Shoji

Director and Senior Executive Officer
Chief Clinical and Regulatory Affairs Officer (CRAO)
Terumo Corporation

19 May, 2016

Our Network in India

Terumo Penpol (Trivandrum)



Terumo India Private Limited (Gurgaon)

Terumo Corporation Chennai Branch

Japanese medical device regulations

Characteristics of Medical device

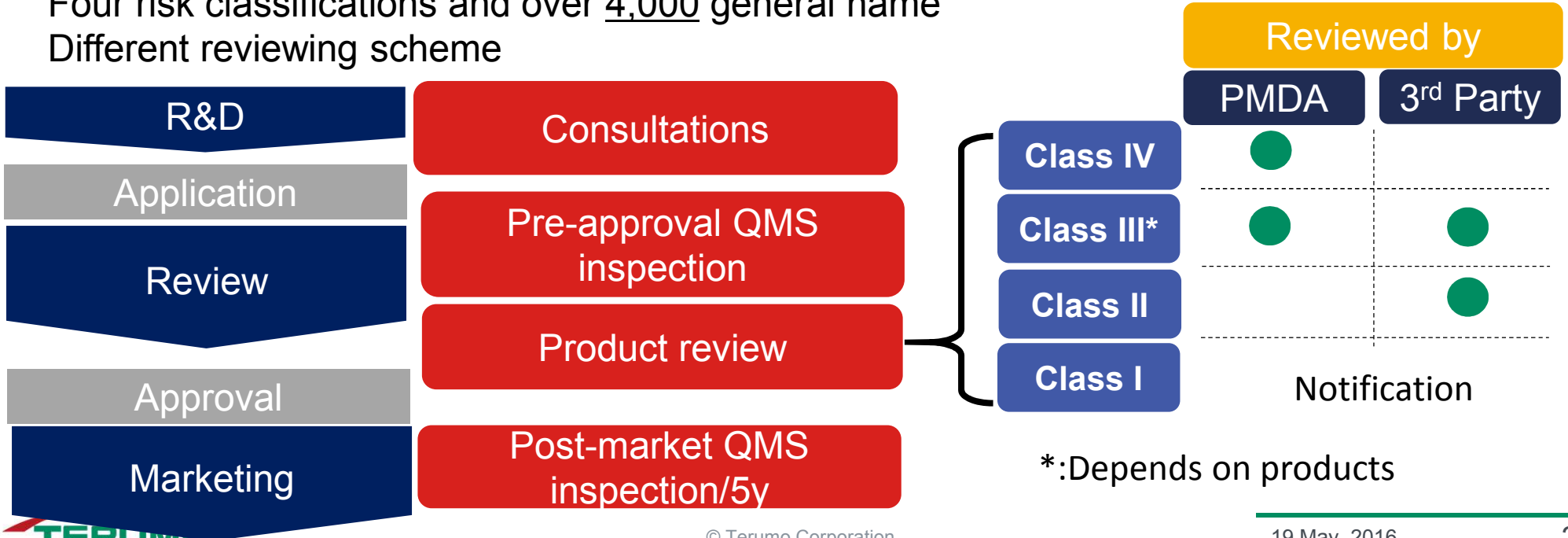
- **Should be regulated because it is used to treat patients**
- **Wide variety of products (ex. From needle to MRI)**

→

- **GCP, GLP are required as same as pharmaceuticals**
- **Classifications/Risk based review are necessary**

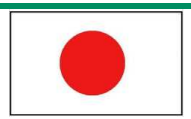
Japanese comprehensive reviewing system

Four risk classifications and over 4,000 general name
Different reviewing scheme



*:Depends on products

Key features and comparison



Risk Classification

•Four Classifications and 4,000 general name Class IV devices are reviewed by PMDA, certified third party is utilized for lower class devices

•14 categories of equipments are defined to be regulated as medical device

Renewal

•Every 5 years, post market QMS inspection is applied to each manufacturing site (Each product design is not reviewed in the process)

•Every 3 years, Plant master file and Device master file are reviewed

Target reviewing time

•Publish target reviewing time for each submission category and the results

•Publish target reviewing time for medical device

Other features in Japanese submission scheme

•PMDA offers consultations before submission
•PMDA publishes approval standard for specific devices
•PMDA has been strengthening resource of reviewers

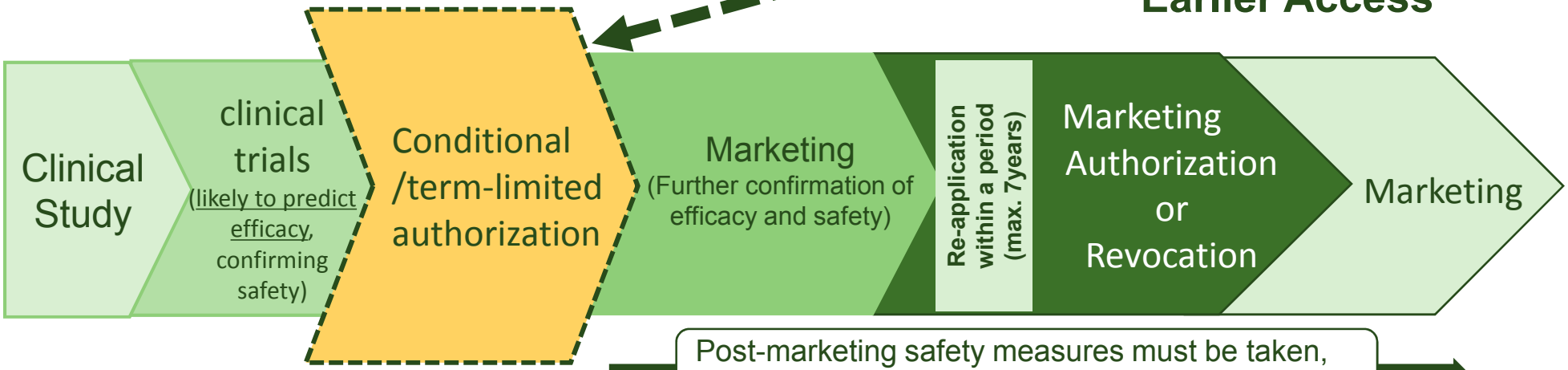
Expedited approval system under PMD Act
- Regenerative Medical Products-

