Results of comparative study on similarities and differences between different CTDs

DCVMN Common Technical Document (CTD) Workshop

Shanghai 21 and 22 March 2018

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This work has been produced by the Developing Countries Vaccine Manufacturers Network (DCVMN) in collaboration with the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) based on data available in the participating companies.

With funding from the Bill and Melinda Gates Foundation (BMGF)

Recommendations from Annual DCVMN meeting 2016 and related Regulatory Panel

- Outcome of the regulatory panel: There is a need for **hard data** to back up the description of constraints faced for registration of vaccines in developing countries

  - Comparative analysis of CTDs from different countries to assess similarities and differences in requirements (contents and numbering)

  - Engagement of IFPMA member companies to work jointly with DCVMN member companies on constraints and proposals for improvements
  - Workshop in Geneva to collect “hard data” on constraints

Workshop in Geneva.

May 15 and 16 2017

Participants: Mary Allin (Pfizer), Abdulaziz M.M Almotiri (Arabio), Paula Barbosa (IFPMA), Nirav Amitkumar Chokshi (Zydus Cadila), Monique Collaço de Moraes Stávale (Bio-Manguinhos), Samir Desai (Zydus Cadila), Shubhangi Ghadge (Serum Institute of India), Tarek Ibrahim (Arabio), Seon Gyeong Jeong (LG Chem). Matthew Marsden (Pfizer), Mic McGoldrick (Merck), YIJIE Qu (CNBG), Christophe Saillez (former GSK), Mira Uton (Biofarma) and Qiaoruo Xiong (CNBG)

Facilitator: Nora Dellepiane (Consultant DCVMN)

Outputs of the workshop:

1. Review accuracy and inputs to the comparative analysis of CTDs, finalization of CTD comparative analysis
2. Comparison of application forms of different countries
3. Comparison of registration process and country specific requirements in 134 countries

Approach
Module I comparison

- ✓ Module 1: CTDs of Australia, China, Europe, the Gulf Cooperation Council (GCC) India, Jordan, PAHO, Tanzania, Thailand, the United States (US) and the (World Health Organization (WHO) are compared to each other, up to node 3 (level 3 of detail).
- ✓ The raw data were organized by aligning the topics on the basis of similarity of content independently of the number assigned to them in each CTD.
- ✓ Similarities and differences between each other were assessed for content and also for the numbering sequences used
- ✓ Contents expressed exactly in the same terms or slightly differently but requiring the same information were considered similar; and contents that differed between the CTDs were considered different
- ✓ For simplicity, the items referring to the application forms were left out of the exercise

Approach
Module I comparison (2)

- ✓ **% of similarity = $\frac{\text{N° items with similar content or numbering}}{\text{N° items compared}} \times 100$**

- ✓ **% of difference= 100- % of similarity**

Approach
Modules 2-5 comparison

- ✓ Modules 2-5: CTDs from PAHO, India, Jordan FDA and Thai FDA are compared to the ICH CTD as implemented by US FDA.
- ✓ The raw data table was constructed by aligning the topics on the basis of similarity of content independently of the number assigned to them in each CTD.
- ✓ Similarities and differences in relation to ICH CTD were assessed for content and also for the numbering sequences used

Approach
Modules 2-5 comparison

CTDs from different countries were considered "different" from the ICH CTD if one of the following situations applied:

- Country X did not require a specific item required in the ICH CTD)
- Country X required data/information not required in the ICH CTD (other information)
- Country X contained in its requirements the same heading (or similar) as contained in the ICH CTD but the data/information expected to be provided under such heading was not specified, while being specified in the ICH CTD
- Country X contained in its requirements the same heading (or similar) as contained in the ICH CTD but the data/information expected to be provided under such heading was specified, while not being specified in the ICH CTD
- Country X requires different information from ICH under the same heading

Calculations of % of similarity and difference

MODULE I

- ✓ % of similarity = N° items with similar content or numbering / N° items compared x 100
- ✓ % of difference= 100- % of similarity

MODULE 2-5

- ✓ % of similarity =
= N° items with similar content or numbering to ICH (CTD) / N° items compared x 100

- ✓ % of difference= 100- % of similarity

CTD CONTENTS
MODULE1

AUSTRALIA, CHINA, EUROPE, GCC, INDIA, JORDAN, PAHO, TANZANIA, THAILAND, US AND WHO

EU	US	CHINA	AUSTRALIA	JORDAN	GCC	PAHO	TANZANIA	INDIA	THAILAND	WHO
MODULE 1 - ADMINISTRATIVE/LEGAL INFORMATION			MODULE 1 - ADMINISTRATIVE INFORMATION AND PRESCRIBING INFORMATION FOR AUSTRALIA	MODULE 1 - ADMINISTRATIVE AND LEGAL INFORMATION		MODULE 1 - ADMINISTRATIVE/LEGAL INFORMATION		MODULE 1 - ADMINISTRATIVE/LEGAL INFORMATION	MODULE 1 - ADMINISTRATIVE AND PRESCRIBING INFORMATION	MODULE 1 - ADMINISTRATIVE AND PRODUCT INFORMATION
			1.0 Correspondence							1.2 Correspondence
1.0 Cover letter	1.2 Cover Letters	1.2 Cover Letters	1.0.1 Cover letter	1.0 Cover Letter	1.0 Cover Letter		1.2 Cover Letter		1.0.2 Cover letter	
			1.0.2 Lifecycle management tracking table 1.0.3 Response to request for information							
	1.1 Forms 1.3 Administrative Information									
1.1 Comprehensive table of content		1.1. Comprehensive table of contents	1.1. Comprehensive table of contents	1.1 Comprehensive Table of Contents (Module 2-5).	1.1 Comprehensive Table of Contents (Module 2-5).	1.1 Table of contents (modules 1 to 5)	1.3 Table of contents (modules 1 to 5)	1.1 Comprehensive table of contents (Modules 1 to 5)	1.0.1 Tracking table	1.1 Table of Contents
1.2 Application Form (Administrative data)	1.5 Application	1.2 Application form	1.2. Administrative information	1.2 Application Forms (JFDA forms):	1.2 Application Forms (JFDA forms):	1.2 Application form	1.4 Application form	1.2 Administrative information	1.2 Application forms Application form annexes	
			1.2.1 Application form							

EU	US	CHINA	AUSTRALIA	JORDAN	GCC	PAHO	TANZANIA	INDIA	THAILAND	WHO
			1.2.2 Pre-submission details 1.2.3 Patent Certification 1.2.4 Change in Sponsor				1.7.8 Patent Information			1.4. Compliance information 1.4.1. Certificate of Establishment Licensing, if required and provided by the National Regulatory Authority (NRA) of the country of manufacture. 1.4.2. Copy of GMP certificate, or other evidence of GMP compliance issued by the NRA of the country of manufacture. Report (English translation if required) of the last GMP inspection (which included in its scope the production of the product submitted for prequalification) by the NRA of the country of manufacture. 1.4.3. Copy of marketing authorizations for all formulations and presentations of the vaccine submitted for prequalification. 1.4.4. Policy for assignment of date of manufacture of each component as well as the final product and diluents.
								1.2.1 Application in Form 44 and Treasury Challan (fee) 1.2.2 Legal and statutory documents 1.2.3 Coordinates related to the application		

EU	US	CHINA	AUSTRALIA	JORDAN	GCC	PAHO	TANZANIA	INDIA	THAILAND	WHO
1.3 Product Information	1.4 Labeling	Product Information (Label, Leaflet/PIL, Artworks/Mock-ups, Description, Compostion)	1.3 Medicine information and labelling	1.3 Product information	1.3 Product information	1.3 Summary of product characteristics and product labelling	1.5 Product Information	1.2.4 General information on drug product		
1.3.1 Summary of Product Characteristics (SPC), Labelling and Package Leaflet			1.3.1 Product information and package insert	1.3.1 SPC (Summary of product characteristics), Labeling, Package leaflet.	1.3.1 SPC (Summary of product characteristics)	1.3.1 Summary of product characteristics	1.5.1 SPC (Summary of product characteristics)		1.3.1 Summary of Product Characteristics, Labelling and Package Leaflet	1.5. Vaccine composition, presentations and scheduling information
					1.3.2 Labeling	1.3.2 Product Labelling	1.5.2 Labeling			
					1.3.3 PIL		1.5.3 PIL			1.5.6. Samples of package inserts (in English) to be used for supply through UN agencies. After finalization of the review of the English version, translation to other languages required by UN procurement agencies (currently French, Portuguese, Russian and Spanish) should be provided.

