

Current status of orphan device development in Japan

*YUKA SUZUKI, Ph.D.
Director of Office of Medical Devices II,
Pharmaceuticals and Medical Devices Agency (PMDA),
Japan*

- Orphan System was established in Japan by amending the Pharmaceutical Affairs Law (PAL) in 1993.

- ✓ Review of orphan medical devices and other products which are highly required in medical practice shall be taken priority. (Article 14(7) of PAL)
- ✓ Orphan medical devices means medical devices whose patients do not exceed 50,000 in Japan, and which, when having been approved, are designated by the MHLW as those with particular use value. (Article 77-2 of PAL)
- ✓ Orphan medical devices shall be subjected to priority review and longer reexamination period(4 to 7 year). (Article 14(7) and 14-4(1) of PAL)
- ✓ Orphan medical devices shall receive grant and preferential treatment on tax. (Article 77-2-2 and 77-2-3 of PAL)

Statistics of Designated Orphan MDs

Fiscal Year	Designation	Approval	Under Development	Rescission
1993	2	2	0	0
1995	2	1	0	1
1996	1	0	0	1
1999	2	2	0	0
2000	1	0	0	1
2001	2	2	0	0
2005	2	1	1	0
2007	1	1	0	0
2008	5	1	4	0
2009	3	0	3	0
2010	1	0	1	0
2011	1	0	0	0
Total	23	10	9	3

(as of July, 2011) N/A: FY1994, 1997, 1998, 2002-2004, 2006

Examples of Approved Orphan MDs

Product (Company)	Generic Name	Designation Shonin (pre-market) Application Approval	Number of Patient in Clinical Trial
Duraheart (TERUMO)	Artificial Heart	2009/3/11 2009/9/17 2010/12/8	Japan 6 Foreign 33
EVAHEART (SUN MEDICAL)	Artificial Heart	2007/7/6 2009/1/19 2010/12/8	Japan 18
CODMAN ENTERPRISE (Johnson & Johnson)	Neurovascular Embolization Implant	2005/12/9 2009/3/12 2010/1/8	Japan 15 Foreign 28
HeartMate XVE LVAS (NIPRO)	Artificial Heart	1999/5/27 2004/2/27 2009/11/18	Japan 6 Foreign 170
Adacolumn (JIMRO)	Apheresis device	2001/4/23 2005/3/18 2008/9/2	Japan 21

(* Some names are abbreviated form)

Concerns/obstacles for orphan MD review

- Challenges in clinical data evaluation
 - Insufficient sample size for clinical trials
 - No established treatment procedure for the diseases to be evaluated
 - Limited Background/baseline information to extrapolate foreign clinical data
- most devices are initially introduced to Japan market which require Japan clinical trial to support compatibility with Japanese patients.

- Improve development
 - Conduct of global clinical trials
 - expects progress of enroll
 - improvement of scientific verification
 - application of pooled data
 - Possible streamlining of clinical trial process
- Improve advanced environment
 - Collecting background information through accumulation of existing treatment results
 - improvement of scientific verification of trials

- Clarify US/JP disparities regarding orphan device regulations and regulatory perspectives in review process
- Propose solutions for disparities preventing prompt introduction
- Prepare initial data for overview of issues and optimization of relevant regulations
- Conduct of global trials and sharing of baseline data
- Minimize the US/JP lag for market introduction of orphan devices

- Review for designation of priority consultation
 - To review and determine the device applicable to priority consultation
 - Consultation on GLP/GCP compliance for medical devices
 - To guide and advise regarding GLP/GCP compliance for priority consultation device with Shonin (Pre-market) application draft materials
- See PMDA website for further information

Thank you for your attention !



<http://www.pmda.go.jp/>

- Orphan System was established in Japan by amending the Pharmaceutical Affairs Law (PAL) in April 1993 and entered into force in 1st October.

(Objectives of PAL)

- This law is intended to provide regulations required to ensure the quality, efficacy and safety of drugs, quasi-drugs, cosmetics and medical devices and to improve the public health and hygiene through necessary measures taken to promote research and development of drugs and medical devices which are of particular importance to medical practice.(Article 1 of PAL)