<Drawback of traditional PAL approval system>
Long-term data collection and evaluation in clinical trials, due to the characteristics of cellular/tissue-based products, such as non-uniform quality reflecting individual heterogeneity of autologous donor patients

<Traditional approval process>

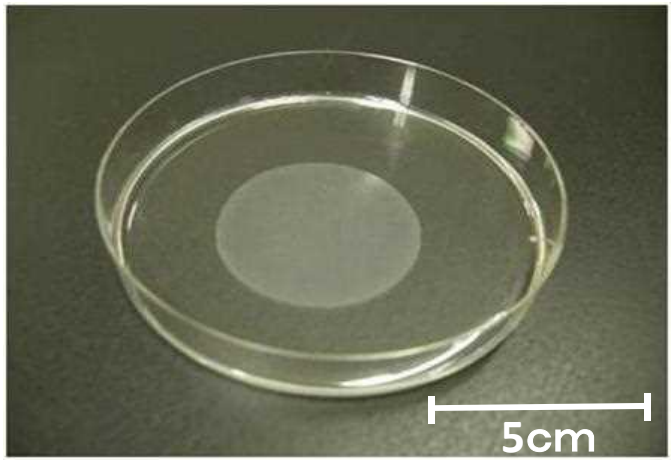
<New Pathway for Regenerative Medical Products>

***Leading to Earlier Access**



Post-marketing safety measures must be taken, including prior informed consent of risk to patients

HeartSheet®



[HeartSheet®]

- Cultured autologous skeletal myoblast cell sheets
- Transplanted in the patient's heart under thoracotomy

[Efficacy of HeartSheet®]

- Improve patient's cardiac function, symptoms and physical function.

[Target Patient]

- Severe Chronic Heart Failure (Ischemic Heart Disease)
- NYHA: Class III, IV
- LVEF<=35%

Collaboration between government and industry

- Annual public-private dialogue for the Creation of Innovative Pharmaceuticals and Medical Devices
- Regular meetings between MHLW and Medical device industry
- Activity of joint working group(PMDA/the industry) for the revision of the Pharmaceutical Affairs Law

Terumo Medical Pranex

Comprehensive training facility to develop and disseminate new healthcare technologies

Medical Pranex = Medical Practice at Annex of R&D

Cooperation to PMDA Medical Devices Training Seminar





Date: 18 February, 2016

Participants: 29 regulatory authorities from 10 countries including India.

Thank you for your attention!

Confidential

OMRON

Way forward to regulate Nebulizer

19th May, 2016

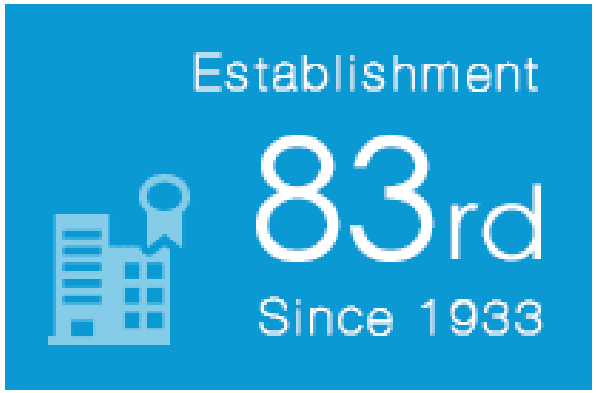
OMRON HEALTHCARE INDIA PVT. LTD.
MASUDA, HISAO

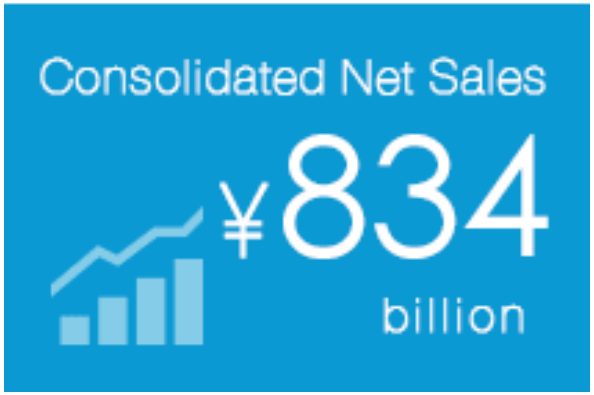
All for Healthcare

Who we are…

"To improve lives and contribute to a better society“

<OMRON Philosophy>





(*INR 520 billion)

Company Philosophy of Omron Healthcare

To help realize healthy and comfortable lives
for Indian people

OMRON'S Blood Pressure Monitor

No.1 trusted bland in the world.
Most preferred choice because of accuracy and quality.

Everyday check,
Accurate measurement

OMRON'S Nebulizer

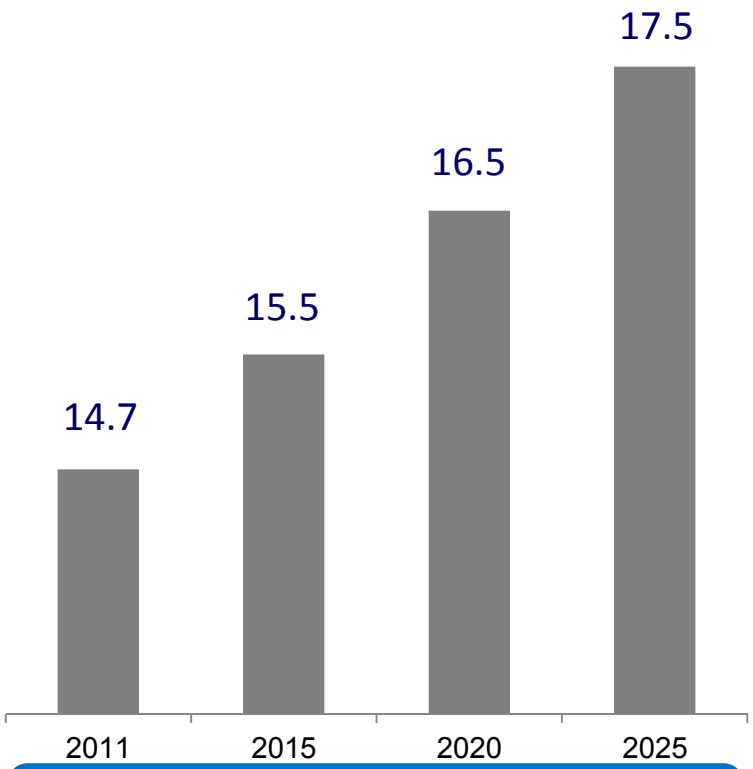
No.1 share* bland in the world.
Most preferred choice because of quality and efficiency.