EU	US	CHINA	AUSTRALIA	JORDAN	GCC	PAHO	TANZANIA	INDIA	THAILAND	WHO
										1.5.1. Description of presentations available to UN agencies, including diluent (if applicable), combination products, forms, dose sizes and type of containers and indicate Vaccine Vial Monitor (VVM) type and location. 1.5.2 Vaccine temperature stability profile Additional to stability information in 3.2.P.8, please provide any additional stability data required to support the assignment of VVM type or to support any on-label claim for elevated temperature storage according Extended Controlled Temperature Conditions guideline (http://who.int/biologicals/areas/vaccines/ectc/en/). 1.5.3 Description of immunization /administration devices to be delivered with the vaccine 1.5.4 Recommended schedule and route of administration
								1.2.5 Summary protocol of batch production and control		1.5.7. Sample of lot summary protocol to be provided to UN agencies, in compliance with WHO-recommended format.
										1.3 Site master file (consistent with WHO Guidance document: WHO Technical Report Series, No 961, Annex 14, 2011) http://apps.who.int/iris/bitstream/10665/44079/1/WHO_TRS_961_eng.pdf
								1.2.6 List of countries where MA or import permission for the said drug product is pending and the date of pendency.		
								1.2.7 List of countries where the drug product has been licensed and summary of approval conditions.	1.3.5 Product Information already approved in Other States	

EU	US	CHINA	AUSTRALIA	JORDAN	GCC	PAHO	TANZANIA	INDIA	THAILAND	WHO
1.3.2 Mock up			1.3.3 label mock-ups and specimens	1.3.2 Mock-up.	1.3.4 Mock-ups		1.5.4 Mock-ups		1.3.2 Mock-up	1.5.5 Samples of labels of primary containers and secondary packaging for the product (including diluents. If applicable)
			1.3.2 Consumer medicines information							
1.3.3 Specimen			1.3.3 Label mock up and specimens	1.3.3 Specimen (One Registration sample).	1.3.5 Samples	1.3.3 Samples	1.13 Samples	1.2.14 Samples of drug product	1.3.3 Specimen	
1.3.4 Consultation with Target Patient Groups									1.3.4 Consultation with Target Patient Groups	
1.3.5 Product Information already approved in the Member States						1.4 List of countries where the product has been licensed and summary of approval conditions	1.10 Regulatory Status			
							1.10.1 Registration status from countries with Stringent Drug Regulatory Authorities (SDRAs)			

EU	US	CHINA	AUSTRALIA	JORDAN	GCC	PAHO	TANZANIA	INDIA	THAILAND	WHO
							1.10.2 Registration status in EAC Partner States 1.10.3 List of countries in which a similar application has been submitted 1.10.4 Statement on whether an application for the product has been previously rejected, withdrawn or repeatedly deferred in the EAC Partner States 1.11 Evidence of API and/or FPP prequalified by WHO			
	1.15 Promotional material									
								1.2.8 List of countries where the drug product is patented. 1.2.10 A brief profile of the manufacturer's research activity 1.2.11 A brief profile of the manufacturer's business activity in domestic as well as global market.		
1.3.6 Braille 1.4 Information about the Experts 1.4.1 Quality 1.4.2 non-clinical 1.4.3 Clinical	1.16 Signed Statement on the Qualified Person		1.4 Information about the experts 1.4.1 Quality 1.4.2 non-clinical 1.4.3 Clinical		1.4 Information about the experts 1.4.1 Quality 1.4.2 non-clinical 1.4.3 Clinical	1.5 Information regarding experts	1.6 Information about the experts	1.2.12 Information about the expert(s)/ Information regarding involvement of experts, if any	1.3.6 Braille 1.4 Information about the Experts 1.4.1 Quality 1.4.2 non-clinical 1.4.3 Clinical	

EU	US	CHINA	AUSTRALIA	JORDAN	GCC	PAHO	TANZANIA	INDIA	THAILAND	WHO
	1.16 Section 6 - RMP Contact Person									
1.5 Specific Requirements for Different Types of Applications		Specific Requirements for Procedures – Applications	1.5 Specific requirements for different types of applications	1.4 Specific Requirements for Different Types of Applications					1.5 Specific Requirements for Different Types of Applications	
1.5.1 Information for Bibliographical Applications	1.4 References		1.5.1 Literature-based submission documents						1.5.1 Information for Bibliographical Applications	
1.5.2 Information for Generic, 'Hybrid' or Bio-similar Applications				1.5.1 Information for application type (Generic, Bio-similar ……..).					1.5.2 Information for Generic, 'Hybrid' or Bio-similar Applications (divided into three sub-sections)	
				1.5.2 Information for submission type (Technology Transfer, under license …..)						
1.5.3 (Extended) Data/Market Exclusivity									1.5.3 (Extended) Data/Market Exclusivity	
1.5.4 Exceptional Circumstances									1.5.4 Exceptional Circumstances	
1.5.5 Conditional Marketing Authorization							1.12 Manufacturing and Marketing authorization		1.5.5 Conditional Marketing Authorization	
									1.5.6 Additional Trade Name Declarations	
			1.5.5 Co-marketed medicines declarations						1.5.7 Co-marketed Medicines Declarations	
			1.5.6 Combination medicines consent							
			1.5.7 OTC New product assurances							
			1.5.8 Umbrella brand assessment							

EU	US	CHINA	AUSTRALIA	JORDAN	GCC	PAHO	TANZANIA	INDIA	THAILAND	WHO
1.6 Environmental Risk Assessment 1.6.1 non-GMO 1.6.2 GMO					1.5 Environmental Risk Assessment 1.5.1 non-GMO 1.5.2 GMO	1.6 Environmental risk assessment		1.2.13 Environmental risk assessment	1.6 Environmental Risk Assessment 1.6.1 non-GMO 1.6.2 GMO	1.4.5 If the vaccine is a Genetically Modified Organism, supply a copy of the Environmental Risk Assessment.
			1.5.3 Genetically modified organisms consents							
			1.6 Master files and certificates of suitability 1.6.1 Relevant external sources 1.6.2 Applicant's declaration 1.6.3 Letters of access		1.7.7 Certificates of Suitability 1.7.9 Letter of access or acknowledgment to DMF		1.7 Certificates of Suitability of monographs of the European pharmacopoeia (CEP) or EAC-APIMF			
1.7 Information relating to Orphan Market Exclusivity 1.7.1 Similarity 1.7.2 Market Exclusivity			1.5.2 Orphan drug designation							
	1.6 Meetings	1.8 Correspondence (Responses to Questions / Meeting minutes)	1.7 Compliance with meetings and pre-submission processes							1.2.2 Agreed minutes of any pre-submission meetings between WHO/PQT and the applicant.

