



BIOFARMA EXPERIENCE WITH ASEAN CTD

**Novotel, Shanghai
Day 4, Thursday 22nd March 2018, CTD session**





ASEAN



Organization membership



Brunei



Cambodia



Indonesia



Laos



Malaysia



Myanmar



Philippines



Singapore



Thailand



Việt Nam

ASEAN CTD (ACTD)



- Established in Jakarta (ASEAN Secretariat), **December 2016**
- Guideline of the agreed upon common format for the preparation of a well-structured Common Technical Dossier (CTD) applications that will be **submitted to ASEAN regulatory authorities** for the registration of pharmaceuticals for human use.
- This guideline merely demonstrates an appropriate write-up format for acquired data. However, **applicants can modify**, if needed, to provide the best possible presentation of the technical information, in order to facilitate the understanding and evaluation of the results upon pharmaceutical registration.

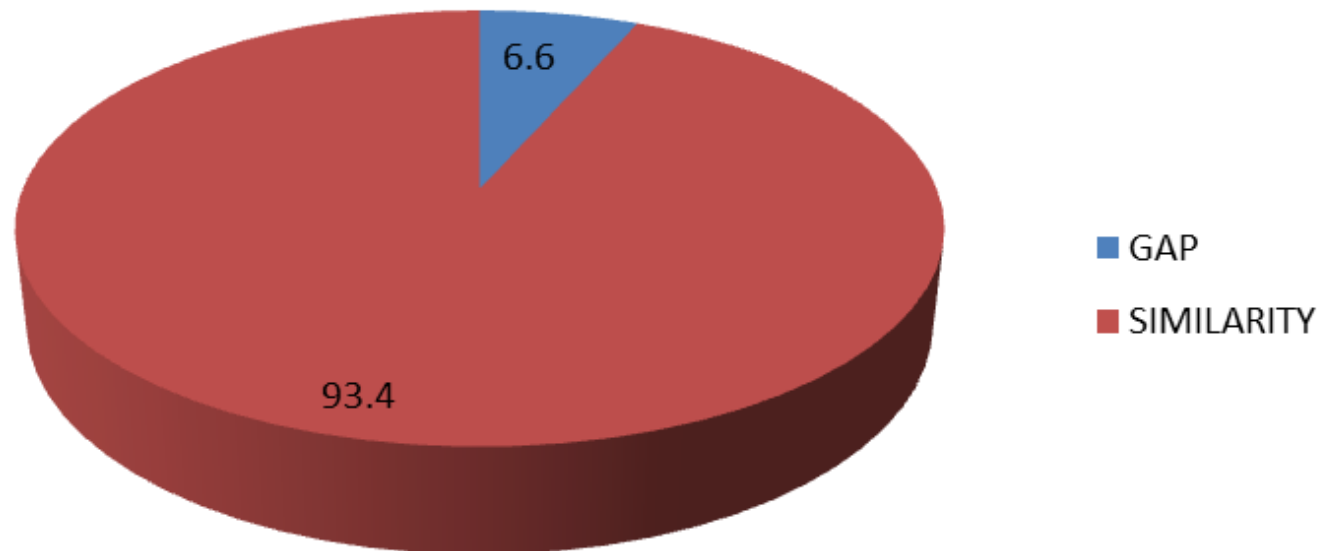
ORGANIZATION Of THE DOSSIER

The Common Technical Document is organized into four parts as follows:

- Part I. Introduction, Table of Contents, Administrative Data and Product Information
- Part II. Quality Document
- Part III. Non-clinical Document
- Part IV. Clinical Document