(*Source : HIS Technology 2014)

Market Overview

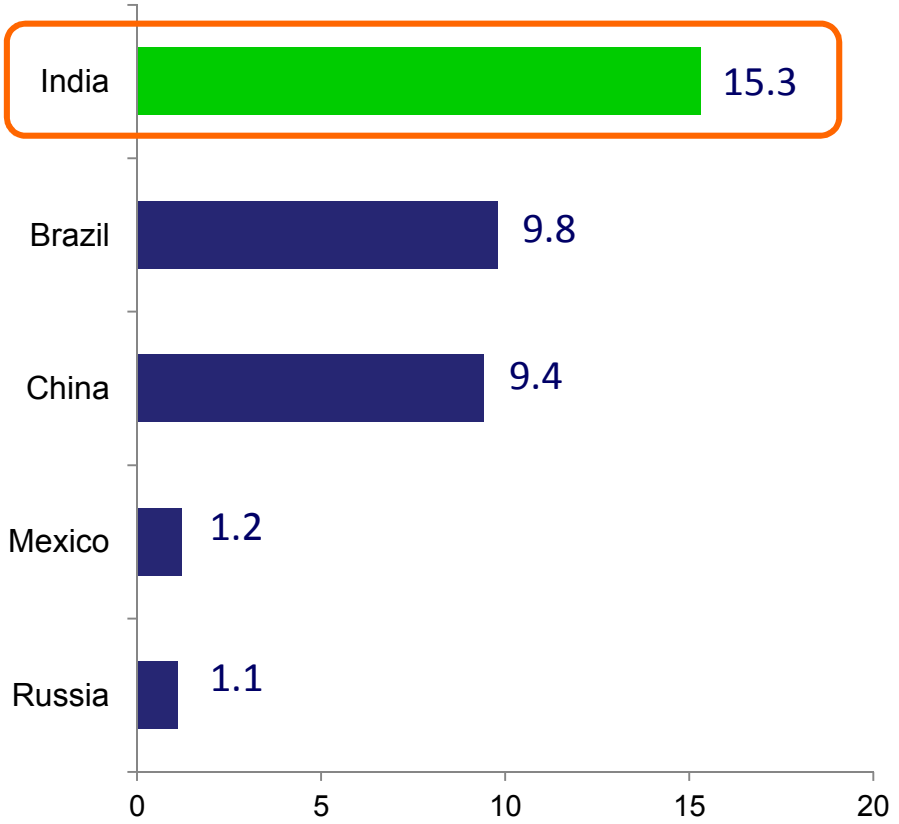
◆India has a large number of Asthma patients compared to other major countries and the market is still expected to grow in the future

