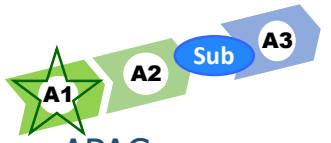
2018 Good Registration Management
Regulatory Science
Center of Excellence Pilot Workshop

Planning of Application

Speakers: Krisana Winitthumkul , Roche/PReMA
Kanokwon Prasitporn, Siam Bheasach /TIPA

Date: 27 June 2018

Disclaimer



The training information and views expressed in this presentation are derived from APAC, we have adapted the case study and do not reflect the views of any other organization.

Thank You for all original source of data and presentation from APAC members

- Sannie Chong
Head, APAC Technical Regulatory Policy,Roche

- Thean Soo (TS) Lo
AP Lead, Global Regulatory Policy & Intelligence,Janssen J&J

- Rosa Fu, Eli Lilly

Thank You for our Thai working group
Wadcharaporn Pothisorn
Head, Regulatory affairs, Mega Lufescineces public co., Ltd., **TPMA**

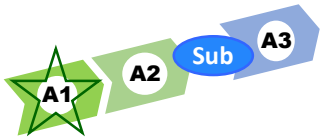
- Thongchai Chomsiri
Assistant RA QA Mgr., Sriprasit Pharma Co.,Ltd, **TPMA**

- Pongparyom Pahulrat
Research and Quality Assurance section officer,Defence Pharmaceutical, **TIPA**

- Duangkamol Tipkate
Senior RA Specialist, Baxter manufacturing (Thailand) Co.,Ltd.,**TIPA**

- Supattra Chirarutsami
Regulatory Affairs, **RAPAT**

Agenda



8:30~8:40	introduction	Krisana
8:40~9:00	What do we want	Krisana
9:00~9:20	What do we need	Kanokwon
9:20~9:40	How do we do it	Kanokwon
9:40~9:50	Q&A	Krisana, Kanokwon
9:50~10:00	Break	
10:05~12:00	Case study	

Glossary

- APEC Asia-Pacific Economic Cooperation
- APAC Asia Partnership Conference of Pharmaceutical Associations
- GSubP Good Submission Practice
- IND Investigational New Drug Application
- NDA New Drug Application
- NGDA New Generic Drug Application
- POC Proof of concept
- TPP Target Product Profile
- TPL Target Product Label
- GRL Global Regulatory Lead
- CMC Chemical Manufacturing Control
- DCDS Developmental Core Data Sheet
- CCDS Company Core Data Sheet
- R&R Role and responsibility
- CoPP Certificate of pharmaceutical product

APEC GSubP Guideline

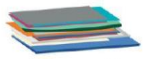
2. PRINCIPLES OF GOOD SUBMISSION

1. Strong Scientific Rationale and Robust Data with Clarification of Benefit-Risk Profile
2. Compliance to Up-to-d
3. Well-Structured Submi
   Appropriate Cross-refe
4. Reliability, Quality, Inte
   Submission Document
5. Effective and Efficient

APAC Asia Partnership Conference of Pharmaceutical Associations

3. MANAGEMENT OF SUBMISSION

- Planning for submission
  - Start discussion on submission strateg[illegible] ***early stage of product development***
  - Use ***support tools*** effectively e.g. check-list, template, glossary
- Preparation and Submission of Application Dossier
  - Provide general instructions on ***report/summary writing, compiling and submission***
  - Encourage creating ***SOPs***
- Quality Check
  - Provide instructions on QC at writing/revision/translation for,
    - ✓ ***Study reports and summary documents***
    - ✓ ***Submission dossier, Electronic dossier***



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ith review authorities
*of **pre-/post- submission***
***nd response** appropriately*
timeline management
amongst applicants
***model, role and responsibility** of*
m & members
working procedure and communication platform

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APEC GSubP Guideline

2. PRINCIPLES OF GOOD SUBMISSION

1. Strong Scientific Rationale and Robust Data with Clarification of Benefit-Risk Profile
2. Compliance to Up-to-date Regulatory Requirements
3. Well-Structured Submission Dossier with Appropriate Cross-references
4. Reliability, Quality, Integrity and Traceability of Submission Documents and Source Data
5. Effective and Efficient Communications

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3. MANAGEMENT OF SUBMISSION

- *Planning for submission*
  - *Start discussion on submission strategy from **early stage of product development***
  - *Use **support tools** effectively e.g. check-list, template, glossary*
- *Preparation and Submission of Application Dossier*
  - *Provide general instructions on **report/summary writing, compiling and submission***
  - *Encourage creating **SOPs***
- *Quality Check*
  - *Provide instructions on QC at writing/revision/translation for,*
    - ✓ ***Study reports and summary documents***
    - ✓ ***Submission dossier, Electronic dossier***

4. COMMUNICATIONS

- *Communications with review authorities*
  - *Make effective use of **pre-/post- submission meetings***
  - *Manage **inquiry and response** appropriately e.g. clarifications, timeline management*
- *Communications amongst applicants*
  - *Confirm **operation model, role and responsibility** of the submission team & members*
  - *Establish **standard working procedure and communication platform***

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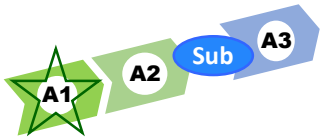
Planning of submission



Purpose of planning

- Give **clear strategic direction** for submission
- **Prepare necessary tools** for submission
- In **compliance with regulatory** requirements

Planning of submission (prior to dossier preparation)

- What do we **want**?
- What do we **need**?
- How do we **do** it?

Planning of submission (prior to dossier preparation)

- **What do we want?**
- What do we need?
- How do we do it?

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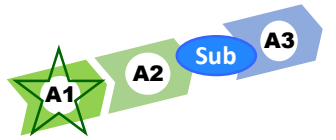
Planning of submission

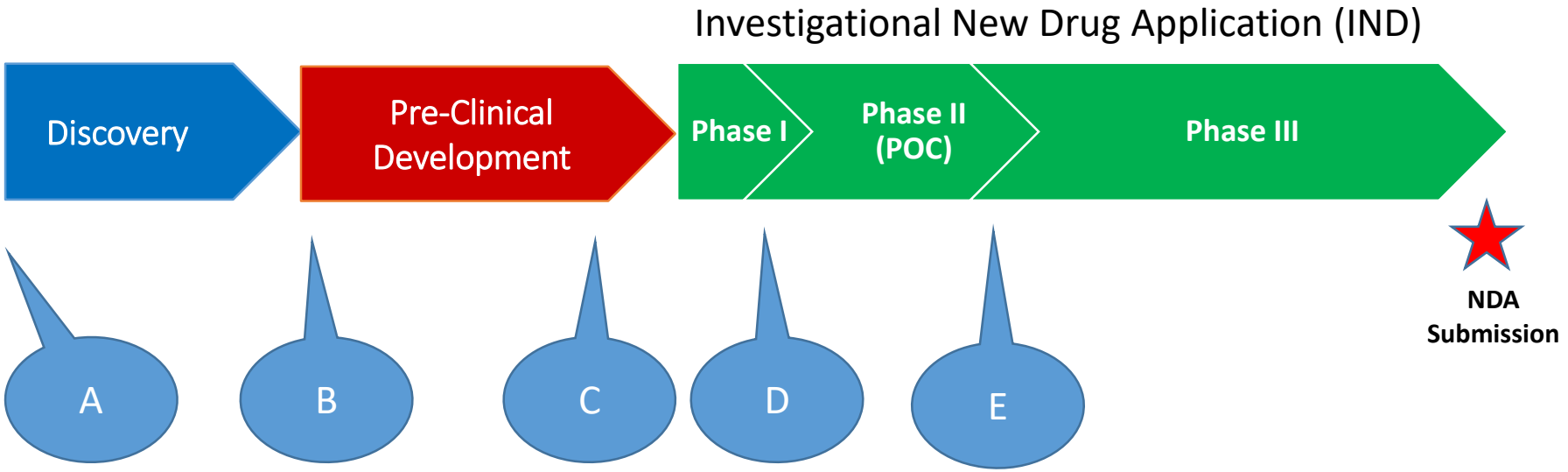
What do we want?

27-Jun-2018

Krisana Winitthumkul , Roche/Prema

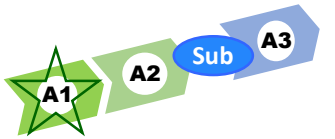
When do we start the planning for submission?

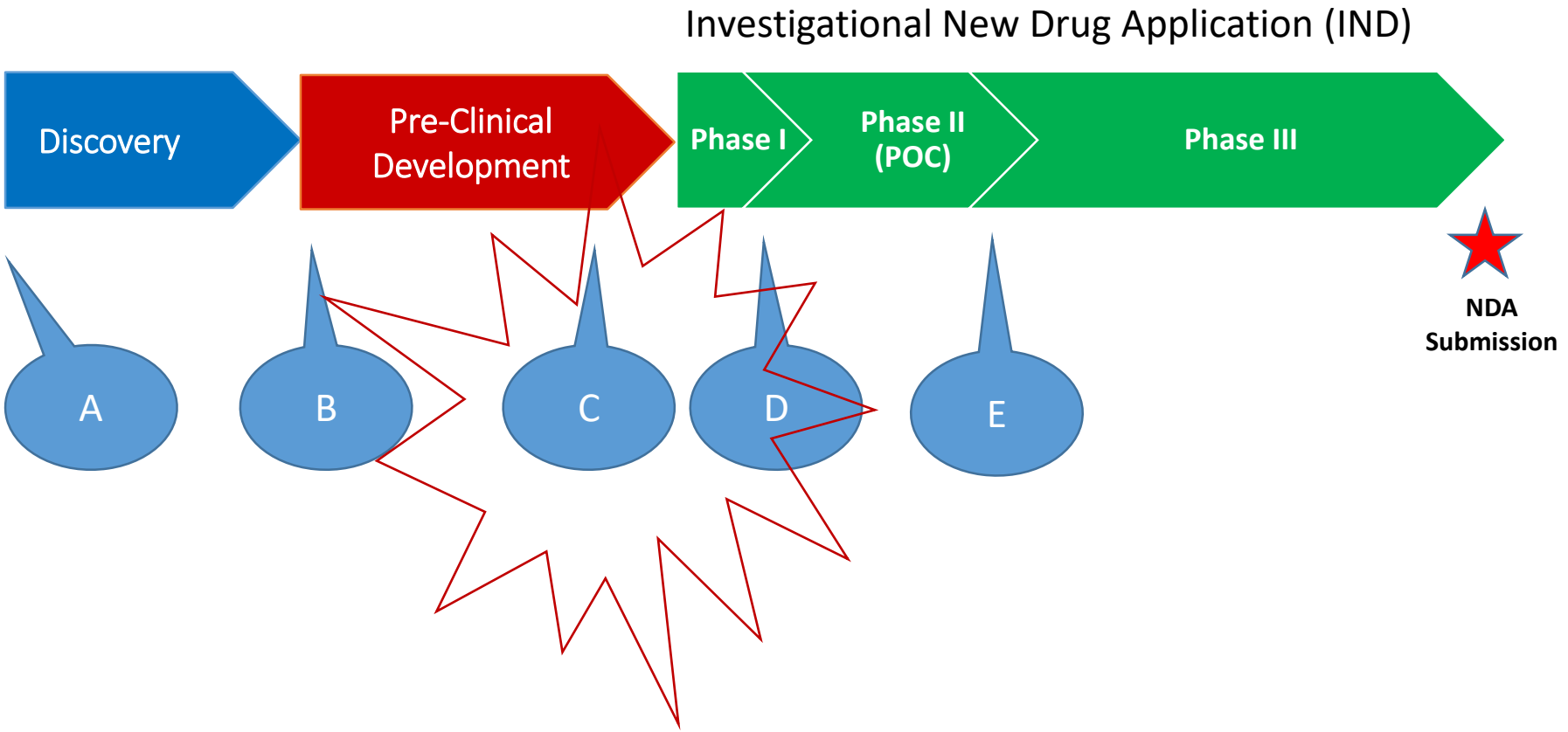




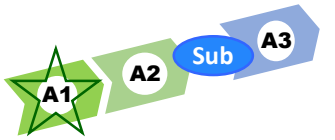
Full Team engaged†

When do we start the planning for submission?



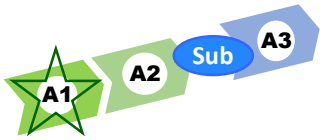


Target Product Profile (TPP)



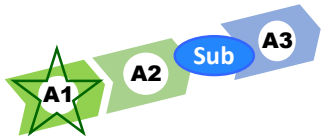
- Definition
  - A TPP is a format for a summary of a drug development program described in terms of labeling concepts.
  - Beginning with the goal! Set the "goalposts" for what we believe will be required to be successful in the marketplace and thus informs our clinical development program / other evidence-generation activities for specific indications.
- Purpose
  - Can be developed as early as the pre-IND phase
  - A TPP could be prepared by a sponsor and then shared with the FDA review staff to facilitate communication regarding a particular drug development program.

