Drug & Device Development & Approval Process for Latin America

(Overview of the Laws/Regulations and Key Requirements)

Latin America Healthcare Compliance Certification Program

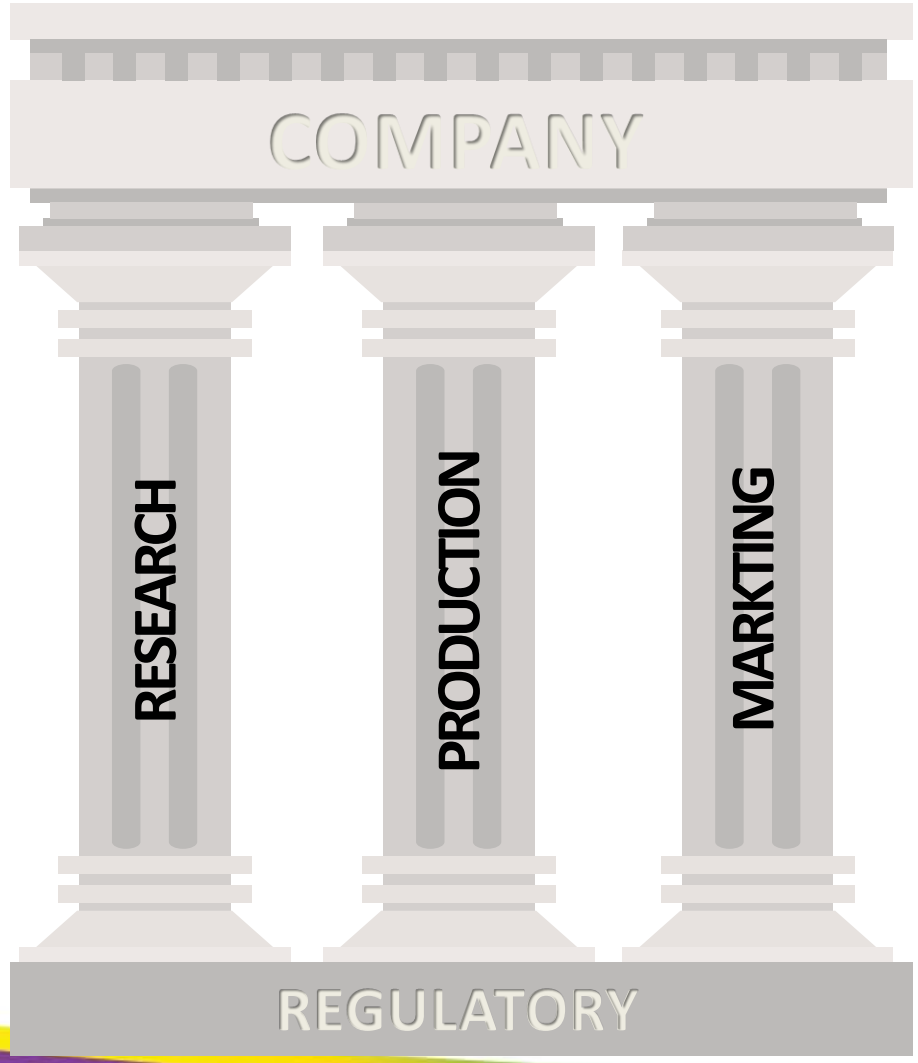
September 25, 2018

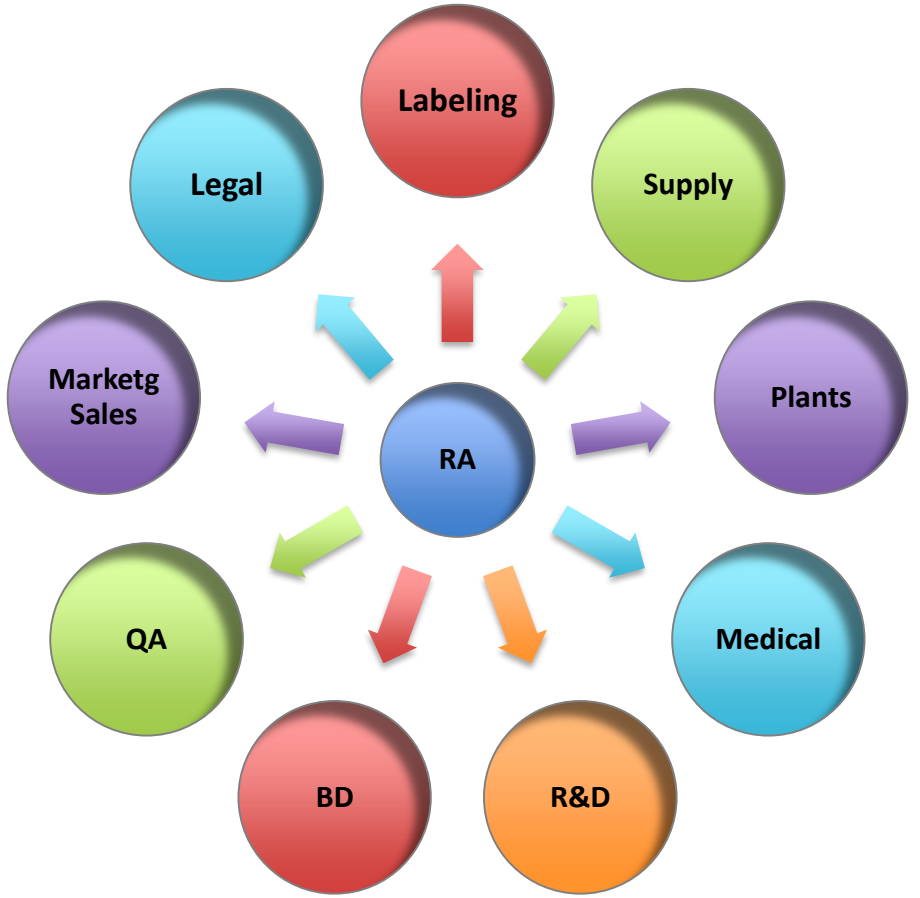
São Paulo, Brazil

LATAM GENERAL OVERVIEW

Regulatory Affairs

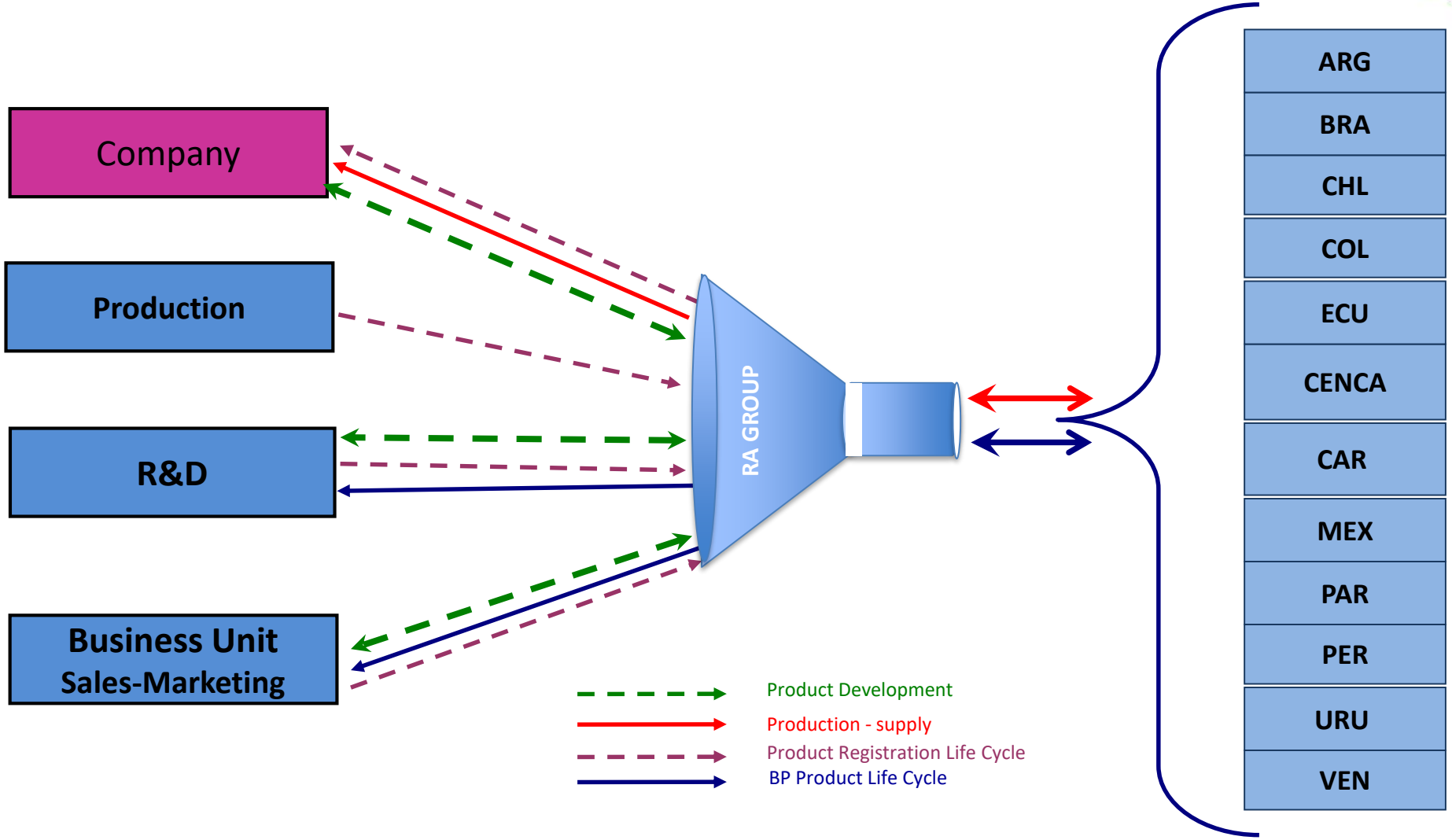
Is the foundation...and the link to compliance





