Introduction
Regulatory Affairs - Europe
Regulatory Affairs - other markets
Career development & personal skills
Introduction

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Regulatory Affairs - other markets

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.

**Background:**

- 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.
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)
Regulatory Affairs

WHAT DO WE DO???

Internally

Drug development
Clinical research
Manufacturing
Marketing

Externally

Interface between companies and Authorities

Regulatory Submission
Regulatory Intelligence
Advertising & Promotion
Technical and Scientific Writing
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.
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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**
Europe

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

Except BQ
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

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

Module 2  Common Technical Document: Table of Contents (Module 2 – 5)

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

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

1.9 Information relating to Clinical-Trials

Responses to Questions

Additional Data
### 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

**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
EVALUATION PROCEDURES: Types of procedures

NATIONAL PROCEDURE (NP)

- Authorisation only in the country.
- Marketing in the country.
EVALUATION PROCEDURES: Types of procedures

**MUTUAL RECOGNITION (MRP)**

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

**DECENTRALIZED PROCEDURE (DCP)**

- If the MP **HAS NOT** 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?????

<table>
<thead>
<tr>
<th>Pre-procedural Step</th>
<th></th>
</tr>
</thead>
</table>
| 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. |

<table>
<thead>
<tr>
<th>Assessment step I</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 0</td>
<td>RMS starts the procedure. The CMSs are informed via CTS.</td>
</tr>
<tr>
<td>Day 70</td>
<td>RMS forwards the Preliminary Assessment Report (PrAR) (including comments on SmPC, PL and labelling) on the dossier to the CMSs and the applicant.</td>
</tr>
<tr>
<td>Until Day 100</td>
<td>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.</td>
</tr>
<tr>
<td>Until Day 105</td>
<td>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.</td>
</tr>
<tr>
<td>Clock-off period</td>
<td>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.</td>
</tr>
<tr>
<td>Day 106</td>
<td>RMS restarts the procedure following the receipt of a valid response or expiry of the agreed clock-step period received. The CMSs are informed via e-mail and CTS will be updated accordingly.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Assessment step II</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 120 (Day 0)</td>
<td>RMS sends the DAR, draft SmPC, draft labelling and draft PL to CMSs and the applicant</td>
</tr>
<tr>
<td>Day 145 (Day 25)</td>
<td>CMSs send comments to RMS, CMSs and the applicant. It may also be sufficient for the CMS to indicate in CTS only in case there are no additional comments.</td>
</tr>
</tbody>
</table>
| 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 |

<table>
<thead>
<tr>
<th>National step</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>5 days after close of procedure</td>
<td>Applicant sends high quality national translations of SmPC, labelling and PL to CMSs and RMS</td>
</tr>
<tr>
<td>30 days after close of the procedure</td>
<td>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).</td>
</tr>
<tr>
<td>30 days after close of CMD referral procedure</td>
<td>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).</td>
</tr>
</tbody>
</table>
Variations: any change on the approved conditions must be submitted/approved

<table>
<thead>
<tr>
<th>TYPE IA &amp; IA IN</th>
<th>TYPE IB</th>
<th>TYPE II</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEFINITION</td>
<td>Do &amp; Tell</td>
<td>Tell, wait &amp; Do</td>
</tr>
<tr>
<td>TIMINGS</td>
<td>15days/20days</td>
<td>20+30days/3-4months</td>
</tr>
</tbody>
</table>
| 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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**CPP**

“Certificate of Pharmaceutical Product”
- Establishes the status of the pharmaceutical product and of the applicant in the exporting country.
- For cosmetics: CLV

**Zone IV**

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

**Legalization**

- Apostille of the Hague
- Legalization through embassy

**Samples**

- Of finished product and WS with <1 year exp.

- Commercialized
- Not commercialized

- Zone IVa: Panama, RD, Peru,
- Zone IVb: ASEAN, Brazil
### Differences Europe & ROW countries

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

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

### Addition of an API manufacturer- CEP

<table>
<thead>
<tr>
<th>ACTIVITY</th>
<th>EUROPE</th>
<th>CHILE</th>
<th>PERU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variation?</td>
<td>Yes, Type IA&lt;sub&gt;IN&lt;/sub&gt;</td>
<td>Yes, no formal legislation</td>
<td>No, as long as the same specifications are kept (Ph Eur)</td>
</tr>
<tr>
<td>Requirements</td>
<td>No stability of the finish product and shelf life is the same as the already approved</td>
<td>Stability of the finished product with the new API. Risk that shelf life could change</td>
<td>NA</td>
</tr>
<tr>
<td>Timing approval</td>
<td>Do &amp; Tell</td>
<td>3-4 months</td>
<td>NA</td>
</tr>
</tbody>
</table>
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Career development & personal skills
Career development & Personal skills for RA

Career

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

Skills

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

KEEP CALM AND
LOVE A
REGULATORY AFFAIRS OFFICER