Prevalence of Asthma in India



Economic loss due to chronic and acute Asthma is estimated at **$700M**

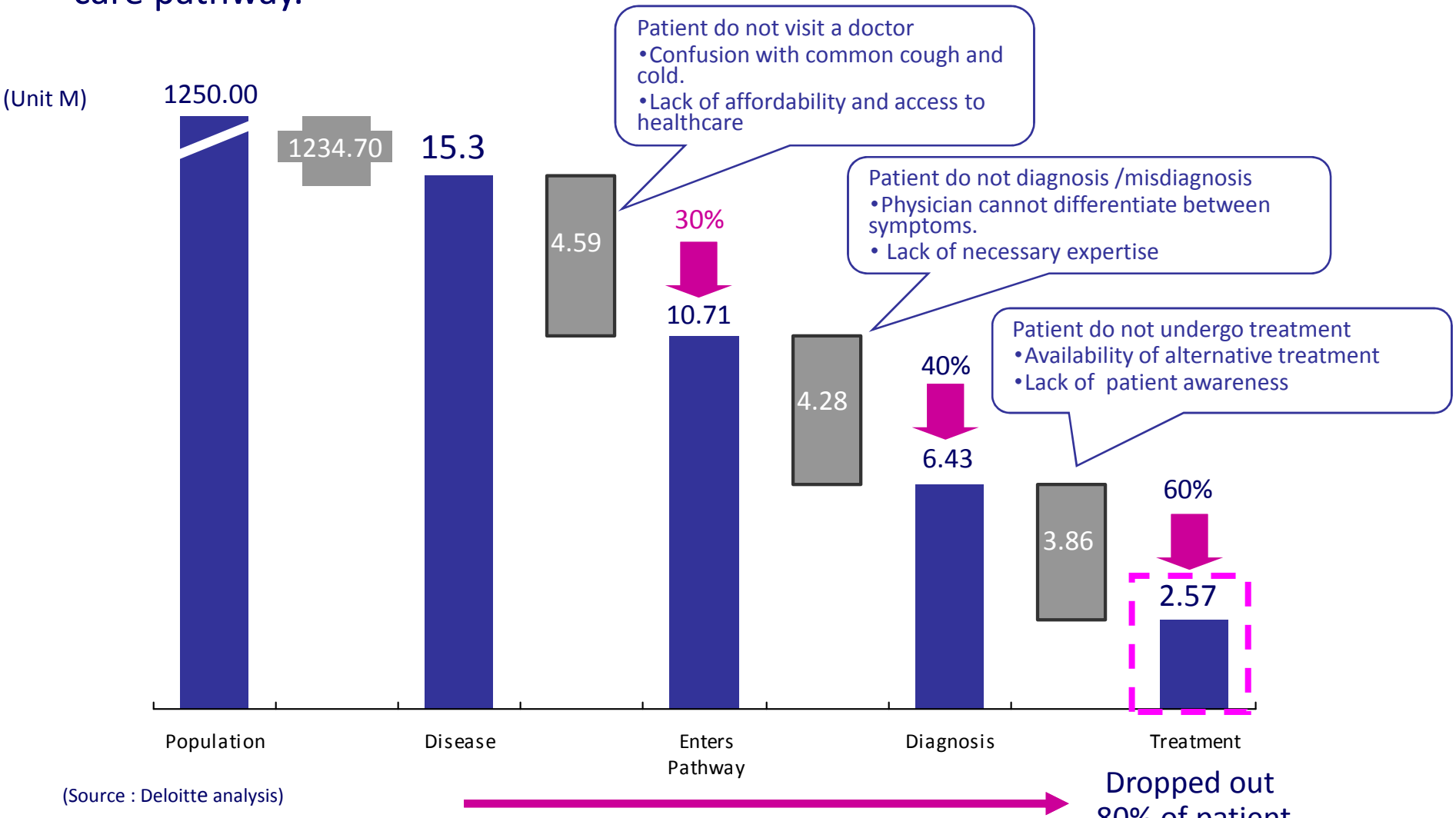
Patient with clinical Asthma, 2014



(Source : Industrial report, Deloitte Analysis)

Market Overview

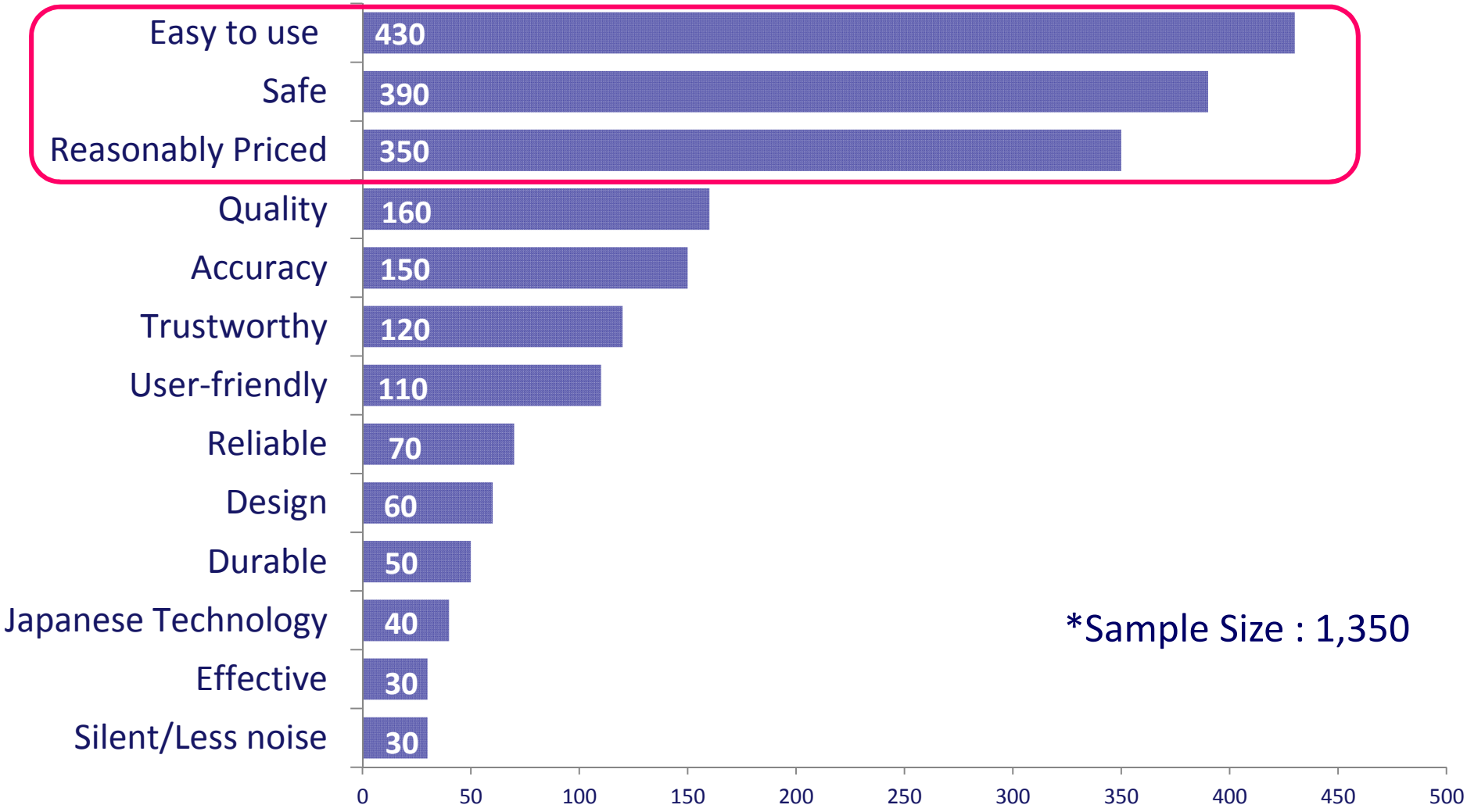
◆There is a significant *"Dropout"* at various stages along the Asthma patient care pathway.



(Source : Deloitte analysis)

Market Overview

◆Ease of use, Safety and Price are the top benefits spontaneously recalled by consumers.



*Sample Size : 1,350

(Researched by DENTSU)

Regulation Scenario <Global>

◆ Home health monitoring devices are globally classified based on their risk level and intended uses

Home health monitoring device classification (Medical)				
Products	Medical Device	US FDA	EU-MDD	JAPAN
Blood Pressure Monitor - CUFF	●	Class II	Class I	Class II
Nebulizer	●	Class II	Class II a	Class I
Weighing Scale/ BFM	●	Class I	Class I	
Thermometer	●	Class II	Class I	

※ Classification are different according to the regulatory authority in each country

Regulation Scenario <India>

◆Some home health monitoring devices are not regulated at all (ex. Nebulizer)

Category	Medical Product		Legal Metrology Model approval		Legal Metrology Packed commodity
	Yes	No	Yes	No	
B.P.M	—	✓	✓	—	✓
W.S & B.F.M	—	✓	✓	—	✓
Thermometer	—	✓	✓	—	✓
NEBULIZER	—	✓	—	✓	✓
PEDOMETER	—	✓	—	✓	✓
BGM STRIPS	✓	—	—	✓	✓
HEARING AID	—	✓	—	✓	✓
MASSAGER	—	✓	—	✓	✓
ECG Monitor	—	✓	—	✓	✓
Nerve Stimulator	—	✓	—	✓	✓