COMPARISON OF ASEAN – ICH CTD

COMPARISON OF ASEAN - ICH CTD





ASEAN regulatory authorities



Indonesia

No	Product Name	Country	Certificate No.	Date of Registration	Status
1	ANTI VENIN SERUM	Indonesia	GKL8502903743A1	28/04/2015	valid
2	ANTI DIPHTHERIA SERUM 20.000 UI	Indonesia	GKL8502903443A1	08/03/2016	valid
3	ANTI TETANUS SERUM 1.500 UI	Indonesia	GKL8502903542A1	08/03/2016	valid
4	ANTI TETANUS SERUM 20.000 UI	Indonesia	GKL8502903543C1	08/03/2016	valid
5	BIOADS (ANTI DIPHTHERIA SERUM)	Indonesia	DKL1102906743A1	21/06/2016	valid
6	BIOSAT 1.5 (ANTI TETANUS SERUM)	Indonesia	DKL1102906643A1	21/06/2016	valid
7	BIOSAT 20 (ANTI TETANUS SERUM)	Indonesia	DKL1102906643B1	21/06/2016	valid
8	BIOSAVE (ANTI VENIN SERUM)	Indonesia	DKL1102906543A1	21/06/2016	valid
9	BIO-TT (TT VACCINE)	Indonesia	DKL0202905843A1	28/04/2015	valid
10	BIVALENT ORAL POLIOMYELITIS VACCINE	Indonesia	GKL1502907036A1	11/05/2015	valid
11	TYPES 1 & 3	Indonesia	GKL1502907036A1	10/08/2015	valid
12	MEASLES VACCINE	Indonesia	GKL9302900544A1	28/04/2015	valid
13		Indonesia	GKL9302900544B1	28/04/2015	valid
14	DT VACCINE	Indonesia	GKL8502901643A1	21/12/2015	valid
15	DTP VACCINE	Indonesia	GKL8502901743A1	03/03/2015	valid
16	DTP-HB 5 VACCINE	Indonesia	GKL0302906043A1	04/12/2013	valid
17	DTP-HB 10 VACCINE	Indonesia	GKL0302906043B1	24/10/2016	valid
18	FLUBIO (INFLUENZA VACCINE)	Indonesia	DKL0902906343A1	22/01/2015	valid
19		Indonesia	DKL0902906343A1	22/01/2015	valid



ASEAN regulatory authorities



Indonesia

No	Product Name	Country	Certificate No.	Date of Registration	Status
20	HEPATITIS B VACCINE	Indonesia	GKL9802905543A1	18/05/2017	valid
21		Indonesia	GKL9802905543A1	28/04/2016	valid
22		Indonesia	GKL9802905543A1	28/04/2016	valid
23		Indonesia	DKL0302905943A1	10/07/2017	valid
24	MONOVALENT ORAL POLIOMYELITIS VACCINE TYPE 1	Indonesia	GKL0502906136A1	20/11/2015	valid
25	POLIOMYELITIS ORAL VACCINE	Indonesia	GKL9402905436A1	04/08/2015	valid
26		Indonesia	GKL9402905436A1	18/09/2015	valid
27		Indonesia	GKL9402905436A1	18/09/2015	valid
28	ADSORBED Td Vaccine	Indonesia	GKL0802901643B1	14/11/2013	valid
29		Indonesia	GKL0802901643B1	01/04/2014	valid
30		Indonesia	GKL0802901643B2	25/11/2014	valid
31	TT VACCINE	Indonesia	GKL8502901443A1	31/05/2013	valid
32	BIO Td	Indonesia	DKL1302906843A1	04/01/2018	valid
33	BCG VACCINE (FREEZED DRIED)	Indonesia	GKL85029000444A1	05/12/2013	valid
34		Indonesia	GKL85029000444A1	05/12/2013	valid
35	Pentabio (DTP-HB-HIB)	Indonesia	DKL1302906943A1	14/11/2013	valid
36		Indonesia	DKL1302906943A1	14/06/2013	valid
37		Indonesia	DKL1302906943A1	21/12/2015	valid
38	DTP-HB-Hib	Indonesia	GKL1502907143A1	04/01/2016	valid



ASEAN regulatory authorities



Indonesia

- Registration Process in Indonesia based on Indonesian NRA regulation No. 24, 2017, on the subject of drug registration procedure (Peraturan Kepala Badan Pengawas Obat dan Makanan RI No. 24 Tahun 2017 Tentang Kriteria dan Tata Laksana Registrasi Obat)
- **ASEAN CTD** and **ICH CTD** format are accepted



