Regulatory Affairs

What do Regulatory Affairs Professionals Do?

Balazs Siminszky, Global Regulatory Lead

Overview

- Why regulate drug development?
- What is regulatory Affairs (RA)?
- Regulatory Affairs – The Basics
- Regulatory Documentation/Tools
- Role of RA During Pre-Approval Phase(R&D)
- Role of RA During Submission Phase
- Role of RA During Post-Approval Phase
- Specializations in Regulatory Affairs
- A Typical Day in Regulatory Affairs

Pharmaceutical Industry: Highly Regulated

Why Regulate Drug Development?

- Drugs are not ordinary consumer products
  - Tightly linked to **Public Health**
  - Professional advice needed for development

Pharmaceutical Industry: Highly Regulated

Common Goal:

- To assure the **high quality, safety and efficacy** of medicinal products

Basic Rules to Assure Safety and Efficacy:

- **Clinical trials** are conducted to test safety and efficacy
- **Marketing authorization**: all medicinal products must be authorized before they can be placed on the market. Authorizations are granted on the basis of the criteria of QUALITY, SAFETY and EFFICACY.
- **Manufacturing**: medicinal products are controlled to ensure their quality (quality standards as described by GMP).
- **Additional rules** related to distribution, advertising, pharmacovigilance

Participants:

- Companies and Regulators

Pharmaceutical Regulation – Driven By Disasters

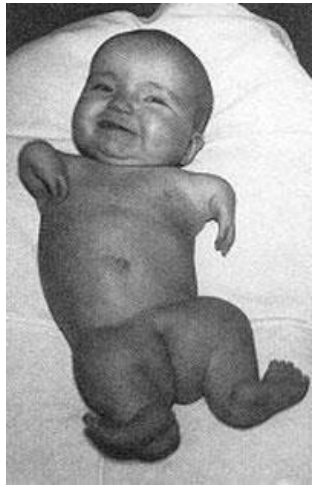
- Unfortunate events development of medicines regulation during 20th century
- 1937 – **Sulfonamide** - diethylene glycol poisoning, 100 people died in the United States died of **diethylene glycol poisoning** following the use of a sulfanilamide elixir, which used the chemical as a solvent without any safety testing.

  US Federal Food, Drug and Cosmetic Act and the birth of New D rug application

- 1956 – **Thalidomide disaster**, Neurosedyn. Sedative. 10000 newborn with deformities. Animal tests did not include tests looking at the effects of the drug during pregnancy. Reduced „morning sickness".

  ➔ modern controls on the sale and supply of pharmaceuticals

  - EU Directive 65/65/EEC



What is Regulatory Affairs (RA)?

Regulatory affairs is a **profession** developed from the desire of governments to protect public health by **controlling the safety and efficacy** of products in areas including pharmaceuticals.

Company's perspective:

- Support the registration of **new medicinal products**
- Gain regulatory approval for **changes to marketed products**
- Goal: fast approval (i.e. place and keep products on the market)

Regulator's perspective:

- To *assess* documentation submitted with the registration- or change application and *surveillanc*e of the use of medicinal products