※as per OMRON study and understanding

Ref.) Particle size of medication

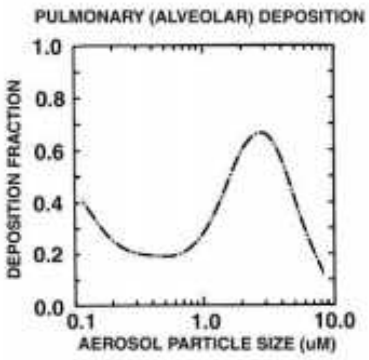
OMRON

◆ US-FDA shows that 2-5μm particle size deposit on tracheobronchial position

U.S. Food and Drug Administration
Protecting and Promoting Public Health
www.fda.gov

Particle Specifications

- **Aerodynamic Particle Size Distribution (APSD)**
  - Particles 2-5 μm have the greatest potential for lung deposition.
    - Likely to be related to clinical response.
  - Extra-fine particles (<1.1 μm) may escape deposition and be exhaled.
  - Course particles (>4.7 μm) deposit in laryngeal and oropharyngeal region
    - No clinical benefit for airway drugs.



Ref.) Effect of particle size on medication

◆Nebulizer is proven as efficient and safety for pediatric asthma patients

< OMRON >

Clinical study on inhalation of budesonid with nebulizer in the treatment of children with asthma

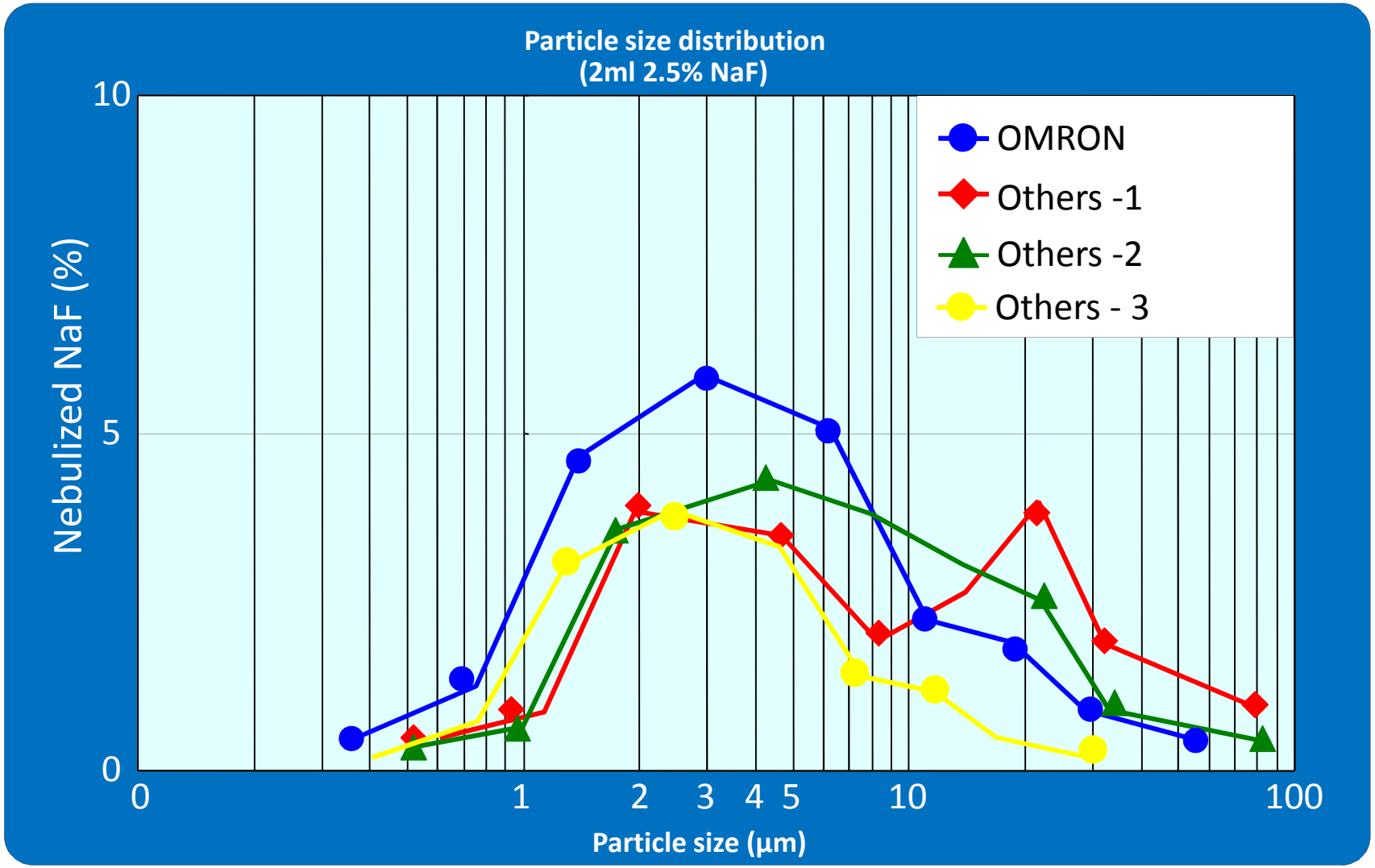
Abstract: **Objectives** To evaluate the clinical effects of inhalation of budesonid with a nebulizer via jet (NE-C28) on children younger than 5 years old with asthma. **Methods** Budesonid were given with nebulizer for 6 weeks in 61 children (aged 5 - 62 months) with recurrent wheeze. Symptomatic score during daytime and night were recorded by the patients each day. Patients were followed-up and the scores were assessed every week after treatment. The differences on symptomatic score every week, between the first week and 2, 3, 4, 5, 6 week after treatment were analyzed. **Results** The differences in the symptom score were significant between the first week and every week after treatment ($P < 0.05$), while the difference in every week after treatment were not significant. The clinical effective rates increased significantly after 2 weeks' treatment (56.8%), and reached to 68.2% in week 6. There were no significant side-effects reported by the patients during the period of treatment. **Conclusions** Inhalation of budesonid with nebulizer is effective for alleviating clinical symptoms of asthma and it is really a safe, well-compliance therapeutic approach for children younger than 5 years old with asthma.

