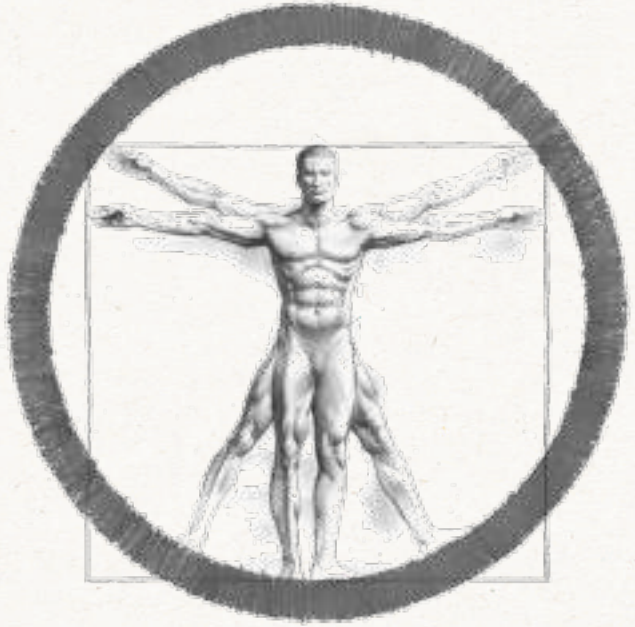
REGULATORY AFFAIRS

UNIVERSITY JOINS INDUSTRY - BARCELONA – MARCH 15TH, 2017

believe in life
Galenicum

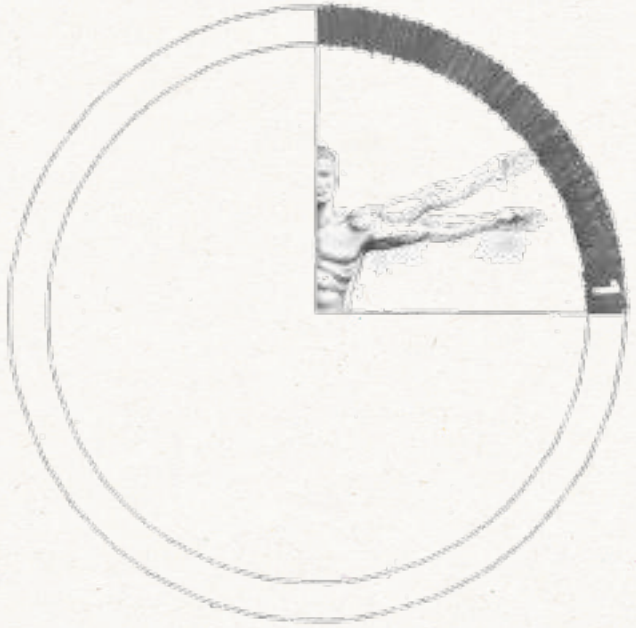


Introduction

Regulatory Affairs-Europe

Regulatory Affairs-other markets

Career development & personal skills



Introduction

Regulatory Affairs-Europe

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Career development & personal skills

Background, key points & basic knowledge

LUISA **SALAZAR**-REGULATORY AFFAIRS B2C MANAGER-GALENICUM HEALTH

- BACHELOR DEGREE: PHARMACY – USAC, GUATEMALA
- MASTER DEGREE: Master in Pharmaceutical Industry-CESIF, BARCELONA
- **MASTER DEGREE-*Graduate Education*:** Quality systems in Pharmaceutical Industry. UB-BARCELONA.

BACKROUND:

- I am a regulatory affairs specialist with more than 8 years experience in the different areas of the Pharmaceutical Industry (QA, QC, manufacturing, RA), and since 2011 located in Barcelona. Specialised in European markets, and currently working also with Latin America, Asia and other emerging markets.

Galenicum Health: is a pharmaceutical company focused in the development of generic products, with a B2B business model in EU & B2C model in other markets.

Well known history.....

THALIDOMIDE NIGHTMARE

Truth Reporter

THIS IS BLACK AUGUST. Mothers all over the world will remember it as the end of a nightmare.

THOUSANDS of malformed babies will have been born because of a colossal medical blunder.

New Zealand may not have escaped.

There is one answer to those who say that thalidomide—which wonder-drugged a pill-taking international public into trusting, deep-sleep acceptance—was not readily available in this country: WRONG!

There was nothing to stop a chemist counter-prescribing this "first-schedule poison." Under the Poisons Act, retail distribution was gave quick sleep, rarely left hangovers, and for would-be suicides it appears it was only expensive.

For expectant mothers it was just the thing.