Target Product Profile (TPP)



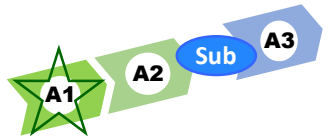
- High-Level TPP
  - Can be developed as early as the pre-clinical stage
  - Information about what any new product would have to aim to deliver to demonstrate meaningful clinical benefit in support of a differentiated value proposition in a disease state
- Global TPP
  - The Global TPP that would apply to any new drug in an indication will be required prior to Phase II
  - Reflects the targeted commercially viable profile
  - Cover all key regions in the world
  - Should change only when substantial environmental or competitive events take place

Target Product Profile (TPP)



- Regional or Country TPP
  - Support Clinical and Commercial decision-making, and informs forecasts based on current data about the asset
  - Defines expected local attributes of an investigational drug candidate
  - Based on existing pre-clinical, clinical, epidemiologic and other data available at the time
  - Reflect the profile of the product most likely to launch, incorporating the latest local information available
  - Be informed by the continuously growing body of clinical evidence, and may change over time

TPP generation process



IND

NDA

Discovery

Pre-Clinical Development

Phase I

Phase II (POC)

Phase III

Submission

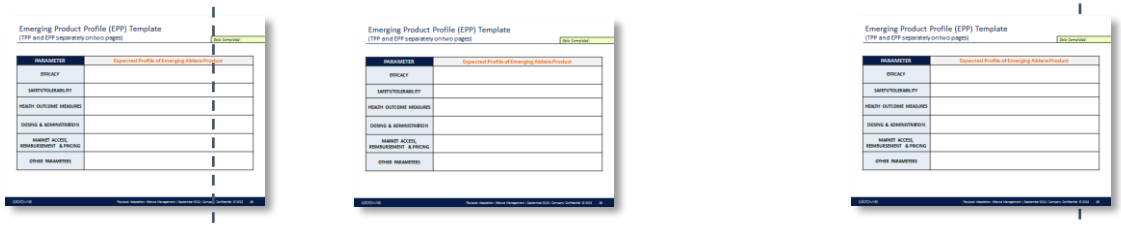
High Level Target Product Profile

Global TPP

Region/ Country TPP

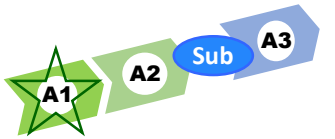
Early clinical data

PoC study data



Full Team engaged†

Target Product Profile (TPP) Template



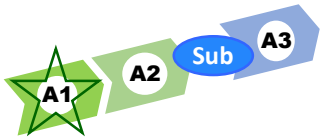
EXAMPLE

Date Completed:

PARAMETER	Expected Profile of Target Product
EFFICACY	
SAFETY/TOLERABILITY	
DOSING & ADMINISTRATION	
MARKET ACCESS, REIMBURSEMENT & PRICING	
OTHER PARAMETERS	

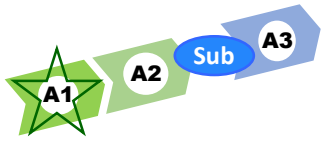
Reflects the profile of the product most likely to launch, incorporating the latest data from all functions

Key consideration of TPP



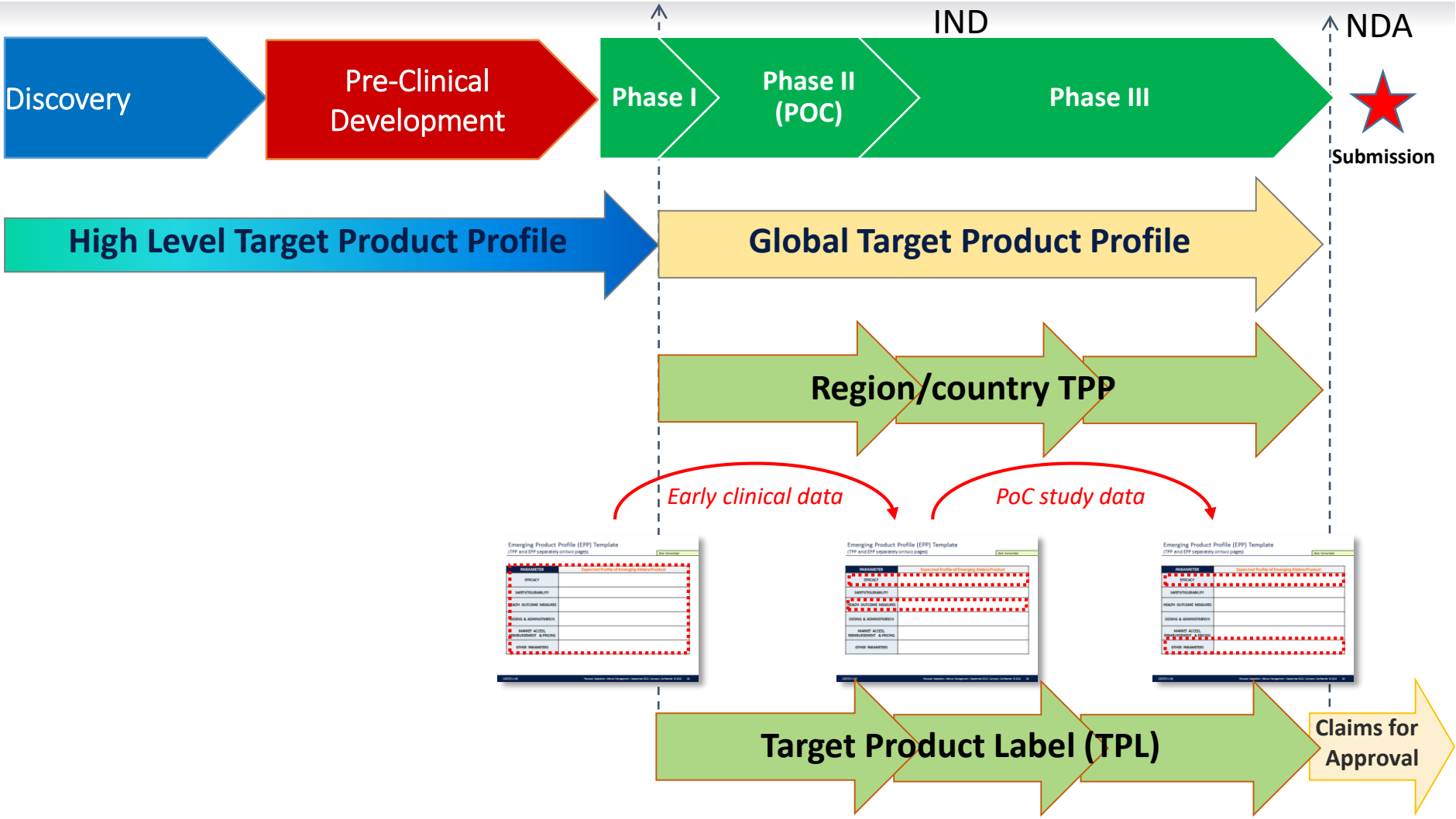
- Can include low, mid, high case in the global TPP for different potential clinical outcomes.
- Possibility for regional/country specific ones
- Global TPP will not be changed frequently unless significant change happened such as regulatory environment change
- Regional/Country TPP can be changed based on the accumulation of clinical evidence

Target Product Label (TPL)

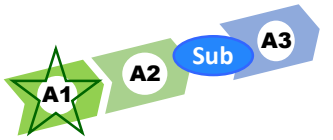


- Begins by capturing categories of claims, but, does not define exact language to be used, supported by proposed and/or completed clinical protocols
- Evolves into claim language representing the best understanding of what to expect to use in materials based on prospective label
- Ends in claim language which is “ready to use” in materials- refined and specific based on anticipated label
- Used to create the Developmental Core Data Sheet (DCDS), then, the Company Core Data Sheet (CCDS)

TPP/TPL generation process

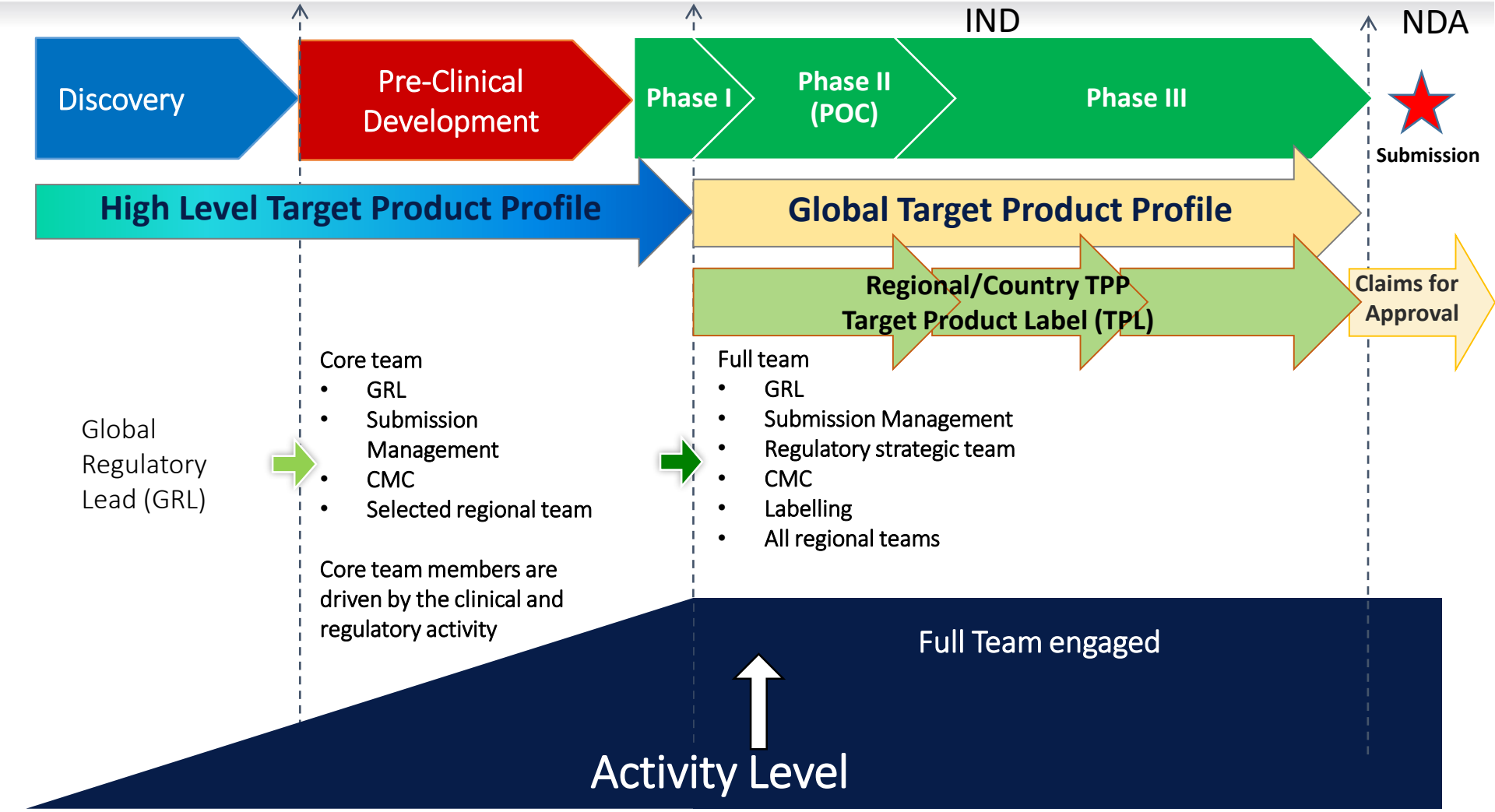


Organizational preparation

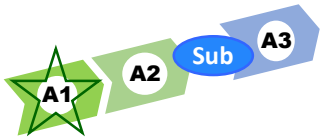


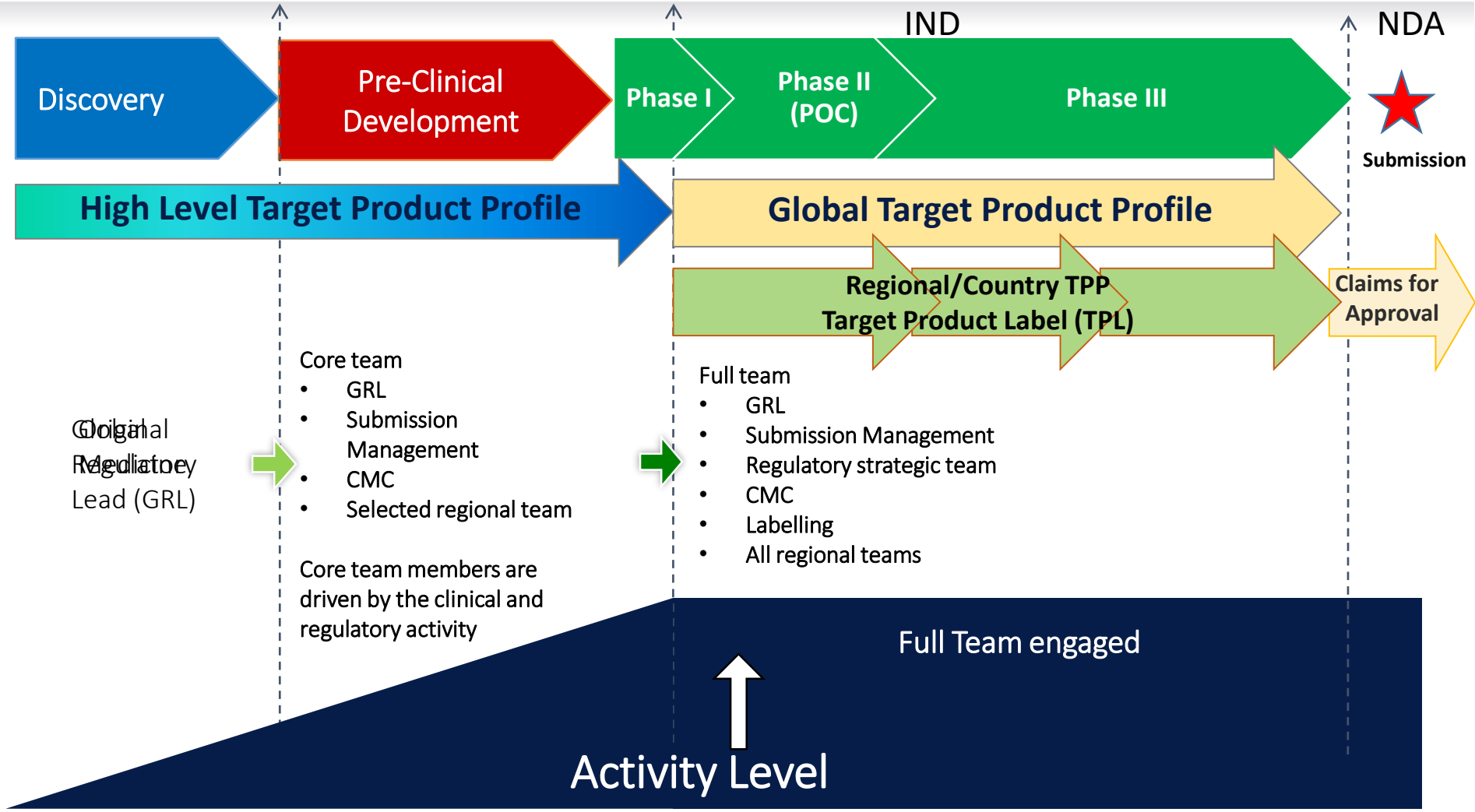
- Key regulatory related functions:
  - Global regulatory lead
  - Submission management
  - CMC
  - Regional/Country team
  - Regulatory strategy team
  - Labelling
- Other important functions:
  - Commercial, Safety, Medical, Clinical, PM
- The level of involvement is increasing with the progress of development