WHY-WHAT-HOW-WHEN

Regulatory Information Flow



Regulatory Affairs Role

1. **Advise** the company on the existence and implications of new regulatory developments in LATAM
2. **Influence** and shape Health Authority positions on matters of importance to the company
3. **Collaborate** with management and global project teams to shape and execute effective regulatory strategies to support its commercial objectives
4. **Lead** and manage the process of preparing, submitting and tracking quality regulatory documents and dossiers
5. **Cultivate** and manage effective Health Authority relationships
6. **Provide** efficient, compliant, technical support to maintain **products on the market**

Challenges

- Regulatory environment continues to get more complex and difficult to manage
- No harmonization in regulatory requirements
- There is no **“one size fits all”** approach
- Constant changes in regulations
- Difference in country labeling
- Limited Health Authorities resources for review
- Local clinical trials/ B.E study
- No formal pre-submission or scientific advice meetings
- Long review timelines
- MOH requesting more detailed documentation i.e. SOPs, validation, API
- Plant inspections (lack of mutual recognition amongst countries within region)

Keys for Success

- Know and be compliant with country local requirements
- Understand the culture
- Establish relationships with local authorities
- Frequent and early communication with Health Authorities
- Early integration of emerging market strategy into development plans (local and regional requirements)

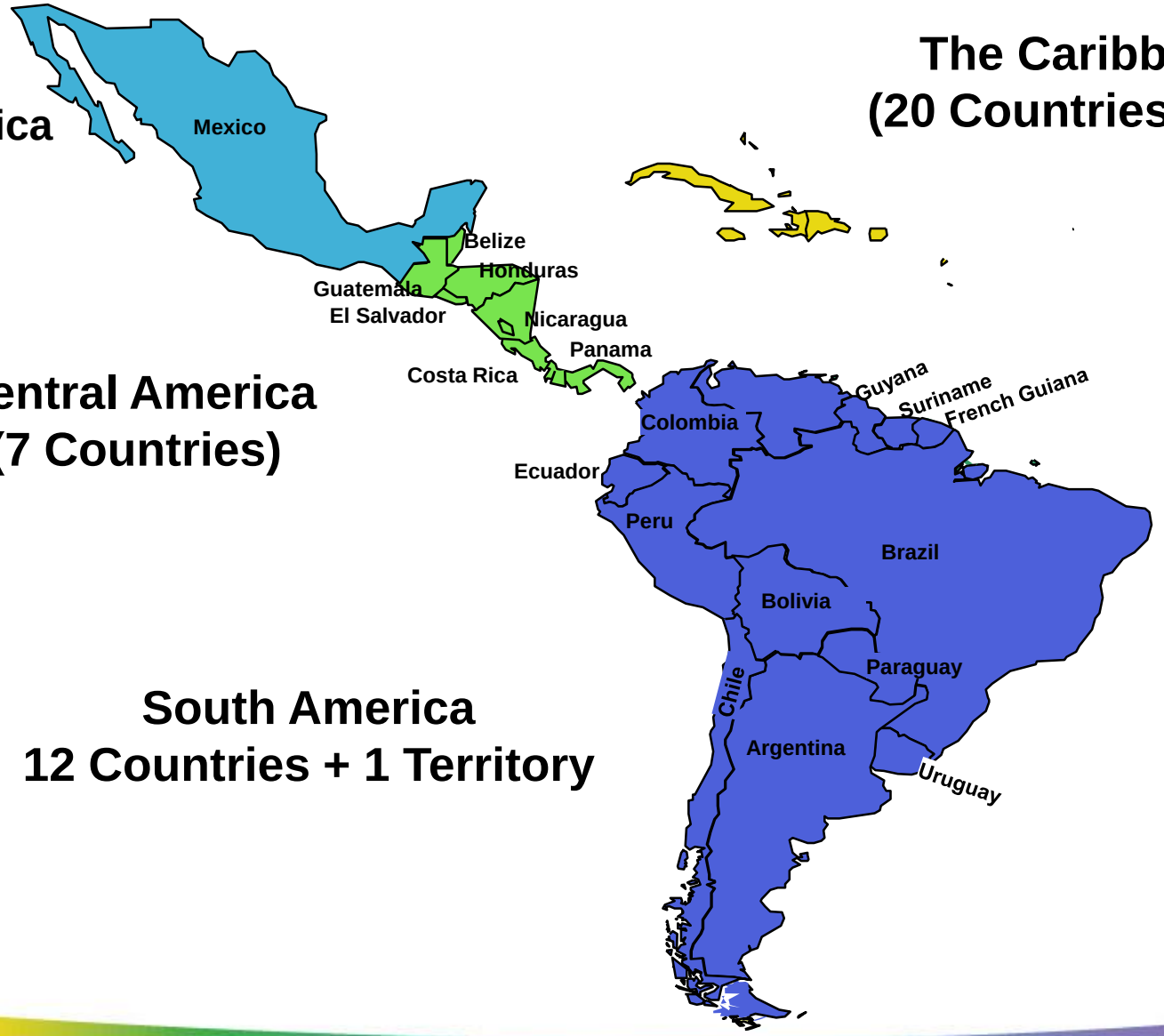
Regulatory Affairs Compliance:

- Describes the outcome of the objective a company would/can achieve by ensuring awareness and **compliance with relevant laws, policies, guidance/regulations**
- Requires robust and clear communication between Regulatory Affairs and company stakeholders at early stages of the project to **provide guidance on strategic regulatory path** (GLOBAL, REGIONAL, LOCAL > i.e. stability studies, fast track, harmonization
- Maintain product life cycle (safety, efficacy and quality)

Latin America Overview

North America

The Caribbean Islands
(20 Countries & Territories)



Central America
(7 Countries)

South America
12 Countries + 1 Territory

+41

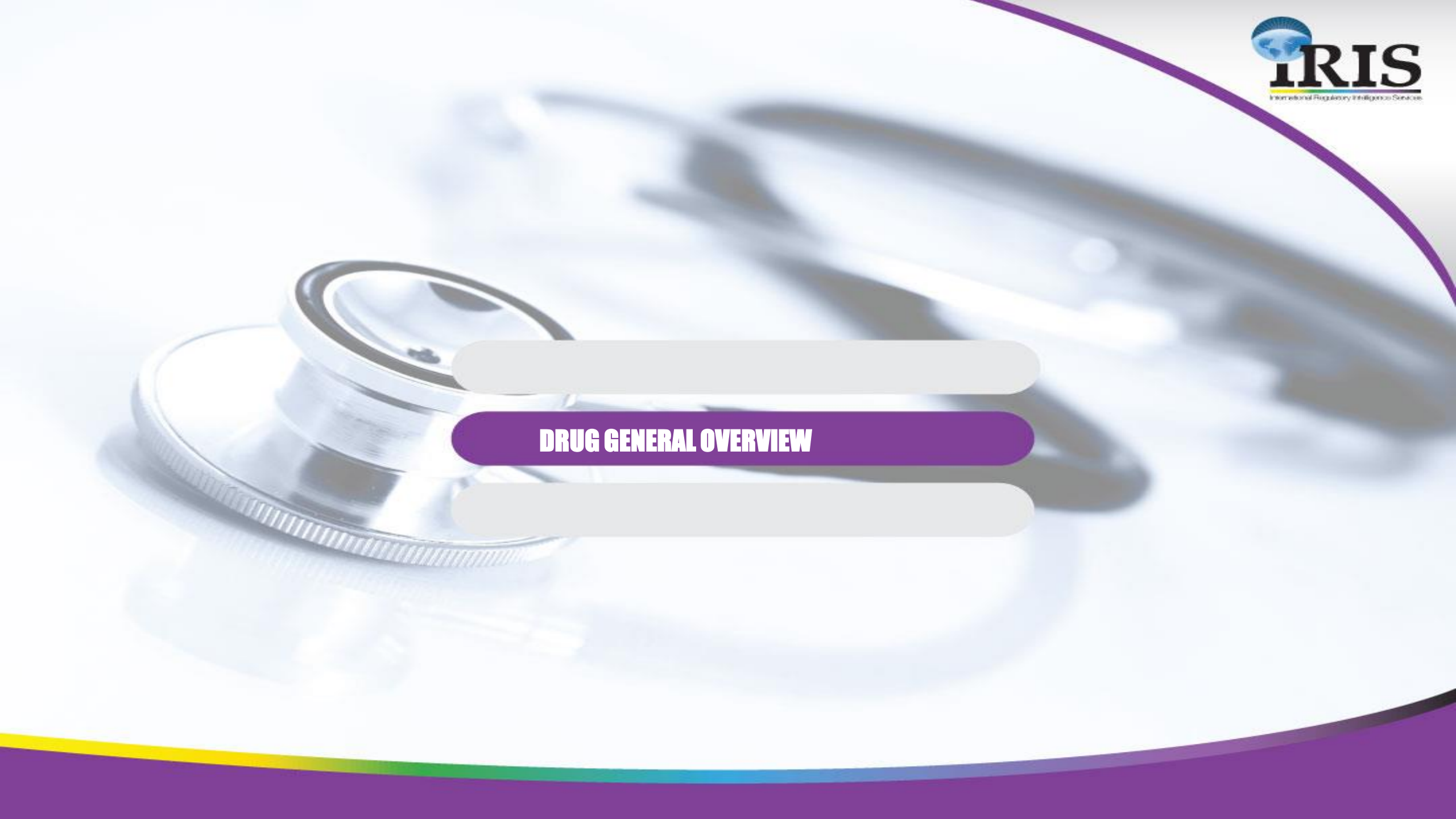
Market Access

General requirements:

- Local legal entity with all the permits for product importation and commercialization (drugs/medical devices), (affiliate/distributor)
- Warehouse and quality control laboratory (manufacturing facility)
- Pharmacist/Technical Director
  - Interphase with the local health authority and product owner/plant
  - Submission of product dossier
  - Change controls
  - Post market surveillance
  - PV and TV
- Marketing authorizations

Distributor vs. Affiliate

Distributor		Affiliate	
+	Min. impact on Corp. resources	--	Impact on Corp. resources
+	Minimal investment	--	Higher investment
--	Partner selection time/risks	+	Corporate presence/image
--	Limited control	+	Full control of operation
--	No registration ownership	+	Registration ownership
--	Limited financial potential	+	Maximizes financial potential
--	Risk low relevance in portfolio	+	Allows intercompany pricing
--	Depends on partner's goodwill (sale/regist)	+	Regulatory control
--	Solvency risks	+	Alignment with corporate vision