Now it stands accused of causing foetal malformation.

When the balloon went up overseas nine months ago, the New Zealand distributors—Distillers Co. Biochemicals (NZ) Ltd., Auckland—properly and promptly went into action.

They whisked the five brands of thalidomide-content pills off the market before the Health Depart-

Eight months before NZ public was warned

World's legacy of tragedy

THE THALIDOMIDE NIGHTMARE will leave a legacy of tragedy in its wake. The global picture:

LONDON: Three hundred deformed babies are expected to be born during the next few weeks as a result of mothers in England and Wales taking thalidomide during early pregnancy.

WASHINGTON: Hundreds of Americans were given the drug on an experimental basis, according to Dr. Frances Kelsey, the Government scientist who blocked the drug for commercial sale.

LIEGE, Belgium: Susanna Vandeput, 25, is in prison accused of murdering her newly-born armless daughter. She took a tranquilliser drug during pregnancy.

SYDNEY: A baby boy, born without arms because of the effects of the drug thalidomide, has been baptised in a Sydney church. Under the trade name of Distaval, the drug

robot arms

every chemist's shop in the country and find a record of every thalidomide disposal since Sedem-

Its remedy is one aspect of the proposed amendment to the Food and Drugs Act, which seeks auth-

"There was very, very little sold," a director told me.

1950-1960s.

Until Thalidomide tragedy, the drugs were being sold by notification to health authority and NO safety, efficacy or quality data were required to be submitted prior marketing.

65/65/EEC came into effect (*mandating that no medicines can be marketed in European Communities until and unless it is not approved by at least one competent authority within Europe)*

Sulfanilamide Elixir

1938 <100 deaths using DEG as solvent

Food, Drug & Cosmetic Act 1938

(Pre-marketing approval of all new drugs was made mandatory and proof of scientific study was asked by FDA)

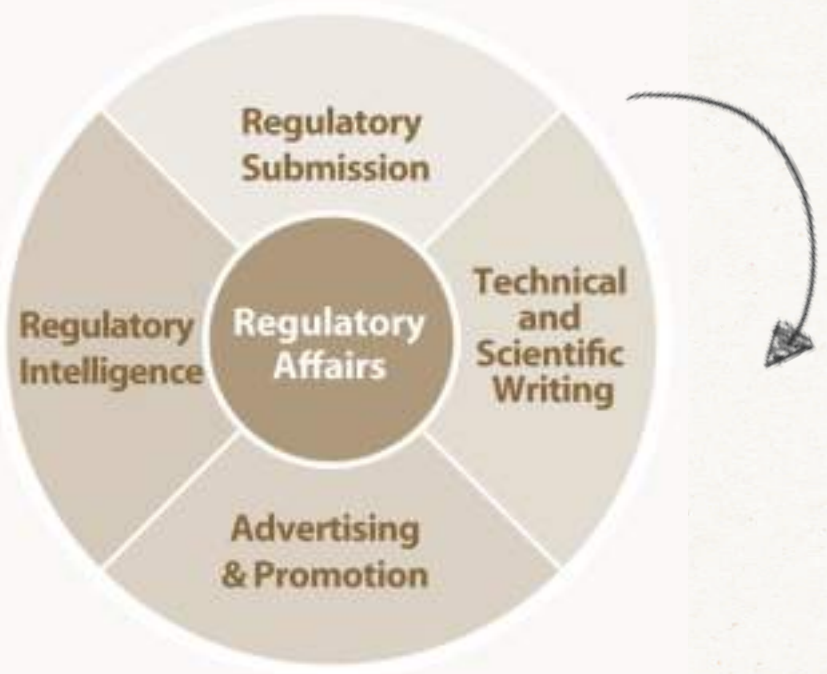
WHAT DO WE DO???

Internally

- Drug development
- Clinical research
- Manufacturing
- Marketing

Externally

- Interface between companies and Authorities



ALL MEDICINAL PRODUCTS REQUIRE PRIOR AUTHORISATION TO BE MARKETED, AND FOR THAT REQUIRE A REGISTRATION, WHICH DOCUMENTS AND ASSURES IT´S QUALITY, SAFETY AND EFFICACY