EU	US	CHINA	AUSTRALIA	JORDAN	GCC	PAHO	TANZANIA	INDIA	THAILAND	WHO
	1.6.1 Meeting request 1.6.2 Meeting background materials 1.6.3 Correspondence regarding meetings		1.7.1 Details of compliance with pre-submission meetings outcomes 1.7.2 Details of any additional data to be submitted 1.7.3 Declaration of compliance with pre-submission planning form and planning letter							
	1.7 Fast track 1.8 Special protocol assessment request 1.9 Pediatric administrative information 1.10 Dispute Resolution 1.11 Information amendment: Information not covered under modules 2 to 5 1.12 Other correspondence									
Responses to Questions		1.8 Correspondence (Responses to Questions / Meeting minutes)			1.9 Responses to Questions				Responses to Questions	
1.8 Information relating to Pharmacovigilance		1.7 PV (+ RMP)	1.8 Information relating to pharmacovigilance	1.5 Information related to Pharmacovigilance	1.6 Information relating to Pharmacovigilance				1.8 Information relating to Pharmacovigilance	1.6.9 Post marketing Safety documentation
1.8.1 Pharmacovigilance System	1.16 Detailed Description of the Pharmacovigilance Plan		1.8.1 Pharmacovigilance system	1.5.1 Pharmacovigilance System.	1.6.1 Pharmacovigilance System				1.8.1 Pharmacovigilance System	

EU	US	CHINA	AUSTRALIA	JORDAN	GCC	PAHO	TANZANIA	INDIA	THAILAND	WHO
	1.16 Annex 3 - Synopsis of ongoing and completed clinical trial program 1.16 Annex 4 - Synopsis of ongoing and completed pharmacoepidemiological study program 1.16 Annex 5 - Protocols for proposed and ongoing studies from Pharmacovigilance Plan 1.16 Annex 6 - Newly available study reports 1.16 Annex 7 - Other supporting data 1.16 Annex 8 - Details of proposed educational program 1.17 Postmarketing studies 1.18 Proprietary names 1.19 Pre-EUA and EUA 1.20 General investigational plan for initial IND									1.6.1 List of pre-clinical studies sponsored by applicant including any important conclusion(s) including and preclinical studies performed after initial licensure of product (and the reasons for these studies) 1.6.2 List of all clinical trials sponsored by the applicant relevant for the application which must contain: • Location of study sites • Number and age of subject • Date of study • Evidence of registration in clinical registry (part of ICTRP) • Indication of whether the study complied with GCP • Rational of each study must be included in the summary table • Statement of final conclusions on safety and immunogenicity (and/or efficacy) 1.6.3 Final approved protocol by ERC and NRA

EU	US	CHINA	AUSTRALIA	JORDAN	GCC	PAHO	TANZANIA	INDIA	THAILAND	WHO
										1.6.4 List of any clinical trials that are known to be currently ongoing not relevant to the current application including the summary of details of the study plan and expected date of result 1.6.5 List of other studies with applicant product for which the applicant is not the sponsor 1.6.6 Complementary Clinical summary supporting the use of the product worldwide by UN agencies 1.6.7 Assessment Report from the NRA(s) 1.6.8 Clinical Independent expert report 1.7 Regulatory actions 1.7.1 Information on refusals, withdrawals, suspensions, including those initiated by the manufacturer 1.7.2 List of lots rejected by an NRA, if applicable 1.7.3 Restrictions on distributions and recalls, including those initiated by the manufacturer 1.7.4 Clinical trial suspensions 1.7.5 Dosage or schedule changes since the initial marketing authorization 1.7.6 Changes in target populations since the initial marketing authorization 1.8 Distribution information 1.8.1 Quantity of finished product distributed in the domestic market and exported in the previous three years, by presentation. Clearly indicate if numbers refer to vials or doses 1.8.2 List of countries where the product has received a Marketing Authorization, with an indication as to whether the product has been supplied in those countries 1.8.3 Description of recording system for distribution, including the release process by the manufacturer and by the NRA/NCL 1.8.4 Summarize the packaging procedures for international shipments for UN agencies and the validation (according to relevant, current WHO guidelines) of this packaging.
				1.7 Other information 1.7.1 List of Similar Product Available in Local Market. 1.7.2 Detailed Comparison between Generic Leaflet & Originator (for generic drugs).						

EU	US	CHINA	AUSTRALIA	JORDAN	GCC	PAHO	TANZANIA	INDIA	THAILAND	WHO
				1.7.3 Declaration from the manufacturer about the ingredient/s from human or animal origin included in the composition of the product and their source and the related certificates (TSE/BSE). 1.7.5 Technical Contract (Open part) in case of contract manufacturing. 1.7.6 Health authority approval of the latest Plasma master file (if the product contain plasma derivatives).						
			1.9 Biopharmaceutic studies 1.9.1 Summary of Bioavailability or bioequivalence study 1.9.2 Justification for not providing biopharmaceutic studies 1.10 Information relating to paediatrics 1.11 Foreign regulatory information							
			1.11.1 Foreign regulatory status	1.7.4 List from manufacturer to declare the worldwide registration status: (registered\Marketed (date), under registration, rejected (with reason)).						
			1.11.2 Foreign product information 1.11.3 data similarities and differences 1.11.4 Foreign evaluation reports							
			1.12 Antibiotic resistance data							
				1.8 Requested Certificates by Jordan FDA	1.7 Certificatesand Documents					
		1.10 Regulatory Certification (GMP, CPP, Manufacturing License)			1.7.1 GMP		1.8 GMP			

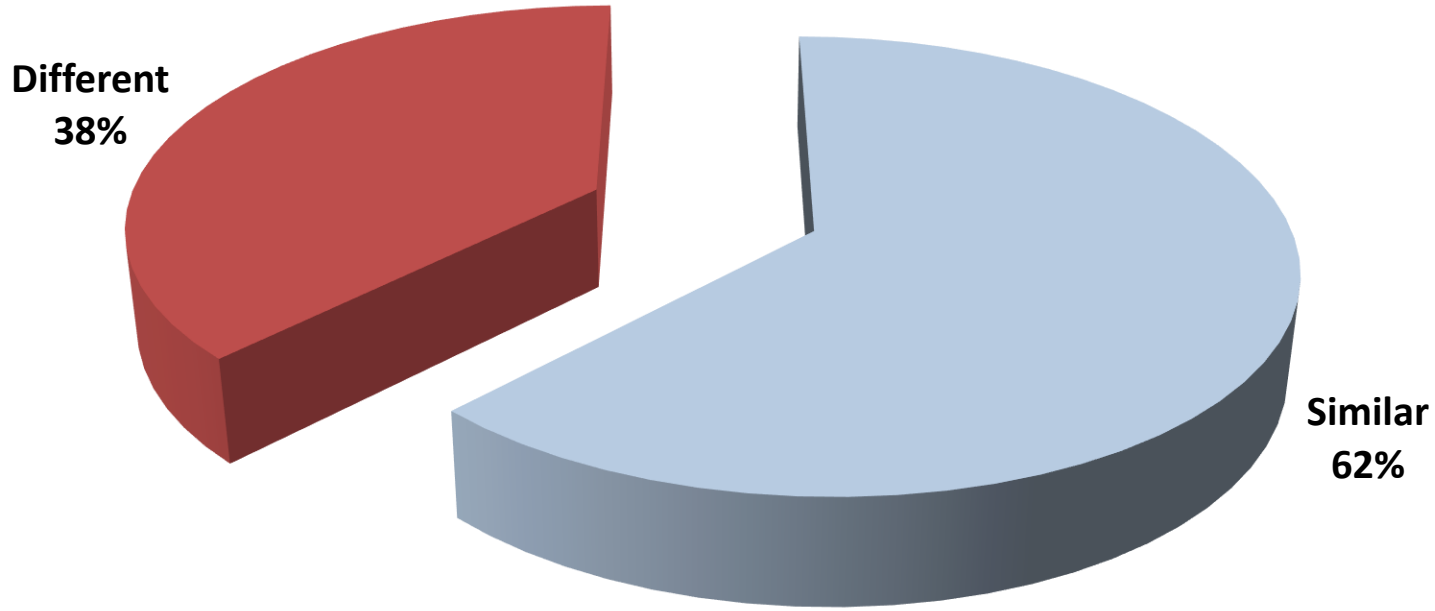
EU	US	CHINA	AUSTRALIA	JORDAN	GCC	PAHO	TANZANIA	INDIA	THAILAND	WHO
				1.8.1 Duly legalized Certificate of Pharmaceutical Product (CPP) according to WHO form	1.7.2 CPP					
					1.7.3-1.7.10 Country specific Documents					
				1.8.2 Pricing certificate informing about the price in the country of origin duly legalized	1.8 Pricing			1.2.9 Domestic price of the drug followed in the countries of origin in INR.		
					1.8.1 Price List					
					1.8.2 Other Documents Related					
				1.8.3 Declaration letter from the manufacturer company to declare the following information: a) The name of the manufacturing company and the address of the manufacturing site b) The name and the address of the MAH company c) The name and address of the company that will issue the invoice d) The export Center (Name of the ciy and name of the airport or seaport) The name and address of the company responsible about the product batch release						
Additional data	1.14+ Additional Information								Additional data	