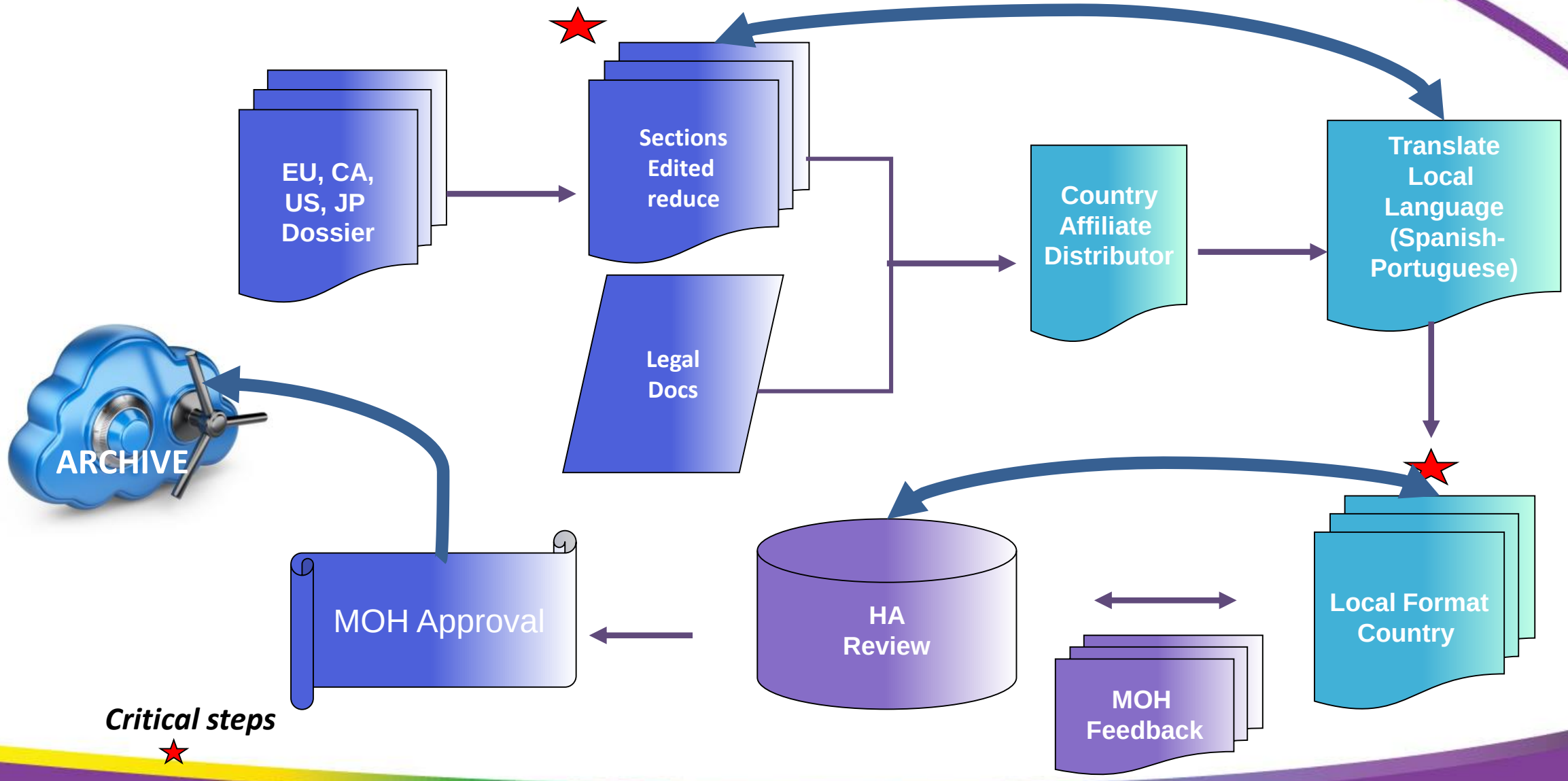
DRUG GENERAL OVERVIEW

Drug – Overview

Approval based on:

- Presentation and evaluation of a dossier **per local country regulations and requirements**
- Product **approval in one of the reference countries** or in a country of high development (i.e. Japan, Canada, Australia, EMEA, USA)
- Presentation of a **CPP – CFS** that includes **GMP** certification **ISO** certificates
- In some countries complete CLINICAL and CMC data of the dossier is required in others summary will be acceptable (2.3. 2.4 2.5 – CTD)
- Product testing/samples, stability studies per country Zone
- Electronic submission – PDF Files uploaded

Submission Dossier Preparation Flow



Drugs General Considerations

Drug registration process is not harmonized, countries have regulations for drugs, GMP, GWP, GCP, Risk Management, life cycle management.

Drug dossier can be build from (e)CTD (Tier 1 countries)

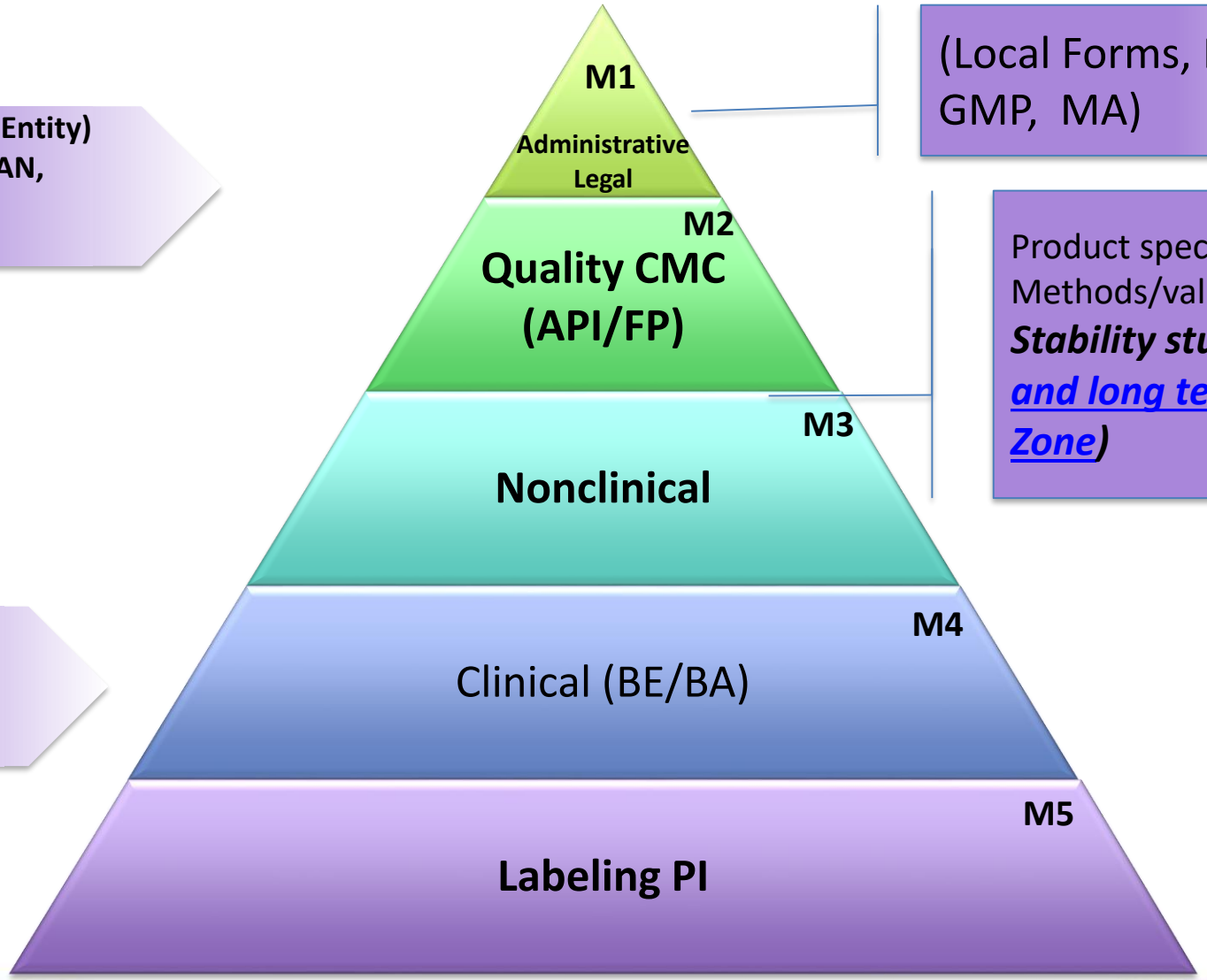
- **eCTD is Not….**
  - a common dossier from A to Z for all Latin America
  - Does not define the *content* of a registration dossier
  - It's not a road towards common review practices across the region, some LA countries interacts with and utilizes ICH standards that have helped with some harmonization of the requirements (stability)

- **eCTD is….**
  - a tool to ease the location of the information needed in each country and build the dossier