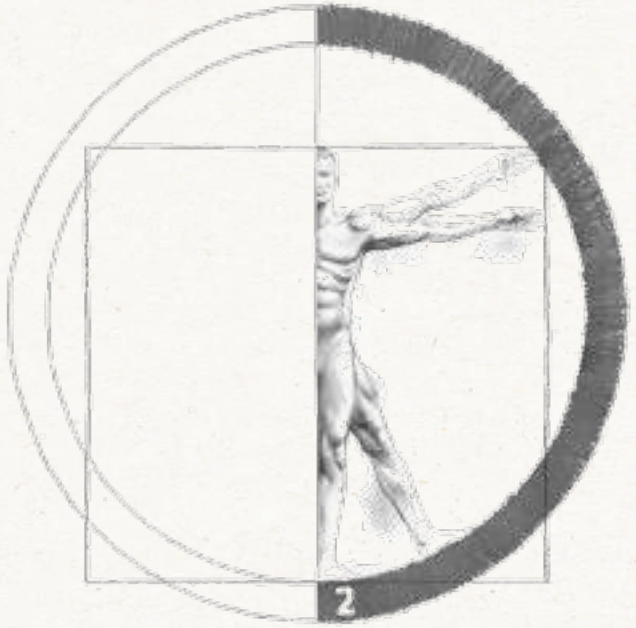
PREPARATION OF DOSSIER

VARIATIONS, Post marketing activities

Research → Approval → Commercialisation

MARKETING AUTHORIZATION

PRICE & REIMBURSEMENT



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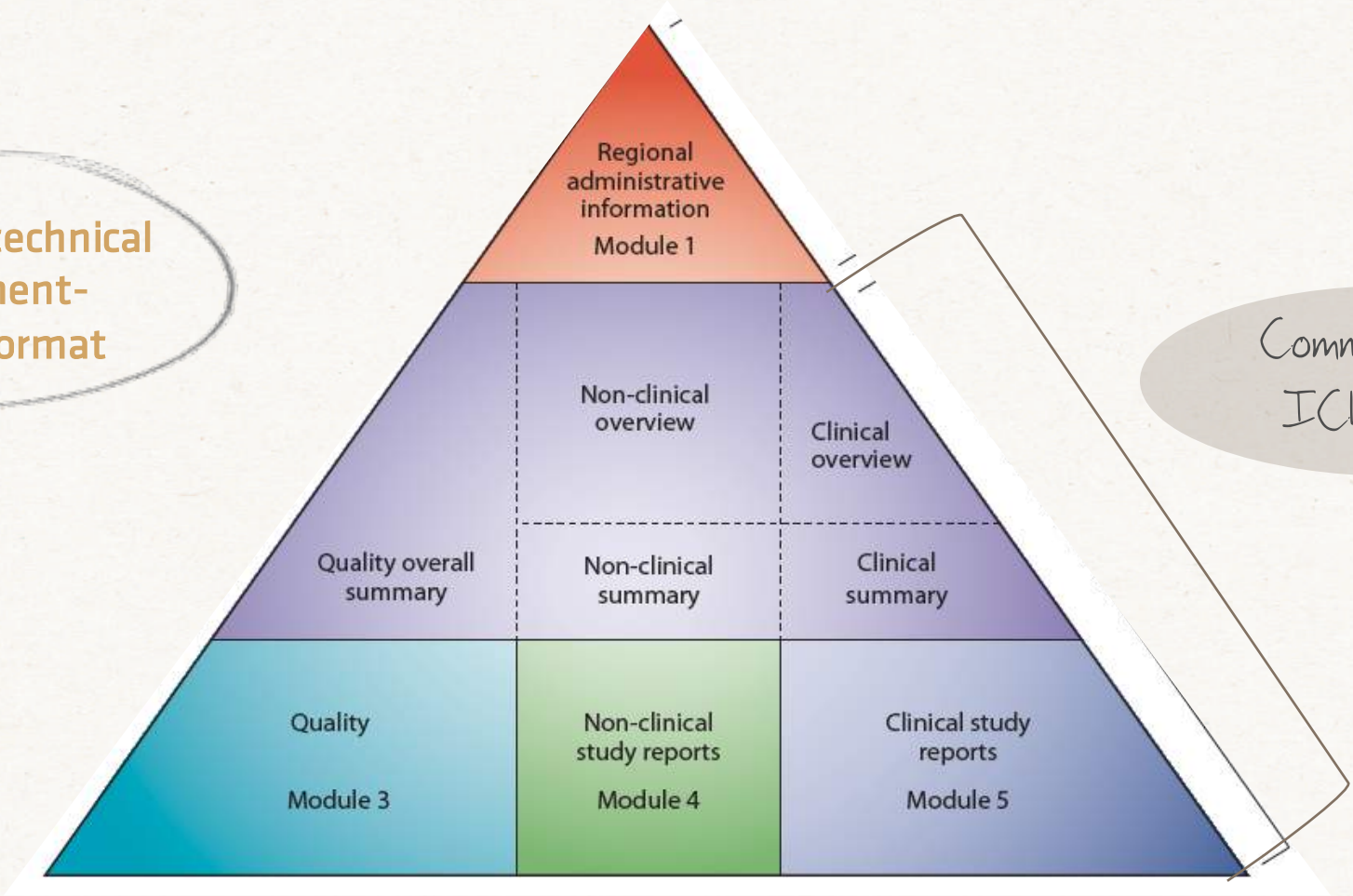
TYPE OF DOSSIERS:
1.COMPLETE/STAND-ALONE: INNOVATOR (Art.8.3) or BIBLIOGRAPHICAL (Art.10a)