Organizational preparation

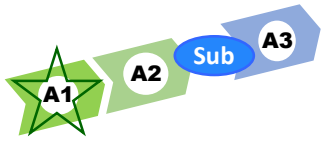


Organizational preparation



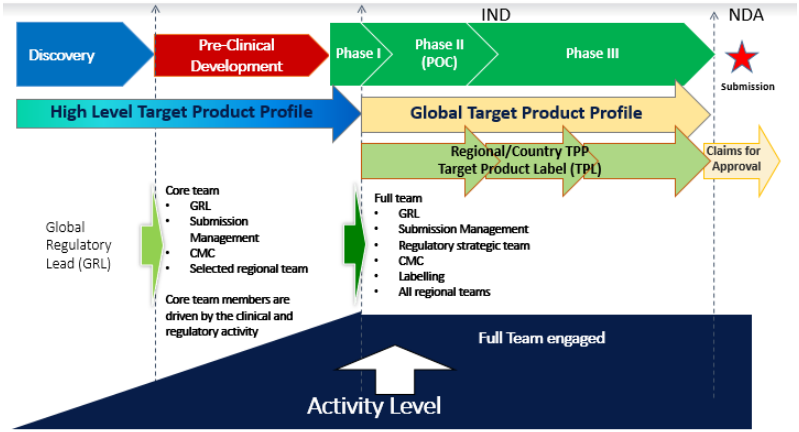


Apply the concept to New Generic



- Prioritize Potential Medicine
- Prioritize Target product (Patented expired)
- Capability of the Manufacturer equipment
- Capacity of the Marketing and sale team
- Plan for Bio Study required
  (BE Study, Biowaiver)

Organizational preparation for NDA



Organizational preparation

NGDA= New Generic Drug Application

New Drug

New Generic

NGDA

Patent expired

Submission and Aprroval

Launch

Launch

Global Target Product Profile

Regional/Country TPP
Target Product Label (TPL)

Product &Claims for Approval

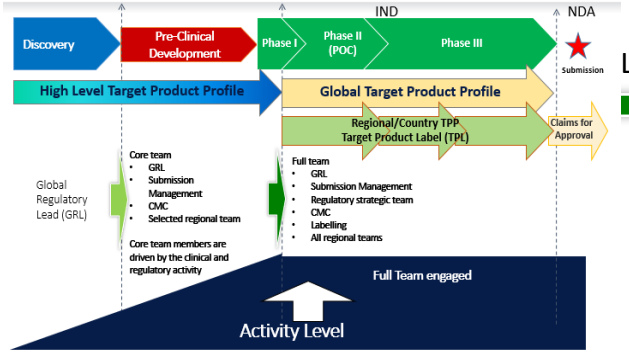
Full team

- Company Strategic team (Owner, R&D,MKT, PD,QC/QA, Purchasing, RA etc.)
- R&D formula & analytical dev
- Country Regulatory Leader
- CMC Team
- **Submission Management**
- **BE/PE study team (if applicable)**

Full Team engaged

Activity Level

Organizational preparation for NDA



Planning of submission (prior to dossier preparation)

- What do we want?
- **What do we need?**
- How do we do it?

2017 Good Registration Management Regulatory Science Center of Excellence Workshop

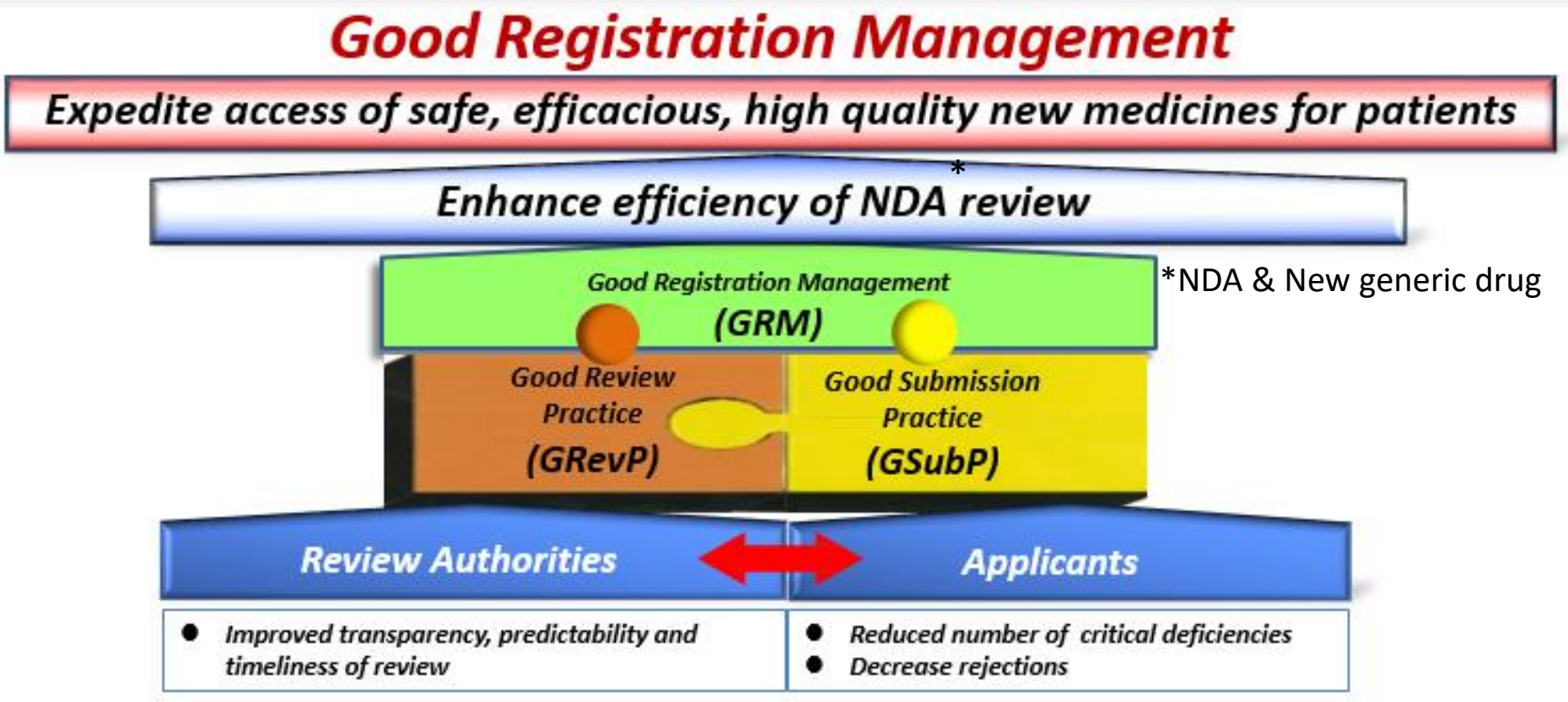
Planning of submission

What do we need?

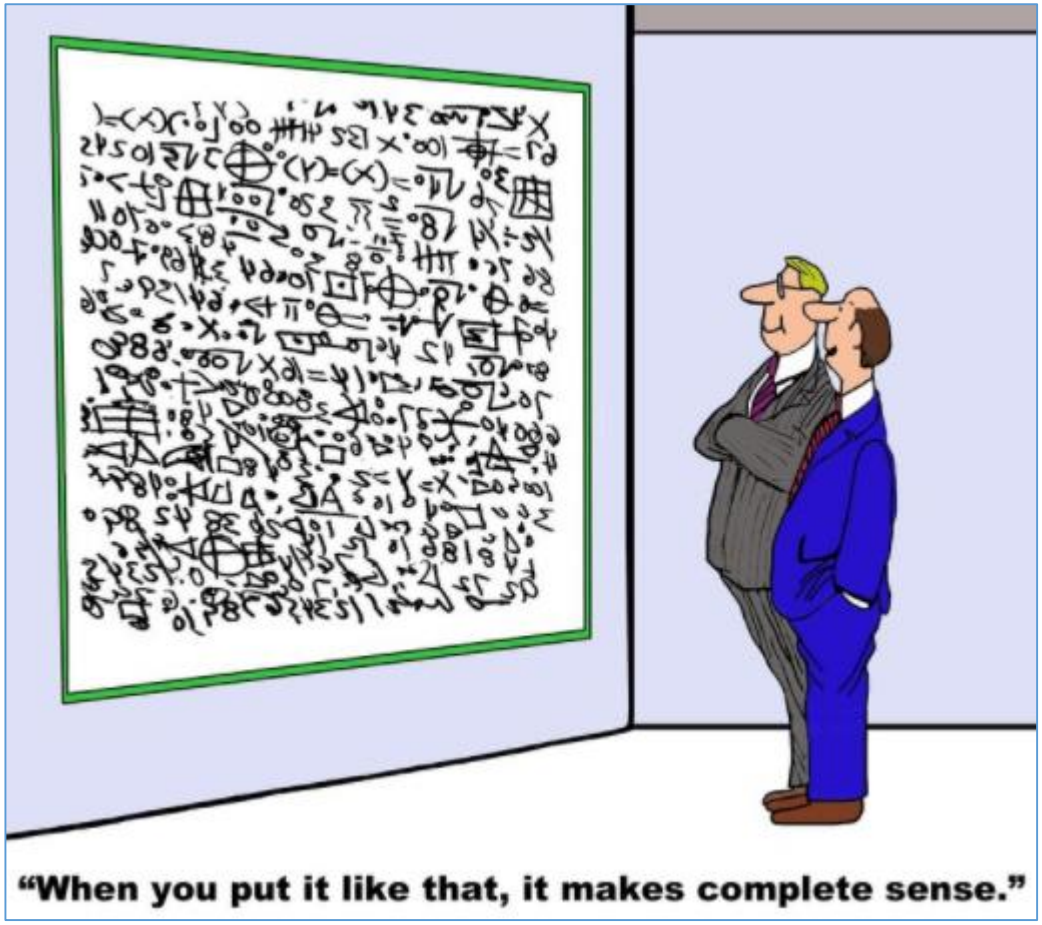
27-Jun-2018

Kanokwon Prasitporn
Director, Regulatory Affairs
SiamBheasach/TIPA Thailand

Good Submission Practice

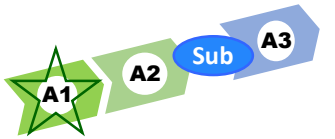


Good Submission Practice



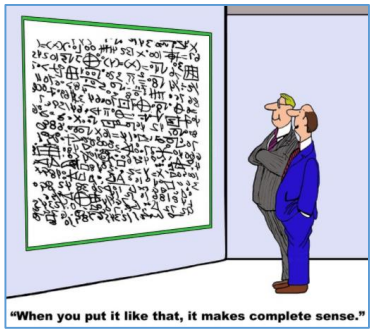
The goal of
Good Submission Practice is to enhance **efficiency** and **quality** of medical product **registration process** which leads to enhance **early access** to these products by patients.

Good Submission Practice Guideline



Good Submission Practice
(GSubP)
Guideline for Applicants

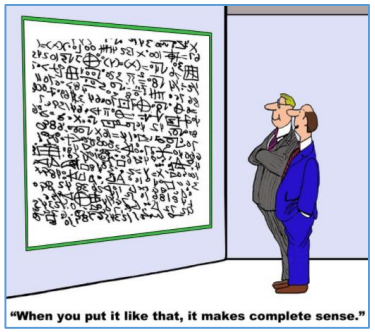
APEC RHSC



Good Submission Practice Guideline

Section 2 - Key Principles of Good Submission

- Clear story, Strong Scientific Rationale and Robust Data with Clarification of Benefit-Risk Profile
- Compliance to Up-to-date Regulatory Requirements
- Well-Structured, Clear & Concise Submission Dossier with Appropriate Cross-references for ease of review
- **R**eliability, **Q**uality, **I**ntegrity and **T**raceability of Submission Documents and Source Data
- Effective and Efficient Communications (with FDA & internal organization)



Good Submission Practice Guideline

Key Principles of a Good Submission

Clear Story and Rationale of Benefit-Risk Profile Based on Scientific Evidence:

A good submission has clear story and rationale with robust scientific evidence as well as integrity, relevance and completeness of technical data.

The nature of the benefits and types of risks should be clarified with sound evidence.

Compliance to Up-to-date Regulatory Requirements:

A good submission is made in compliance with the up-to-date regulations nationally and regionally. In addition, it should keep reasonable consistency with internationally harmonized regulatory standards.

Well-Structured and Reviewer Friendly Submission Dossier:

A good submission will be made with well-structured dossier complying with the required format in that economy. For ease of review, it is encouraged to make each technical and summary document clear, concise and use appropriate cross-references in the dossier.

Reliability, Quality, Integrity and Traceability of Submission Documents and Source Data:

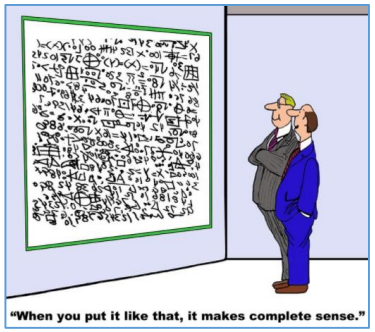
A good submission is made ensuring the reliability, quality, integrity, and traceability of information and data described in submission documents and source data.

Effective and Efficient Communications (with the Review Authorities and within the Applicants' Organization):

A good submission can only be achieved by keeping effective and efficient communications with the review authorities throughout the product development and registration process. In addition, good communications within the applicants' organization(s) are essential for successful submission and approval.

Good Submission Practice
(GSubP)
Guideline for Applicants

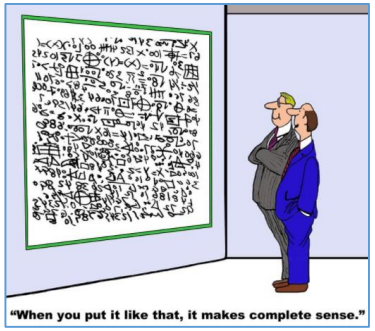
APEC RHSC



Good Submission Practice Guideline

Section 3.1 - Planning for Submission

- In order to plan and manage an application submission efficiently, applicants are recommended to prepare and use the following tools.
  - Checklist
  - Glossary
  - Template
  - Timeline Table



Good Submission Practice Guideline

3.1 *Planning for Submission*

Preparation for application submission usually starts with planning phase. As noted, submission for product registration generally takes place in the last stage of lengthy product development process. Even so, applicants need to initiate discussions on submission strategy from an early stage of product development and establish a clear strategy for submission. Clarification of product profile is a critical part of such strategic discussions. For that purpose, some companies use a document so-called 'Target Product Profile', a summary format of a drug development program described in terms of labeling concepts.

It is also important for applicants to study and understand the up-to-date regulatory standards, guidelines and regulations in each stage of product development, and conduct clinical and non-clinical studies in compliance with them. It should be noted that progress has been made in regulatory convergence and harmonization by regional and international cooperation scheme among the regulatory authorities, e.g. ICH and ASEAN pharmaceutical harmonization. It is necessary that applicants keep eyes on not only local but also regional and international standards, guidelines and regulations, and update their own submission strategy accordingly.