Drugs Registration Requirements

NME (New Molecule Entity)
BIOLOGIC, ORPHAN,
VACCINES
M1 – M5

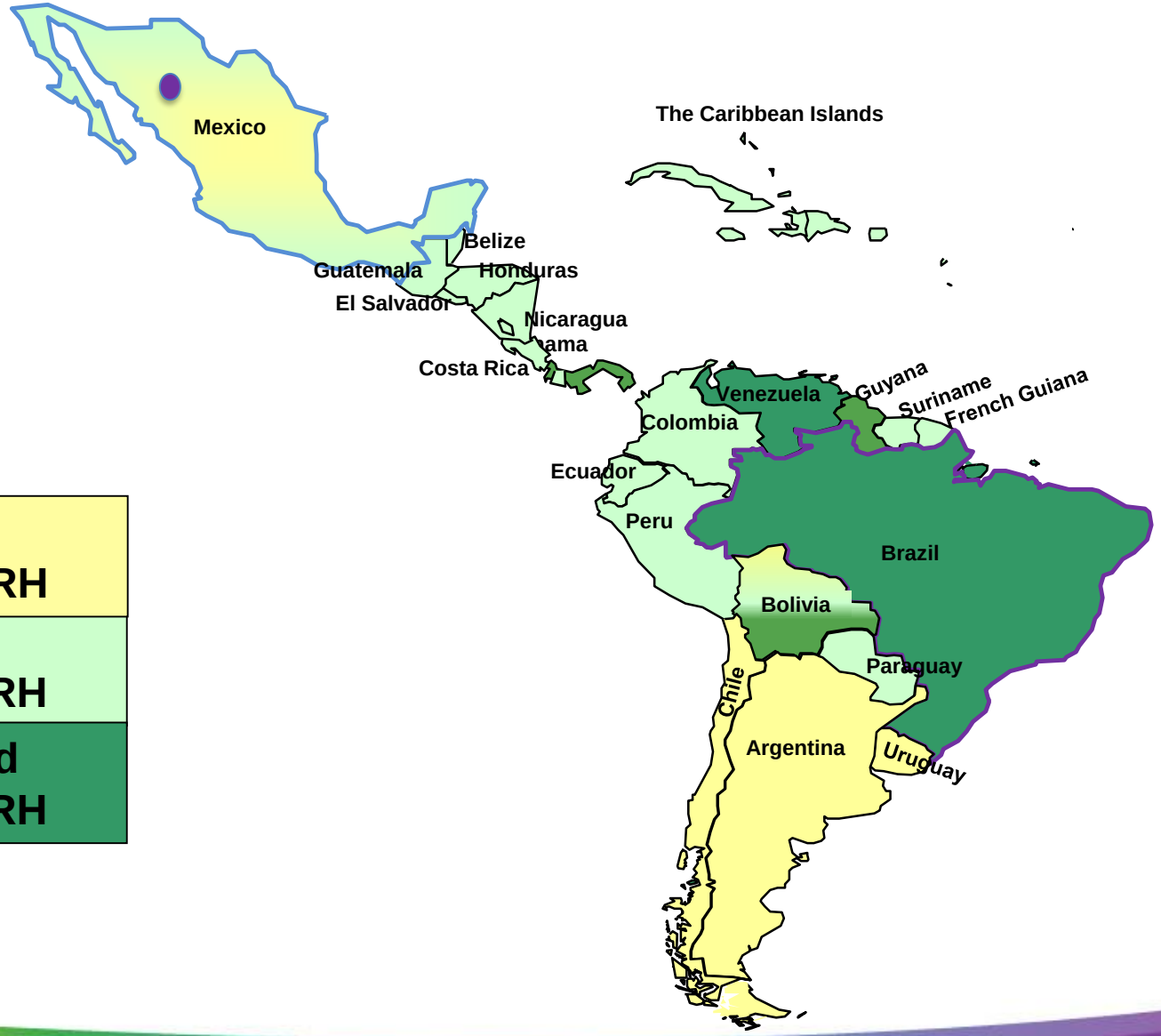
GENERIC/SIMILAR
M1, M2, M4 (BE), M5



(Local Forms, POA, CPP*, GMP, MA)

Product specifications, Formula, COA
Methods/validations, Packaging specifications
Stability studies (3 batches accelerated and long term according the country Zone)

Countries Climate Classification



Zone II **25° C±2° C/60%±5%RH**
Zone IVa Hot and Dry **30° C±2° C/65%±5%RH**
Zone IVb Hot and Humid **30° C±2° C/75%±5%RH**

Finish Product Stability Studies

Zone	NEW SUBMISSION/VARIATIONS Shelf life granted based on 6 mo data (24mos) Or complete long term data		RENEWAL Assigned Shelf Life	Reference	Comments
	ACCELERATED	LONG TERM	LONG TERM		
II 25°C±2°C/**60**%±5 %RH	3 Batches 6 months 0, 1, 2, 3, 6 (4,5)	3 Batches 6 months 0, 3, 6, 9, 12, 18, 24	3 Batches 0, 3, 6, 9, 12, 18, 24- 1 batch (annually)	Local regulations, ICH, WHO (Mercosur)	Legalized Originally signed
IVa 30°C±2°C/**65**%±5 %RH Hot and Dry	3 Batches 6 months 0, 1, 2, 3, 6 (4,5)	3 Batches 6 months 0, 3, 6, 9, 12, 18, 24	3 Batches 0, 3, 6, 9, 12, 18, 24- 1 batch (annually)	Local regulations, ICH, WHO	Legalized Originally signed
IVb 30°C±2°C/**75**%±5 %RH Hot and Humid	3 Batches 6 months 0, 1, 2, 3, 6	3 Batches 6 months 0, 3, 6, 9, 12, 18, 24	3 Batches 0, 3, 6, 9, 12, 18, 24- 1 batch (annually)	Local regulations, ICH, WHO	Legalized Originally signed

Refer to country specific stability guidelines for additional information for different type of products

South America Summary

	Argentina	Bolivia	Chile	Colombia	Ecuador	Mexico	Paraguay	Peru	Uruguay	Venezuela
Language		Spanish			Spanish -		Spanish	Spanish	Spanish	Spanish
Agency	**ANMAT -** Argentine National Administration of Drugs, Food & Medical Technology	Ministry of Health – UNIMED	Instituto de Salud Pública - ISP	National Institute for the Surveillance of Drugs and Food - INVIMA	Agencia Nacional de Regulación, Control y Vigilancia Sanitaria (ARCSA)	The Federal Commission for the Protection against Sanitary Risk (COFEPRIS)	Ministerio de Salud Publica y Bienestar Social	DIGEMID (Dirección General de Medicamentos, Insumos y Drogas)	Ministry of Health - DIGESA	Instituto Nacional de Higiene "Rafael Rangel" (INHRR)http://www.inhrr.gob.ve
Regulations – Drug	Decree 150: New Product Registrations implemented 1992 updates 1890/92, and 177/93	Ley 1737 Dic. 17/96	Decreto Supremo 1.876 de 1.995	Decree 2092 of 1986 and Decree 677 of 1995 (additional amendments)	Acuerdo 0586 Cap II Gov. Price	Ley General de Salud and its modifications (1983-12-26)	Mercosur; Decree 17057/97; Resol No. 23/95 52/96 Gov. Price	Ley General de Salud 26842 D.S. 010-97-SA, y sus modificatorias MD: Decree 016 (2016)	Law 15443: Decree 521/984: Law 15443. Decree 324/999 Decree 38/2015 - Biotecnology	000 Medicines Law, which came into effect in 2002
Samples - Quality Control Lab	Yes product tested	No	Yes	No	No	No	First Lot Tested	Yes product tested	No	Yes, product tested
website	www:anmat.org.ar	http://www.minsalud.gob.bo	http://www.ispch.cl/	https://www.invima.gov.co/	http://www.arcsa.gob.ec/	http://www.cofepris.gob.mx	www.vigisalud.gov.py	http://www.digemid.minsa.gob.pe	http://www.msp.gub.uy	http://www.inhrr.gov.ve
Mutual Recognition	Mercosur	No	No - Pacific Alliance in process	Pacific Alliance in process	Yes	Yes - Pacific Alliance in process	Mercosur	No - Pacific Alliance in process	Mercosur	-
Approval timeline	90-120 days	9-12 mo	12 mo	10 mo	6-9 mo	12 mo	6-9 months	12mo	9-12 months	18-24 mo
Product Renewal	5 years	5 years	5 years	**PP - 5 year MD-10 years**	5 years	5 years	5 years	5 years	5 years	**7 years**
PSUR	Yes	No	No*	No*	Yes ICH B'date	Yes Norm 220	No*	Yes ICH B'date	Yes ICH B'date	No*
GMP Audit	Yes: Colombia Mexico	No	Yes	Yes Recon: Argentina	No	Yes Recon: Argentina	No	Yes – FDA, EMA, ANVISA	No	No

Central America Drug Regulatory Overview

- Harmonization initiative resulted in the creation of the Central American Technical Regulation RTCA Regulation (drugs)
  - Mutual Recognition among member countries if products are manufactured in one of the member
  - El Salvador – Level IV Agencies (USA, Canada, Austria, Switzerland, Japan, EU (Mexico Agreement)
  - Panama adopted some of the RTCA regulation
- MA validity in CA - 5 years (most countries)
- Some countries requires products samples and testing at time (prior) of submission
- Standards – COA
- Zone IVa stability
- Member countries reserve the right to request additional information aside form the ones in the RTCA
- Each country has its own PV regulation in process of being implemented
- All the documents must be in Spanish, legal documents must be apostille/consularized with a validity of minimum 1 year (CFS, GMP, POA, Declarations)

Member Countries: Costa Rica, El Salvador, Guatemala, Honduras and Nicaragua

Associate Member Country: Panama

Central America Summary

	COSTA RICA	EL SALVADOR	GUATEMALA	HONDURAS	NICARAGUA	PAMANA
Language	Spanish - dossier					
Evaluation Agencies	Ministry of Health - Dirección Regulación de Productos Interes Sanitario	Ministry of Health - Dirección Nacional de Medicamentos	Ministry of Public Health - Departamento de Regulación y Control de Productos Farmacéuticos y Afines	Secretariat of Health - Dirección General de Regulación Sanitaria	Ministry of Health - Dirección General de Regulación Sanitaria / Dirección de Farmacia	Ministry of Health - Dirección Nacional de Farmacia y Drogas
website	http://www.ministeriodesalud.go.cr	http://www.medicamentos.gob.sv	http://medicamentos.mspas.gob.gt/	https://arsa.gob.hn/	http://www.minsa.gob.ni	http://www.minsa.gob.pa
Regulations – Drug	Central American Technical Regulation (RTCA) 11.03.59:11-11.01.02:04			(RTCA) 11.03.59:11-11.01.02:04 Resolución 254 de la Dirección de Farmacia y Drogas	(RTCA) 11.03.59:11-11.01.02:04	Decrees 178 de 12 de julio 2001; 105 de 15 April 2003; 340 of27 August 2007; 197 of 14 April 2009; 321 of 17 June 2009. (RTCA) 11.03.59:11-11.01.02:04
Samples - Quality Control Lab	Yes - Laboratorio de Análisis y Asesorías Farmacéuticas (LAYAFA) de la Universidad de Costa Rica	Yes - Unidad de Control de Calidad en el Pre y Post Registro de Medicamentos	Yes -Laboratorio Nacional de Salud-LNS	Yes -Laboratorio de Especialidades Farmacéuticas- Colegio de Químico Farmacéutico de Honduras	Yes -Laboratorio de Control de Calida de Medicamentos de la Universidad Nacional Autónoma de Nicaragua	Yes -Instituto Especializado de Análisis-IEA
Mutual Recognition	Yes	Yes	Yes	Yes	Yes	No
Regulatory Alliances	Cofepris agreement on drugs. Oct-2013	Cofepris drugs. Feb-2013	USP just as technical training	none	none	Cofepris agreement on drugs. Apr-2014
Approval timeline	6-12 mo	4-8 mo	9-12 mo	6-9 mo	6-12 mo	9-12 mo
Product Renewal	5 years	5 years	5 years	5 years	5 years	5 years
Generall	QA agreement/Declaration; QQ formula by unit of dose - original signed; Methods per RTCA, with copy of the validation report; Clinical studies not older than 10 years; Product samples					