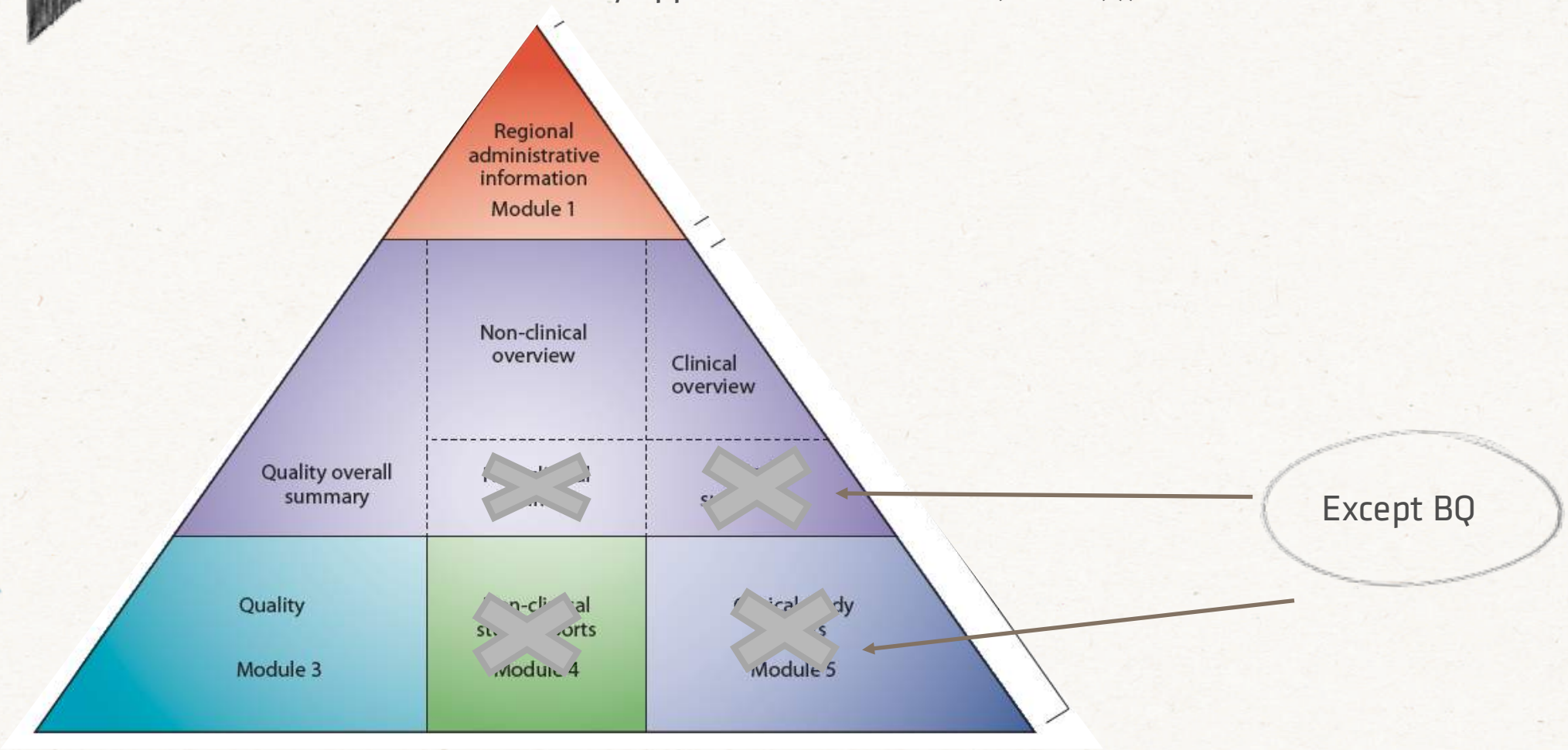
Common technical document- eCTD Format



Common for all ICH regions

TYPE OF DOSSIERS:

2.ABRIDGED: linked to one already approved, ex. GENERIC (Art.10(1))



Research

Module 1 Table of Content

1.0 Cover Letter

1.1 Comprehensive Table of Contents

1.2 Application Form

1.3 Product Information

- 1.3.1 SPC, Labelling and Package Leaflet
- 1.3.2 Mock-up
- 1.3.3 Specimen
- 1.3.4 Consultation with Target Patient Groups
- 1.3.5 Product Information already approved in the Member States
- 1.3.6 Braille

Texts

1.4 Information about the Experts

- 1.4.1 Quality
- 1.4.2 Non-Clinical
- 1.4.3 Clinical

1.5 Specific Requirements for Different Types of Applications

- 1.5.1 Information for Bibliographical Applications
- 1.5.2 Information for Generic, 'Hybrid' or Bio-similar Applications
- 1.5.3 (Extended) Data/Market Exclusivity
- 1.5.4 Exceptional Circumstances
- 1.5.5 Conditional Marketing Authorisation

1.6 Environmental Risk Assessment

- 1.6.1 Non-GMO
- 1.6.2 GMO

Administrative summary: type procedure, legal basis, prescription, companies, formula

1.7 Information relating to Orphan Market Exclusivity

- 1.7.1 Similarity
- 1.7.2 Market Exclusivity

1.8 Information relating to Pharmacovigilance

- 1.8.1 Pharmacovigilance System
- 1.8.2 Risk-management System

Pharmacovigilance

1.9 Information relating to Clinical Trials

Responses to Questions

Additional Data

Module 2.1	Common Technical Document Table of Contents (Module 2 – 5)
Module 2.2	Introduction
Module 2.3	Quality Overall Summary
Module 2.4	Nonclinical Overview
Module 2.5	Clinical Overview
Module 2.6	Nonclinical Summary
Module 2.7	Clinical Summary

Module 2

Drug substance (API)

Module 3	
3.1	MODULE 3 TABLE OF CONTENTS
3.2	BODY OF DATA
3.2.S	DRUG SUBSTANCE
3.2.S.1	General Information
3.2.S.2	Manufacture
3.2.S.3	Characterisation
3.2.S.4	Control of Drug Substance
3.2.S.5	Reference Standards or Materials
3.2.S.6	Container Closure System
3.2.S.7	Stability
3.2.P	DRUG PRODUCT
3.2.P.1	Description and Composition of the Drug Product
3.2.P.2	Pharmaceutical Development
3.2.P.3	Manufacture
3.2.P.4	Control of Excipients
3.2.P.5	Control of Drug Product
3.2.P.6	Reference Standards or Materials
3.2.P.7	Container Closure System
3.2.P.8	Stability

Drug Product

Module 3 (Cont.)	
3.2.A	APPENDICES
3.2.A.1	Facilities and Equipment
3.2.A.2	Adventitious Agents Safety Evaluation
3.2.A.3	Novel Excipients
3.2.R	REGIONAL INFORMATION
3.3	LITERATURE REFERENCES

NATIONAL PROCEDURE (NP)

- Authorisation only in the country.
- Marketing in the country.

EVALUATION PROCEDURES: Types of procedures

MUTUAL RECOGNITION (MRP)

- If the medicinal product <u>already has</u> a national Marketing Authorisation (MA) in the EU.
- Marketing in the countries of the EU included in the MRP.

DESCENTRALIZED PROCEDURE (DCP)

- If the MP <u>HAS NOT</u> a previous national MA in the EU.
- Marketing in the countries of the EU included in the DCP.

EVALUATION PROCEDURES: Types of procedures

CENTRALIZED PROCEDURE (CP)

- Mandatory: Bio tech products-HIV-cancer-Neuro-Diabetes-AI disease Orphan drugs, viral diseases.
- Optional for new AS, and GENERICs of prod approved via CP (ej: Olanzapine, Sildenafil).
- Marketing in all the EU.

Authorization...when?????