In order to plan and manage an application submission efficiently, applicants are recommended to prepare and use the following tools.

Check-list:

Applicants are encouraged to make use of a kind of check-list which covers all required components to be incorporated into submission dossier. Such list is useful not only to check if there is any missing component but also to manage the whole process of submission preparation efficiently

Glossary:

It is important to keep consistency of terminology used throughout a submission dossier. Applicants are recommended to create a list of general glossary before initiating preparation of technical documents and summaries.

Template:

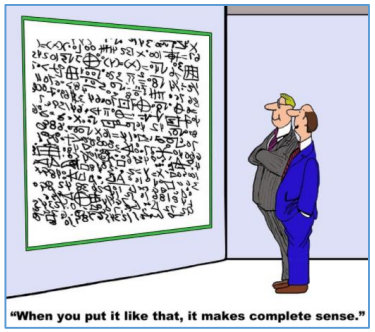
Templates help the author to prepare each component document in structured and consistent manner. It will also enhance efficiency of preparation. Submission with defined format of technical documents and summaries also enables reviewers to perform review smoothly.

Timeline table:

Development and management of timeline is one of the most important tasks in submission planning phase especially when the submission is performed by collaborations among multiple parties of applicants. It is recommended that applicants generate and keep updating a timeline table or a Gantt chart to manage the whole process of submission preparation.

Good Submission Practice
(GSubP)
Guideline for Applicants

APEC RHSC



Developing your GSubP "Needs"

Planning Your Submission

Your Needs: Submission Plan

Identify Specific Needs

Build/Develop Your Tools

Developing your GSubP "Needs"

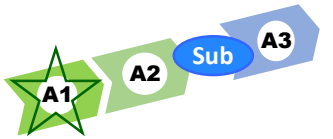
Planning Your Submission Methodology

Your Needs: Submission Plan → **Identify Specific Needs** → **Build/Develop Your Tools**

Review your product development plan	Identify your specific Needs	How should you proceed to meet these needs?

Product Development Plan

Developing your GSubP "Needs"

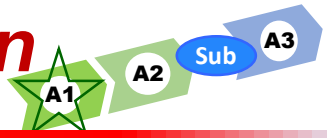


Planning Your Submission Methodology

1. Reference Your Product Development Plan
2. Identify Your Submission Needs
3. Specify Actions to Meet Needs
4. Identify Activity List for Each Action

5. Your Final Submission Plan

1. Reference Your Product Development Plan



R&D

Commercial

Supply Chain

Key Activities

- **Regulatory Strategy**
- **Regulatory Intelligence**
- **Health Authority meetings**
- **Draft Labeling**
- Phase I Deliverables

CMC Process development

EARLY DEV to PH1

- Finalize strategy for health authority interactions
- **Plan for submission**
- Phase II Deliverables
- Pediatric investigational plans (PIPs)

CMC Tech transfer & manufacturing

PH II a/b

- **Plan for submission**
- **Prepare for Advisory Committee**
- Phase III deliverables

CMC Process validation & submission planning

PH III

SUBMISSION & APPROVAL

- Align submission plan with launch strategies
- File registration
- Plan for health authority questions
- Plan for launch
- Negotiate labels

POST-APPVL POST-DEV

- Maintain License/ Lifecycle Management Activities
- Maintain Labels
- Support Phase IV commitments

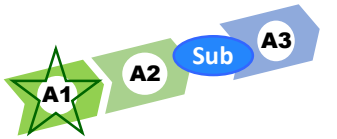
2. Identify Your Submission Needs

Your Specific Needs

Your Needs: Submission Plan

1. Regulatory Strategy
2. Regulatory Intelligence
3. Draft Labeling – Safety & Effcicacy
4. Health Authority Meetings
5. CMC - Quality Consideration
6. Input from Business Partners
7. Final Submission Plan
8. Health Authority Engagement Plan

3. Specify Actions to Meet Needs

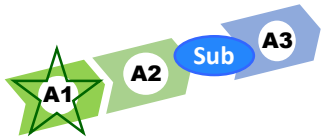


List Activities (Tools) to achieve Your Specific Needs

1. Review Regulatory requirements & guidance
2. Review Regulatory intelligence database
3. Understand Competitive intelligence
4. Planning for HA meetings
5. Form Project teams
6. Develop SOPs, WIs, processes
7. Finalize requirements, request for document, samples, others
8. Finalize Dossier structure & checklist
9. Finalize Timeline Table/Tracker

Your Tools

4. Identify Activity List for Each Action

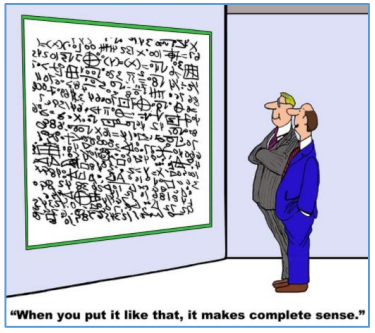


	Your Tools	Examples of Activities
1.	Review Regulatory requirements & guidance.	Review list of guidelines. Review relevant GL for project – eg pathways (expedited, accelerated, standard, abridged, full review, specific GL)
2.	Review Regulatory intelligence database	Country specific requirements, soft intelligences, past experiences, timelines, market information
3.	Understand Competitive intelligence	Competitor list, competitor strategies, define own strategy (timelines, TPP, etc ..)
4.	Planning for HA meetings	HA meeting template. Gathering what you need to prepare for a pre-submission meeting, relevant GL, TPP, tentative strategy
5.	Form Project teams	Cross functional, communication, consulting, collaboration with project team members to define strategy – marketing, medical affairs (RA), logistics, CMC
6.	Develop SOPs, WIs, processes	Prepare, review relevant SOPs or WIs, internal GL, develop project specific SOPS, if necessary
7.	Finalize requirements, request for document, samples, etc	Using generic template, define product specific dossier structure, review product profile, module 1, 2, 3, 4 data, country specific CMC, GMP certification, CoPP, samples
8.	Finalize Dossier structure & checklist	Dossier structure & checklist to ensure all requirements compiled, references
9.	Finalize Timeline Table/Tracker	Prepare GANTT charts, MS project, MS excel tracking sheets

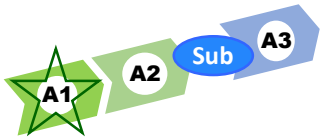
Summary - What do we need?

Examples of Tools/Activities

1. List of Regulations & Guidelines
2. List of Country Specific Requirements
3. Competitors database
4. HA Meeting template
5. Project Team composition, R&R
6. List of SOPs & WIs
7. Dossier structure template
8. Timeline Table/Tracker



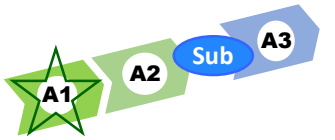
4a. Timeline Table/Tracker



Elements in a Timeline Table/Tracker

- Management decisions
- Project teams
- HA Pre-submission meeting
- Clinical trial programs or BE study plan for NG
- Market definition, market intelligence
- Product profile (indications, spec)
- Logistics planning
- Artwork, labels & inserts
- Dossier structure & development
  - ✓ Develop SOPs, WIs, processes
  - ✓ Core dossier availability
  - ✓ Finalize requirements, request for document, samples, etc
  - ✓ Country specific CMC
  - ✓ CoPP requirement
  - ✓ GMP certification – manufacturing, packaging sites
  - ✓ Registration samples
- Finalize Timeline Table
- Post submission elements

What do we need?

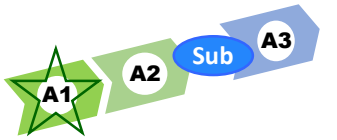


"Needs"	"Tools"	"The Activities"
1. Regulatory Strategy Sample strategy document content • Executive summary • Product background information • Project specific regulatory strategy • Project specific plan for risk assessment & mitigation • Global support plan • Global clinical development • CMC regulatory strategy • List of core documents required.	• Regulatory requirements & guidance	✓ Review relevant GL for project – eg pathways (expedited, accelerated, standard, abridged, full review, specific GL
	• Regulatory intelligence database	✓ Country specific requirements, more subtle types of information, soft intelligences, past experiences, timelines, market information
	• Competitive intelligence	✓ Competitor list, competitor strategies, define own strategy (timelines, TPP, etc ..)
	• Planning of pre-submission meeting	✓ Gathering what you need to prepare for a pre-submission meeting, relevant GL, TPP, tentative strategy
	• Project teams	✓ Cross functional, communication, consulting, collaboration with project team members to define strategy – marketing, medical affairs, logistics, CMC
	• SOPs	✓ Review relevant SOPS, internal GL, develop project specific SOPS, if necessary
	• Dossier structure & checklist	✓ Using generic template, define product specific dossier structure, review product profile, module 1, 2, 3, 4 data

"Needs"	"Tools"	"The Activities"
2. Regulatory Intelligence	• Regulatory requirements & guidance	✓ Review relevant GL for project – eg pathways (expedited, accelerated, standard, abridged, full review, specific GL
	• Regulatory intelligence database	✓ Country specific requirements, more subtle types of information, soft intelligences, past experiences, timelines, market information
	• Competitive intelligence	✓ Competitor list, competitor strategies, define own strategy (timelines, TPP, etc ..)
	• Planning of pre-submission meeting	✓ Gathering what you need to prepare for a pre-submission meeting, relevant GL, TPP, tentative strategy
	• Project teams	✓ Cross functional, communication, consulting, collaboration with project team members to define strategy – marketing, medical affairs, logistics, CMC
	• SOPs	✓ Review relevant SOPS, internal GL, develop project specific SOPS, if necessary
	• Dossier structure & checklist	✓ Using generic template, define product specific dossier structure, review product profile, module 1, 2, 3, 4 data

"Needs"	"Tools"	"The Activities"
3. Health Authority Meetings	• Regulatory requirements & guidance	✓ Review relevant GL for project – eg pathways (expedited, accelerated, standard, abridged, full review, specific GL
	• Regulatory intelligence database	✓ Country specific requirements, more subtle types of information, soft intelligences, past experiences, timelines, market information
	• Competitive intelligence	✓ Competitor list, competitor strategies, define own strategy (timelines, TPP, etc ..)
	• Planning of pre-submission meeting	✓ Gathering what you need to prepare for a pre-submission meeting, relevant GL, TPP, tentative strategy
	• Project teams	✓ Cross functional, communication, consulting, collaboration with project team members to define strategy – marketing, medical affairs, logistics, CMC
	• SOPs	✓ Review relevant SOPS, internal GL, develop project specific SOPS, if necessary
	• Dossier structure & checklist	✓ Using generic template, define product specific dossier structure, review product profile, module 1, 2, 3, 4 data

What do we need?



"Needs"	"Tools"	"The Activities"
4. Draft Labeling	• Regulatory requirements & guidance	✓ Review relevant GL for project – eg pathways (expedited, accelerated, standard, abridged, full review, specific GL
	• Regulatory intelligence database	✓ Country specific requirements, more subtle types of information, soft intelligences, past experiences, timelines, market information
	• Competitive intelligence	✓ Competitor list, competitor strategies, define own strategy (timelines, TPP, etc ..)
	• Planning of pre-submission meeting	✓ Gathering what you need to prepare for a pre-submission meeting, relevant GL, TPP, tentative strategy
	• Project teams	✓ Cross functional, communication, consulting, collaboration with project team members to define strategy – marketing, medical affairs, logistics, CMC
	• SOPs	✓ Review relevant SOPS, internal GL, develop project specific SOPS, if necessary
	• Dossier structure & checklist	✓ Using generic template, define product specific dossier structure, review product profile, module 1, 2, 3, 4 data

"Needs"	"Tools"	"The Activities"
5. Plan for submission	• Regulatory requirements & guidance	✓ Review relevant GL for project – eg pathways (expedited, accelerated, standard, abridged, full review, specific GL
	• Regulatory intelligence database	✓ Country specific requirements, more subtle types of information, soft intelligences, past experiences, timelines, market information
	• Competitive intelligence	✓ Competitor list, competitor strategies, define own strategy (timelines, TPP, etc ..)
	• Planning of pre-submission meeting	✓ Gathering what you need to prepare for a pre-submission meeting, relevant GL, TPP, tentative strategy
	• Project teams	✓ Cross functional, communication, consulting, collaboration with project team members to define strategy – marketing, medical affairs, logistics, CMC
	• SOPs	✓ Review relevant SOPS, internal GL, develop project specific SOPS, if necessary
	• Dossier structure & checklist	✓ Using generic template, define product specific dossier structure, review product profile, module 1, 2, 3, 4 data

"Needs"	"Tools"	"The Activities"
6. Finalize Strategy for Health Authority interactions	• Regulatory requirements & guidance	✓ Review relevant GL for project – eg pathways (expedited, accelerated, standard, abridged, full review, specific GL
	• Regulatory intelligence database	✓ Country specific requirements, more subtle types of information, soft intelligences, past experiences, timelines, market information
	• Competitive intelligence	✓ Competitor list, competitor strategies, define own strategy (timelines, TPP, etc ..)
	• Planning of pre-submission meeting	✓ Gathering what you need to prepare for a pre-submission meeting, relevant GL, TPP, tentative strategy
	• Project teams	✓ Cross functional, communication, consulting, collaboration with project team members to define strategy – marketing, medical affairs, logistics, CMC
	• SOPs	✓ Review relevant SOPS, internal GL, develop project specific SOPS, if necessary
	• Dossier structure & checklist	✓ Using generic template, define product specific dossier structure, review product profile, module 1, 2, 3, 4 data