Caribbean Drug Regulatory Initiative

CARIBBEAN REGULATORY SYSTEM (CRS) is the initiative of the Caribbean Community and Common Market (CARICOM); Caribbean Public Health Agency (CARPHA) responsible:

- Manage centralized medicines registration process
- Abbreviated review procedure leveraging information on registration and marketing authorizations granted by Reference Authorities based on safety, quality and efficacy, one common registration will be issue to those that meet the following criteria:
  - current approval/registration in a “reference authority”
  - product is on the WHO Essential Medicine List or PAHO Strategic Fund that includes innovative and generic medicines, and vaccines
- Recommends reviewed products to CARICOM Member States
- Carries out PV and post market surveillance of medicines and vaccines in the region.

Member States: Antigua and Barbuda, Bahamas, Barbados, Belize, Dominica, Grenada, Guyana, Haiti, Jamaica, Montserrat, Saint Lucia, St. Kitts and Nevis, St. Vincent and the Grenadines, Suriname, and Trinidad and Tobago, Anguilla, Bermuda, British Virgin Islands, Cayman Islands, and Turks and Caicos Islands

Reference Countries: Argentina, Brazil, Canada, Chile, Colombia, Cuba, European Union, Mexico, United States or WHO prequalification

http://carpha.org/What-We-Do/Laboratory-Services-and-Networks/CRS

Caribbean Drug Technical Requirements

1. Cover Letter – confirming submission is true and accurate and product is sold in other countries
2. Marketing authorization status – copy of other country approvals
3. Product information SmPC and PIL
4. Manufacture API – address/GMP and inspection reports if available
5. Manufacture FP - address/GMP and inspection reports if available
6. Certificate of Analysis FP
7. **Signed** Finished Product Specifications – with analytical test procedure
8. Stability Studies - Zone IVB conditions:
   - Long term: 30±2°C - 75%± 5%RH
   - Accelerated: 40oC±2°C - 75%±5% RH
9. Color Pictures of Product – all sides of the product; Primary secondary packaging, insert – product may be requested
10. Proof of Therapeutic equivalence/clinical summaries - (i.e. bioequivalence/bioavailability studies, when applicable, or comparative in vitro dissolution tests, when applicable).
11. PSUR (periodic safety update report) /PBRER (periodic benefit risk evaluation report

Caribbean – General Information

	ANTIGUA BARBUDA	BAHAMAS	BARBADOS	CAYAMAN ISLANDS	CURACAO	GRENADA	GUYANA	HAITI	JAMAICA	SAINT LUCIA	SAINT VINCENT GRENADINE	SINT MAARTEN	SURINAME	TRINIDAD AND TOBAGO	DOMINICAN REPUBLIC
MOH	NATIONAL DRUG FORMULARY COMMITTEE REGULATE THE PURCHASE AND USE OF DRUGS	Bahamas National Drug Agency (BNDA), under the Ministry of Health	Pharmacy Council and the Barbados Drug Service are both departments under the Ministry of Health National Drug Formulary Committee	Department of Health Regulatory Services Pharmacy Council	INSPECTORATE OF PUBLIC HEALTH BUREAU OF PHARMACEUTICAL AFFAIRS	Ministry of Health Medicines Regulatory Authority (MRA)	Ministry of Health structure, Food and Drug Department and Office of the Chief Pharmacist both report to the Chief Medical Officer	Directorate for Pharmacy, Medicines & Traditional Medicines (DPM/MT) in the Ministry of Health	Pharmaceutical and Regulatory Affairs Department	Ministry of Health, Wellness, Human Services and Gender Relations	Ministry of Health, Wellness and The Environment Pharmacy Council SVG Pharmacy Act	Ministry of Public Health, Social Development and Labor	Ministry of Health	Drug Inspectorate Division (DID) and the Chemistry Food and Drug Department (CFDD), both are part of the Ministry of Health,	Ministerio de Salud Pública y Asistencia Social
Other Agencies	OECS/PPS Procurement of pharmaceuticals and medical supplies			NA	Drug Registration Board	OECS/PPS Procurement of pharmaceuticals and medical supplies				OECS/PPS Procurement of pharmaceuticals and medical supplies	OECS/PPS Procurement of pharmaceuticals and medical supplies	NA	Pharmaceutical Inspectorate Registration Committee		Dirección General de Medicamentos, Alimentos y Productos Sanitarios (DIGEMAPS)
Regulations	Pharmacy Act, 1995	Pharmacy Act 2009	Pharmacy Act, 1986 National Drug Policy (being revised)	NA	Registration_guidelines Curacao	Pharmacy Act (Cap 241) of 1987, Medical Products (Regulations) Act, 1995, Food and Drugs Law, 1986 and Antibiotics Act.	Pharmacy and Poisons Ordinance 1956, Food & Drugs Act 1971 as well as in the Food & Drugs Regulations 1977.	Low of 1955, enforeced as of 1997			Pharmacy Act No. 54 of 2002, the Drug (prevention of misuse) Act of 1998	NA	Medicine or Registration Act of 1973	National Drug Policy	1. Decreto 246-06 Reglamento de Medicamentos 2. DGDF-RP-LI-011 3. DGDF-RP-LI-020
Quality Control Lab (Drugs)	Caribbean Regional Drug Testing Laboratory (CRDTL)	Caribbean Regional Drug Testing Laboratory (CRDTL)			Local Lab	Caribbean Regional Drug Testing Laboratory (CRDTL)			Caribbean Regional Drug Testing Laboratory (CRDTL)			NA	Caribbean Regional Drug Testing Laboratory (CRDTL)		Departamento de Análisis de Medicamentos del Laboratorio Nacional
Website	http://www.ab.gov.ag/detail_page.php?page=29	http://www.bahamas.gov.bs/	http://www.health.gov.bb/	http://www.ministryofhealth.gov.ky/	http://gobiernu.cw/	http://www.gov.gd/ministries/health.html	http://www.health.gov.gy/moph/index.php/contact-us	http://mspp.gouv.ht/newsite/	http://moh.gov.jm/divisions-agencies/divisions/standards-and-regulation-division/guidelines-forms-lists/	http://health.govt.lc/	http://www.health.gov.vc/health/	http://www.sintmaartengov.org/government/VSA/Pages/About.aspx	http://health.gov.sr/sr/ministerie-van-volksgezondheid	http://www.health.gov.tt/sitepages/default.aspx?id=93	http://www.msp.gob.do
Drug Med Device - Regultory Framework	Drug & MD are not regulated and have no regulatory registration system. Medicines are sold in pharmacies. Quality control of samples analysis is done.	Drug & MD can be marketed submitting CPP/CFS from an EU agency or USA FDA. Import permit granted importers/ wholesalers. Produts must meet	Drug legislation in process. require a local agent.	No regulatory process. Product can be freely imported if freely sold and registered in the USA, Canada, Europpean Union.	Drug & MD regulation exists. Prior approval of registration need to import products. Tier 1 Pharmacopoeias are accepted as reference.	Registration required per Medical Product Act of 1995, system not operational. The premises that conduct business of pharmaceutical products need to be inspected prior registration.	The product has to be registered by the importer/wholeseller. (dossier & samples for testing) No registration renewal. Annual import license	Registration legislation since 1955, but in practice only started in 1997. 5 year validity. Registration is voluntary, not all the medications sold in Haiti are specifically authorized .	Regulation for registration, PV and marketing of medicines exist. Product tested prior to obtaining MA. A permit to import the dRug is issued by PRAD.	There is no registration policy in St. Lucia. Medicines are imported by the fomulatry of OECS/PPS. Testing is requierd for prequalification for public procurement, tno post-marketing testing.	Local regulations require marketing authorization but not being enforced. Rely on drug registrations in U.S. and EU to ensure drugs are safe.	Products are not required to be registered or laboratory tested.	Medicines are registered by their INN (International Non-proprietary Names) or Brand name+INN. Sampling of imported products for testing is required for new MA.	Product registration is required. No legal provision for renewal, MA has no expiration date. Variations must be filed. Certificate of a Pharmaceutical Product (CPP), tech dossier.	Yes
Mutual Recognition	Argentina, Brazil, Canada, Chile, Colombia, Cuba, European Union, Mexico, United States or WHO prequalification)														
Regulatory Alliences	CARIBBEAN REGULATORY SYSTEM (CRS) initiative CARICOM (Caribbean Community and Common Market). The CRS helps states perform key regulatory functions. Relys on reference authorities and a focus on essential medicines. Conducts reviews of product dossiers for safety, quality, and efficacy of medicines and vaccines														