LEGEND

	Similar
	Different

COMPARISON OF CTD MODULE 1 CONTENT FROM AUSTRALIA, CHINA, EUROPE, GCC, INDIA, JORDAN, PAHO, TANZANIA, THAILAND, US AND WHO

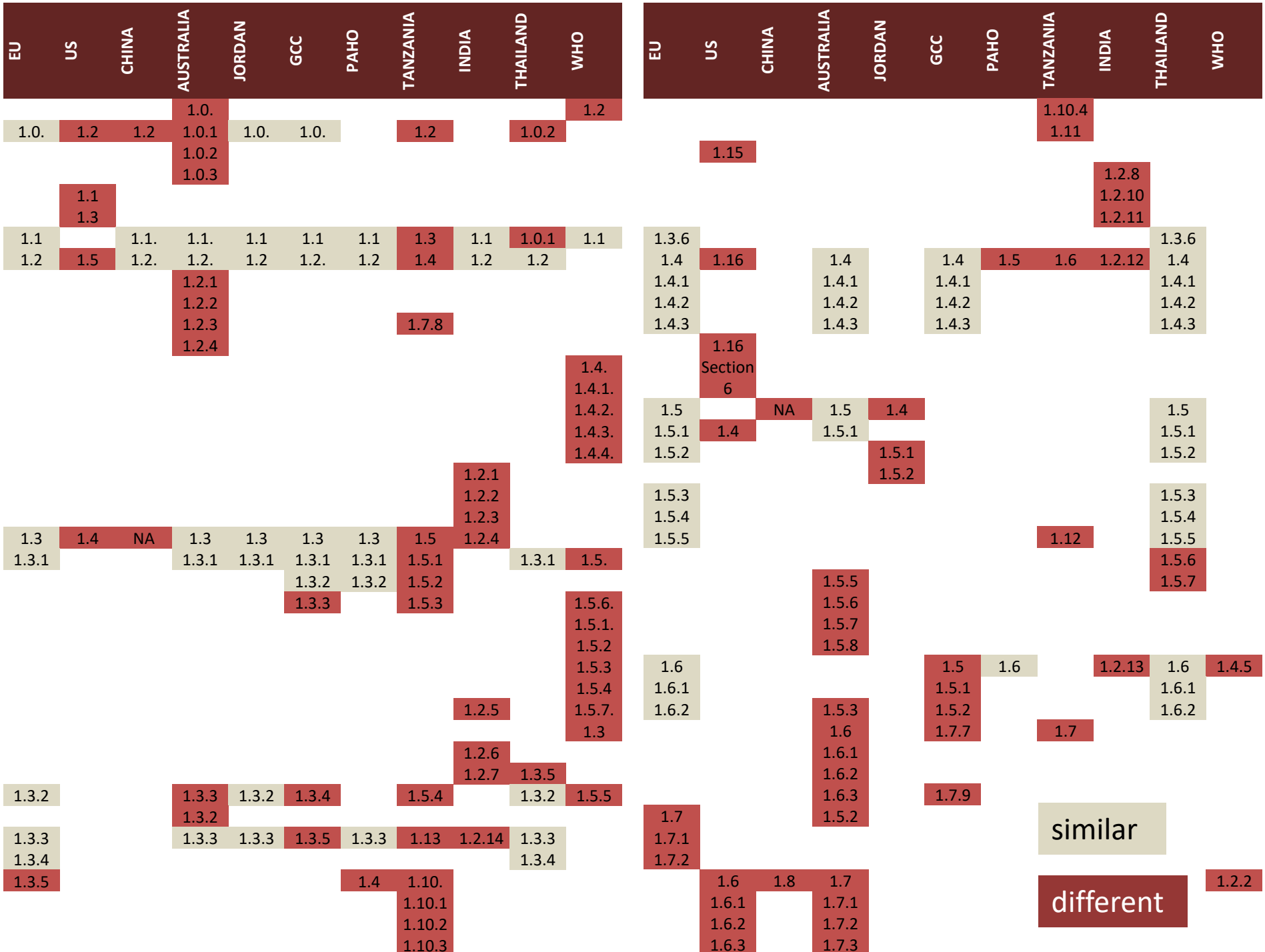
NON HARMONIZED MODULE



Comparability	Similar	Different	Total
Number of items	189	114	303

CTD NUMBERING – MODULE1

AUSTRALIA, CHINA, EUROPE, GCC, INDIA, JORDAN, PAHO, TANZANIA, THAILAND, US AND WHO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similar
different

EU	US	CHINA	AUSTRALIA	JORDAN	GCC	PAHO	TANZANIA	INDIA	THAILAND	WHO
	1.7 1.8 1.9 1.10. 1.11 1.12									
NA		1.8			1.9				NA	
1.8		1.7	1.8	1.5	1.6				1.8	1.6.9
1.8.1	1.16		1.8.1	1.5.1	1.6.1				1.8.1	
1.8.2	1.16		1.8.2	1.5.2	1.6.2				1.8.2	
	1.16			1.6						
									1.8.3	
1.9									1.9	1.6
									1.7	
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	Annex 5									
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	Annex 6									

EU	US	CHINA	AUSTRALIA	JORDAN	GCC	PAHO	TANZANIA	INDIA	THAILAND	WHO
	1.16 Annex 7 1.16 Annex 8 1.17 1.18 1.19 1.2									
										1.6.1
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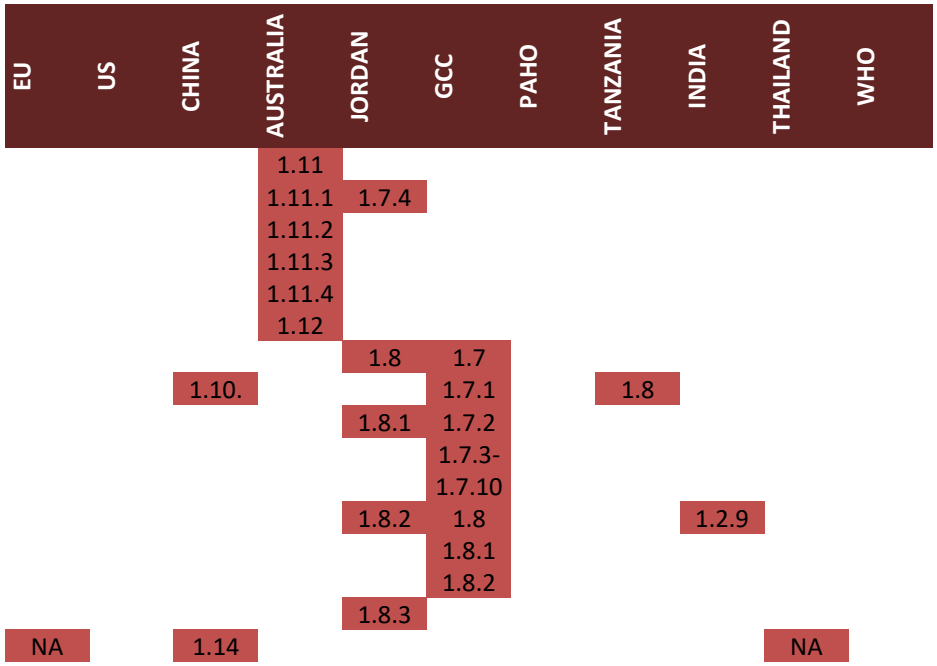
										1.6.5
										1.6.6
										1.6.7
										1.6.8
										1.7
										1.7.1
										1.7.2
										1.7.3
										1.7.4
										1.7.5
										1.7.6
										1.8
										1.8.1
										1.8.2
										1.8.3
										1.8.4
				1.7						
				1.7.1						
				1.7.2						
				1.7.3						
				1.7.5						
				1.7.6						
			1.9							
			1.9.1							
			1.9.2							
			1.10.							