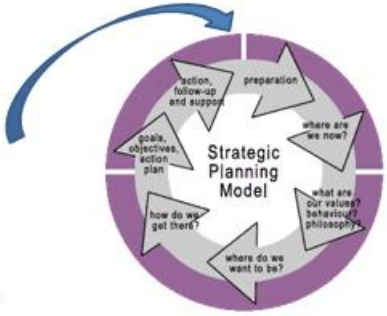
5. Your Final Submission Plan

Dossier Plan

+

Timeline Tracker

→ Final Submission Plan



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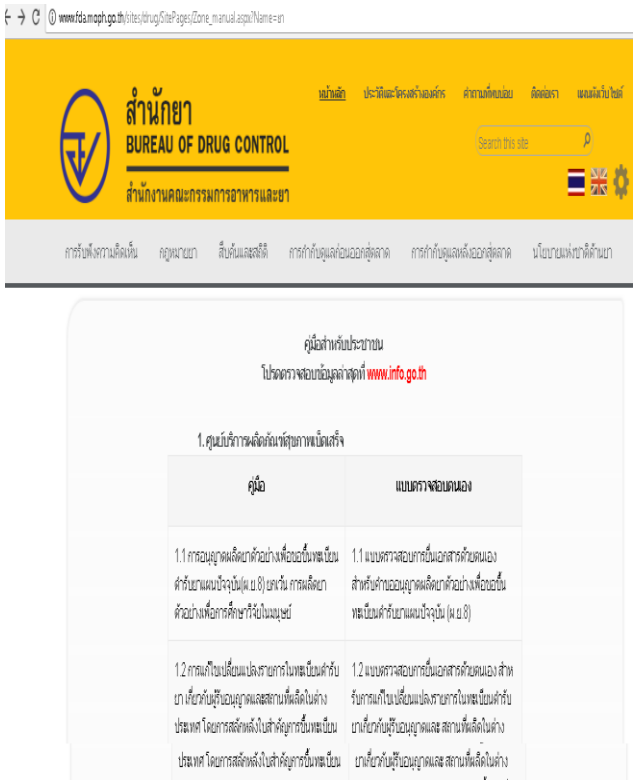
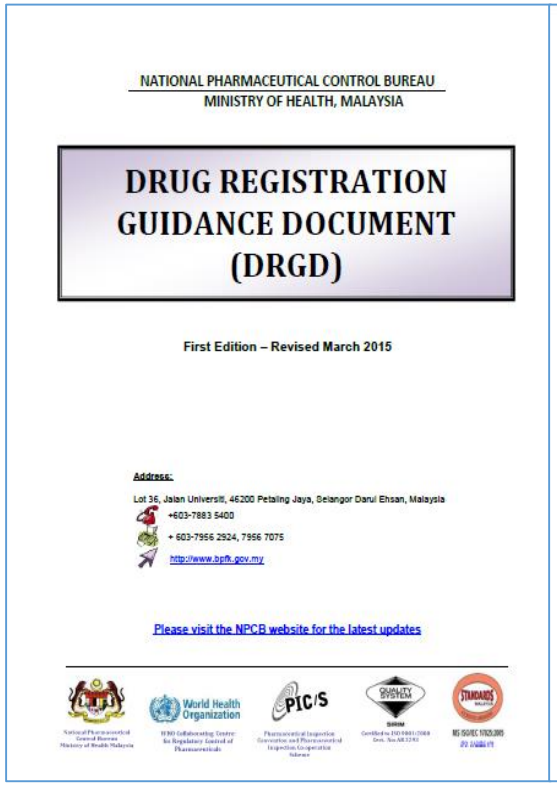
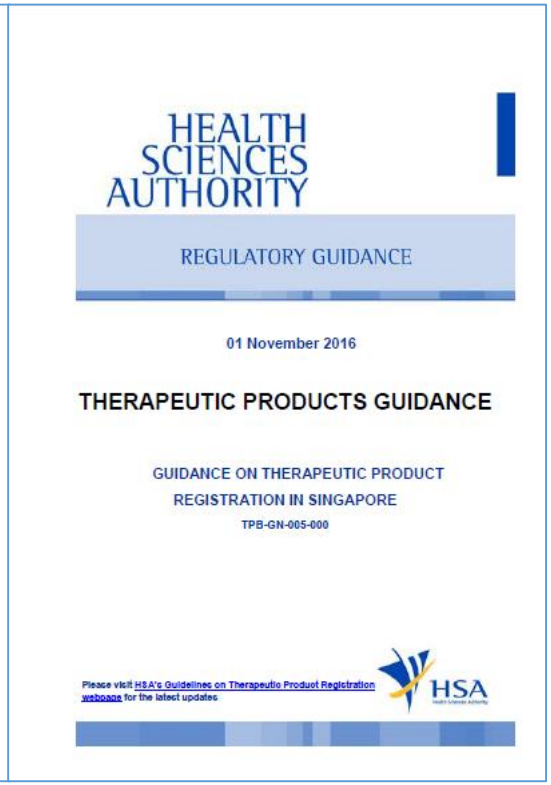
Example: List of Regulations & Guidelines



*From THAI FDA Guidance



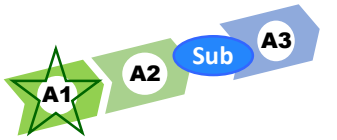
*From Malaysia NPRA Guidance



*From Singapore HSA Guidance

Example: Dossier Checklist

Thai FDA



แบบ SAR-NDL

หน้า 1

แบบตรวจสอบการยื่นเอกสารด้วยตนเองสำหรับ
คำขอขึ้นทะเบียนตำรับยาใหม่ (ยกเว้นยาชีววัตถุ)

1. ชื่อยา ..... เลขรับที่ .....

☐ ยาเดี่ยว ☐ ยาผสม

ประเภทยาใหม่

☐ New Chemical Entity (NCE) ☐ New Indication (NI)

☐ New Combination (NCO) ☐ New Delivery System (NDS)

☐ New Route of Administration (NR) ☐ New Dosage form of Approved NCE (NDOS)

☐ New Strength of Approved NCE (NS)

กลุ่มยา .....

2. รายการที่ยื่น

รายการเอกสาร	ผลการตรวจคำขอ (สำหรับผู้รับอนุญาต)		ผลการตรวจรับคำขอ (สำหรับเจ้าหน้าที่)	
	มี	ไม่มี	มี	ไม่มี
ส่วนที่ 1 (Part 1) : เอกสารข้อมูลทั่วไปและข้อมูลผลิตภัณฑ์ (ADMINISTRATIVE DATA AND PRODUCT INFORMATION)	☐	☐	☐	☐
ตอนที่ A (Section A) : คำนำ (Introduction)	☐	☐	☐	☐
ตอนที่ B (Section B) : สารบัญ (Table of Contents)	☐	☐	☐	☐
ตอนที่ C (Section C) : เอกสารที่ยื่น	☐	☐	☐	☐
1. แบบฟอร์มคำขอขึ้นทะเบียนตำรับยา (แบบ ย.1)	☐	☐	☐	☐
2.หนังสือรับรองต่างๆ (Certificates)	☐	☐	☐	☐
2.1 กรณีที่ผลิตในต่างประเทศ	☐	☐	☐	☐
2.1.1 สำเนาใบอนุญาตผลิตยาแผนปัจจุบัน	☐	☐	☐	☐
2.1.2 หนังสือรับรอง GMP ของผู้ผลิต	☐	☐	☐	☐
2.1.3 Certificate of Origin ของ active ingredient raw material	☐	☐	☐	☐
2.2 กรณีที่ผลิตในต่างประเทศแต่มีสาขาในประเทศไทย	☐	☐	☐	☐
2.2.1 สำเนาใบอนุญาตนำเข้าวัตถุดิบยาแผนปัจจุบัน สำเนาใบอนุญาตประกอบโรคศิลปะ	☐	☐	☐	☐
2.2.2 หนังสือรับรองผลิตภัณฑ์ยา (Certificate of Pharmaceutical	☐	☐	☐	☐

*From TH FDA Guidance

แบบตรวจสอบการยื่นเอกสารด้วยตนเองสำหรับคำขอการขึ้นทะเบียนตำรับยาสามัญและยาสามัญใหม่

ชื่อยา.....	ชื่อผู้รับอนุญาต.....	เลขรับที่.....
.....	.....	วันที่ยื่นคำขอ.....
.....	เลขที่ใบอนุญาต.....	

รายละเอียดการตรวจสอบเอกสาร

เป็นโรงงานผู้ผลิตรายใหม่หรือไม่

☐ ใช่ผู้ผลิตรายใหม่

☐ มีหนังสือรับรองว่าผ่านการ Accredit จากกลุ่มกำกับดูแลหลังออกสู่ตลาด หน้า.....

☐ ไม่มีหนังสือรับรองว่าผ่านการ Accredit จากกลุ่มกำกับดูแลหลังออกสู่ตลาด

☐ ไม่ใช่ผู้ผลิตรายใหม่โดยมีเลขทะเบียนอ้างอิงสถานที่ผลิต คือ.....

เป็นยาที่ต้องแนบรายงานการศึกษาชีวสมมูล ☐ ใช่ ☐ ไม่ใช่

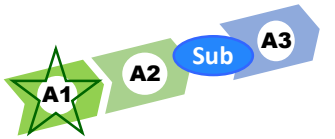
1) ชื่อยา	2) สูตรยา
☐ เป็น generic name ☐ ไม่ซ้ำ ☐ ซ้ำ ☐ คล้าย กับยาชื่อ..... เลขทะเบียนที่..... ☐ ตัวยาสำคัญเดียวกัน ☐ ตัวยาสำคัญต่างกัน เติมคือ..... ☐ dosage form เดียวกัน ☐ dosage form ต่างกัน เติมคือ..... ☐ ประเภทยาเดียวกัน ☐ ประเภทยาต่างกัน เติมคือ..... ☐ มีเจ้าของเดียวกัน คือ..... ☐ ผู้ผลิตเดียวกัน ☐ ผู้ผลิตต่างกัน เติมคือ..... ☐ มีหนังสือยินยอมให้ใช้ชื่อยาเดียวกัน	☐ ยาเดี่ยว ☐ ยาผสม ☐ ตัวยาสำคัญเติม ☐ dosage form เดิม ☐ ความแรงเดิม เหมือนกับยาชื่อ..... เลขทะเบียนที่..... ☐ ตัวยาสำคัญต่าง เติมคือ..... ☐ dosage form ต่าง เติมคือ..... ☐ แบบ Available dosage form ☐ ความแรงต่าง เติมคือ..... ☐ แบบ Available strength ประเภทยา ☐ ยาสามัญ ☐ ยาอันตราย ☐ ยาสามัญประจำบ้าน ☐ ยาควบคุมพิเศษ จัดเป็นยา ☐ ยาสามัญ ☐ ยาสามัญใหม่ / ยาใหม่ → ไปตรวจต่อกลุ่มยาใหม่

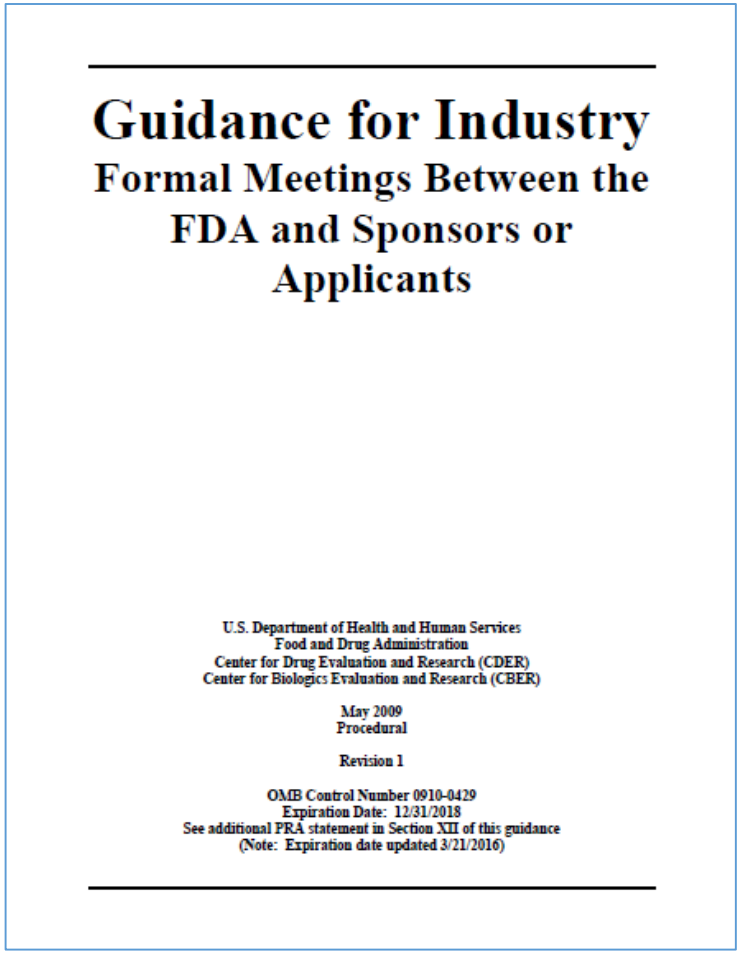
รายการเอกสาร	แท็บ/หน้า	ผลการตรวจสอบคำขอฯ				รายละเอียดข้อบกพร่องที่ต้องแก้ไขและเอกสารที่ต้องยื่นเพิ่ม
		ผู้รับอนุญาต		เจ้าหน้าที่		
		มี	ไม่มี	มี	ไม่มี/ไม่ใช่	
ส่วนที่ 1 : ข้อมูลทั่วไปและข้อมูลของผลิตภัณฑ์ยา ประกอบด้วย 3 ตอน คือ						
ตอนที่ A และ B (ข.ท.ย. A1)						
ข.ท.ย. AR						
แบบฟอร์มบันทึกข้อมูล						

ผู้รับอนุญาต ..... ผู้ตรวจรับคำขอ..... หน้า 1/17

Example: HA Meeting Template

US





Guidance for Industry

Formal Meetings Between the FDA and Sponsors or Applicants

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

May 2009
Procedural

Revision 1

OMB Control Number 0910-0429
Expiration Date: 12/31/2018
See additional PRA statement in Section XII of this guidance
(Note: Expiration date updated 3/21/2016)

*From US FDA Guidance

Meeting Package Content

1. Product name and application number (if applicable).
2. Chemical name and structure.
3. Proposed indication.
4. Dosage form, route of administration, and dosing regimen (frequency and duration).
5. An updated list of sponsor or applicant attendees, affiliations, and titles.
6. A background section that includes the following:

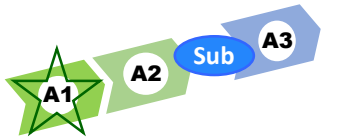
a. A brief history of the development program and the events leading up to the meeting.

b. The status of product development (e.g., the target indication for use).

7. A brief statement summarizing the purpose of the meeting.
8. A proposed agenda.
9. A list of the final questions for discussion grouped by discipline and with a brief summary for each question to explain the need or context for the question.
10. Data to support discussion organized by discipline and question. For example, for an end-of-phase 2 meeting, this section should include the following, if not already provided in the background section (refer to item #6 above): description and results of controlled trials conducted to determine dose-response information; adequately detailed descriptors of planned phase 3 trials identifying major trial features such as trial population, critical exclusions, trial design (e.g., randomization, blinding, choice of control group, with explanation of the basis for any noninferiority margin if a noninferiority trial is used), choice of dose, primary and secondary trial endpoints; and major analyses (including planned interim analyses and adaptive features, and major safety concerns).