Regulatory Intelligence / TOC - Pharma

Documentation requirements	GTM NEW (ALO, ORP, GEN)	GTM RNW	GTM MOD	GTM TRN MA	GTM LBL Chng	GTM MNF site chr
Agency Information						
Name of Health Authority	Ministerio de Salud Pública y Asistencia Social	Ministerio de Salud Pública y Asistencia Social	Ministerio de Salud Pública y Asistencia Social	Ministerio de Salud Pública y Asistencia Social	Ministerio de Salud Pública y Asistencia Social	Ministerio de Salud Pública y Asistencia Social
Drug Evaluation/Regulatory Agency	Departamento de regulación y control de productos farmaceuticos y afines	Departamento de regulación y control de productos farmaceuticos y afines	Departamento de regulación y control de productos farmaceuticos y afines	Departamento de regulación y control de productos farmaceuticos y afines	Departamento de regulación y control de productos farmaceuticos y afines	Departamento de regulación y control de productos farmaceuticos y afines
Acronym of the Agency	NA	NA	NA	NA	NA	NA
Website	http://www.medicament	http://www.medicame	http://www.medicamen	http://www.medicament	http://www.medicamen	http://www.medicamento
Address	6 avenida 3-45 Zona 11, Guatemala,	6 avenida 3-45 Zona 11, Guatemala,	6 avenida 3-45 Zona 11, Guatemala,	6 avenida 3-45 Zona 11, Guatemala,	6 avenida 3-45 Zona 11, Guatemala,	6 avenida 3-45 Zona 11, Guatemala,
Telephone	T: 24752121 T: 24752122	T: 24752121 T: 24752122	T: 24752121 T: 24752122	T: 24752121 T: 24752122	T: 24752121 T: 24752122	T: 24752121 T: 24752122
E-mail address within the country agency for general questions						
Hague Member	No	No	No	No	No	No
Regulatory Alliances	Yes	Yes	Yes	Yes	Yes	Yes
Requirements for Manufacturing Site						
Manuf Site GMP'S	Yes	Yes	Yes	Yes	Yes	Yes
Declaration of relationship between manuf site and coporate office	Yes	Yes	Yes	Yes	Yes	Yes
Local Manufacturing License	Yes	Yes	Yes	Yes	Yes	Yes
In Situ GMP Inspection	No	No	No	No	No	No
3rd party manufacturing is allowed	Yes	Yes	Yes	Yes	Yes	Yes
Secondary manufacturing site allowed	Yes	Yes	Yes	Yes	Yes	Yes
If secondary manf site is alowed, can it be on the same MA?	No	No	No	No	No	No
Legal Requirements in Country						
Do you need local wharehouse?	Yes	Yes	Yes	Yes	Yes	Yes
Warehouse technical director	Yes	Yes	Yes	Yes	Yes	Yes
Technical director	Yes	Yes	Yes	Yes	Yes	Yes
Pharmacovigilance system in place	Yes	Yes	Yes	Yes	Yes	Yes
Pharmacovigilance reports					Yes	
If yes, will your country accept other countries PSURs or reports?						
Regulations for promotional material						
If yes, provide the regulation number						
Dossier General Requirements						
Dossier Language	Spanish	Spanish	Spanish	Spanish	Spanish	Spanish
Dossier type	Local	Local	Local	No	No	Local
SMF - finished product	No	No	No	No	No	No
SMF - API	No	No	No	No	No	No
Quality statements sign and legalize	Yes	Yes	Yes	No	No	Yes
Patent Molecule (does not apply to generics)	Recommended	No	No	No	No	No
Patent Formula (does not apply to generics)	Recommended	No	No	No	No	No
No patent Molecule certificate (only for generics)	No	No	No	No	No	No
Climatic Zones	Zone IV	Zone IV	Zone IV	No	No	Zone IV
Accelerated Stability (months)	6	6	6	No	No	6
Shelf life (months)	At least 6	At least 6	At least 6	No	No	At least 6
Local clinical studies		No	No	No	No	No
New Molecule	No					
Biologics						
Orphan	No					
Generics						
Local bioequivalence studies (only for generics) needed	No	No	No	No	No	No
Bioequivalence studies are accepted from what countries						
Number of Samples for Registration						

IRIS

Medicamentos
Lista de Verificacion de Documentos Requeridos
Registro Nuevo y Renovación

Perú

Producto:
P.A. y Concentración:
Forma Farmacéutica:
Fabricante: Nombre / Dirección
Titular:: Nombre / Dirección
Solicitante: Nombre del Titular Local
Importado Desde: País de origen
Vida Útil: ## meses
Presentación Comercial:
Contenido:

Item	Documentos	Responsable	Estatus
1.	**Requisitos cuyos principios activos o asociaciones se encuentran en el Petitorio Nacional Único de Medicamentos Esenciales (Categoría 1).** Solicitud con carácter de Declaración Jurada dirigida al Director Ejecutivo de Autorizaciones Sanitarias, suscrita por el Representante Legal y el Químico Farmacéutico regente o director técnico, según formato. - Información del Solicitante - Información del Medicamento - Información Técnica del Medicamento		
2.	Especificaciones y técnica analítica de los principios activos y		

6.	Estudios de Estabilidad según Reglamento aprobado por la Autoridad de Salud del Perú. (Perú: zona climática IVa, que es de temperatura de 30°C ±20°C y una humedad relativa de 65±5%)		
7.	Estudios de Equivalencia Terapéutica para demostrar intercambiabilidad cuando aplique, según Reglamento aprobado por la Autoridad de Salud del Perú. (cuando corresponda)		
8.	Proyecto de ficha técnica e inserto		
9.	Proyecto de rotulado en idioma español de los envases mediato e inmediato.		
10.	Certificado de producto farmacéutico emitido por la Autoridad competente del país de origen o del exportador, tomando como base el modelo de la Organización Mundial de la Salud (OMS) o Certificado de Libre Comercialización, para productos importados.		
11.	Certificado de Buenas Prácticas de Manufactura (BPM) del fabricante nacional o extranjero, emitido por la Autoridad de Salud del Perú. Se aceptarán los certificados de Buenas Prácticas de Manufactura de los países de alta vigilancia sanitaria a que hace referencia el numeral 2 del Artículo 50º de la Ley General de Salud y de los países con los cuales exista reconocimiento mutuo.		
12.	Comprobante de pago por concepto de Registro Sanitario.		
Nota: Para los efectos de la protección de datos de prueba u otros datos sobre seguridad y eficacia, no divulgados, conforme a lo previsto en el Artículo 5º del D.S. Nº 002-2009-SA, se acompañará a la solicitud de registro sanitario lo siguiente:			
13.	Declaración jurada de que el solicitante es la persona que generó los datos de prueba u otros datos sobre seguridad y eficacia, no divulgados; o que ha sido autorizada por esta persona, por escrito, para usar dicha información; así como		

15.	Declaración jurada que los datos de prueba u otros datos sobre seguridad y eficacia, sobre los que se solicita la protección, no han sido divulgados		
16.	Declaración jurada de no haber sido sancionado, según decisión firme de la autoridad administrativa o judicial, por conductas o prácticas declaradas contrarias a la libre competencia, si la sanción se encuentra directamente referida al uso de los datos de prueba u otros sobre seguridad y eficacia no divulgados.		
Requisitos cuyos principios activos o asociaciones no se encuentran en el Petitorio (Categoría 2) Presentar los requisitos señalados en los numerales del 1 al 12 y los siguientes:			
13.	Información sobre eficacia y seguridad del principio activo si es un medicamento monofármaco o de la asociación si el producto tiene más de un principio activo		
14.	Declaración jurada de que el solicitante es la persona que generó los datos de prueba u otros datos no divulgados, o que ha sido autorizada para el uso de los mismos, cuando el producto se refiera a entidades químicas sujetas a protección de datos de prueba que no hayan sido aprobadas en Perú y que hayan sido aprobadas en un país de alta vigilancia sanitaria		
Nota: Para los efectos de la protección de datos de prueba u otros datos sobre seguridad y eficacia, no divulgados, conforme a lo previsto en el Artículo 5º del D.S. Nº 002-2009-SA, se acompañará a la solicitud de registro sanitario lo siguiente			
15.	Declaración jurada de que el solicitante es la persona que generó los datos de prueba u otros datos sobre seguridad y eficacia, no divulgados; o que ha sido autorizada por esta persona, por escrito, para usar dicha información; así como dicha autorización		
16.	En el caso que un producto proceda de un país extranjero, constancia de aprobación de comercialización otorgada en el país extranjero donde se obtuvo por primera vez el Registro Sanitario del producto farmacéutico que contenga una nueva entidad química, debiéndose indicar la fecha y lugar de su otorgamiento, de ser el caso		
17.	Declaración jurada que los datos de prueba u otros datos sobre seguridad y Eficacia, sobre los que se solicita la protección, no han sido divulgados.		
18.	Declaración jurada de no haber sido sancionado, según decisión firme de la autoridad administrativa o judicial, por conductas o prácticas declaradas contrarias a la libre		

	competencia, si la sanción se encuentra directamente referida al uso de los datos de prueba u otros sobre seguridad y eficacia no divulgados.		
Requisitos cuyos principios activos no se encuentran considerados en las Categorías 1 y 2 (Categoría No. 3): Presentar los requisitos señalados en los numerales del 1 al 12 y los siguientes:			
13.	Estudios y documentos que sustenten la eficacia y seguridad del producto		
Nota 1:Para los efectos de la protección de datos de prueba u otros datos sobre seguridad y eficacia, no divulgados, conforme a lo previsto en el Artículo 5º del D.S. Nº 002-2009-SA, se acompañará a la solicitud de registro sanitario lo siguiente:			
14.	Declaración jurada de que el solicitante es la persona que generó los datos de prueba u otros datos sobre seguridad y eficacia, no divulgados; o que ha sido autorizada por esta persona, por escrito, para usar dicha información; así como dicha autorización.		
15.	En el caso que un producto proceda de un país extranjero, constancia de aprobación de comercialización otorgada en el país extranjero donde se obtuvo por primera vez el Registro Sanitario del producto farmacéutico que contenga una nueva entidad química, debiéndose indicar la fecha y lugar de su otorgamiento, de ser el caso.		
16.	Declaración jurada que los datos de prueba u otros datos sobre seguridad y eficacia, sobre los que se solicita la protección, no han sido divulgados		
17.	Declaración jurada de no haber sido sancionado, según decisión firme de la autoridad administrativa o judicial, por conductas o prácticas declaradas contrarias a la libre competencia, si la sanción se encuentra directamente referida al uso de los datos de prueba u otros sobre seguridad y eficacia no divulgados.		

Nota:
Para la Solicitud de Inscripción en el Registro Sanitario:
- Periodo de validez tentativo:
  - El solicitante debe presentar el reporte de los estudios de estabilidad obtenidos de los 6 meses del estudio de estabilidad acelerado y de los primeros 6 meses del estudio a largo plazo, en el envase cierre propuesto para circular en el mercado.
- Periodo de validez comprobado:
  - El solicitante debe presentar los resultados obtenidos de los estudios a largo plazo por el periodo de vida útil solicitado, en el envase propuesto para circular en el mercado.