Regulatory Affairs (Regulators) - Various Health Agencies

FDA:
Covering the US

EMA:
Covering the EU

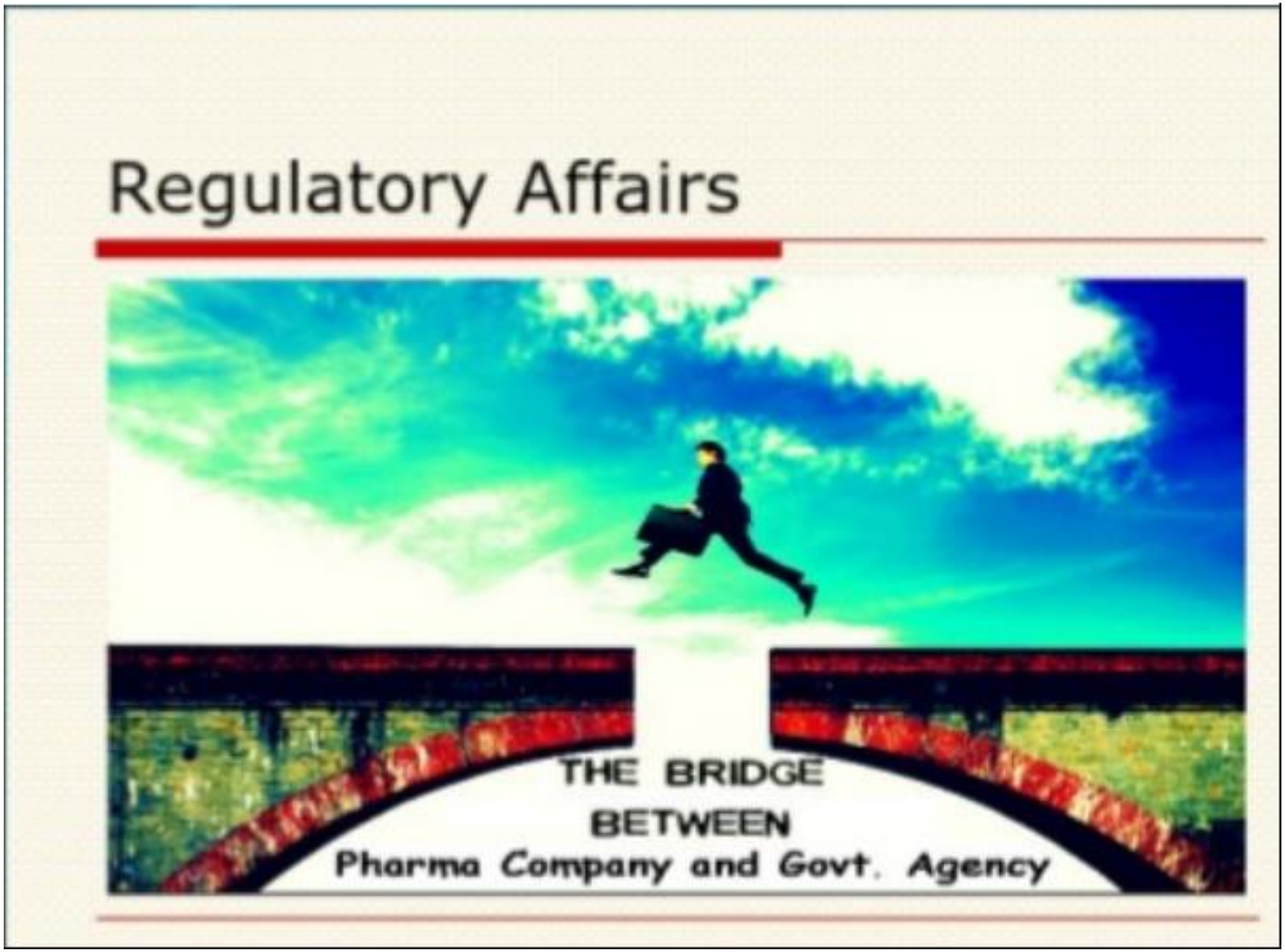
Health Canada:
Covering Canada

TGA:
Covering Australia

Országos Gyógyszerészeti és Élelmezés-egészségügyi Intézet
(OGYEI)
Covering Hungary (if not Centralized Procedure)

Regulatory Affairs (Company) – The Basics

The Role of Regulatory Affairs (Company)



The Role of Regulatory Affairs (Company)

Common Goal: High quality, Safe, efficacious medicinal products

Compliance at each stage of product development

These phases include:

- research and development,
- clinical trials,
- regulatory submissions,
- manufacturing,
- marketing, distribution,
- reimbursement, and
- post-market surveillance