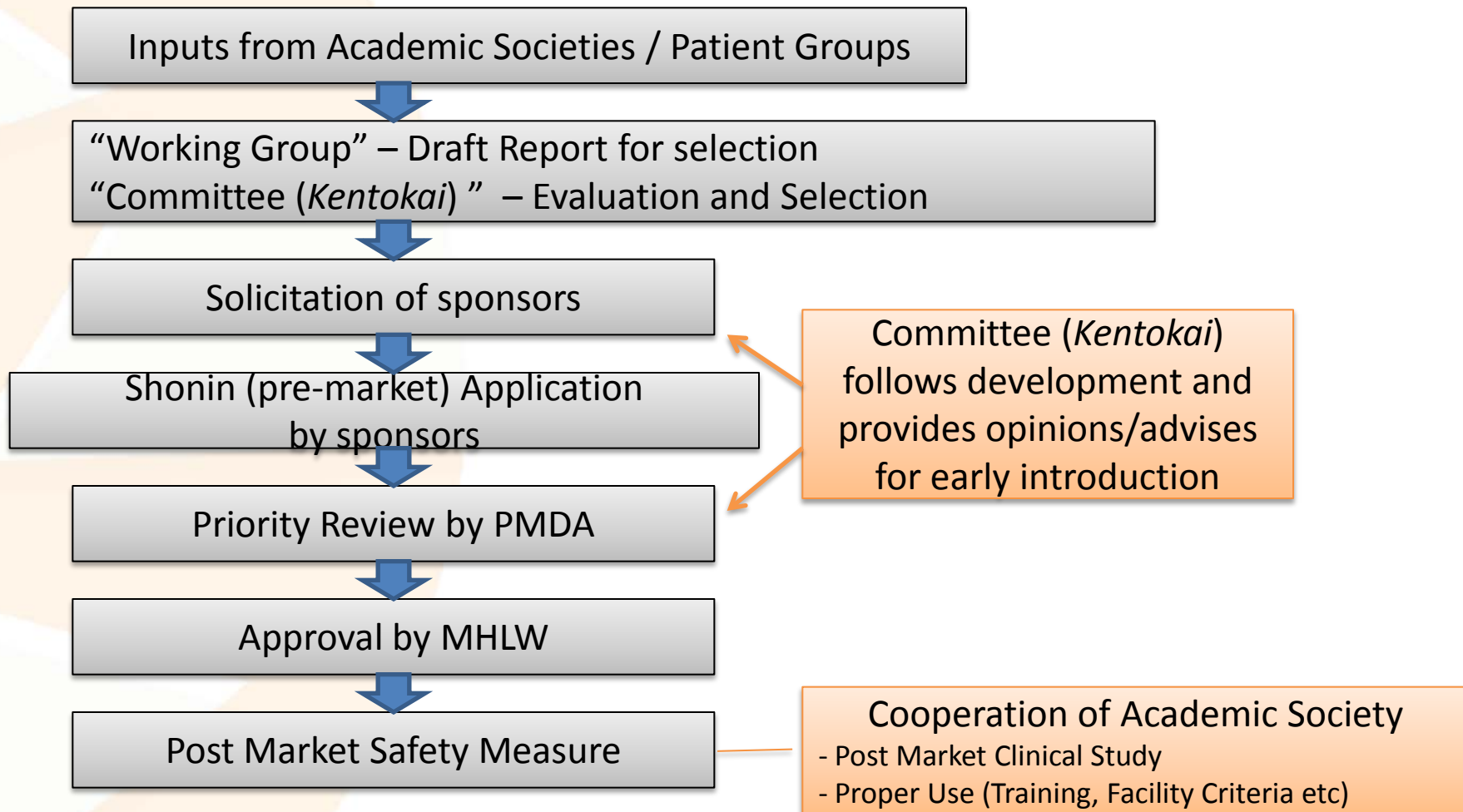
Priority Review and Orphan MD

- Review of orphan medical devices and other products which are highly required in medical practice shall be taken priority. (Article 14(7) of PAL)
- Orphan medical devices means medical devices whose patients do not exceed 50,000 in Japan, and which, when having been approved, are designated by the MHLW as those with particular use value. (Article 77-2 of PAL)
- Orphan medical devices shall be subjected to priority review and longer reexamination period(4 to 7 year). (Article 14(7) and 14-4(1) of PAL)
- Orphan medical devices shall receive grant and preferential treatment on tax. (Article 77-2-2 and 77-2-3 of PAL)

“Committee on early introduction of innovative medical devices highly needed” (from 2006)

- Investigating clinical needs from academia/patients society and seeking a pathway to promote early introduction of devices have highly needs.
- Agreed to promote the early introduction of 36 MDs, and 16 of them has already been approved as of Jan 2011.

2011 Summary Process of “Committee on early introduction of innovative medical devices highly needed”



The review of orphan devices/devices with high medical necessity

	Orphan devices	Devices with high medical necessity	Other general devices
General perspective of approval review (Conditions for rejection)	J-PAL, a14, i2	J-PAL, a14, i2	J-PAL, a14, i2
Applicability of priority review	Priority review (J-PAL, a14, i7)	Determine with PFSB/ELD No. 0227016 notification	Determine with PFSB/ELD No. 0227016 notification
Applicability of new medical device	applicable	Yes if J-PAL, a14-4-1 would applicable	Yes if J-PAL, a14-4-1 would applicable
Re-examination period for new medical device	4-7 years	-4 years	-4 years

Examples for clinical trials on orphan devices

- CODMAN ENTERPRISE VRD (J&J)
 - Neurovascular Embolization Implant
 - JAPAN 15pts, US 28pts
 - Endpoints
 - Procedure success
 - Aneurysm occlusion rate, Implant success, Satisfactory coil mass position, VRD patency rate, Neurological evaluation, Adverse event

- # Examples for clinical trials on orphan devices
- EVAHEART (Sun Medical)
 - Artificial Heart
 - Japan 18pts
 - Endpoints: 6-month survival, Adverse event, Device failure
 - DuraHeart (Terumo)
 - Artificial Heart
 - Japan 6pts, EU 33pts
 - Endpoints
 - Performance: 13-week (26-week) survival
 - Safety: Adverse event