ASEAN regulatory authorities



Thailand

No	Product name	Countries	Date of registration (initial)	Certificate No	Status*)
1	Bio TT Vaccine	Thailand	11-Jun-04	1C 106/47	Valid
2	TT Vaccine 10 ds	Thailand	01-Nop-03	1C 236/46	Valid
3	Bio Td Vaccine	Thailand	24-Feb-16	2C 1/59 (B)	Valid
4	Adsorbed Td Vaccine 1 ds	Thailand	07-Jul-14	2C 4/55 (B)	Valid
5	Adsorbed Td vaccine 10 ds	Thailand	13-Dec-12	2C 4/55 (B)	Valid
6	DT vaccine 10 ds	Thailand	11-Jun-04	2C 29/47	Valid
7	DTP vaccine 10 ds	Thailand	30-Sep-04	2C 63/47	Valid
8	DTP-HB vaccine 10 ds	Thailand	03-Feb-06	2C 57129/56 (NB)	Valid
9	mOPV1 vaccine 20 ds	Thailand	18-Okt-07	1C 267/50	Valid
10	bOPV types 1 dan 3 20 ds	Thailand	21-Mar-16	2C 2/59 (B)	Valid
11	Measles vaccine 10 ds	Thailand	22-Jun-06	1C 173/49	Valid
12	OPV 10 ds	Thailand	20-May-05	2C 36/48	Valid
13	OPV 20 ds	Thailand	27-Mar-06	2C 20/49	Valid
14	Pentabio 1, 5 and 10 ds	Thailand	17-Jan-2018	2C 2/61 (NBC)	Valid

*) Valid as long as import license provided



ASEAN regulatory authorities



Thailand

Name of countries	Dossier	FORMAT	Year of submission
Thailand	ACTD Td 10 DS/2009	ASEAN CTD	2009
	ACTD Measles 10 DS/2009	ASEAN CTD	2009
	ACTD TT 10 DS/2010	ASEAN CTD	2010
	ACTD DTP-HB 10 DS/2010	ASEAN CTD	2010
	ACTD RTF/final bulk Td/2013	ASEAN CTD	2013
	CTD bOPV (I-CTD-ICH/bOPV/November 2013)	ICH CTD	2013
	I/CTD/ICH/Td/July 2013	ICH CTD	2014
	I/CTD-ICH/PENTABIO/APRIL 2014)	ICH CTD	2014

Note:

ASEAN CTD was accepted. However, Thai FDA tend to request ICH CTD in the recent years.



ASEAN regulatory authorities



Malaysia

No	Product name	Countries	Date of registration (initial)	Certificate No	Status
1	TT Vaccine 10 ds	Malaysia	05-Agust-04	MAL20041042A	Valid
2	DT vaccine 10 ds	Malaysia	05-Agust-04	MAL20041069A	Valid
3	DTP vaccine 10 ds	Malaysia	5-Agust-04	MAL20041068A	Valid
4	Measles vaccine 10 ds	Malaysia	27-Mei-04	MAL20040877A	Valid
5	OPV 10 ds	Malaysia	09-Sep-04	MAL20041126A	Valid
6	OPV 20 ds	Malaysia	09-Sep-04	MAL20041126A	Valid
7	Bio TT Vaccine	Malaysia	28-Jan-16	-	In process registration
8	Pentabio Vaccine 1, 5, 10 ds	Malaysia	31-Des-15	-	In process registration
9	bOPV types 1 and 3 20 ds	Malaysia	15-Des-15	-	In process registration
10	bOPV types 1 and 3 10 ds	Malaysia	15-Des-15	-	In process registration
11	Adsorbed Td vaccine 10 ds	Malaysia	28-Jan-16	-	In process registration