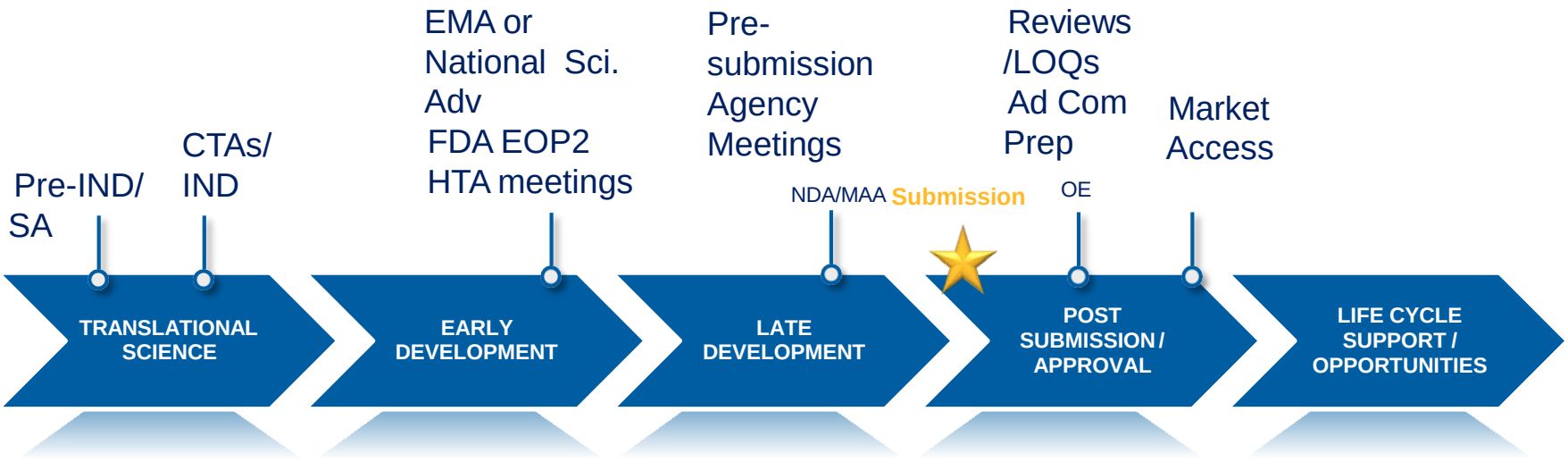
The Role of Regulatory Affairs (Company)

Main responsibilities

- **Keeps track of the ever-changing legislation** in all the regions in which a company wishes to distribute its products
- **Provides advice** on legal and scientific restraints and requirements
- **Collects, collates and evaluates** scientific data
- **Presents registration documents to regulatory agencies** and carries out any subsequent **negotiations** necessary to obtain or maintain marketing authorization for the products concerned
- **Gives strategic and technical advice** at the highest level in their companies, making an important contribution both commercially and scientifically to the success of a **development program** and the company as a whole
- **Helps the company avoid problems** caused by badly kept records, inappropriate scientific thinking or poor presentation of data.

The Role of Regulatory Affairs (Company)

Main responsibilities: Interactions with Regulators



Fit to purpose pre clinical programs

Phase 1
Breakthrough
PRIME
Acceleration strategies

Phase 2
Dose Selection,
Phase III design,
Integrated Regulatory/ MA plan,
Pediatric Plans