Approval

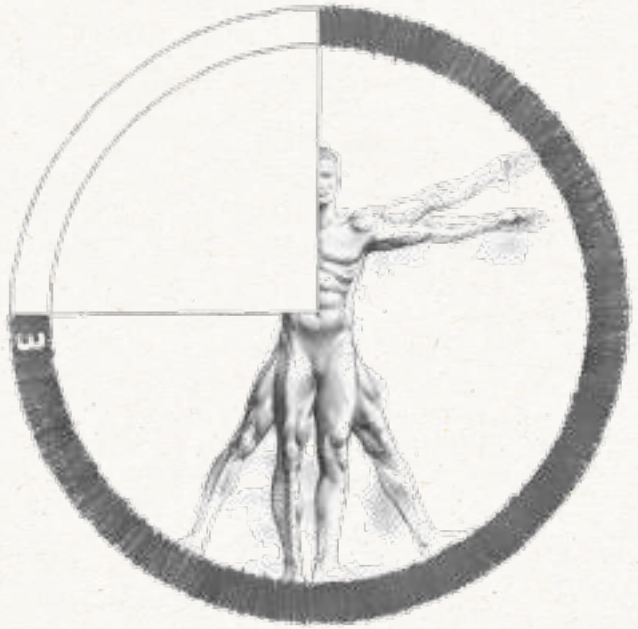
Pre-procedural Step	
Before Day -14	Applicant discussions with RMS RMS allocates procedure number. Creation in CTS.
Day –14	Submission of the dossier to the RMS and CMSs Validation of the application. Positive validation should only be indicated in CTS, not via e-mail.
Assessment step I	
Day 0	RMS starts the procedure. The CMS are informed via CTS.
Day 70	RMS forwards the Preliminary Assessment Report (PrAR) (including comments on SmPC, PL and labelling) on the dossier to the CMSs and the applicant
Until Day 100	CMSs send their comments to the RMS, CMSs and applicant. It may also be sufficient for the CMS to indicate in CTS only in case there are no additional comments
Until Day 105	Consultation between RMS and CMSs and applicant. If consensus not reached RMS stops the clock to allow applicant to supplement the dossier and respond to the questions.
Clock-off period	Applicant may send draft responses to the RMS and agrees the date with the RMS for submission of the final response. Applicant sends the final response document to the RMS and CMSs within a period of 3 months, which can be extended by a further 3 months.
Day 106	RMS restarts the procedure following the receipt of a valid response or expiry of the agreed clock-stop peri received. The CMS are informed via e-mail and CTS will be updated accordingly.
Assessment step II	
Day 120 (Day 0)	RMS sends the DAR, draft SmPC, draft labelling and draft PL to CMSs and the applicant
Day 145 (Day 25)	CMSs send comments to RMS, CMSs and the applicant. It may also be sufficient for the CMS to indicate in CT comments.
Day 150 (Day 30)	RMS may close procedure if consensus reached Proceed to national 30 days step for granting MA
Until 180 (Day 60)	If consensus is not reached by day 150, RMS to communicate outstanding issues with applicant, receive any additional clarification, prepare a short report and forward it to the CMSs and the applicant
Day 195 (at the latest)	A Break-Out Session (BOS) may be held at the European Medicines Agency with the involved MSs to reach consensus on the major outstanding issues
Between Day 195 and Day 210	RMS consults with the CMSs and the applicant to discuss the remaining comments raised.
Day 210 (Day 90)	Closure of the procedure including CMSs approval of assessment report, SmPC, labelling and PL, or referral to Co-ordination group. Proceed to national 30 days step for granting MA.
Day 210 (at the latest)	If consensus on a positive RMS AR was not reached at day 210, points of disagreement will be referred to the Co-ordination group for resolution
Day 270 (at the latest)	Final position adopted by Co-ordination Group with referral to CHMP/CVMP for arbitration in case of unsolved disagreement
National step	
5 days after close of procedure	Applicant sends high quality national translations of SmPC, labelling and PL to CMSs and RMS
30 days after close of the procedure	Granting of national marketing authorisation in RMS and CMSs if outcome is positive and there is no referral to the Co-ordination group. (National Agencies will adopt the decision and will issue the marketing authorisation subject to submission of acceptable translations).
30 days after close of CMD referral procedure	Granting of national marketing authorisation in RMS and CMSs if positive conclusion by the Co-ordination group and no referral to the CHMP/CVMP. (National Agencies will adopt the decision and will issue the marketing authorisation subject to submission of acceptable translations).

DESCENTRALIZED PROCEDURE (DCP)

Constantly UPDATING the dossier

Variations: any change on the approved conditions must be submitted/approved

	TYPE IA & IA IN	TYPE IB	TYPE II
DEFINITION	Do & Tell	Tell, wait & Do	Major variations
TIMINGS	15days/20days	20+30days/3-4months	15+90[+60]days/8-10months
EXAMPLES	• Change of name and/or direction of MAH • Add packagers and releasers; • Change batch size of API	• Change name of the product; • MINOR change in the manuf process of API and FP; • Change expiry date & storage conditions of API & FP;	• Add and/or change of supplier for API with DMF; • Change of compostion; • Change of specifications.
FEES	ES: 717.25€ IE:NA EMA: 3000€	ES: 1236.85€ IE: 345€ EMA: 6900€	ES: 7051.73€ IE: 1797€ EMA: 61800€