ASEAN regulatory authorities



Malaysia

Name of countries	DOSSIER	FORMAT	Year of submission
Malaysia	I-CTD-ACTD-bOPV-OCTOBER 2015(bOPV 20 ds)	ASEAN CTD	2015
	I/CTD-ICH/PENTABIO/APRIL 2014)	ICH CTD	2015
	II-CTD-ACTD-Td-NOVEMBER 2015	ASEAN CTD	2016
	I-CTD-ACTD-TT-OCTOBER 2013	ASEAN CTD	2016
	I-CTD-ACTD-bOPV 10-JANUARY 2016 (Bopv 10)	ASEAN CTD	2016

Note:

ASEAN and ICH CTD are accepted by Malaysia Authority



Việt Nam

ASEAN regulatory authorities



No	Product name	Countries	Date of registration (initial)	Certificate No	Status
1	Diphtheria Bulk (DAM)	Vietnam	29-Des-09	QLVX-0284-09	Renewal
2	Tetanus Bulk (TAM)	Vietnam	24-Nop-08	QLVX-0146-08	Renewal
3	Pertussis Bulk (PFB)	Vietnam	29-Des-09	QLVX-0285-09	Renewal
4	Bio TT Vaccine	Vietnam	24-Nop-08	QLVX-0145-08	Renewal



ASEAN regulatory authorities



Philippines

No	Product name	Countries	Date of registration (initial)	Certificate No	Status
1	Bio TT Vaccine	Philippines	25-Nop-08	BR-663	Valid
2	DTP-HB vaccine 10 ds	Philippines	25-Nop-08	BR-662	Renewal
3	OPV 10 ds	Philippines	20-Feb-12	BR-847	Expired
4	-	Philippines	23-Mei-17	CDRR-NCR-DI/W-1872	GMP certification-Valid
5	Adsorbed Td vaccine 10 ds	Philippines	04-Des-13	-	In process registration



ASEAN regulatory authorities



Philippines

Name of countries	DOSSIER	FORMAT	Year of submission
Philippine	ACTD Measles 10 DS/2009	ASEAN CTD	2009
	ACTD OPV/2009	ASEAN CTD	2009
	I/CTD-ACTD/Td/November 2013	ASEAN CTD	2013

Note:

Philippines accepts ASEAN CTD. Bio Farma is having no experience using ICH CTD in registration process to Philippines.



ASEAN regulatory authorities



Myanmar

No	Product name	Countries	Date of registration (initial)	Certificate No	Status
1	Bio TT Vaccine	Myanmar	28-Agust-06	1108 A 8909	Renewal
2	Adsorbed Td Vaccine 1 ds	Myanmar	16-Jun-16	2106AA9638	Valid
3	Tetanus Toxoid bulk (PTT)	Myanmar	22-Des-17	-	In process registration
4	bOPV types 1 and 3 10 ds	Myanmar	30-Jun-16	-	In process registration
5	Adsorbed Td vaccine 10 ds	Myanmar	29-Mei-15	-	In process registration



ASEAN regulatory authorities



Myanmar

Name of countries	DOSSIER	FORMAT	Year of submission
Myanmar	I/CTD-ACTD/Td/November 2013	ASEAN CTD	2013
	I-CTD-ACTD-bOPV 10-JANUARY 2016 (Bopv 10)	ASEAN CTD	2016
	I/CTD-ICH/PTT/DECEMBER 2017	ICH CTD	2017

Note:

Myanmar accepts ASEAN and ICH CTD

ASEAN regulatory authorities



No	Product name	Countries	Date of registration (initial)	Certificate No	Status
1	Bio TT Vaccine	Laos	27-Jun-07	06 I 2932/07	Renewal
2	Adsorbed Td vaccine 1 ds	Laos	04-Des-13	-	In process registration
3	bOPV types 1 and 3 20 ds	Laos	24-Mar-17	-	In process registration
4	bOPV types 1 and 3 10 ds	Laos	24-Mar-17	-	In process registration
5	Adsorbed Td vaccine 10 ds	Laos	04-Des-13	-	In process registration



ASEAN regulatory authorities



Name of countries	DOSSIER	FORMAT	Year of submission
Laos	I/CTD-ACTD/Td/November 2013	ASEAN CTD	2013

Note:

Laos accepts ASEAN CTD. Bio Farma is having no experience using ICH CTD in registration process to Laos.



