IGDRP ASMF/DMF Working Group
Project 3 : Gap analysis survey

Pharmaceuticals and Medical Devices Agency (PMDA)
Office of Generic Drugs
Maki Matsuhama

2014.11.4
7th International Generic Drug Regulators Meeting
at Orchard City Centre, Singapore

Outline

1. Outline of ASMF/DMF System
2. Application Scheme Gap
3. Document for Submission of ASMF/DMF
4. Technical Requirement Gap
5. Assessment Report
6. Procedure of Changing Gap
7. Other Topics

2

1. Outline of ASMF/DMF System (1)

Existing for ASMF/DMF (likely) System

(TGA, ANVISA, HC, EMA, PMDA, HSA, Swissmedic, TFDA, WHO, EDQM)

30 APIs are mandatory for registration (All APIs will be mandatory for registration by 2020)

1. APIMF procedure
2. API Prequalification

CEP

Non-Existing for ASMF/DMF likely system

(MCC)

In developing for ASMF/DMF system (pilot phase)

- ✓ Not mandatory for submission
- ✓ No upper limit for the number of application of same API

APIs
(TGA, ANVISA, HC, EMA, PMDA, HSA, Swissmedic, TFDA, WHO, EDQM)

Excipients
(HC, PMDA, EDQM)

Others:
Materials for medical devices, etc.
(PMDA)

- ✓ Intermediate ASMF/DMF can be included in API ASMF/DMF (TGA, HC, PMDA, HSA,EDQM)
- ✓ Different polymorphic form can be included in the same ASMF/DMF (ANVISA, HC)
- ✓ Different synthetic routes can be included in the same ASMF/DMF (HSA, TFDA, (HC, EDQM: not recommended))

3

1. Outline of ASMF/DMF System (2)

What is the purpose of ASMF/DMF system?

TGA
Part of submission to register a drug product

WHO
To avoid repeated assessment
To ensure a single source of API information

To protect the technical know-how of the API manufacturers

EMA, Swissmedic
Whilst allowing the MAH to take full responsibility for quality and quality control of the API

TFDA
To clarify the quality of API and the suitability of specification

Who applies for the ASMF/DMF submission?

API manufacturers or importers, etc.

- ➢ ANVISA : Regulatory body must be based in Brazil
- ➢ PMDA, TFDA : In-country-caretaker or agent (when foreign manufactures)
- ➢ HC : North American agent (strongly recommended)

Any Guideline?

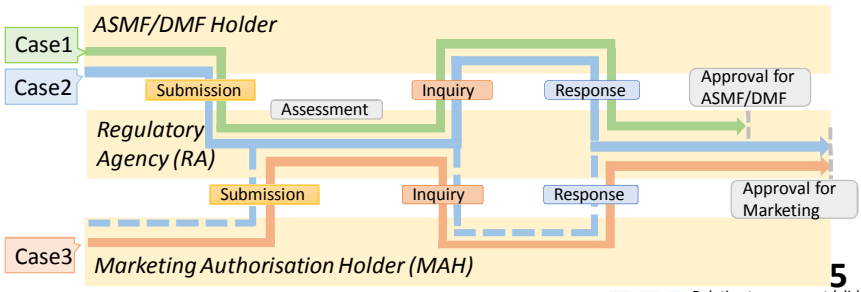
- ➢ TGA, EMA, Swissmedic : EU guideline
- ➢ Others : other domestic guideline

4

2. Application Scheme (1) Gap

- ✓ Application scheme is classified into 3 patterns.
- ✓ Differences between 3 patterns are on submission, inquiry, response, and approval.

	Classification	Regulatory Agency (fee)
Case1	Independent of a drug product application	ANVISA (no fee), TFDA (50USD), WHO(API Prequalification) (tiered fee structure), EDQM (3000euros)
Case2	In conjunction with a drug product application	TGA, EMA, PMDA, HSA, Swissmedic, WHO(APIMF) : no fee HC: 416Cdn
Case3	Non-ASMF/DMF scheme	MCC

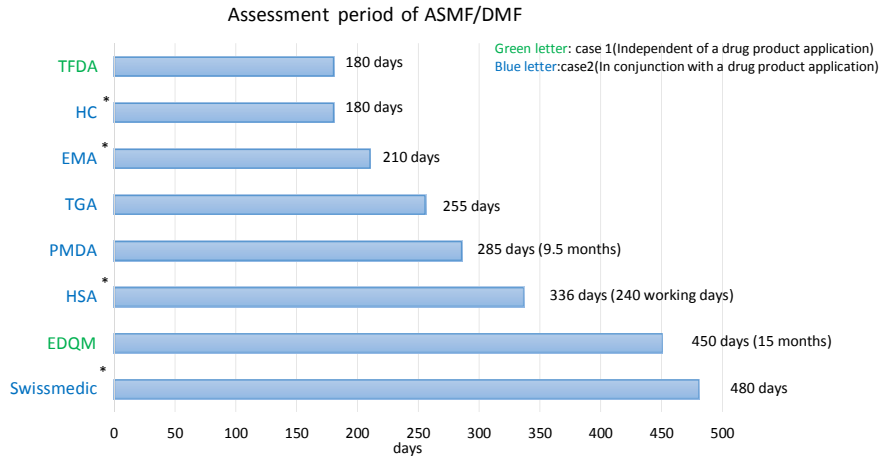


5

: Relative to open part (slide p.8)