Phase 3
Confirmatory Clinical studies
Integrated Regulatory/ MA plan

Final Labeling
Risk Management
Pricing Negotiation
Training

Line Extensions
Implement RMPs/ REMs
Pediatric studies New indications

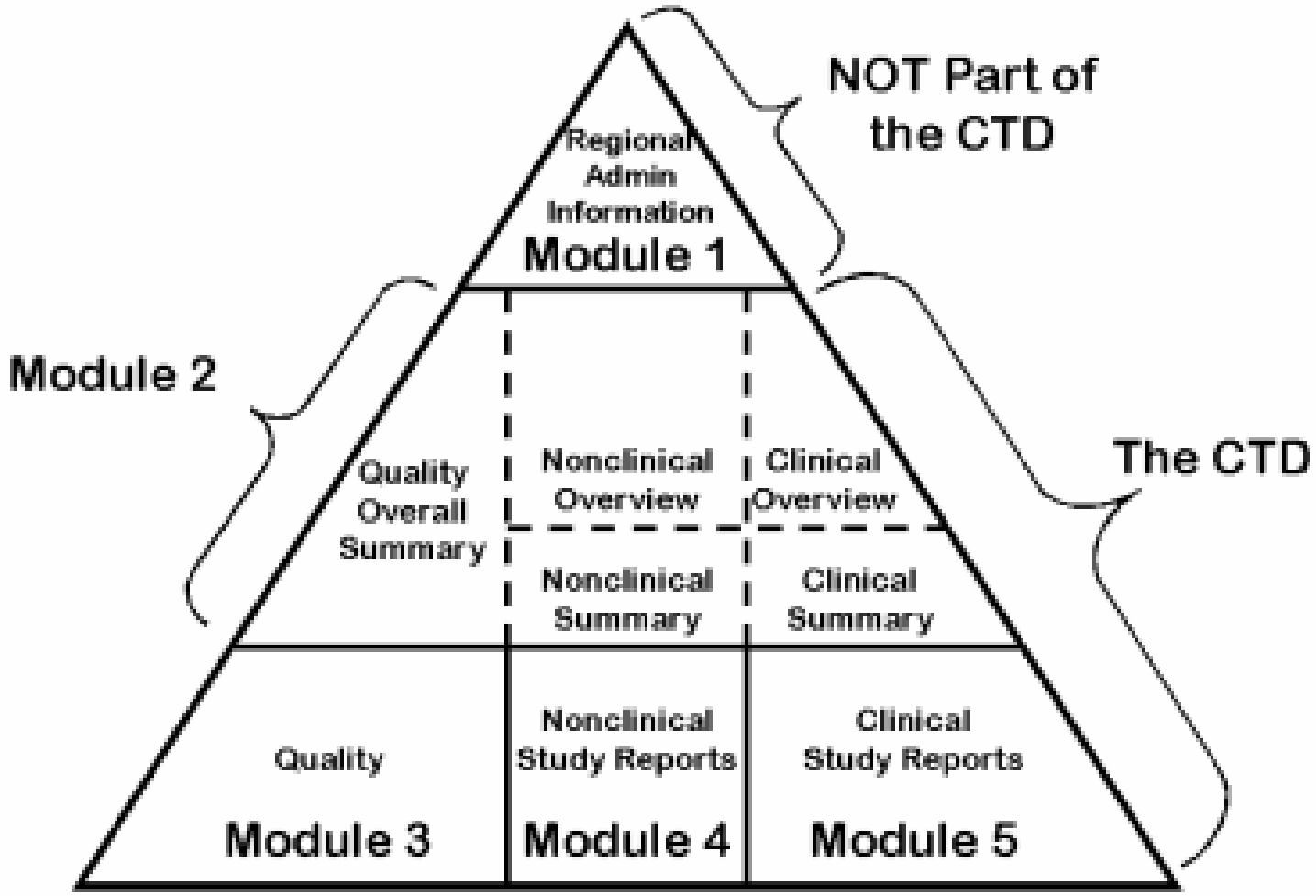
Regulatory Documentation/Tools

- In the past the regulatory documentation presented to the authorities was printed on paper and organized in binders.

- Common Technical Document (CTD) is the standard format used for Marketing Authorization Applications (MAAs, EU) and New Drug Applications (NDAs, US)

- Common agreed structure for the main sections (SAFETY, QUALITY, EFFICACY) of a regulatory submission

The CTD Triangle



The common technical document - CTD

The Common Technical Document is divided into five modules:

- Module 1 Administrative and prescribing information
- Module 2 Overview and summary of modules 3 to 5
- Module 3 Quality (Pharmaceutical documentation)
- Module 4 Preclinical (Pharmacology/Toxicology)
- Module 5 Clinical - efficacy (Clinical Trials)

Role of RA During Product Life Cycle

Pre-Approval Phase (R&D)

The Role Of Regulatory Affairs: Pre-approval

- **Strategic**
  - Participates in decision making on new projects or in-licensing.
  - Formulates strategies as to how a product be documented?
  - Contributes to risk assessments, time plans
  - Assesses how quick can the product be on the market? Which is the best way?