(J Clin Pediatr, 2008, 26(3): 226-229)

Availability in India

Internal Analysis

◆Inhalation efficiency simulation of nebulizer as per different particle size and “3µm” deposit on constant position



(*OMRON’S internal study)

Comparison Data

OMRON

◆Chemicals used in Mask / neb-kit which are not healthy for human body

	OMRON			Company "A"	Company "B"	Company "C"
				Non OMRON Brand		
Type	Compressor Nebulizer	Compressor Nebulizer	Compressor Nebulizer	Compressor Nebulizer	Compressor Nebulizer	Compressor Nebulizer
Noise	60db	60db	43 db	48db	58.1 dB	54.4 dB
Nebulization	0.40ml	0.20ml	0.10ml/min	0.15ml	0.3 ml/min	0.2 ml/min
Particle Size (MMAD)	3.4µm	3.6µm	3.0µm	4.5µm	4.0µm	5.3µm
Medication capacity	7ml	6ml	7ml	6ml	6ml	6ml
Phthalic Acid in Mask	**Not Used**	**Not Used**	**Not used**	**Used**	**Used**	**Used**

※Phthalic Acid has side effect on Human Body (*OMRON'S internal study)

Ex. disturb the human hormonal system and human, sexual development and reproduction.
Additionally, phthalates are suspected to trigger asthma and dermal diseases in children

Technical Background

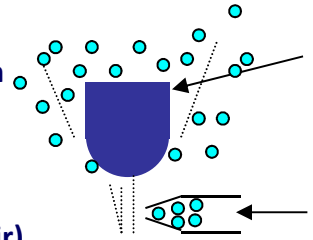
◆Neb –kit is a essential part of Nebulizer , it store the medicine & generate it in to fine mist in required particle size.

<Configuration>

Nebulizer kit
(to turn liquid medication into a fine mist)

Compressor
(to make a compressed air)

<Nebulization>

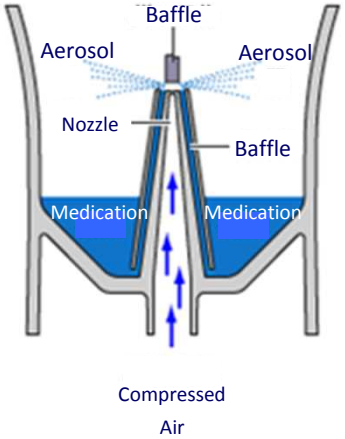


Baffle

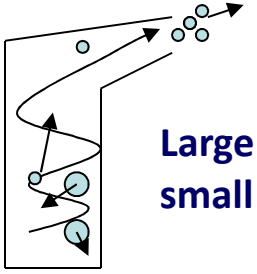
Sucking liquid medication
(Venturi effect)

Compressed Air

<Configuration of Nebulizer Kit>



***Filtering effect**



Large particles drop down and small particles are blow out.

Advantage : Almost every solutions can be nebulized

Conclusion

◆ Standardization & regulation will help to *Provide*, *Protect*, *Promote* best of the devices to intended users

Provide

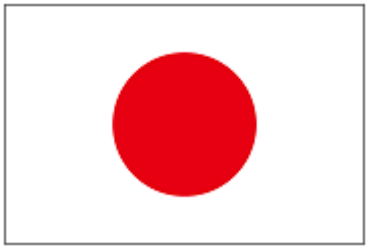
- Insure that each manufacturer/brand they adhere to standards
- Clear delectation to industry

Protect

- Protect the intended users from the sub-standard devices & services

Promote

- Better quality will reduce high import burden and promote long term needs effective & sustainable healthcare
- Will motivate manufacturer to man future locally which will help to transfer Know- How



Thank you !!

Our Experience with the PMDA

Nandakumar Subburaman (Nandu)
CEO
Perfint Healthcare

Perfint Healthcare

A pioneering ***medtech start-up from India*** in the minimally invasive, image guided cancer therapies space ***: Interventional Oncology.***

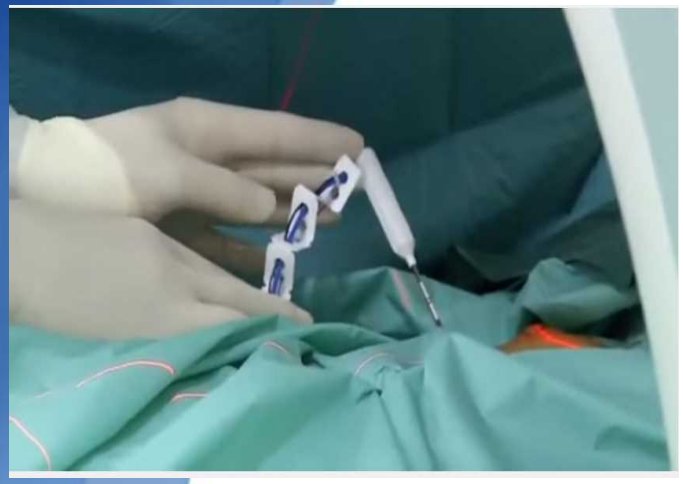
Flag ship product - ***MAXIO™ : A patented, Robotically assisted CT Guided Tumor Ablation* solution.***

Cleared by USFDA, CE & Japanese PMDA, China CFDA

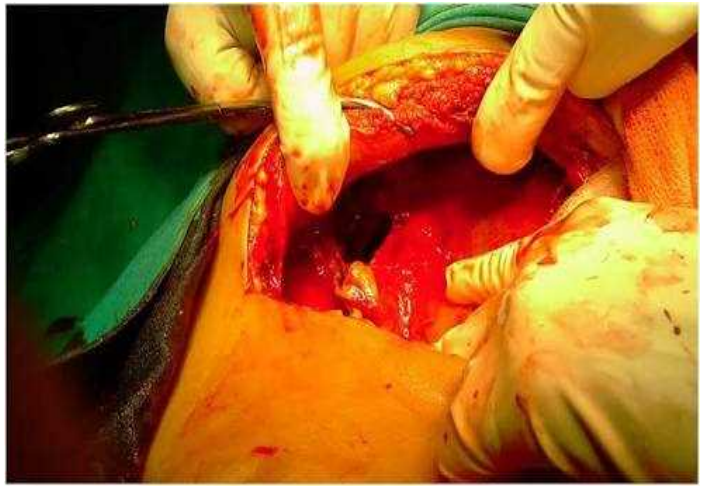
Tumor Ablation : Significantly tolerable than surgery