2. Application Scheme (2) Gap

- ✓ Assessment period of ASMF/DMF is variable in each RA.
  - In HC, EMA, TGA, PMDA, HSA and Swissmedic, the assessment period of ASMF/DMF is as the same as the drug product assessment period.
  - ANVISA and WHO have no limit. (but change soon in WHO)



*Data of HC, EMA, HSA, Swissmedic from regulatory gap survey by ANVISA

6

2. Application Scheme (3) Gap

- ✓ *If the drug product application (that is linked to the ASMF/DMF) is rejected or withdrawn before acceptable of ASMF/DMF,*
  - TGA, ANVISA and TFDA continue reviewing the ASMF/DMF.
  - HC, EMA, PMDA, HSA, Swissmedic and WHO suspend reviewing the ASMF/DMF.

- ✓ *After ASMF/DMF is accepted, when ASMF/DMF which has been assessed is used with different a new drug product,*

TGA, WHO	don't reassess the ASMF/DMF.
Swissmedic	don't reassess if the version is same.
HC, EMA, TFDA	assess suitability for use in the new drug product.
HSA	assess the updated which are submitted between the previous assessment and current product application.
PMDA	reassess by scientific standards at that time. reassess including minor change notification which is submitted by then.
ANVISA	reassess the ASMF/DMF.

Green letter: case 1(Independent of a drug product application)
Blue letter:case2(In conjunction with a drug product application)

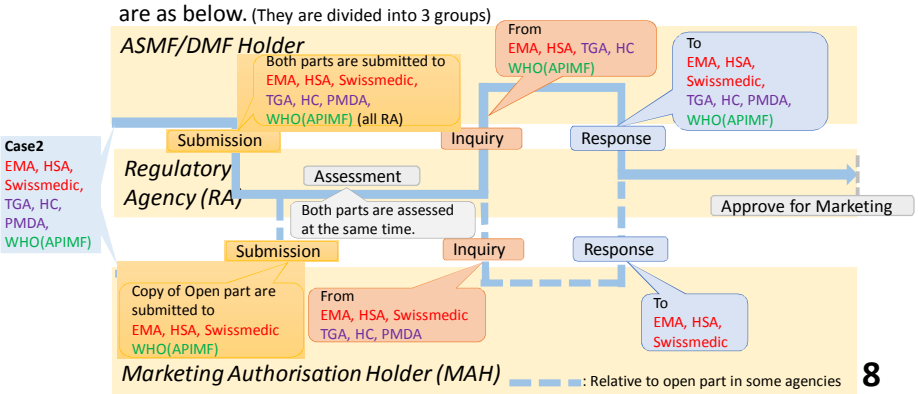
7

3. Document for Submission of ASMF/DMF

- ✓ Application form
- ✓ CTD (or technical document) Module 3.2.S1-7
  - Module2.3.S1-7 is required in HC, HSA, Swissmedic, WHO
- ✓ Others : Letter of Access, GMP certification, Fee form, etc.

} Common set, but contents of AF is variously

- ➢ Open / Closed part structure (adopted in Case 2 procedure)
  - Classification is Prescribed in guideline (HC, EMA, PMDA)
  - 3.2.S.2.2 - 3.2.S.2.6 are mainly possible to include in closed part. (see guideline)
  - The destination/sender of submission, inquiry and response relative to open part are as below. (They are divided into 3 groups)



8

4. Technical Requirement

Gap

- ✓ Possible to set different specification between those in ASMF/DMF and for the drug product.
- ✓ Stability test is required in all RA.

	Pharmacopoeia which accepted as specifications of ASMF/DMF (Accepted in / Not accepted in)		
EP	TGA, ANVISA, HC, EMA, PMDA, HSA, Swissmedic , TFDA, WHO, EDQM , (MCC)		
USP	TGA, ANVISA, HC, EMA, PMDA, HSA, Swissmedic, TFDA, WHO, (MCC)		EDQM
BP	TGA, ANVISA, HC, HSA, TFDA,WHO, (MCC)	EMA, PMDA, Swissmedic, EDQM	
JP	ANVISA, PMDA, HSA, TFDA, WHO, (MCC)	TGA, HC, EMA, Swissmedic, EDQM	
Ph.Int	ANVISA, TFDA, WHO, (MCC)	TGA, HC, EMA, PMDA, HSA, Swissmedic, EDQM	
CEP	TGA, HC, EMA, HSA, MCC, Swissmedic, TFDA, WHO	ANVISA,PMDA	EDQM