MEDICAL DEVICE OVERVIEW

Medical Device General Considerations

- *Medical Device dossier* can be build referencing the USA 510(k), EU STED (Summary Technical Documentation) dossier and filed as soon as clearance is received from USA/EU to maximize the entrance of the LATAM market.
- The complexity of the approval process depends on the risk classification of the product.
- Each national agency has guidelines that define risk classification based on the technology and the regulatory process
- Individual country regulatory requirements is a challenge
- Early identification of required documentation is advised
- Original signature – company stamps on several sections of the documents
- Product samples
- Product testing

General Medical Device Classification

Class			Risk	Examples	Safety Controls
I	I	A	Low risk to patients Non Invasive	Tongue depressor, bandages, thermometers	No clinical trial require – notification to MOH – QMS
II a	II	B	Moderate low risk (non life sustaining)	Hearing aids, sutures, x-rays, ***surgical gloves/condoms***	May require clinical trials – Registration QMS
II b	III	C	Moderate high risk (Implantable/ life sustaining	Implantable devices (orthopedic, glucose monitors, hemodialysis systems, infusion pumps	Required clinical trials – Registration QMS Facility inspection
III	IV	D	High (critical) Risk – Presents a potential risk of illness or injury to patients – Long Term Invasive	Heat valves, pacemaker Implants Dental	Requires clinical trails – Registration QMS Facility Inspection

MEDICAL DEVICE REGULATIONS

21%

- Regulations enforced
- Limited Regulation
- Regulation Not Enforced
- No regulation

*Voluntary registration

Medical Device Common requirements

- In country local infrastructure/legal entity
- Legal documents (POA/Declarations)
- Technical Dossier content based on device classification; Chemical, Physical and Biological Properties; Microbial Contamination; Sterility
- Quality systems (specification/methods/validations/ electrical) Aging studies
- CFS country of manufacture/origin (legalized)
- Product labeling
- Clinical

CA Medical Device Requirements

REQUIREMENTS	GT	SV	HN	NI	CR	PA	DO
Form	✓	✓	✓	✓	✓	✓	✓
CFG/US-FSC/CoE, ISO Certificat*	✓	✓	✓	✓	✓	✓	✓
Finished product specifications	✓ (signed)	✓ (signed)	✓ (signed)	✓ (signed)	✓	-	✓
Certificate of Analysis	✓ (signed)	-	-	✓ (signed)	**✓ (signed)**	-	**✓ (signed)**
Safety Report	-	-	-	✓	-	-	-
Primary, secondary and shipping label	✓	✓ (signed)	✓	✓	✓ Original/PDF	✓	✓
Instructions for Use	✓	✓	✓	✓	✓	✓	✓
Picture of the product	✓	-	-	-	✓	-	✓
Product description	✓	✓	✓	✓	✓	-	✓
Material description (list)				x	x		
Legal representation power of attorney	✓	✓	✓	✓	✓	✓	✓
Samples	✓	-	-	✓	-	-	✓
Operational Manual	✓	✓	✓	✓	✓	-	
Copy of local permits - representative	-	-	-	✓	-	-	✓
Manufacturing Process (flow chart)	-	-	-	-	-	-	✓
Quality Agreement - CMO	-	-	-	-	-	-	✓
General Technical documentation to demonstrate safety and efficacy (shelf life, sterilization, medical specifications (Structure, Material, composition and functions of the medical device)	✓	✓	✓	✓	✓	-	✓
UL Certificate apostille	-	-	-	✓	-	-	-
Technovigilance report/Control	-	-	-	✓	-	-	-
Regulation	Norm 37 V. 5-2016	Law MD (c02-rs-01-urim.Gui01)	Reglamento control sanitario 6-2005.	Normativa-064, norma para el registro de dispositivos médicos	Decree#. 34482-s, Reg Class, Import and control of MD	Resolución 600/2018 + ley 90	**DGDF-RP-LI-018 version 01**
*** Documents must be apostille/consularize**							

Regulatory Intelligence/TOC Medical Devices

	A	B	H	I	J	K	L	M	N	O
1	REQUIREMENTS	REQUERIMIENTOS	COLOMBIA					Republica Dominica		
2			NEW	RNW	MOD	Trnsf MA	Mnf St Chng	NEW	RNW	MOD
3	Agency Information	Informaction de la Agencia								
14	Requirements for Manufacturing site	Requisitos para el Sitio de Fabricación								
24	Legal Requirements in Country	Requerimientos Legales del Pais								
36	Dossier General Requirements	Dossier- Requerimientos Generales								
64	Product Related Local Req	Producto Relacionado (Requerimiento Local)								
83	MA Characteristics	Caraterísticas del Registro Santiario								
84	Validity of the MA	Cual es el tiempo de validez del Registro	10 years	10 years	10 years	10 years	10 years	5 years	5 years	5 years
85	MA validity based on the submission dossier? Y/N	La validacion del Registro Sanitario es basado del sometimiento del dossier? SI/NO	Yes	Yes	Yes	Yes	Yes			
86	MA can be transferred from one distributor to another	El Registro Sanitario puede ser Transferible de un distrubuidor a otro distribuidor?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
87	MA can be transferred from one company to another	El Registro Sanitario puede ser Transferible de una empresa a otra empresa?			Yes			Yes	Yes	Yes
88	Is a second manufacturing facility accepted? Y/N	Es aceptable una segunda planta de fabricacion? SI/NO	No	No	No	No		Yes	Yes	Yes
89	Two MAs can exist for the same product, each from a different manufaturing site	Pueden existir dos registros para un mismo producto? Cada uno de diferente sitio de fabricacion?	No	No	No	No	No			
90	One MA can list two manufacturing sites	Un registro se puede listar en dos sitios de fabricacion?	No	No	No	No	No			
91	Submission	Sometimiento								
130	Timing	Tiempo								
152	Labeling/Container	Etiquetado/Contenedor								
158	Label Primary	Etiqueta Primario								
175	Label Secondary	Etiqueta Secundario								
176	1. Name of the device	Nombre del dispositivo	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
177	2. Name and address of the manufacturer	Nombre y direccion del fabricante	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
178	3. Name and address of the	Nombe y direccion del importador/distribuidor	Yes	Yes	Yes	Yes	Yes	No	No	No
179	4. Name and address of the legal manufacturer (owner of the product)	Nombe y direccion del fabricante legal (Dueno del producto)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
180	5. Date of manufacture; serial - model (if applicable)	Fecha de fabricacion; Modelo- serie (si es aplicable)	Yes	Yes	Yes	Yes	Yes	No	No	No
181	6. Expiration date	Fecha de caducidad	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
182	7. Storage conditions	Condiciones de Almacenamiento	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
183	8. Shelf life	Vida Util	Yes	Yes	Yes	Yes	Yes	No	No	No
184	9. Intended use of the product	Uso previsto del producto	Yes	Yes	Yes	Yes	Yes	No	No	No
185	10. Identification of use (single - multiple)	Identificacion de uso (unico- multiple)	Yes	Yes	Yes	Yes	Yes	No	No	No
186	11. Name of qualified person	Nombre de la persona calificada						No	No	No
187	12. Registration number	Numero de Registro Sanitario	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
188	13. Batch number or Serial No.	Numero de Lote o Numero de Serie.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
189	14. Definition of symbols and warnings	Definiction de simbolos y precauciones	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
190	15. Presentation	Presentacion	Yes	Yes	Yes	Yes	Yes	No	No	No
191	16. Other	Otro								
192	Insert	Inserto								
193	1. Name of the device	Nombre del dispositivo	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

IRIS

Medical Devices
Verification List of Requirements
New Registration & Renewal (Class I & IIA)

Colombia

Product:
Components List:
Pharmaceutical Form:
Manufacturer: Name / Address
MA Holder: Name / Address
Requested by: Name of
Import from: Country of Origin
Shelf Life: ## months
Presentation:
Contents:

Item	Documents	Responsible	Status
1.	Forms endorsed by the technical diretor (nationals), or the responsible person for the manufacture (Import)		
2.	Receipt of proof of payment of fees		
3.	Free Sale Certificate - Apostiled (import products)		
4.	Authorization from manufacturer to importer ((import products). Authorization from manufacturer to the MA holder		
5.	Proof of Constitution and legal representation of the importer, the manufacturer and MA holder as appropriate. Medical and legal documents that demonstrate the existence document.		
6.	Indicate the date and the case number in which the Certificate of Storage Capacity (CCAA) or of Good Manufacturing Practices of Medical Devices (BPM) was issued by the Anti-procedural Decree 019 of 2012 will be reviewed within the Institute.		
7.	Description of the medical device. The description refers only to: indications, contraindications, warnings, main components, accessories, relation with patients and description of the operation; in Spanish.		
8.	Technical Studies and analytical tests. The requirement must be understood with the presentation of any of the following		

	requirements. A) Summary Design of Verification and validation documents: The declaration of conformity that relates to compliance with international reference standards can be complied with; or B) Certificate of Analysis of the finished product containing the specifications, indicating values or acceptable ranges.		
9.	Method of sterilization, when applicable. The requirement is with the statement of the method and the reference standard on which it is based in accordance with the registered product.		
10.	Disposal Method or the final diposal product, when applicable. Certification will be accepted in which will be declared the local standards for disposal waste.		
11.	Final Arts and Inserts. Submit a representative design indicating the information of the product.		
12.	Declaration letter regarding the biomedical equipment, when applicable. The commitment to deliver to the user the final operating manual which are available in Spanish language and will have the maintenance and operation manuals available when necessary		
13.	Scientific information to support product safety. Class IIa, IIb and III. The biocompatibility tests only apply to materials that signify innovations (those that do not have international reference standards) and on them can be requested the summary of studies and tests.		
14.	Risk of Analysis in the stage of design, class IIa, IIb and III. Description of measures to comply with the essential safety requirements. Class IIa, IIb and III.		
15.	List of standards used in Class IIa, IIb and III. It will be listed in the declaration of conformity.		
16.	History Commerce (Imported products). This document may be signed by the responsible health person in Colombia.		