- **Operational**
  - Submits applications to authorities (structure and format)
  - Formulates time plans
  - Assures compliance

- **Responsive**
  - Responds to questions
  - Solves problems

The Role Of Regulatory Affairs: Pre-approval

- **Ensures that the legislative requirements are met**
  - Defines regulatory strategy
  - Participates in cross-functional project teams
  - Ensures application of guidelines
  - Advices on studies to demonstrate safety, quality and efficacy
  - Prepares of submission of application for clinical trials

The Role Of Regulatory Affairs: Pre-approval

Preparation of Product Information

Product Information	Function
Labels	Information on the packaging
Summary of Product Characteristics (SmPC)	Summary for the prescribers
Package Information Leaflet (PIL)	Information for the patient

- Indication and dosing
- Precautions and warnings
- Interactions with other drugs
- Undesirable effects

The claims in the Product Information needs to be supported by scientific data in the dossier.

Coordinates input from different parties.

The Role Of Regulatory Affairs: Pre-approval

Prepares High-level Documents

In all submission dossiers there will be overviews of the:

- non-clinical part
- quality part
- clinical part

  - It is an introduction to the data with a critical assessment of the results.
  - It justifies any deviations from guidelines
  - It justifies the development and testing strategy.

Role of RA – Application Phase

Routes to Registration

Centralized Procedure	Mutual Recognition procedure	Decentralized Procedure	National Procedure

Role of RA - Submission and Application Phase

- Leads application procedure
- Executes Electronic submission
- Leads/participates authority meetings/hearings
- Checks progress of evaluation and anticipates questions
- Clarifies questions, plans response and strategies with other departments
- Negotiates approval and Product Information with agencies

Approval!
Marketing Authorization (MA) Granted

An agreement with the authorities

- Valid for a period of 5 years.
- After 5 years renewal required

Role of RA – Post-Approval Phase

The Role of Regulatory Affairs – Post Approval Phase

- Submits variations
- Coordinates/Submits Renewals
- Pharmacovigilance
- Reviews Product Information
- New indications / New formulations
  - Provides regulatory input to development plans
- Regulatory Intelligence
  - What does the future hold?

LIFE CYCLE MANAGEMENT

The Role of Regulatory Affairs - Summary

- **Get the Product on the Market Quickly**

  (Meet the legislative requirements and present the company position in the best light to maximize competitiveness)

- **Keep the Product on the Market for a Long Time**

Specializations in Regulatory Affairs

The Various Roles within Regulatory Affairs

By Product Life Cycle

- R&D (Pre-approval)
- Submission management
- Maintenance management (Post-approval)

By Specialty

- CMC specialist (quality)
- Pre-clinical/Clinical specialist
- Labelling expert
- Regulatory intelligence

The Various Roles within Regulatory Affairs

Regulatory Intelligence

- Is a systematic process initiated by a defined need
- It is a collection of data and analysis of the data linked to a strategy
- It is legal and ethical (not espionage/hacking)
- So much information available on websites/databases
- Typical question – what other modified release products with indications x and y exist in Europe? What clinical trials supported the approval?

The Various Roles within Regulatory Affairs

By Scope (Global versus Local)

- Global/Head office
  - Strategies
  - Specialized
  - Contact with experts
  - Compile common documents and variations and send to affiliates
  - Contact with manufacture, sales and logistics
- Affiliate/local/market
  - Specialist in local requirements – adapt the common documents
  - Translations
  - Contact with market, sales and logistics
  - Customer complaints and questions

The Various Roles within Regulatory Affairs

By Product Type (Original versus Generics)

	Generics	Originator
Production	Often contract manufacturing	Own facilities
Products	High number of different products and different types of products	Few high volume products

An Average Day at Work Depends on all these factors

- Generic vs Originator
- HQ vs Affiliate
- Generalist vs Specialist
- Strategic (R&D) vs Operational (Post-approval)
- Small molecule vs Biologics
- Quality vs Clinical

Typical Daily Activities (Regardless of Function)

- Project management
  - planning, coordinating, summarizing
- Read, review, write
  - Interpret legislations and, guidelines etc.
- Communication/collaboration – meetings/e-mails/TC
  - Business Partners, CROs, manufacturers, consultants and other experts
  - Medicines Agencies
  - Colleagues
- Small details versus bigger picture
- Fast paced but still precise…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