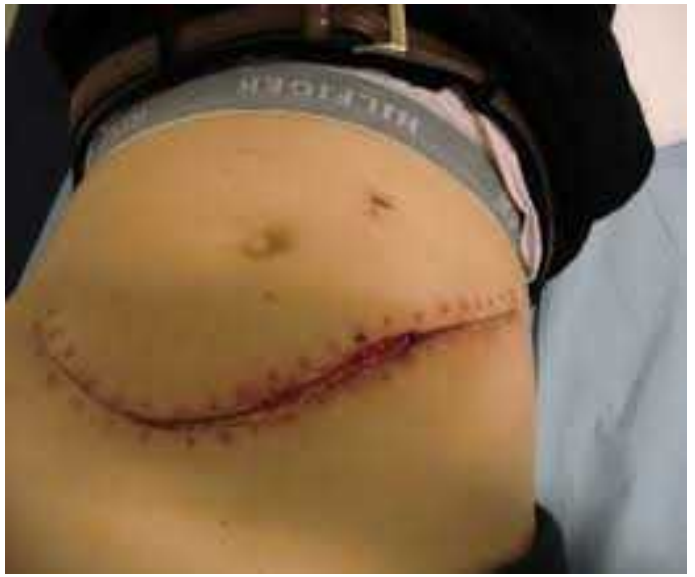
Perfint

Ablation

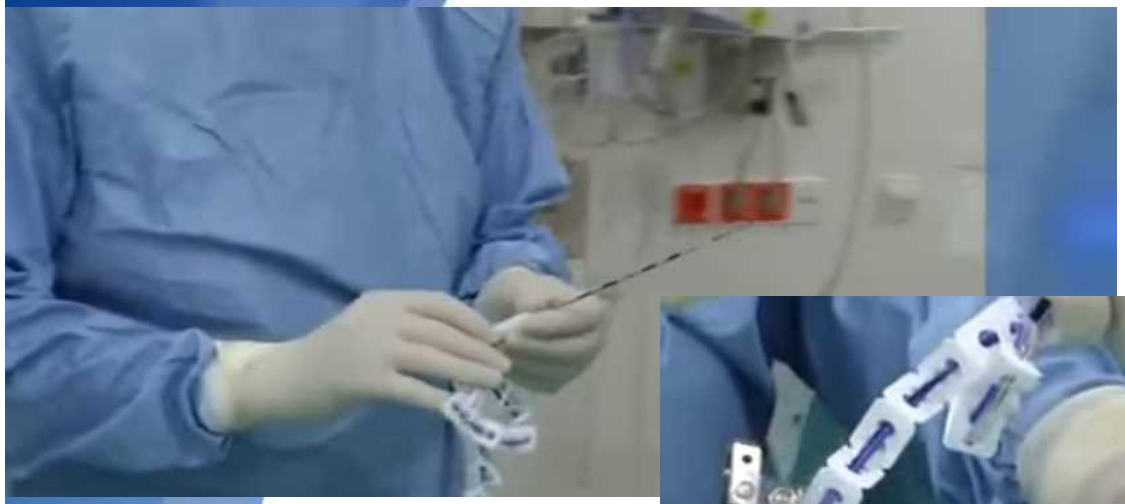


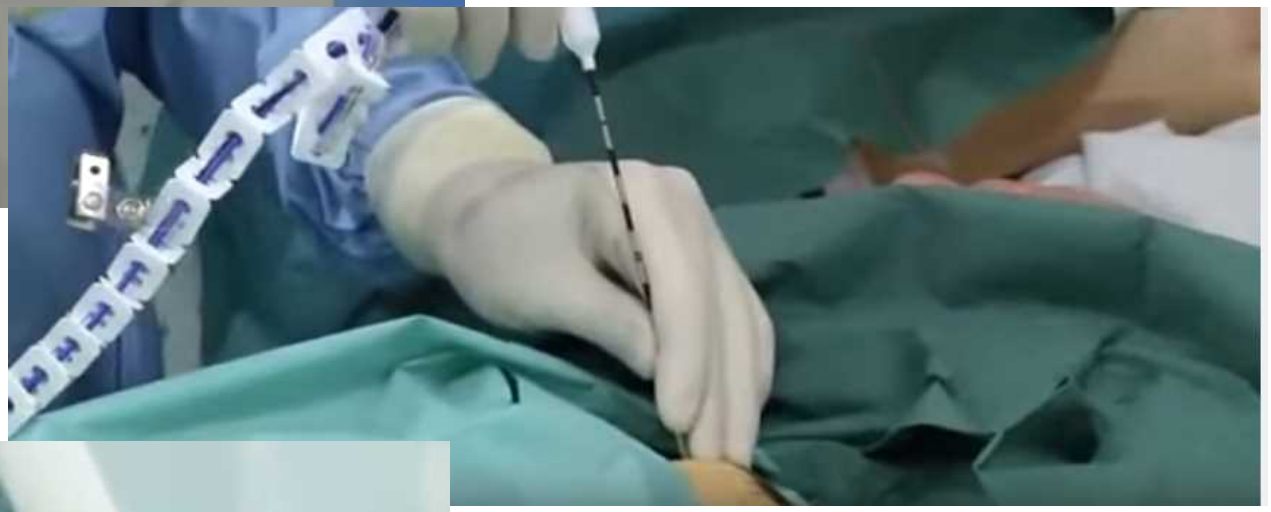
Surgery





Ablation electrode placement …





Prof Thomas Vogl
Microwave ablation of lung tumor
Univ Clinic, Frankfurt

Perfint's current products …

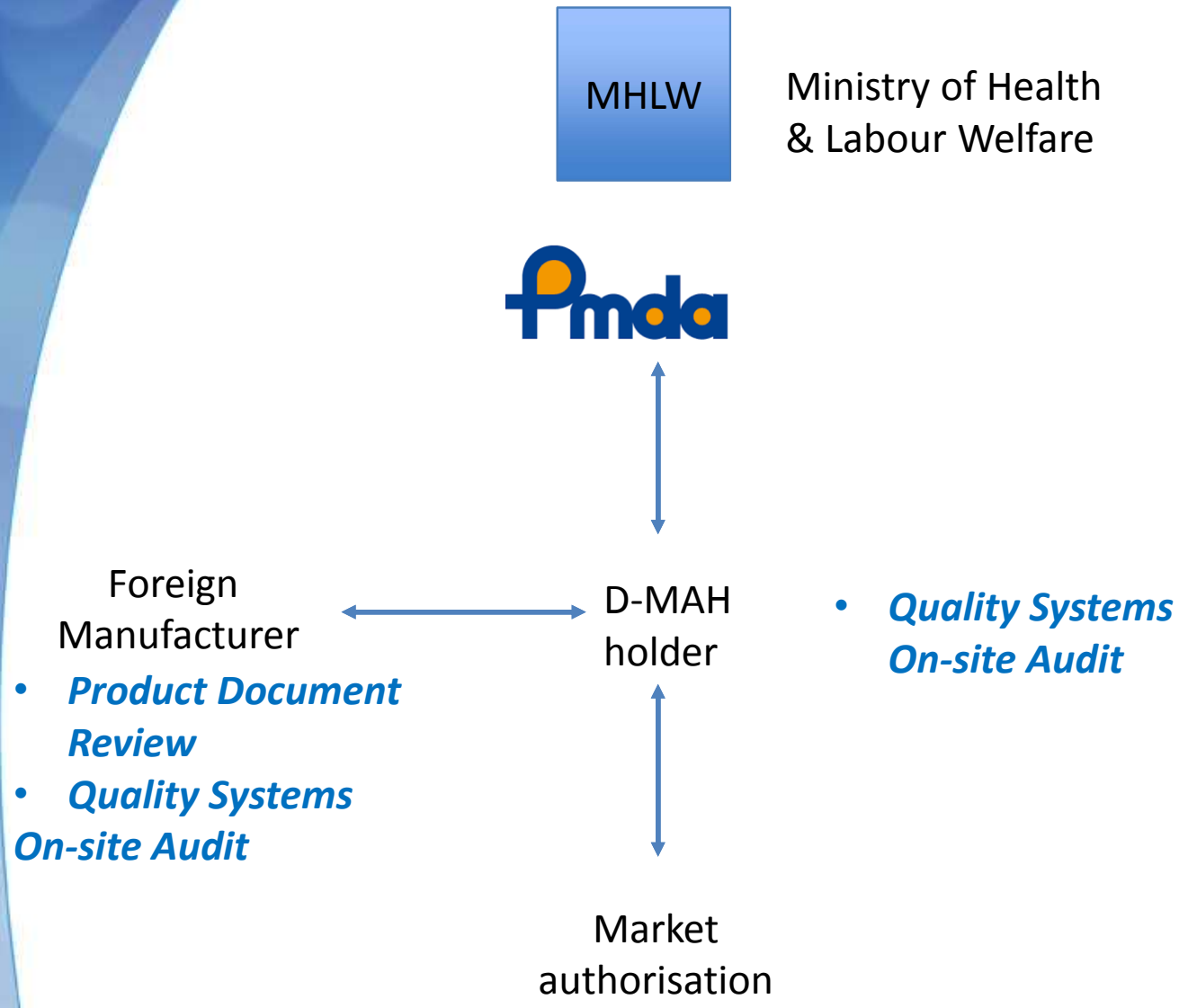
2013

MAXIO™

*An Integrated system for **Treatment Planning + Robotic Navigation of electrodes** for CT Guided Tumor Ablation*

The PMDA process & experience

Foreign Manufacturer Device Approval …



Classification and Regulation of Medical Devices

Class	Risk base Medical Device Classification	Classification	Clearance / Approval
Class Ⅰ	Devices with extremely low risk to the human body in case of problems. Examples: In vitro diagnostic devices, steel made small devices (including a scalpel, tweezers), X-ray film, devices for dental technique	General Medical Device	Pre- Market Submission (**Todokede)** by MAH holder, No review / assessment by PMDA
Class Ⅱ	Devices with relatively low risk to the human body in case of problems/ Examples: MRI devices, electronic endoscope, catheter for digestive organs, ultrasonic devices, dental alloy	Specfied Controlled Devices	Pre- Market Certification by PMDA **(Ninsho)** – similar to Notified body approval in CE
Class II non-specified, Class III, Class IV	Devices with relatively high risk to the human body, highly invasive and with life threatening risk in case of problems Examples: Dialyzer, bone prosthesis, mechanical ventilation	Highly Controlled Devices	Pre-Market Approval from PMDA **(SHONIN)**

Role of D-MAH (Marketing Authorization Holder)