	Reference guideline (ICH&EMA/ICH/Other/Nothing)		
Stability Test Condition	TGA, HC, EMA, PMDA, HSA, Swissmedic, TFDA, EDQM	ANVISA, WHO	MCC
Impurity	TGA, EMA, WHO	HC, PMDA, HSA, MCC, Swissmedic, TFDA, WHO, EDQM	ANVISA
Starting Material	TGA, HC, EMA, PMDA, HSA, Swissmedic, TFDA, WHO, EDQM	ANVISA (EDQM)	MCC
Others (Validation, Residual Solvents, etc)	TGA, ANVISA, HC, EMA, HSA, Swissmedic, TFDA, WHO, EDQM	PMDA, MCC	
	(FDA guidance: ANVISA, HC, TFDA, Others: WHO, EDQM)		

9

5. Assessment Report

	TGA	ANVISA	HC	EMA	PMDA	HSA	MCC (non ASMF/DMF)	Swiss-medic	TFDA	WHO	EDQM (CEP)
1. Are there assessment reports of generic drug products?	Yes				No						N/A
2. Are there assessment reports of ASMF/DMF?	Yes										
3. Are assessment reports of ASMF/DMF separated from drug products part?	Yes						No				
4. Are assessment reports of ASMF/DMF description form?	Yes						No				
5. How many pages do assessment reports of ASMF/DMF have ?	About 1～50 pages (various)										
6. Are there English version assessment reports of ASMF/DMF ?	Yes	No									
7. Are assessment reports of ASMF/DMF published?	No										
8. Are assessment reports of ASMF/DMF provided to applicant?	No	Yes									
9. Is there public assessment reports?	No		Yes								
10. Is the assessment of responses included in assessment reports?	Yes		No								
11. Is the assessment of update included in assessment reports?	Yes										

Answer is as an API part

Only in the case of new drugs (PMDA)

For non/NCE and ANDA (TFDA)

Except for new drugs (PMDA)

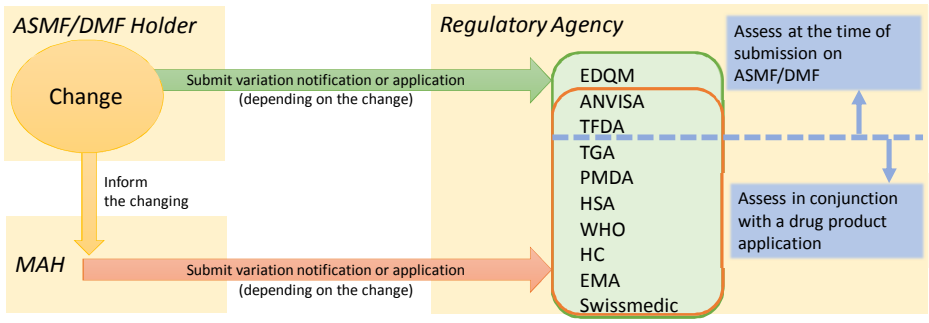
Except for new drugs (TFDA)

On request only (Swissmedic)

10

6. Procedure of Changing

Gap



- ✓ Type of change procedure for ASMF/DMF (e.g.)
  - Partial Change Approval Application/ Minor Change Notification (PMDA)
  - Annual Notification / Immediate Notification / Minor Amendments / Major amendments (WHO)
  - Notification / Minor Change / Major Change / Renewal (EDQM)
  - Under discussion (ANVISA)
- ✓ Periodically update
  - Every 2 years (HC, WHO)
  - Every 5 years (ANVISA, TFDA)

11

7. Other Topics (1)

✓Application by electronic/non-electronic

- ✓HC, EMA, PMDA, HSA, Swissmedic, TFDA, WHO and EDQM accept electronic application (only electronic in HSA and WHO) .
- ✓The paper version is the official version in HC and PMDA.
- ✓TGA and ANVISA are under development.

✓Coding system(link to project14)

- There is a coding system. (except TGA)
- Not required number change when ASMF/DMF version is updated (All RA)

✓Lexicon(link to project 13)

ANVISA, HC(guideline), PMDA(ICH guideline) have.

12

7. Other Topics (2)

✓GMP inspection / certification

GMP certification is mandatory	GMP certification is not mandatory
TGA, ANVISA, HC, PMDA, WHO *By when?* ASMF/DMF submission : ANVISA, WHO Drug product submission : HC Drug product approval : TGA, PMDA *Who applies?* API manufacture : ANVISA, HC, WHO Sponsor : TGA, ANVISA, PMDA	HSA, EMA, MCC, Swissmedic, TFDA, EDQM • Qualified Person GMP statement is required. (EMA, Swissmedic) • GMP certification will be required to approve ASMF/DMF in 2016. (TFDA)

✓Mutual recognition(link to ultimate goal)

- EMA : among the national competent authorities within EU
- EDQM : exchanging AR with EMA (pilot)

✓Review guide(link to project 6)

ANVISA, HC(in creating), EMA(guideline), HSA, TFDA, WHO, EDQM have.

13

Back up

14

8. Discussion points

- What are the barriers to share and utilize ASMF/DMF assessment from other RA?
  - Differences in application scheme linked to drug products?
  - Differences in technical requirements?
  - Differences in procedure of changing?
  - Other reasons?
- How do we consider the results of Gap analysis survey…

15

Thank you for attention!!

16