Example: Dossier Checklist

HSA Singapore



APPENDIX 2A *APPLICATION CHECKLIST (ICH CTD – NDA AND GDA)*

This Application Checklist should be used to
and GDA applications only.

All documents required under Module 1 mus

Colour scanned copy of the original docume

However, HSA reserves the rights to reques
submitted scanned document is not an accu

To use this Checklist, check against the doss

Note:

- Cells with ☐ indicate that the documents
- Cells with ☐ with an asterisk * indicate th
- Cells without ☐ indicate that the docume
- If a mandatory document is not included i
  for the omission must be provided in the c

Please refer to the *Guidance on Therapeuti*
documents for a submission in ICH CTD for

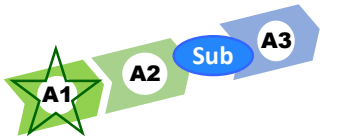
Module 1 – Administrative Documentation

Section	Documents			Application Type & Evaluation Route					HSA Screening	
				NDA			GDA			
				F	A	V	A	V	Submitted/ Acceptable?	Remarks
1.0	PRISM Application Form			☐	☐	☐	☐	☐		
	1.0.1	Section 1: Company Particulars		☐	☐	☐	☐	☐		
		▪ Company shall be based and registered in Singapore.								
	1.0.2	Section 2: Applicant Particulars		☐	☐	☐	☐	☐		
		▪ The applicant of a product registration refers to the local company that is applying for the product registration. The applicant company may authorise officers, permanent employees, or designated external parties, all of whom are referred to as the "applicant representative", to submit the application for product registration in Singapore. ▪ The NRIC/FIN of the applicant representative entered must be the same as that used to login to access the PRISM application.								
		▪ Note: Section 2.4.5 of the PRISM application form does not support entry of multiple email addresses.								
	1.0.3	Section 3: Application Details								
			Pre-filled syringes of different strengths (total weight/concentration) are to be submitted as separate product applications							
			Injectable products in the form of solid powder for solution are to be submitted as separate product applications if the amount of powder in each container closure system is different							
		3.1	Type of Application	☐	☐	☐	☐	☐		
		3.2	Type of Product	☐	☐	☐	☐	☐		
		3.3	Reference Product	☐*	☐*	☐*	☐	☐		
			▪ All GDA applications – specify Singapore reference product's SIN number.							
			▪ If GDA-2 application not submitted at the same time as GDA-1 application, specify both the Singapore reference product's and the GDA-1 product's SIN numbers.							
			▪ Applicants should ensure that data protection is not infringed on.							

*From Singapore HSA Guidance

** Can create timeline/project tracker from HA Application Checklist

Example: Guideline & Checklist



衛接性試驗基準

接受國外臨床資料之族群因素考量

ETHNIC FACTORS IN THE ACCEPTABILITY

OF FOREIGN CLINICAL DATA

行政院衛生署

中華民國 98 年 7 月

*From Taiwan FDA Guidance

*Checklist for bridging study evaluation

附錄F、衛接試驗評估之查檢表

衛接性試驗評估之查檢表		資料提供 有 無	資料冊數，頁數
I、藥品於各國之臨床試驗現況		□ □	
II、完整臨床試驗數據資料（Complete Clinical Data Package），至少應包含新藥查驗登記資料之專家審查報告（NDA expert report）或試驗主持人手冊（Investigator's Brochure），且宜有藥品之適應症與用法用量資訊 (含有不同族群間的比較分析，請一併提供)		□ □	
III、有關亞洲族群的藥動、安全性及療效性資料		□ □	
IV、亞洲族群的藥動、安全性及療效性資料和其他族群比較		□ □	
V、自我評估(請舉證評估之參考依據或文獻資料)	是 否 未知	□ □	
1、在臨床治療劑量下，藥品有效成分是否顯示具非線性藥動學性質者？	□ □ □	□ □	
2、藥品在建議劑量及用法範圍內，療效及安全性與藥效學相關曲線是否成聚升趨勢者？	□ □ □	□ □	
3、藥品之療效範圍是否狹窄？	□ □ □	□ □	
4、是否為高度代謝藥品，特別是經單一代謝途徑，因而導致藥品交互作用可能性增加者？	□ □ □	□ □	
5、藥品代謝是否需經由具族群差異性質之基因多形性酵素，且具臨床重要性者？	□ □ □	□ □	
6、是否為前趨藥品方式給藥，而該藥品會經具族群差異性質之酵素轉換者？	□ □ □	□ □	
7、藥品之生體可用率是否會因個體差異而產生極大差異者？	□ □ □	□ □	
8、藥品是否因生體可用率低，而易受飲食影響吸收者？	□ □ □	□ □	
9、藥品是否為常需與其他多種藥物併用者？	□ □ □	□ □	
10、藥品是否為常易被濫用者？例如止痛劑及鎮靜劑	□ □ □	□ □	
11、主要試驗族群與我國適用此藥之適應症族群的流行病學現象(含自然病史、致病機轉及盛行率、對類似藥品之療效與安全性)，是否不同？	□ □ □	□ □	
12、其他重要具有族群敏感性的因素(例如醫療行為是否有所不同)	□ □ □	□ □	
VI、藥品上市後之安全性資料		□ □	
自我總結評估 (以上因素請自我評估有無臨床意義，並評估申請藥品的利害權衡，例如藥品所申請的適應症是否為嚴重疾患，藥品是否有其他替代療法，藥品資料所顯示之族群差異是否可容忍等)		□ □	

說明事項：

請填寫清楚所附資料的冊數，頁數，以方便審查；必要時，除了頁數之外，並於該頁數該段落處標

Example: Guideline & Checklist

衛接性試驗基準

接受國外臨床資料之族群因素考量

ETHNIC FACTORS IN THE ACCEPTABILITY

OF FOREIGN CLINICAL DATA

Checklist for bridging study evaluation for Taiwan at TFDA website

行政院衛生署

中華民國 98 年 7 月

*From Taiwan FDA Guidance

*Checklist for bridging study evaluation

Checklist for Bridging study Evaluation		Data Yes No	Vol. No. (Page No.)
I、Worldwide regulatory status		□□	
II、NDA expert report or Investigator's Brochure (Please provide information of comparison between different ethnic groups if available)		□□	
III、Clinical data on pharmacokinetic, safety and efficacy from Asian populations		□□	
IV、Clinical data on PK, safety and efficacy in Asians and its comparison with other ethnic groups.		□□	
V、Self evaluation (Please provide data or literature underlying the evaluation)	Unknown	□□	
1. Non-linear pharmacokinetics in therapeutic dosage range?	□□ □	□□	
2.A steep pharmacodynamic (effect-concentration) curve for both efficacy and safety in the range of the recommended dosage and dose regimen	□□ □	□□	
3. A narrow therapeutic dose range.	□□ □	□□	
4.Highly metabolized, especially through a single pathway, thereby increasing the potential for drug-drug interaction.	□□ □	□□	
5.Metabolism by enzymes known to show genetic polymorphism which present clinical significance.	□□ □	□□	
6.Administration as a prod rug, with the potential for ethnically variable enzymatic conversion.	□□ □	□□	
7.High inter-subject variation in bioavailability.	□□ □	□□	
8.Low bioavailability, thus more susceptible to dietary absorption effects.	□□ □	□□	
9.High likelihood of use in a setting of multiple co-medications.	□□ □	□□	
10.High likelihood for inappropriate use, e.g., analgesic and tranquilizers.	□□ □	□□	
11、Different indications and/or epidemiology (including natural history of disease, disease mechanism, disease prevalence, and efficacy/safety of similar drugs)	□□ □	□□	
12、Other important factors of ethnic sensitivity (e.g. medical practice)	□□ □	□□	
VI、Post marketing safety surveillance		□□	
Conclusion of Self-Evaluation Based upon the above considerations, please evaluate whether the drug under assessment is of any clinical or risk/benefit impact, such as whether indications are for serious disorders, whether there are alternative therapies and whether the ethnic differences are tolerable.		□□	

*English translation

Example: Dossier Preparation Guidance

iMPRO 專區

首頁 > iMPRO 專區

食品藥物管理署整合藥品審查工作小組專區

(Integrated Medicinal Product Review Office, 簡稱 iMPRO)

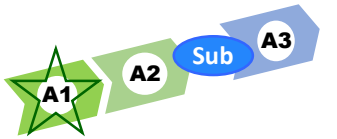
2011 年 6 月 1 日食品藥物管理署整合藥品審查工作小組 (Integrated Medicinal Product Review Office, 簡稱 iMPRO) 正式成立，請各位配合事項如下：

送件

1. 申請案件仍須依原規定檢送紙本文件，一律送至行政院衛生福利部食品藥物管理署 **聯合服務中心**，受文者為：**食品藥物管理署藥品組**。
   - 收文單位請儘量勿使用「食品藥物管理署」或「財團法人醫藥品查驗中心」
   - 行政院衛生署食品藥物管理局地址：115-61 台北市南港區昆陽街161-2號
2. 申請案請依「廠商應提供資料清單」提供電子檔。
3. 申請案一律須附上「案件類別表」、「案件基本資料表」，以便收文之順暢。
   (請見 100 年 9 月 19 日署授食字第 1001405584 號公告)
4. 紙本文件份數原則：
   - 臨床試驗申請新案：一正六副。
   - 臨床試驗申請申復案：一正六副。
   - 臨床試驗申請變更案：一正三副。

*From Taiwan FDA Guidance - Guideline for dossier preparation

Example: Timeline Tracker



RESPONSIBLE STAFF	ACTIVITIES	DURATION (Days)	Target START DATE	Target END DATE	COMPLETION DATE
Local RA	DOSSIER SUBMISSION PROJECT DURATION	365	02-Dec-19	01-Dec-20	
	Review Regulatory requirements & guidance.	30	01-Jan-19	31-Jan-19	
	Review Regulatory intelligence database	30	01-Jan-19	31-Jan-19	
	Management decisions	30	01-Jan-19	31-Jan-19	
	Project teams				
	HA Pre-submission meeting				
	Clinical trial programs				
	Market definition, market intelligence				
	Product profile (indications)	15	14-Feb-19	01-Mar-19	
	Logistics planning				
	Artwork, labels & inserts	15	14-Feb-19	01-Mar-19	
	Dossier structure & development				
	Develop SOPs, WIs, processes				
	Core dossier availability				
	Finalize requirements, request for document, samples, etc				
	Country specific CMC				
	CoPP requirement				
	GMP certification – manufacturing, packaging sites				
	Registration samples	30	31-Oct-19	30-Nov-19	
	Finalize Timeline Table	30	02-Dec-18	01-Jan-19	
	Post Submission Elements	30	02-Dec-18	01-Jan-19	
	TARGET SUBMISSION DATE @ 20-DEC-2020				


Thank
You

Planning of submission (prior to dossier preparation)

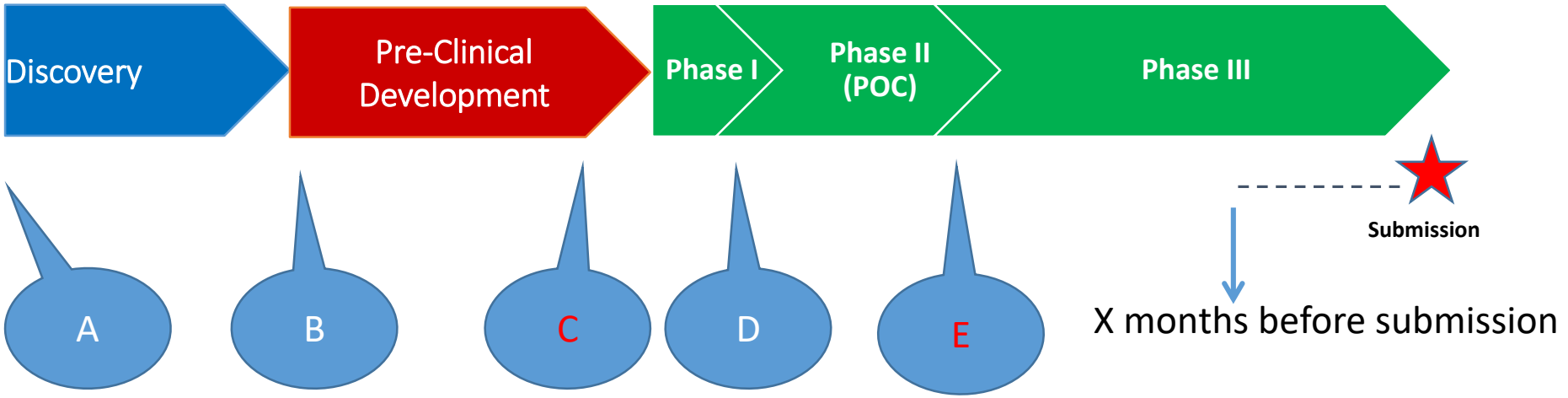
- What do we want?
- What do we need?
- **How do we do it?**

2018 Good Registration Management
Regulatory Science
Center of Excellence
Pilot Workshop

Planning of submission

How do we do it?

How to interpret the intelligence into strategic plan
How do we do it?



Strategic plan at various stages:

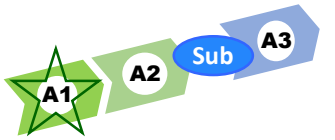
(1) Point C: Planning for submission: Consider a selected list of countries on top of ICH countries (Factors to consider include e.g. indication, etc.)

(2) During/after Phase II: Decision to expand (consider e.g. local trials, operation feasibility, etc)

(3) X Months before submission

(Factors to consider – see next slide)

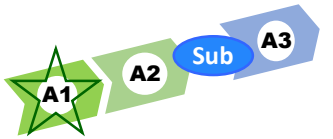
Interpret the intelligence into strategic plan How do we do it?



X months before the submission

1. Strategic fundamentals
    - (a) ICH countries' requirements
    - (b) Local clinical data result/analysis
    - (c) CPP
    - (d) Country specific requirements
    - (e) Samples and Sourcing scenario

Interpret the intelligence into strategic plan How do we do it?



X Months before the submission

1. Strategic fundamentals

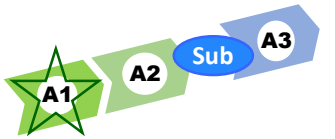
   (a) ICH countries requirements

   - Why ICH? (Transparent, science-based, prior approval required (CPP), etc.)

   (b) Local clinical data and/or results/analysis

   (c) CPP – Exercise 1

Interpret the intelligence into strategic plan
How do we do it?