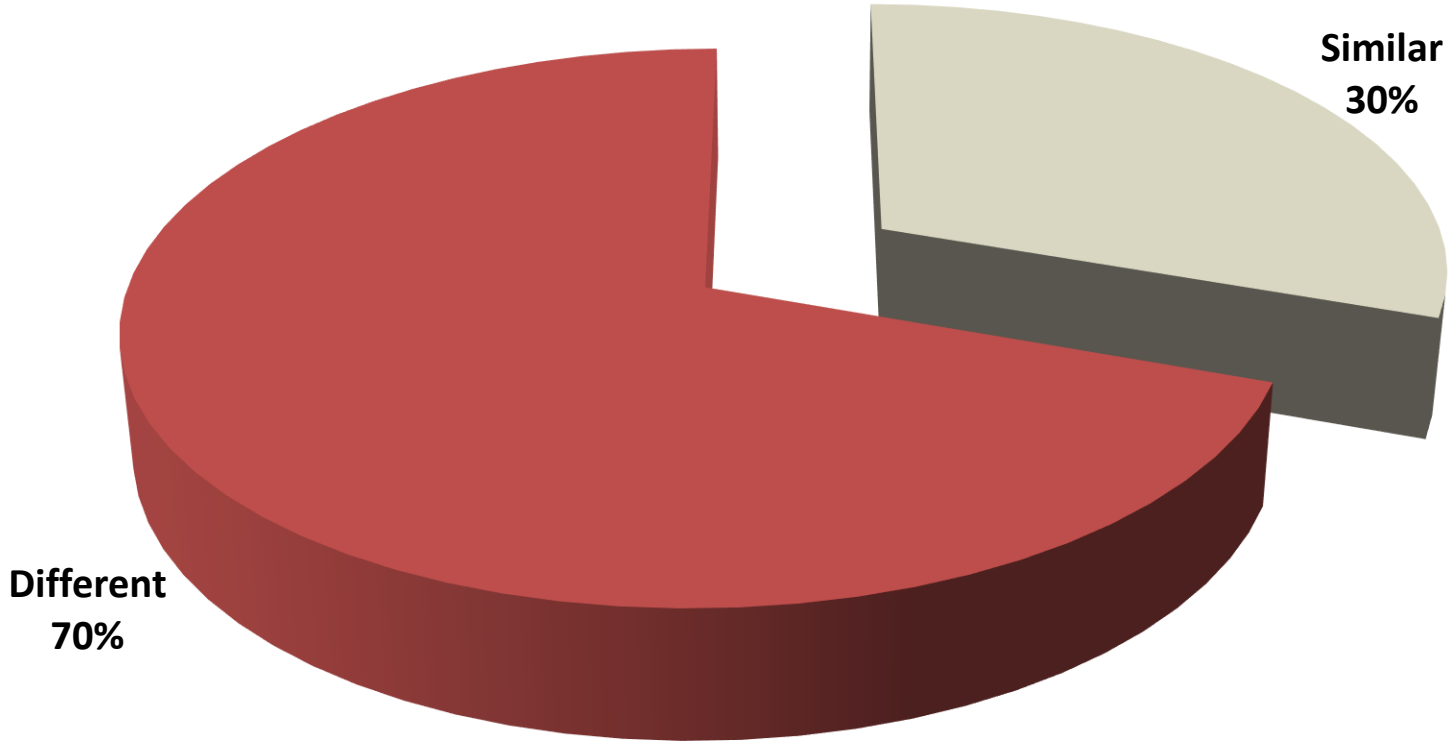
LEGEND

Same

Different

COMPARISON OF CTD MODULE 1 NUMBERING FROM AUSTRALIA, CHINA, EUROPE, GCC, INDIA, JORDAN, PAHO, TANZANIA, THAILAND, US AND WHO

NON HARMONIZED MODULE



Comparability	Same	Different	Total
Number of items	92	211	303

CTD CONTENTS MODULES 2-5

ASEAN, INDIA, JORDAN, PAHO AND THAILAND Vs. ICH (FDA)

Comparison between ASEAN and ICH

- The structure of the ASEAN CTD is completely different from the ICH CTD.
- Information required in Module 2 of the ICH CTD is embedded in the other sections in the ASEAN CTD
- Due to these structural differences
  - ASEAN is not included in the tables as for the other countries/regions because the comparison between the ICH and the ASEAN CTDs was done separately from that done for other countries
  - Comparison between the ICH and the ASEAN CTDs resulted in 93% of similarities and 7% differences

ICH (FDA) REFERENC	ICH (FDA) NAME	PAHO Vs ICH	INDIA Vs ICH	JORDAN Vs ICH	THAILAND Vs ICH
2	MODULE 2 - COMMON TECHNICAL DOCUMENT SUMMARIES				
2.4	Nonclinical Overview	Similar	Similar	Similar	Similar
		Different	Different		
2.4.1	Overview of the Nonclinical Testing Strategy	Different	Similar	Different	Different
2.4.2	Pharmacology	Different	Similar	Different	Different
		Different			
2.4.3	Pharmacokinetics	Different	Similar	Different	Different
		Different			
2.4.4	Toxicology	Different	Similar	Different	Different
		Different			
2.4.5	Integrated Overview and Conclusions	Different	Similar	Different	Different
2.4.6	List of Literature Citations	Different	Similar	Different	Different
2.5	Clinical Overview	Similar	Similar	Similar	Similar
2.5.1	Product Development Rationale	Different	Different	Different	Different
2.5.2	Overview of Biopharmaceutics	Different	Different	Different	Different
2.5.3	Overview of Clinical Pharmacology	Different	Different	Different	Different
		Different	Different		
		Different	Different		
		Different	Different		
		Different	Different		
2.5.4	Overview of Efficacy	Similar	Similar	Different	Different
2.5.5	Overview of Safety	Similar	Similar	Different	Different
2.5.6	Benefits and Risks Conclusions	Similar	Similar	Different	Different
2.5.7	References	Similar	Similar	Different	Different

ICH (FDA) REFERENC	ICH (FDA) NAME	PAHO Vs ICH	INDIA Vs ICH	JORDAN Vs ICH	THAILAND Vs ICH
2	MODULE 2 - COMMON TECHNICAL DOCUMENT SUMMARIES				
2.6	Nonclinical Written and Tabulated Summaries	Similar	Similar	Similar	Similar
2.6.1	Introduction	Similar	Similar	Different	Different
2.6.2	Pharmacology Written Summary	Similar	Similar	Different	Different
2.6.2.1	Brief Summary	Different	Different	Different	Different
2.6.2.2	Primary Pharmacodynamics	Different	Different	Different	Different
2.6.2.3	Secondary Pharmacodynamics	Different	Different	Different	Different
2.6.2.4	Safety Pharmacology	Different	Different	Different	Different
2.6.2.5	Pharmacodynamic Drug Interactions	Different	Different	Different	Different
2.6.2.6	Discussion and Conclusions	Different	Different	Different	Different
2.6.2.7	Tables and Figures	Different	Different	Different	Different
2.6.3	Pharmacology Tabulated Summary	Similar	Similar	Different	Different
2.6.4	Pharmacokinetics Written Summary	Similar	Similar	Different	Different
2.6.4.1	Brief Summary	Different	Different	Different	Different
2.6.4.2	Methods of Analysis	Different	Different	Different	Different
2.6.4.3	Absorption	Different	Different	Different	Different
2.6.4.4	Distribution	Different	Different	Different	Different
2.6.4.5	Metabolism (interspecies comparison)	Different	Different	Different	Different
2.6.4.6	Excretion	Different	Different	Different	Different
2.6.4.7	Pharmacokinetic Drug Interactions	Different	Different	Different	Different
2.6.4.8	Other Pharmacokinetic Studies	Different	Different	Different	Different
2.6.4.9	Discussion and Conclusions	Different	Different	Different	Different
2.6.4.10	Tables and Figures	Different	Different	Different	Different