- Ensure the marketing, quality, and safety standards of your products to be placed on the market.
- Act as your primary contact point for all Japanese regulatory authorities.
- Assist in incident reporting in Japan as needed.
- Communicate with your distributor(s) to create your Import Procedures, prepare your Import Submissions, and clear products through Japanese Customs.
- Communicate with your registered warehousing manufacturer for a final product to develop the Quality Agreement and prepare Manufacturing Standard (Seihinhyojunsho) for labeling, and warehousing as applicable.
- Procure all government import licenses on your behalf.
- Conduct audits of your facility, when applicable.
- Report manufacturing or in-process control changes to authorities as applicable.
- Show their audit records if requested by Japanese authorities.

MHLW Ministerial Ordinance No. 87 ..

- ***Quite Similar to ISO 13485, 84 Articles***
- ***Manufacturing Site, Responsible Engineering Manager, D-MAH***
- ***Communicate thro D-MAH (local rep)***
- ***Communication in Japanese – time taking, error prone***
- ***Lost 2+ years in erroneous classification. Eventually re-submitted as Improvised Medical Device w/o clinical trials***
- ***Lengthy document review followed by audits of D-MAH holder and site***
  - *Provision of resources*
  - *Responsibility & authority*
  - *CAPA*
  - *Process validation*
  - *Training*
  - *Top management engagement*
- ***While enabling access to safe and effective devices to enhance public health, is also concerned with alignment to Japanese clinical practices***

Thanks