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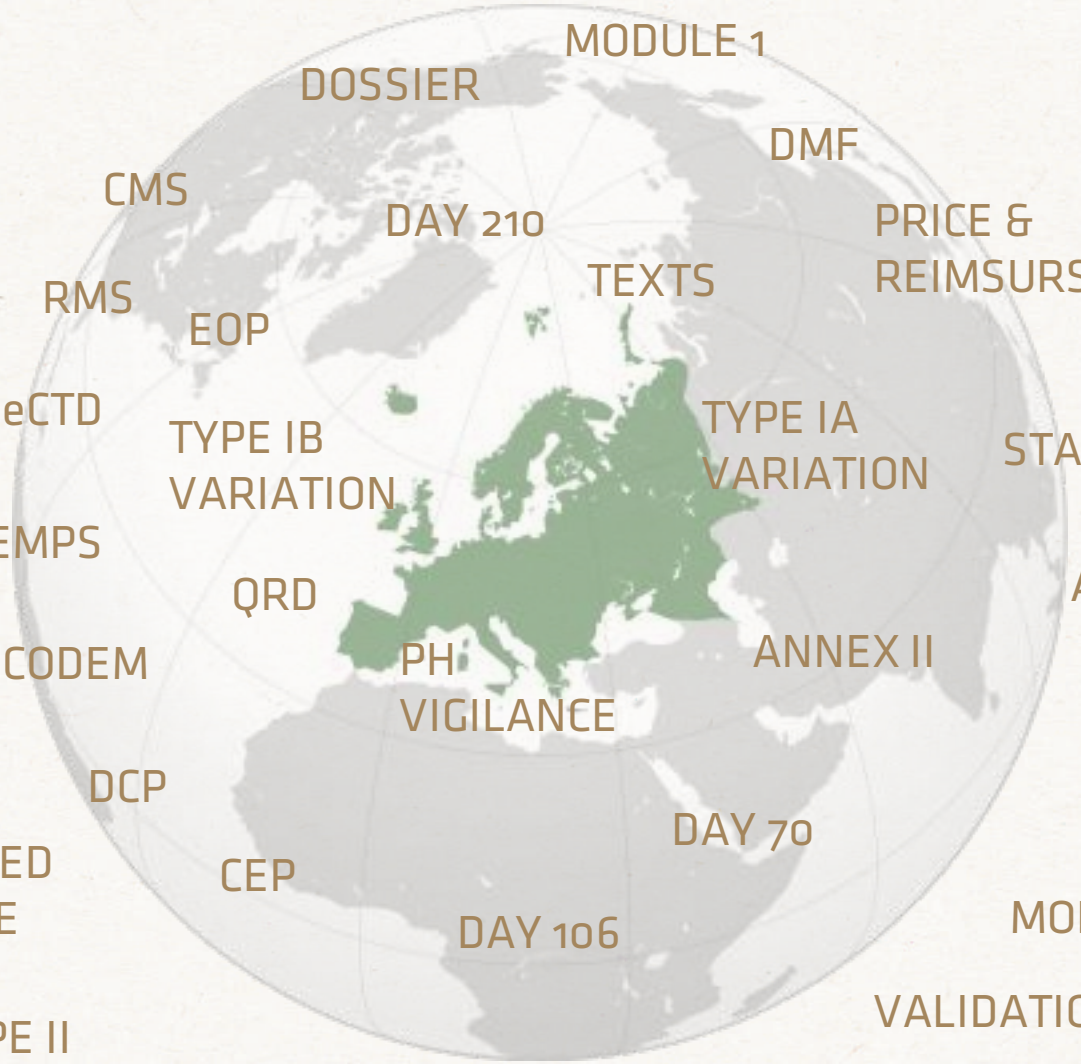
REGULATORY AFFAIRS-EUROPE



MODULE 1
DOSSIER
DMF
HOLDER
CMS
DAY 210
PRICE &
REIMSURSEMENT
TEXTS
RMS
EOP
PH EUR
eCTD
TYPE IA
VARIATION
STABILITY
TYPE IB
VARIATION
CONTROL &
RELEASE
AEMPS
ASMF
QRD
ANNEX II
CODEM
PH
VIGILANCE
MODULE 2
MUTUAL
RECOGNITION
DCP
SLOT
DAY 70
CENTRALIZED
PROCEDURE
CEP
MODULE 3
DAY 106
VALIDATION
TYPE II
VARIATION
READABILITY
TEST
BIOEQUIVALENCE

ROW COUNTRIES

CPP

"*Certificate of Pharmaceutical Product*"

- Establishes the status of the pharmaceutical product and of the applicant in the exporting country.
- For cosmetics: CLV

- Commercialized
- Not commercialized

Zone IV

- Zone IVa: 30°C/65%
- Zone Ivb 30°C/75%

- Zone IVa: Panama, RD, Peru,
- Zone IVb; ASEAN, Brazil

Legalization

- Apostille of the Hague
- Legalization through embassy

Samples

Of finished product and WS with <1 year exp.