ICH (FDA) REFERENC	ICH (FDA) NAME	PAHO Vs ICH (FDA)	INDIA Vs ICH (FDA)	JORDAN Vs ICH (FDA)	THAILAND Vs ICH (FDA)
2	MODULE 2 - COMMON TECHNICAL DOCUMENT SUMMARIES				
2.6.5	Pharmacokinetics Tabulated Summary	Similar	Similar	Different	Different
2.6.6	Toxicology Written Summary	Similar	Similar	Different	Different
2.6.6.1	Brief Summary	Different	Different	Different	Different
2.6.6.2	Single-Dose Toxicity	Different	Different	Different	Different
2.6.6.3	Repeat-Dose Toxicity	Different	Different	Different	Different
2.6.6.4	Genotoxicity	Different	Different	Different	Different
2.6.6.5	Carcinogenicity	Different	Different	Different	Different
2.6.6.6	Reproductive and Developmental Toxicity	Different	Different	Different	Different
2.6.6.7	Local Tolerance	Different	Different	Different	Different
2.6.6.8	Other Toxicity Studies (if available)	Different	Different	Different	Different
2.6.6.9	Discussion and Conclusions	Different	Different	Different	Different
2.6.6.10	References	Different	Different	Different	Different

ICH (FDA) REFERENC	ICH (FDA) NAME	PAHO Vs ICH	INDIA Vs ICH	JORDAN Vs ICH	THAILAND Vs ICH
2	MODULE 2 - COMMON TECHNICAL DOCUMENT SUMMARIES				
2.6.7	Toxicology Tabulated Summary	Similar	Similar	Different	Different
2.7	Clinical Summary	Similar	Similar	Similar	Similar
		Different	Different		
		Different	Different		
		Different	Different		
2.7.1	Summary of Biopharmaceutic and Associated Analytical Methods	Different	Different	Different	Different
2.7.1.1	Background and Overview	Different	Different	Different	Different
2.7.1.2	Summary of Results of Individual Studies	Different	Different	Different	Different
2.7.1.3	Comparison and Analyses of Results Across Studies	Different	Different	Different	Different
2.7.1.4	Appendix	Different	Different	Different	Different
2.7.2	Summary of Clinical Pharmacology Studies	Different	Different	Different	Different
2.7.2.1	Background and Overview	Different	Different	Different	Different
2.7.2.2	Summary of Results of Individual Studies	Different	Different	Different	Different
2.7.2.3	Comparison and Analyses of Results Across Studies	Different	Different	Different	Different
2.7.2.4	Special Studies	Different	Different	Different	Different
2.7.2.5	Appendix	Different	Different	Different	Different
2.7.3	Summary of Clinical Efficacy	Similar	Similar	Different	Different
2.7.3.1	Background and Overview of Clinical Efficacy	Different	Different	Different	Different
2.7.3.2	Summary of Results of Individual Studies	Different	Different	Different	Different
2.7.3.3	Comparison and Analyses of Results Across Studies	Different	Different	Different	Different
2.7.3.3.1	Study Populations	Different	Different	Different	Different
2.7.3.3.2	Comparison of Efficacy Results Across All Studies	Different	Different	Different	Different
2.7.3.3.3	Comparison of Results in Sub-Populations	Different	Different	Different	Different
2.7.3.4	Analysis of Clinical Information Relevant to Dosing Recommendations	Different	Different	Different	Different
2.7.3.5	Persistence of Efficacy and/or Tolerance Effects	Different	Different	Different	Different

ICH (FDA) REFERENC	ICH (FDA) NAME	PAHO Vs ICH	INDIA Vs ICH	JORDAN Vs ICH	THAILAND Vs ICH
2	MODULE 2 - COMMON TECHNICAL DOCUMENT SUMMARIES				
2.7.3.6	Appendix	Different	Different	Different	Different
2.7.4	Summary of Clinical Safety	Similar	Similar	Different	Different
2.7.4.1	Exposure to the Drug	Different	Different	Different	Different
2.7.4.1.1	Overall Safety Evaluation Plan and Narratives of Safety Studies	Different	Different	Different	Different
2.7.4.1.2	Overall Extent of Exposure	Different	Different	Different	Different
2.7.4.1.3	Demographic and Other Characteristics of Study Population	Different	Different	Different	Different
2.7.4.2	Adverse Events	Different	Different	Different	Different
2.7.4.2.1	Analysis of Adverse Events by Organ System or Syndrome	Different	Different	Different	Different
2.7.4.2.2	Narratives	Different	Different	Different	Different
2.7.4.2.3	Deaths	Different	Different	Different	Different
2.7.4.2.4	Other Serious Adverse Events	Different	Different	Different	Different
2.7.4.3	Clinical Laboratory Evaluations	Different	Different	Different	Different
2.7.4.4	Vital Signs, Physical Findings, Observations Related to Safety	Different	Different	Different	Different
2.7.4.5	Safety in Special Groups and Situations	Different	Different	Different	Different
2.7.4.5.1	Intrinsic Factors	Different	Different	Different	Different
2.7.4.5.2	Extrinsic Factors	Different	Different	Different	Different
2.7.4.5.3	Drug Interactions	Different	Different	Different	Different
2.7.4.5.4	Use in Pregnancy and Lactation	Different	Different	Different	Different
2.7.4.5.5	Overdose	Different	Different	Different	Different
2.7.4.5.6	Drug Abuse	Different	Different	Different	Different
2.7.4.5.7	Withdrawal and Rebound	Different	Different	Different	Different
2.7.4.5.8	Effects on Ability to Drive or Operate Machinery or Impairment of Mental Ability	Different	Different	Different	Different
2.7.4.6	Post-Marketing Data	Different	Different	Different	Different
2.7.4.7	Appendix	Different	Different	Different	Different
2.7.5	References	Similar	Different	Different	Different
2.7.6	Synopses of Individual Studies	Different	Different	Different	Different

ICH (FDA) REFERENC	ICH (FDA) NAME	PAHO Vs ICH	INDIA Vs ICH	JORDAN Vs ICH	THAILAND Vs ICH
3	MODULE 3 - QUALITY				
3.1	Comprehensive Table of Contents for Module 3	Similar	Similar	Different	Different
		Similar	Similar		Similar
3.2	Drug Substance	Similar	Similar	Similar	Similar
					Different
3.2.S.1	General Information	Different	Different	Similar	Similar
3.2.S.1.1	Nomenclature	Different	Different	Different	Different
3.2.S.1.2	Structure	Different	Different	Different	Different
3.2.S.1.3	General Properties	Different	Different	Different	Different
		Different	Different		
		Different	Different		
		Different	Different		
		Different	Different		
		Different	Different		
		Different	Different		
3.2.S.2	Manufacture	Similar	Similar	Similar	Different
3.2.S.2.1	Manufacturer(s)	Similar	Similar	Similar	Similar
3.2.S.2.2	Description of Process and Process Controls	Similar	Similar	Similar	Different
		Different	Different		
		Different	Different		
		Different	Different		
		Different	Different		
		Different	Different		
		Different	Different		
		Different	Different		
		Different	Different	Different	
3.2.S.2.3	Control of Materials	Similar	Different	Similar	Different
3.2.S.2.4	Control of Critical Steps and Intermediates	Similar	Similar	Similar	Different
			Different		
3.2.S.2.5	Process Validation and/or Evaluation	Similar	Similar	Similar	Different
			Different	Different	