Exercise 1

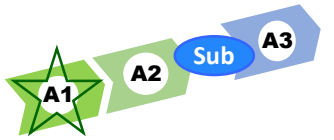
(i) Trainee to list out CPP requirement in the country

- How many?
- Preferred country?
- Issued by country of origin or..?
- At the point of submission?
- Language?
- Others?

(ii) Trainee to share the CPP requirement with two other Trainees. Is there any specific requirement?

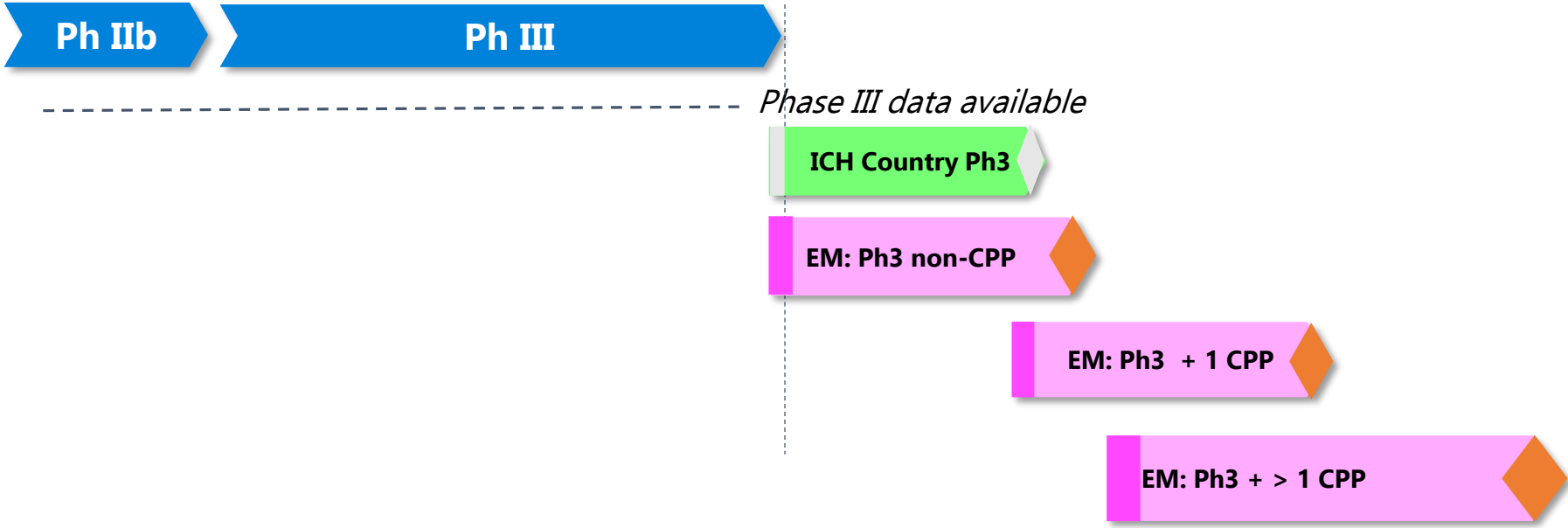
(iii) Together, plan the submission priority based on CPP requirements in these countries

Interpret the intelligence into strategic plan How do we do it?

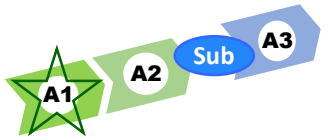


Exercise 1 Discussion:

CPP requirement differs from country to country. Use the intelligence when planning for submission.



Interpret the intelligence into strategic plan
How do we do it?



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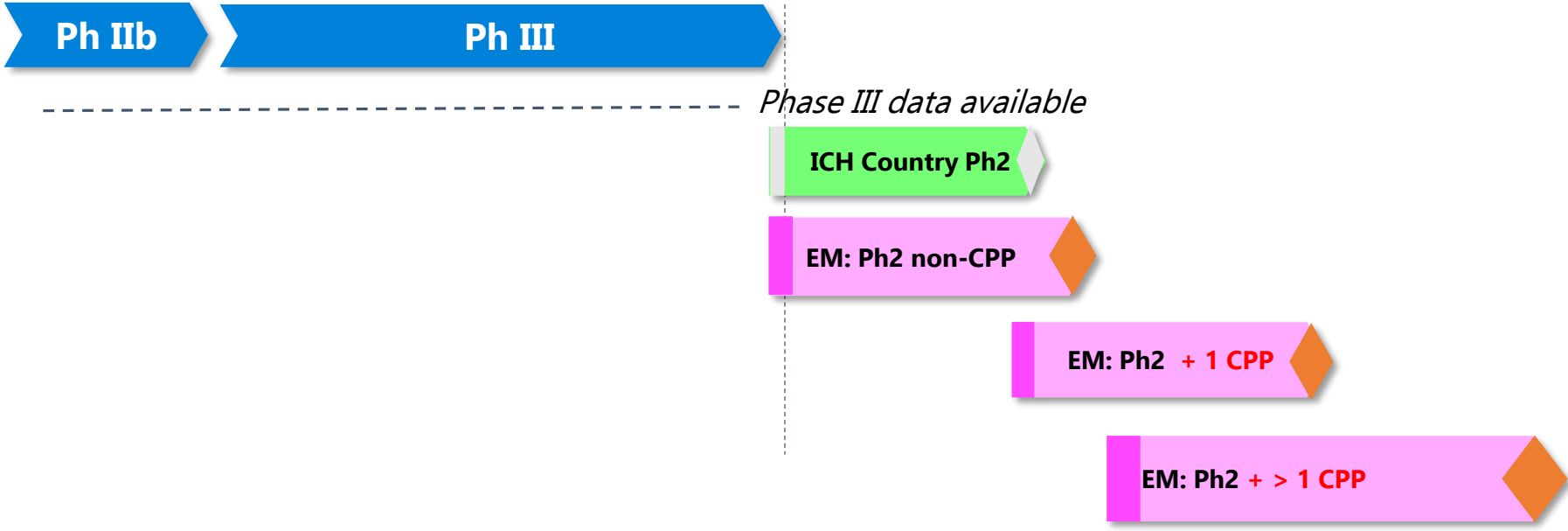
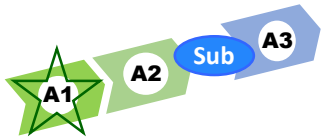
CPP requirement differs from country to country. Use the intelligence when planning for submission.



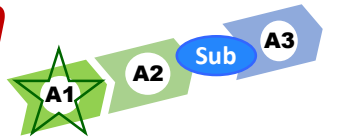
Interpret the intelligence into strategic plan How do we do it?



X Months before the submission

1. Strategic fundamentals
   - (a) ICH countries' requirements
   - (b) Local clinical data result/analysis
   - (c) CPP
   - (d) Country specific requirements
   - (e) Samples and Sourcing scenario

Interpret the intelligence into strategic plan
How do we do it?



Exercise 2: Country specific requirements (CSR)

(i) Trainee to list the CSR in the country e.g.

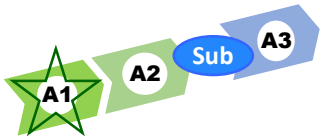
- Electronic platform versus e-CTD
- CMC information e.g. formula, full stability data
- Artworks: Wording of indication, actual carton box

(ii) Trainee to share the CSR with two other Trainees

(iii) Together, share the points to consider when planning the submission based on the CSR

(iV) Practice with the submission priorities decided and apply the CSR.

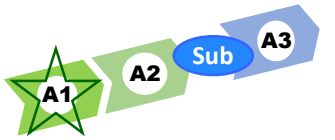
Interpret the intelligence into strategic plan
How do we do it?



Months before the submission

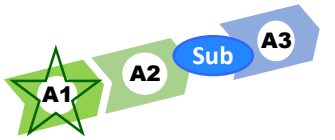
1. Strategic fundamentals
   - (a) ICH countries' requirements
   - (b) Local clinical data result/analysis
   - (c) CPP
   - (d) Country specific requirements
   - (e) Samples and Sourcing scenario
     - Ordering samples
     - Shelf life remaining
     - Others considerations

Interpret the intelligence into strategic plan How do we do it?



1. Strategic fundamentals
2. Operational effectiveness
   - Success factor: Two-way engagement with affiliates and cross-functional partners
   - Formal resource allocation: country specific requirement can be planned for and requested earlier
   - Improved tools and processed: Support in place for country specific requirements
   - Publishing and operations process (HQ/Affiliates)
   - Pre-approval inspection
   - Intent to file tracker
   - Q&A/Approval tracking
   - Pre-submission meeting

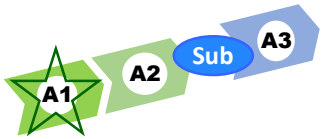
Interpret the intelligence into strategic plan How do we do it?



Planning for pre-submission meeting

- Meeting materials availability
- Module document ordering
- Capacity awareness: Team can only address questions after responses have been provided to ICH country
- Experience (affiliates)
- Communication plan
- Estimated timelines
- Points to consider due to limited data
- Regulatory pathway

Expected output – How do we do it?

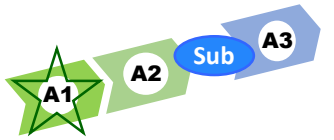


What kind of information do I need to gather?
What activities do I need to perform?

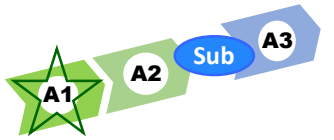
How do we do it?	Case study
Strategy planning	Communication with strategy planning: how to survive? - Ways to expedite local filing - Consider local critical impact data requirement (COA, stability data) - CMC review (Chemical, Manufacturing, control) - Country specific requirements (monograph) - Samples and sourcing
Operational effectiveness	Communicate to achieve operational effectiveness: - Locked in global resources of API, Excipients, Mfger/infrastructure to support - Ordering samples
Sourcing	Readiness to market: - Consider the manufacturing site to supply - Pre-approval inspection
Pre-submission meeting	Y, N? Communication with Health Authority - Ways to expedite local filing 6mths accelerate& LT? - Ways to overcome hurdles

Planning of submission (prior to dossier preparation)

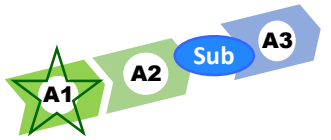
- What do we want?
- What do we need?
- How do we do it?



Thank You!



Q & A



Case study

Ms. SAKURA

Nation :

GREEN Country

Company :

Flower pharm co.

Local subsidiary

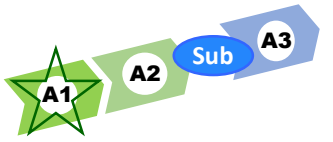
Under the Asia region head of multi-national company

Work Experience :

SAKURA graduated from the university two years ago, She joined the company in order to fultfil her dream that patients access innovative drugs early in her country.

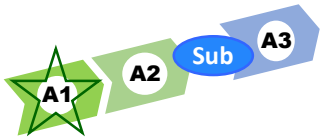
She has worked hard and learned the role of regulatory affairs. Now she is appointed regulatory leader of the project(s).

Case study 1 Plan for new product submission



- Global development project:
  - Cardiovascular product (anti-hyperlipid)
  - Novel product with superior efficacy and safety profile
  - Developed by multi-national company with global support and global TPP available
  - Ongoing global pivotal phase III study (Asia countries are not involved in this global study)
  - Target NDA submission in US in Nov 2018, EU submission in Dec 2018.
  - Conducted PK in US/Japanese subjects living in US and no ethnic difference observed in PK profile
  - Manufacturing site: US, UK
  - US/EU submission package available according to US/EU requirement
  - Target to launch in all Asian countries

Case study

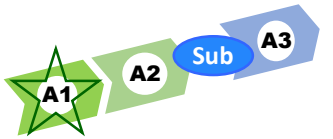


- Breakup to 6 team (~10 per team)
- Designate a lead and a scribe
- Discussion time: 15 minutes

use the concept "What do we want?" and "What do we need?" and "How do we do it?"

- Questions to answer
  - What kind of **information** do I need to gather?
  - What **activities** do I need to perform?
  - What best practice to recommend to HA?
  - List one improvement you will implement in your submission planning?
- Report back: 10 minutes group 1,3,5
- Group 2,4,6 to add on

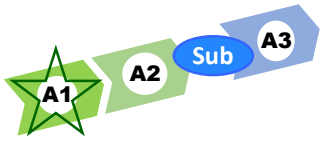
Duration



- 60 min for case 1

Discussion time: 15 minutes	15
Report back: 10 minutes for group 1,3,5	30
Group 2,4,6 to add on	15

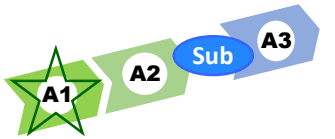
Expected output – What do we want?



What kind of information do I need to gather? What activities do I need to perform?	
What do we want?	**Case study**
TPP	Review Global TPP and determine country TPP
TPL	Check whether we can follow the global TPL
Organization	Establish country project team

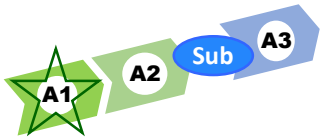
What do we need

Identify Activity List for Each Action



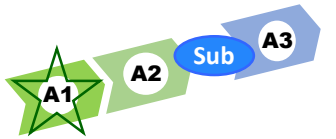
	Your Tools	Examples of Activities
1.	Review Regulatory requirements & guidance.	Review list of guidelines. Review relevant GL for project – eg pathways (expedited, accelerated, standard, abridged, full review, specific GL)
2.	Review Regulatory intelligence database	Country specific requirements, soft intelligences, past experiences, timelines, market information
3.	Understand Competitive intelligence	Competitor list, competitor strategies, define own strategy (timelines, TPP, etc ..)
4.	Planning for HA meetings	HA meeting template. Gathering what you need to prepare for a pre-submission meeting, relevant GL, TPP, tentative strategy
5.	Form Project teams	Cross functional, communication, consulting, collaboration with project team members to define strategy – marketing, medical affairs (RA), logistics, CMC
6.	Develop SOPs, WIs, processes	Prepare, review relevant SOPs or WIs, internal GL, develop project specific SOPS, if necessary
7.	Finalize requirements, request for document, samples, etc	Using generic template, define product specific dossier structure, review product profile, module 1, 2, 3, 4 data, country specific CMC, GMP certification, CoPP, samples
8.	Finalize Dossier structure & checklist	Dossier structure & checklist to ensure all requirements compiled, references
9.	Finalize Timeline Table/Tracker	Prepare GANTT charts, MS project, MS excel tracking sheets

Expected outcome - What do we need?