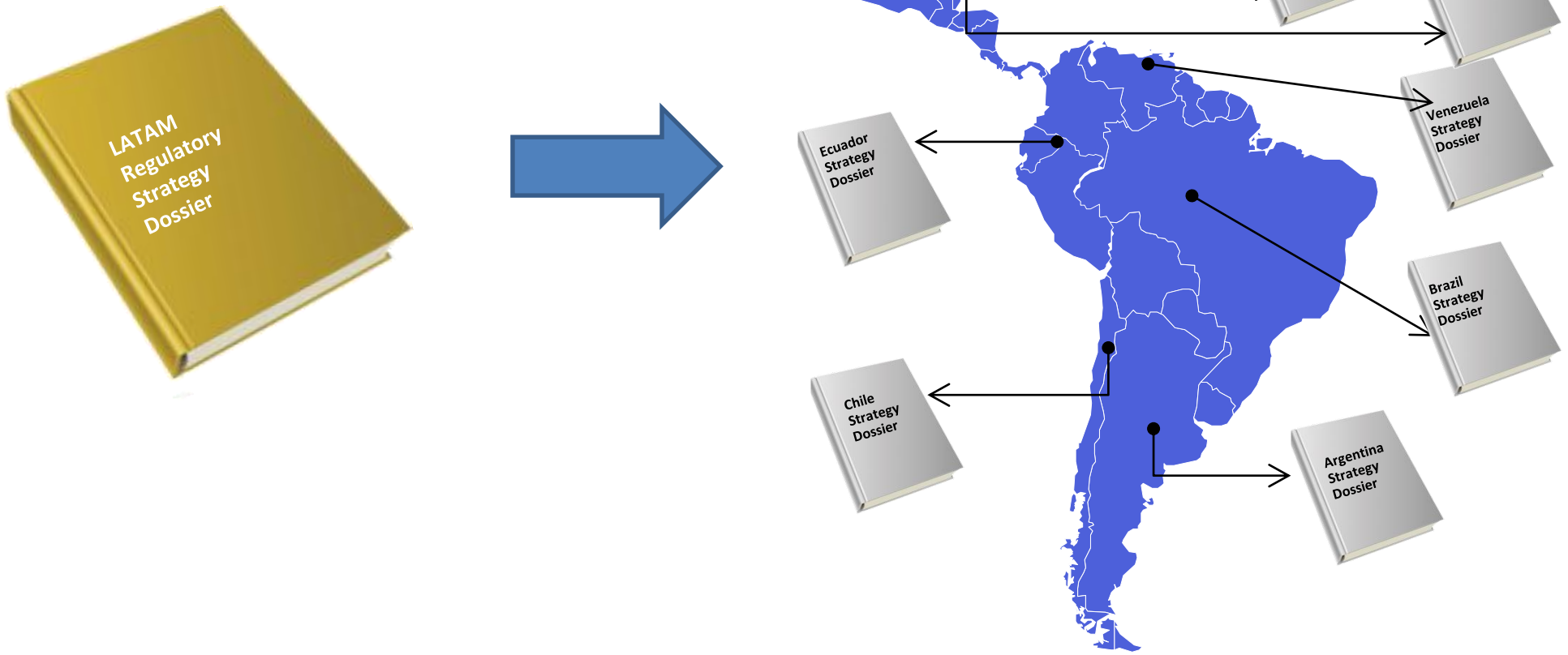
Note:

1) Differences in classification of devices and equipment: The classification of the manufacturer that is within the types of risk defined in the Decree, will be accepted.

2) Translation: Studies may come in a language other than Spanish, with a summary in Spanish.

3) Stability requirements shall be deemed to be met by the stability test summary when the declaration of conformity or Certificate of Analysis of the finished product is not indicated.

Master LATAM Dossier - Strategy



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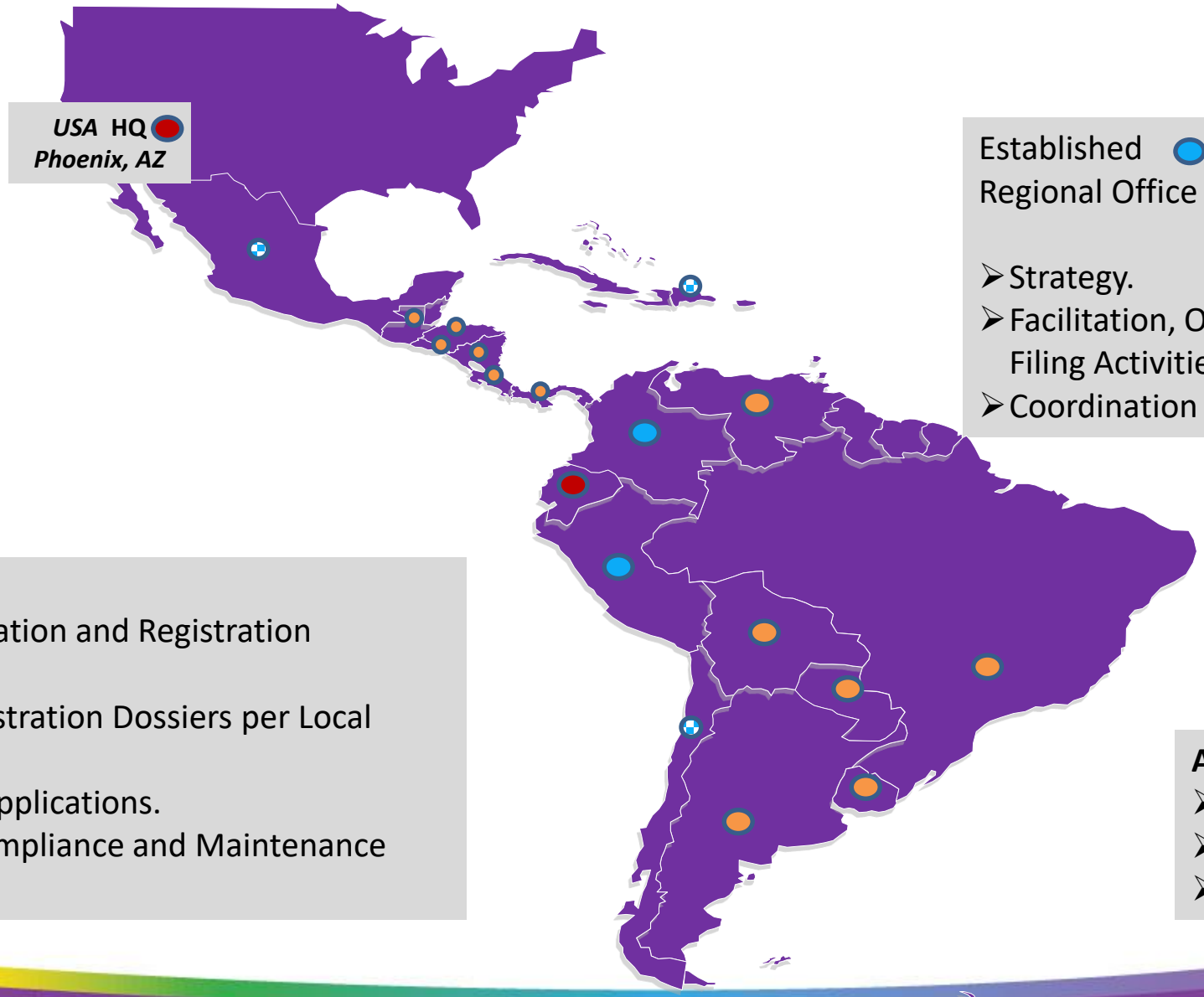
IRIS - Network



Established Regional Office

In Process Iris Agents

- Strategy.
- Facilitation, Oversight and Coordination of Filing Activities.
- Coordination and Harmonization Efforts.

IRIS Agents:

- Knowledge of Regulation and Registration Process.
- Preparation of Registration Dossiers per Local Requirements.
- Administration of Applications.
- Management of Compliance and Maintenance Issues.

Advantages of Our Network

- Centralized Management
- Globlocal®
- Structure and Management

Thank you!
¡Gracias!

LATAM – Health Authorities websites

AMRO - ?**Regional Office for the Americas**

1. Antigua and Barbuda: no website identified
2. Argentina: http://www.anmat.gov.ar/
3. Bahamas: http://www.phabahamas.org/hospitals_overview_bnda.php
4. Barbados: no website identified
5. Belize: no website identified
6. Bolivia:http://www.sns.gov.bo/snis/enlaces_salud/dinamed/index.htm
7. Brazil: http://www.anvisa.gov.br/eng/index.htm
8. Canada: http://www.hc-sc.gc.ca/dhp-mps/index-eng.php
9. Chile: http://www.ispch.cl/
10. Colombia: www.invima.gov.co/
11. Costa Rica: http://www.ministeriodesalud.go.cr/ MoH department with information on site
12. Cuba: http://www.cecmed.sld.cu/
13. Dominica: no website identified
14. Dominican Republic: http://www.drogasyfarmacias.gov.do/
15. Ecuador: no website identified
16. El Salvador: no website identified
17. Grenada: no website identified
18. Guatemala: http://portal.mspas.gob.gt/regulacion_y_control_de_productos_farmaceuticos_y_afines.html MoH department with information on site

AMRO - ?**Regional Office for the Americas**

19. Guyana: MoH department http://www.health.gov.gy/prg_adm_food_drugs.php
20. Haiti: website does not exist
21. Honduras: http://www.dgrs.gob.hn/
22. Jamaica: http://www.pcoj.org/ pharmacies and pharmacists, not medicines
23. Mexico: http://www.cofepris.gob.mx/
24. Nicaragua: no website identified
25. Panama: http://www.minsa.gob.pa/ MoH department with information on site
26. Paraguay: http://www.mspbs.gov.py/programas/index.php?id=6
27. Peru: http://www.digemid.minsa.gob.pe/
28. Saint Kitts and Nevis: no website identified
29. Saint Lucia: no website identified
30. Saint Vincent and the Grenadines: no website identified
31. Suriname: no website identified
32. Trinidad and Tobago: http://www.health.gov.tt/sitepages/default.aspx?id=93
33. United States of America: http://www.fda.gov/
34. Uruguay: http://www.msp.gub.uy/subcategorias_8_1.html
35. Venezuela (Bolivarian Republic of): http://www.inhrr.gov.ve/