ICH (FDA) REFERENC	ICH (FDA) NAME	PAHO Vs ICH	INDIA Vs ICH	JORDAN Vs ICH	THAILAND Vs ICH
3	MODULE 3 - QUALITY				
3.2.S.3	Characterization	Similar	Similar	Similar	Similar
3.2.S.3.1	Elucidation of Structure and Other Characteristics	Different	Similar	Similar	Different
			Different		
3.2.S.3.2	Impurities	Different	Similar	Similar	Different
3.2.S.4	Control of Drug Substance	Similar	Similar	Similar	Similar
3.2.S.4.1	Specifications	Similar	Similar	Similar	Similar
3.2.S.4.2	Analytical Procedures	Similar	Similar	Similar	Similar
3.2.S.4.3	Validation of Analytical Procedures	Similar	Similar	Similar	Similar
3.2.S.4.4	Batch Analyses	Similar	Similar	Similar	Similar
3.2.S.4.5	Justification of Specification	Similar	Similar	Similar	Similar
3.2.S.5	Reference Standards or Materials	Similar	Similar	Similar	Similar
3.2.S.6	Container/Closure Systems	Similar	Similar	Similar	Similar
			Different		
			Different		
3.2.S.7	Stability	Similar	Similar	Similar	Similar
3.2.S.7.1	Stability Summary and Conclusions	Similar	Similar	Different	Different
3.2.S.7.2	Post-approval Stability Protocol and Commitment	Similar	Similar	Different	Different
3.2.S.7.3	Stability Data	Similar	Different	Different	Different
		Different	Different		
		Different			
3.2.P	Drug Product	Similar	Similar	Similar	Similar
					Different
3.2.P.1	Description and Composition of the Drug Product	Similar	Similar	Similar	Similar
3.2.P.2	Pharmaceutical Development	Similar	Similar	Similar	Similar
3.2.P.2.1	Composition of Drug Product	Different	Different	Similar	Different
		Different	Different	Similar	
				Different	
		Different	Different	Different	
3.2.P.2.2	Formulation, Overages, Properties	Different	Different	Different	Different
				Different	
				Different	
3.2.P.2.3	Manufacturing Process Development	Similar	Similar	Similar	Different
3.2.P.2.4	Container/Closure System	Similar	Similar	Similar	Different
3.2.P.2.5	Microbiological Attributes	Different	Different	Similar	Different
3.2.P.2.6	Compatibility	Similar	Similar	Similar	Different
		Different	Different		

ICH (FDA) REFERENC	ICH (FDA) NAME	PAHO Vs ICH	INDIA Vs ICH	JORDAN Vs ICH	THAILAND Vs ICH
3	MODULE 3 - QUALITY				
3.2.P.3	Manufacture	Similar	Similar	Similar	Similar
3.2.P.3.1	Manufacturer(s)	Similar	Similar	Similar	Different
3.2.P.3.2	Batch Formula	Similar	Similar	Similar	Different
3.2.P.3.3	Description of Manufacturing Process and Process Controls	Similar	Similar	Similar	Different
3.2.P.3.4	Controls of Critical Steps and Intermediates	Similar	Similar	Similar	Different
3.2.P.3.5	Process Validation and/or Evaluation	Similar	Similar	Similar	Different
		Different	Different		
3.2.P.4	Control of Excipients	Similar	Similar	Similar	Similar
					Different
3.2.P.4.1	Specifications	Similar	Similar	Similar	Different
3.2.P.4.2	Analytical Procedures	Similar	Similar	Similar	Different
3.2.P.4.3	Validation of Analytical Procedures	Similar	Similar	Similar	Different
3.2.P.4.4	Justification of Specifications	Similar	Similar	Similar	Different
3.2.P.4.5	Excipients of Human or Animal Origin	Similar	Similar	Similar	Different
3.2.P.4.6	Novel Excipients	Similar	Similar	Similar	Different
3.2.P.5	Control of Drug Product	Similar	Similar	Similar	Similar
3.2.P.5.1	Specifications	Similar	Similar	Similar	Similar
3.2.P.5.2	Analytical Procedures	Similar	Similar	Similar	Similar
3.2.P.5.3	Validation of Analytical Procedures	Similar	Similar	Similar	Similar
3.2.P.5.4	Batch Analyses	Similar	Similar	Similar	Similar
3.2.P.5.5	Characterization of Impurities	Similar	Similar	Similar	Similar
3.2.P.5.6	Justification of Specifications	Similar	Similar	Similar	Similar
		Different	Different		
3.2.P.6	Reference Standards or Materials	Similar	Similar	Similar	Similar
3.2.P.7	Container/Closure System	Similar	Similar	Similar	Similar
		Different	Different		
		Different	Different		
3.2.P.8	Stability	Similar	Similar	Similar	Similar
3.2.P.8.1	Stability Summary and Conclusions	Similar	Similar	Similar	Different
		Different	Different		
		Different			
3.2.P.8.2	Post-Approval Stability Protocol and Stability Commitments	Similar	Similar	Similar	Different
3.2.P.8.3	Stability Data	Similar	Different	Similar	Different
		Different	Different		

ICH (FDA) REFERENC	ICH (FDA) NAME	PAHO Vs ICH	INDIA Vs ICH	JORDAN Vs ICH	THAILAND Vs ICH
3	MODULE 3 - QUALITY				
3.2.A	Appendices	Similar	Similar	Different	Similar
3.2.A.1	Facilities and Equipment	Similar	Similar	Different	Similar
3.2.A.2	Adventitious Agents Safety Evaluation	Similar	Similar	Different	Similar
3.2.A.3	Novel Excipients	Different	Different	Different	Similar
3.2.R	Regional Information	Different	Different	Different	Similar
3.2.R.1	Batch Records	Different	Different	Different	Different
	Lot #### (STRENGTH)	Different	Different	Different	Different
	Lot #### (STRENGTH)	Different	Different	Different	Different
3.2.R.2	Methods Validation Packet	Different	Different	Different	Different
3.3	Key Literature References	Similar	Similar	Different	Similar
4	MODULE 4 - NON-CLINICAL STUDY REPORTS	Similar	Similar	Similar	Similar
				Different	
				Different	
4.1	Comprehensive Table of Contents for Module 4	Similar	Similar	Similar	Different
4.2	Study Reports	Similar	Similar	Similar	Similar
4.2.1	Pharmacology	Similar	Similar	Similar	Similar
4.2.1.1	Primary Pharmacodynamics	Similar	Similar	Different	Similar
4.2.1.2	Secondary Pharmacodynamics	Similar	Similar	Different	Similar
4.2.1.3	Safety Pharmacology	Different	Different	Different	Similar
4.2.1.4	Pharmacodynamic Drug Interactions	Different	Different	Different	Similar
4.2.2	Farmacokinetics	Similar	Similar	Similar	Similar
4.2.2.1	Analytical Methods and Validation Reports	Different	Different	Different	Similar
4.2.2.2	Absorption	Different	Different	Different	Similar
4.2.2.3	Distribution	Different	Different	Different	Similar
4.2.2.4	Metabolism	Different	Different	Different	Similar
4.2.2.5	Excretion	Different	Different	Different	Similar
4.2.2.6	Pharmacokinetic Drug Interactions	Different	Different	Different	Similar
4.2.2.7	Other Pharmacokinetic Studies	Different	Different	Different	Similar