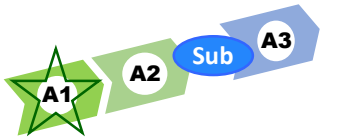
Identify Elements to create a Timeline Table/Tracker	
Management decisions	Management update, When? Decision on TPP
Project teams	Market access, sales, marketing, logistics, etc. What decision required?
HA Pre-submission meeting	When? Identify issues. Time to discuss & resolve issue
Clinical trial programs	Local data requirement for submission, for access
Market definition, market intelligence	Market access consideration on TPP. What decision required?
Product profile (indications)	Timeline for decision on TPP
Logistics planning	Supply chain, artwork approvals
Artwork, labels & inserts	Approvals

Expected outcome - What do we need?



Identify Elements to create a Timeline Table/Tracker	
Dossier structure & development	Develop SOPs, WIs, processes Core dossier availability Finalize requirements, request for document, samples, etc Country specific CMC CoPP requirement GMP certification – manufacturing, packaging sites Registration samples
Finalize Timeline Table	
Post submission elements	HA communication plan, tracking progress of review

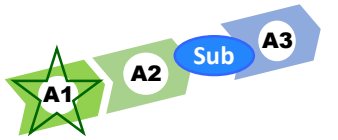
Expected output – How do we do it?



What kind of information do I need to gather?
What activities do I need to perform?

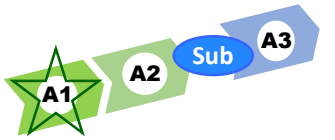
How do we do it?	Case study
Strategy planning	Communication with strategy planning: - Ways to expedite local filing - Consider local clinical data requirement - Reference Agencies' approval/CPP - Country specific requirements - Samples and sourcing
Operational effectiveness	Communicate to achieve operational effectiveness: - Locked in global resources/infrastructure to support - Publishing - Ordering samples
Sourcing	Readiness to market: - Consider the actual manufacturing site to supply - Pre-approval inspection
Pre-submission meeting	Communication with Health Authority - Ways to expedite local filing - Ways to overcome hurdles

Case study 1 (Importation) Timeline



ข้อ	กิจกรรม	ระยะเวลา	2018		2019				2020				หมายเหตุ
			Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	
1	New Drug Plan US/ EU approval			submission				Approval					
2	Evaluate/check gap of US/EU Submission package and generate evaluation report - CMC - Stability Zone IVB - Formulation/ Batch Size - In-vitro BE study (PE)	2 เดือน	x										
3	Communicate & Follow-up the lacking documents (ie.,stab zone IVB)			x	x	x	x	X					
4	Apply GMP clearance for all manufacturing plants (US & UK)	2 เดือน			X								Prepare in advance and renew the cert (GMP cert before expire 6mths)
5	Package Insert Translation	3 เดือน						X					
6	Prepare mock-up labels	2 เดือน						X					
7	Check CPP - Manufacturer name & address - Expiry date - Market in country of origin							X					Get CPP after approval in US/EU
8	Apply Import permit(นย8) for registration sample	5 วัน					X						
9	Budget Planning for submission	5 วัน					X						
10	Prepare Administrative document								X				
11	Submission to Thai FDA								submission				
12	Official application number								x				New Drug review :240 (WD)
13	First comment and correspondence									x			
14	Approval											Approval	New Drug review :240 (WD)

Case study 2 Post Approval Variations



โจทย์ Workshop – Planning for Variation

ทางสำนักงานคณะกรรมอาหารและยา ได้เรียกประชุม เพื่อชี้แจง “ร่าง คำสั่งกระทรวงสาธารณะสุข และ ร่าง ประกาศสำนักงานคณะกรรมการอาหารและยา เรื่อง การแก้ไขทะเบียนตำรับยาเซตไทริซีน (Cetirizine Tablet)”
โดยมีเนื้อหาของรายละเอียดตามเอกสารแนบ

ร่าง คำสั่งกระทรวงสาธารณสุข

อาศัยอำนาจตามความในมาตรา 86 ทวิ แห่ง พรบ.ยา พ.ศ. 2510 แก้ไขเพิ่มเติมโดย พรบ.ยา (ฉบับที่ 3) พ.ศ. 2522 .....มีคำสั่ง....

1.ให้แก้ไขทะเบียนตำรับยาเซตไทริซีน (Cetirizine Tablet) ให้เป็นไปตามข้อกำหนดตามตำรายา USP40 หรือ BP2017 หรือฉบับใหม่กว่า

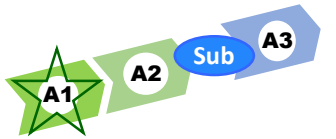
2.การแก้ไข....ให้เป็นไปตามหลักเกณฑ์ วิธีการ และเงื่อนไขที่อย.กำหนด (รายละเอียดตามเอกสารร่าง ประกาศฯ)

3.ให้ยื่นแก้ไขทะเบียนตำรับยาภายใน 180 วัน นับแต่วันถัดจากประกาศในราชกิจจานุเบกษา เมื่อพ้นกำหนดแล้วกระทรวงสาธารณสุขจะดำเนินการเพิกถอนทะเบียนตำรับยาที่ไม่ได้ดำเนินการแก้ไขตามกฎหมายต่อไป

Hint : บริษัทส่วนใหญ่ พบว่า impurities ไม่ผ่าน

บริษัทมีทะเบียนตำรับยา Cetirizine Tablet ซึ่งเป็นผลิตภัณฑ์หลักที่ขายดี (Top 5) ของทางบริษัท
จากเดิม FPS ของตำรับยา Cetirizine Tablet ในทะเบียนของบริษัท In-house method
RA ต้องทำการเตรียมความพร้อมให้สอดคล้องกับในร่าง คำสั่งฯ และ ร่าง ประกาศฯ ดังกล่าว

Case study 2 Plan for Post Approval Variations



เอกสารประกอบเพิ่มเติม

Current Formulation

Ingredients	Function	Quantity per tablet
Cetirizine Hydrochloride	API	10.0 mg
Lactose Monohydrate	Diluent	100.0 mg
Pregelatinized Starch	Diluent/ Disintegrant	30.0 mg
Povidone K90	Binder	4.0 mg
IPA*	Solvent	10.0 mcL
Croscarmellose Sodium	Disintegrant	3.0 mg
Talcum	Glidant	1.5 mg
Magnesium Stearate	Lubricant	1.5 mg

*To be removed during process

Current Finished Product Specification

SPECIFICATION	LIMITS	Reference
Appearance	White round tablet	In-house method
Average weight per tablet	150 mg ± 7.5%	In-house method
Assay	90.0 – 110.0 % LA	In-house method
Content uniformity	85.0 – 115.0 %	In-house method
Dissolution	Not less than 75% LA in 45 minutes	In-house method

Case study 2 Post Approval Variations

Hint : impurity

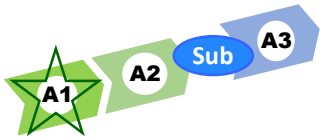
Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Cetirizine lactose ester[a]	0.56	1.0	0.5
Cetirizine	1.0	—	—
Cetirizine ethanol[b]	1.67	1.2	0.4
Any unspecified degradation product	—	—	0.2
Total impurities	—	—	1

[a] 6-*O*-[2-(2-{4-[(4-Chlorophenyl)(phenyl)methyl]piperazin-1-yl} ethoxy)acetyl]-β-D-galactopyranosyl-(1→4)β-D-glucopyranose.

[b] 2-[4-[(4-Chlorophenyl)phenylmethyl]piperazin-1-yl]ethanol.

Duration

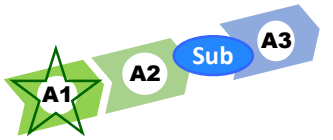


- 60 min for case 2
- Discussion time: 15 minutes

use the concept "What do we want?" and "What do we need?" and "How do we do it?"

- Questions to answer
  - What kind of **information** do I need to gather?
  - What **activities** do I need to perform?
  - What best practice to recommend to HA?
  - List one improvement you will implement in your submission planning?
- Report back: 10 minutes group 2,4,6
- Group 1,3,5 to add on

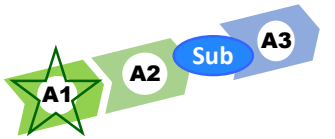
Expected output – What do we want?



What kind of information do I need to gather? What activities do I need to perform?	
What do we want?	**Case study 2**
Regulation /standard compliance	Compliance to regulation
Target product profile (CMC)	QSE concern => follow to monograph
Strategic plan	Survive in market

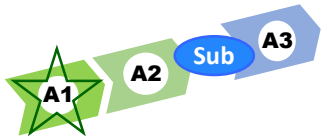
What do we need

Identify Activity List for Each Action



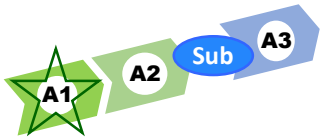
	Your Tools	Examples of Activities
1.	Review Regulatory requirements & guidance.	Review list of guidelines. Review relevant GL for project – eg pathways (expedited, accelerated, standard, abridged, full review, specific GL)
2.	Review Regulatory intelligence database	Country specific requirements, soft intelligences, past experiences, timelines, market information
3.	Understand Competitive intelligence	Competitor list, competitor strategies, define own strategy (timelines, TPP, etc ..)
4.	Planning for HA meetings	HA meeting template. Gathering what you need to prepare for a pre-submission meeting, relevant GL, TPP, tentative strategy
5.	Form Project teams	Cross functional, communication, consulting, collaboration with project team members to define strategy – marketing, medical affairs (RA), logistics, CMC
6.	Develop SOPs, WIs, processes	Prepare, review relevant SOPs or WIs, internal GL, develop project specific SOPS, if necessary
7.	Finalize requirements, request for document, samples, etc	Using generic template, define product specific dossier structure, review product profile, module 1, 2, 3, 4 data, country specific CMC, GMP certification, CoPP, samples
8.	Finalize Dossier structure & checklist	Dossier structure & checklist to ensure all requirements compiled, references
9.	Finalize Timeline Table/Tracker	Prepare GANTT charts, MS project, MS excel tracking sheets

Expected outcome - What do we need?



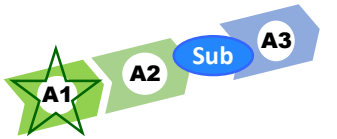
Identify Elements to create a **Timeline Table/Tracker 1**	
Management decisions	Management update, When? Decision on TPP
Project teams	Market access, sales, marketing, logistics, R&D,PD, QC,QA, RA etc. What decision required?
HA Pre-submission meeting	When? Identify issues. Time to discuss & resolve issue
CMC Adjustment programs	Local data requirement for submission, for access
Logistics planning	Supply chain, artwork approvals
Artwork, labels & inserts	Approvals

Expected outcome - What do we need?



Identify Elements to create a **Timeline Table/Tracker 2**	
Dossier structure & development	Develop SOPs, WIs, processes Core dossier availability Finalize requirements, request for document, etc Country specific CMC CoPP requirement (import case :if change formula) GMP certification – API source, manufacturing, packaging sites Registration sample -- (if change formula)
Finalize Timeline Table	
Post submission elements	HA communication plan, tracking progress of review, submit ongoing stability study

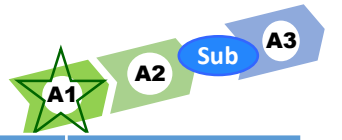
Expected output – How do we do it?



What kind of information do I need to gather?
What activities do I need to perform?

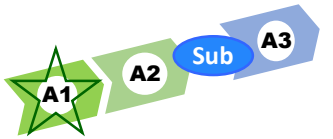
How do we do it?	Case study
Strategy planning	Communication with strategy planning: how to survive? - Ways to expedite local filing - Consider local critical impact data requirement (COA, stability data) - CMC review (Chemical, Manufacturing, control) - Country specific requirements (monograph) - Samples and sourcing
Operational effectiveness	Communicate to achieve operational effectiveness: - Locked in global resources of API, Excipients, Mfger/infrastructure to support - Ordering samples
Sourcing	Readiness to market: - Consider the manufacturing site to supply - Pre-approval inspection
Pre-submission meeting	Y, N? Communication with Health Authority - Ways to expedite local filing 6mths accelerate& LT? - Ways to overcome hurdles

Case Study 2 (Variation) Timeline

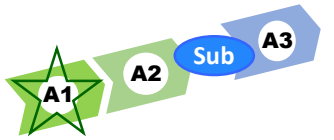


ข้อ	กิจกรรม	หน่วยงานที่เกี่ยวข้อง	ระยะเวลา	เดือน												กำหนดเสร็จ	หมายเหตุ
				1	2	3	4	5	6	7	8	9	10	11	12		
1	เรียกประชุมหน่วยงานที่เกี่ยวข้อง เพื่อรับทราบประกาศฯ และให้ข้อมูลรายละเอียดทั้งหมด รวมถึงค่าใช้จ่ายที่ต้องใช้	RA, QA, QC, PD, SCM, BD	2 วัน	X													ได้ Proposed FPS (USP, BP, In-house)
2	ประเมินสถานการณ์ของผลิตภัณฑ์ในทุกๆ ด้าน - Stability and Impurity profile - API source available	QC, PD	ภายใน 30 วัน	X													
3	เรียกประชุมหน่วยงานที่เกี่ยวข้อง เพื่อสรุปผล และเสนอผู้บริหารเพื่อตัดสินใจ	RA, QA, QC, PD, SCM, BD, Management, CEO	2 วัน	X													
4	หาซื้อสารมาตรฐาน วัตถุดิบ	SCM	30-60 วัน		x	X											
5	ทำ Analytical Method Verification/ Validation	QC, QA	30-60 วัน				x	X									
6	Formulation Development (Experimental scale)	PD	30-60 วัน				X	x									
7	Comparative DS profile between old and proposed formulation	PD	10 วัน					X									
8	ทำ Pilot Scale 3 batches (optimization)	PD	20 วัน						X								
9	Stability study - Accelerated - Long term - Stress test	PD	3-6 เดือน						x	x	x	x	x	x			
10	Process validation 3 batches	Production	2-3 เดือน									x	x	X			
11	รวบรวมข้อมูล และตรวจสอบความครบถ้วน	RA/ QA	7 วัน						x	x	x	x	x	x	X		
12	ประชุมสรุปเพื่อดำเนินการยื่นคำขอแก้ไขตามประกาศ	RA, QA, QC, PD, SCM, BD, Management, CEO	1 วัน												x		

Wrap Up



- The planning of application should start as early as possible. There should be proper organizational preparation and resource planning.
- Necessary documents and tools are the key success factors. Those documents and tools include but not limited to TPP, Regulatory Intelligence Database and Checklist etc.
- Strategic plan will be the guidance document for the application preparation.
- The same principle can be adapted for all kinds of applications including post approval variations.



Thank You!