Cambodia

ASEAN regulatory authorities



No	Product name	Countries	Date of registration (initial)	Certificate No	Status
1	Bio TT Vaccine	Cambodia	15-Jan-07	039/07	Valid



ASEAN regulatory authorities



Cambodia

Name of countries	DOSSIER	FORMAT	Year of submission
Cambodia	ACTD BIO TT/2010	ASEAN CTD	2012

Note:

Cambodia accepts ASEAN CTD. Bio Farma is having no experience using ICH CTD in registration process to Cambodia.



ASEAN regulatory authorities



Singapore

No	Product name	Countries	Date of registration (initial)	Certificate No	Status
1	TT Vaccine 10 ds	Singapore	8-Jul-2015	x	Process was terminated
2	Bio TT 1 ds	Singapore	8-Jul-2015	x	Process was terminated



ASEAN regulatory authorities



Singapore

Name of countries	DOSSIER	FORMAT	Year of submission
Singapore	I-CTD-ACTD-TT-OCTOBER 2013	ASEAN CTD	2015

Note:

Format was not an issue. Insufficient clinical studies was highlighted.

We, Novem Healthcare Pte Ltd, having principal place of business at Solstice Business Center, 23 New Industrial Road #03-08 Singapore 536209, hereby state that TT (TT 10ds vaccine from PT. Bio Farma (Persero), at Jalan Pasteur No. 28 Bandung 40161-Indonesia) registration in Singapore is no longer continued. Based on the reasons found during pre-registration consultation process with the Health Sciences Authority, Therapeutic Products Branch, Singapore, the available clinical studies are insufficient to support vaccines registration and hence the dossier could not be accepted for registration in Singapore.



[Brunei](#)

ASEAN regulatory authorities



- Bio Farma is currently not having registered product in Brunei.

ASEAN CTD for Non ASEAN Countries



- ASEAN CTD also accepted in Non ASEAN countries.
- Bio Farma registered bOPV 10 doses and 20 doses to **Ghana** and approved on 2 October 2017 using ASEAN CTD
- Bio Farma registered bOPV 20 doses, mOPV 1 20 doses, OPV 10 and 20 doses to **Nigeria**, approved on 7 August 2012 (bOPV and OPV) and 31 May 2007 (mOPV 1)

ASEAN CTD for Non ASEAN Countries



- Bio Farma registered DTP-HB 10 and TT vaccine in Egypt, approved on 24 June 2015 and 17 June 2015 respectively, using ASEAN CTD

Conclusion



- **Format** is not always be an issue in submitting registration.
- The most challenging part in registration is having different references in particular **subject**. For example: for stability study, NRA might refer to general pharmaceutical product which consider humidity as environmental factor, in addition to temperature; whereas in vaccine, temperature should be the only environment factor considered.

WHO TRS 962 Annex 3 Guidelines for stability evaluation of vaccines, page 179, it is mentioned that *“Among the environmental factors considered to influence pharmaceuticals, the only one that affects characteristics of all vaccines over time is temperature. The impact of humidity is not relevant for the vast majority of vaccines due to their liquid formulation, and the protective nature of the packaging, providing that the closure system of the vial or ampoule is appropriate”*.

Conclusion



- Other issue might also arise during registration is the incomplete data for old product. Example: Having no data in pre-clinical and limited data in clinical study. Bio Farma had experience with Singapore authority in TT Vaccine registration and the process was terminated due to insufficient clinical studies.

We, Novem Healthcare Pte Ltd, having principal place of business at Solstice Business Center, 23 New Industrial Road #03-08 Singapore 536209, hereby state that TT (TT 10ds vaccine from PT. Bio Farma (Persero), at Jalan Pasteur No. 28 Bandung 40161-Indonesia) registration in Singapore is no longer continued. Based on the reasons found during pre-registration consultation process with the Health Sciences Authority, Therapeutic Products Branch, Singapore, the available clinical studies are insufficient to support vaccines registration and hence the dossier could not be accepted for registration in Singapore.

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Thank You