Differences Europe & ROW countries

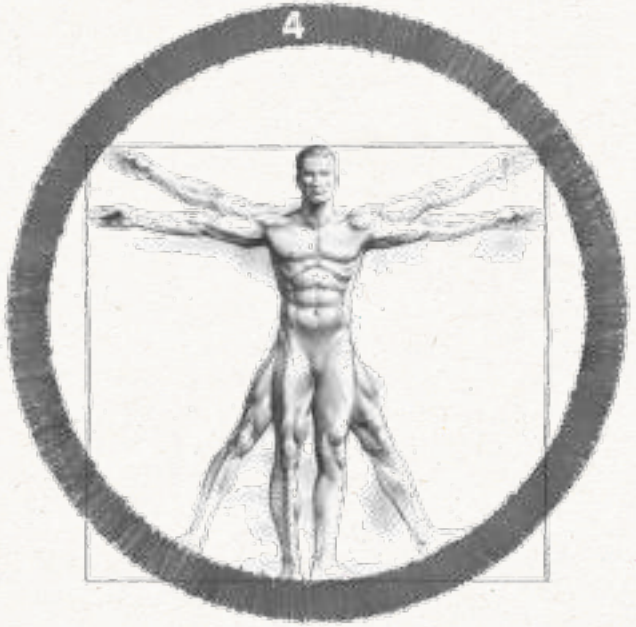
ACTIVITIES	EUROPE	ROW COUNTRIES
Format of dossier	Electronic format, in English-CD or CESP submission	Electronic format (Chile, Peru) Paper (Panama, Rep Dom)
Administrative/legal	Scanned copies OK	CPP, GMP legalized and apostilled
Stability	Zone II Min: 6 months	Zone II or Zone IV Min: 3 or 6 or 12 months (depends country)
Content Dossier	Modules 1-5	Extracts of the European dossier.
Timings approval	Around 1 year	No legislation on this: Chile 6-8 months Peru: 10-18 months Panama: >12 months RD: >12 months but can commercialized before
Samples (local analysis)	Required for some countries	Yes, Panama and RD. Same samples as CPP
Bioequivalence	Mandatory	Mandatory for some countries (Colombia, Chile, Singapore, MY) MY, VN, Mexico: local BQ

Differences Europe & ROW countries

ACTIVITIES	EUROPE	ROW COUNTRIES
Manufacturer of API	Mandatory DMF or CEP. >1 API manufacturer allow	Mandatory in some countries and >1 allow with stab data (Chile, SG, MY) Specifications only: Peru, RD-NO DMF
Manufacturer of FP	More than 1 allow	Just one allow in LATAM SG, MY more than one (with stab studies)
Manufacturing contracts	NA	Yes if manufacturer is different than holder in the country. Legalized
Holder	European MAH	Chile, Peru, Colombia, ASEAN: Local holder Panama, RD, Central America: Local holder not mandatory
Validation phase	1-2 months	No validation. Some countries there is something called "la ventanilla"
Name of the product	INN + Name Holder + strength and FF	Invented name (Vitae) is OK. Some countries is allow generic name + vitae. Chile, Mexico have different requirements.

Addition of an API manufacturer- CEP

ACTIVITY	EUROPE	CHILE	PERU
Variation?	Yes, Type IA_{IN}	Yes, no formal legislation	No, as long as the same specifications are kept (Ph Eur)
Requirements	**No stability of the finish product and shelf life is the same as the already approved**	**Stability of the finished product with the new API. Risk that shelf life could change**	**NA**
Timing approval	Do & Tell	3-4 months	NA



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Career development & Personal skills for RA

Career

- Graduate in Health Science, preferibly Pharmacy (Biology, Medicine, etc)
- Normally, post-graduate focused in Industry required, including intership. Ex: CESIF, UB, etc
- High English level

Skills

- Attitude: self-motivated, easy learning, hustler, multi-task, ...
- Organised, tidy, responsible, focused, ...

thank you!