ICH (FDA) REFERENC	ICH (FDA) NAME	PAHO Vs ICH	INDIA Vs ICH	JORDAN Vs ICH	THAILAND Vs ICH
4	MODULE 4 - NON-CLINICAL STUDY REPORTS				
4.2.3	Toxicology	Similar	Similar	Similar	Similar
		Different	Different		
		Different	Different		
		Different	Different		
4.2.3.1	Single-Dose Toxicity	Different	Different	Different	Similar
4.2.3.2	Repeat-Dose Toxicity	Different	Different	Different	Similar
		Different	Different		
		Different	Different		
		Different	Different		
		Different	Different		
		Different	Different		
4.2.3.3	Genotoxicity	Similar	Similar	Different	Similar
4.2.3.3.1	*In vitro* Studies	Different	Different	Different	Similar
4.2.3.3.2	*In vivo* Studies	Different	Different	Different	Similar
		Different	Different		
4.2.3.4	Carcinogenicity	Similar	Similar	Different	Similar
					Different
					Different
					Different
4.2.3.5	Reproductive and Developmental Toxicity	Similar	Different	Different	Similar
4.2.3.5.1	Fertility and Embryonic Development	Different	Different	Different	Similar
4.2.3.5.2	Embryo-Fetal Development	Different	Different	Different	Similar
4.2.3.5.3	Pre- and Post-natal Development & Maternal Function	Different	Different	Different	Similar
4.2.3.5.4	Offspring, Juvenile, Second & Third-Generation Studies	Different	Different	Different	Similar
4.2.3.6	Local Tolerance	Different	Different	Different	Similar
4.2.3.7	Other Toxicity Studies	Different	Different	Different	Similar
4.2.3.7.1	Antigenicity	Different	Different	Different	Similar
4.2.3.7.2	Immunotoxicity	Different	Different	Different	Similar
4.2.3.7.3	Mechanistic studies (not included elsewhere)	Different	Different	Different	Similar
4.2.3.7.4	Dependence	Different	Different	Different	Similar
4.2.3.7.5	Metabolites	Different	Different	Different	Similar
4.2.3.7.6	Impurities	Different	Different	Different	Similar
4.2.3.7.7	Other	Different	Different	Different	Similar
			Different		
		Different	Different		
		Different	Different		
4.3	Literature References	Similar	Similar	Similar	Similar

ICH (FDA) REFERENC	ICH (FDA) NAME	PAHO Vs ICH	INDIA Vs ICH	JORDAN Vs ICH	THAILAND Vs ICH
5	MODULE 5 - CLINICAL STUDY REPORTS				
				Different	
5.1	Comprehensive Table of Contents for Module 5	Similar	Similar	Different	Different
5.2	Tabular Listing of all Clinical Studies	Similar	Similar	Different	Similar
5.2.1	CLIENT Studies	Different	Different	Different	Different
5.2.2	Tabular Listing of Clinical Investigators	Different	Different	Different	Different
		Different	Different		
		Different	Different		
		Different	Different		
			Different		
		Different	Different		
		Different	Different		
		Different	Different		
		Different	Different		
			Different		
5.3	Clinical Study Reports	Similar	Different	Similar	Similar
5.3.1	Reports of Biopharmaceutic Studies	Different	Different	Different	Similar
5.3.1.1	Bioavailability (BA) Study Reports	Different	Different	Similar	Similar
					Different
					Different
					Different
5.3.1.1.1	CLIENT Studies	Different	Different	Different	Different
	• Protocol #### (Food-Effect)	Different	Different	Different	Different
	• Protocol #### (Food-Effect) (continued)	Different	Different	Different	Different
	• Protocol #### (Food-Effect) (continued)	Different	Different	Different	Different
	• Protocol #### (Food-Effect) (continued)	Different	Different	Different	Different
5.3.1.1.2	REFERENCE LISTED DRUG SPONSOR STUDIES	Different	Different	Different	Different
	• Fill in data from NDA Summary Basis of Approval Review	Different	Different	Different	Different
	NA				
	NA				
5.3.1.1.3	Published Studies	Different	Different	Similar	Different
5.3.1.1.4	Summary	Different	Different	Different	Different
				Different	
				Different	
				Different	
				Different	

ICH (FDA) REFERENC	ICH (FDA) NAME	PAHO Vs ICH	INDIA Vs ICH	JORDAN Vs ICH	THAILAND Vs ICH
5	MODULE 5 - CLINICAL STUDY REPORTS				
5.3.1.2	Comparative BA & BE Study Reports	Different	Different	Different	Similar
5.3.1.2.1	CLIENT Studies	Different	Different	Different	Different
	· Protocol ####	Different	Different	Different	Different
	· Appendices 16.0	Different	Different	Different	Different
	· Appendices 16.1 – Study Information	Different	Different	Different	Different
	· Appendices 16.1.1 – Protocol & IRB Approval	Different	Different	Different	Different
	· Appendices 16.1.2 – Sample Case Report Form (CRF)	Different	Different	Different	Different
	· Appendices 16.1.3 – IRB Membership Roster	Different	Different	Different	Different
	· Appendices 16.1.4 – List of Investigators	Different	Different	Different	Different
	· Appendices 16.1.5 – Signature Page	Different	Different	Different	Different
	· Appendices 16.1.6 – Table of Dosing Dates and Times	Different	Different	Different	Different
	· Appendices 16.1.7 – Randomization Scheme and Codes	Different	Different	Different	Different
	· Appendices 16.1.8 – Audit Certificate	Different	Different	Different	Different
	· Appendices 16.1.9 – Statistical Report	Different	Different	Different	Different
	· Protocol #### (continued)	Different	Different	Different	Different
	· Appendices 16.1.9 – Statistical Report (continued)	Different	Different	Different	Different
	· Appendices 16.1.10 – Analytical Report	Different	Different	Different	Different
	· Addendum to Method Validation Report	Different	Different	Different	Different
	· Protocol #### (continued)	Different	Different	Different	Different
	· Appendices 16.1.10 – Analytical Report (continued)	Different	Different	Different	Different
	· Appendix 16.1.11 – Publications Based on this Study (NA)	Different	Different	Different	Different
	· Appendix 16.1.12 – Publications Referenced in Report (NA)	Different	Different	Different	Different
	· Appendix 16.2 – Subject Data Listings	Different	Different	Different	Different
	· Appendix 16.2.1 – Discontinued Subjects	Different	Different	Different	Different
	· Appendix 16.2.2 – Protocol Deviations (none)	Different	Different	Different	Different
	· Appendix 16.2.3 – Concomitant Medications	Different	Different	Different	Different
	· Appendix 16.2.4 – Subject Demographics	Different	Different	Different	Different
	· Appendix 16.2.5 – Table of Deviations from Scheduled Collections	Different	Different	Different	Different
	· Appendix 16.2.6 – Individual Efficacy Response (NA)	Different	Different	Different	Different
	· Appendix 16.2.7 – Adverse Event Listings	Different	Different	Different	Different
	· Appendix 16.2.8 – Listing of Individual Lab Measurements ((NA)	Different	Different	Different	Different
	· Appendix 16.3 – Case Report Forms (CRF) (Subjects 1 – 44)	Different	Different	Different	Different
	· Appendix 16.3.1 – CRFs for Deaths, Serious AE, & Discontinuations	Different	Different	Different	Different
	· Appendix 16.3.2 – Other CRFs Submitted (NA)	Different	Different	Different	Different
	· Appendix 16.4 – Individual Patient Listings	Different	Different	Different	Different

ICH (FDA) REFERENC	ICH (FDA) NAME	PAHO Vs ICH	INDIA Vs ICH	JORDAN Vs ICH	THAILAND Vs ICH
5	MODULE 5 - CLINICAL STUDY REPORTS				
	· Protocol ####	Different	Different	Different	Different
	· Protocol ####	Different	Different	Different	Different
	· Appendices 16.0	Different	Different	Different	Different
	· Appendices 16.1 – Study Information	Different	Different	Different	Different
	· Appendices 16.1.1 – Protocol & Protocol Amendments	Different	Different	Different	Different
	· Appendices 16.1.2 – Sample Case Report Form (CRF)	Different	Different	Different	Different
	· Appendices 16.1.3 – IRB Membership & Sample Informed Consent	Different	Different	Different	Different
	· Appendices 16.1.4 – List of Investigators	Different	Different	Different	Different
	· Appendices 16.1.5 – Signature Page	Different	Different	Different	Different
	· Appendices 16.1.6 – List of Subjects Receiving Test Drugs from Multiple Batches (NA)	Different	Different	Different	Different
	· Appendices 16.1.7 – Randomization Scheme and Codes	Different	Different	Different	Different
	· Appendices 16.1.8 – Audit Certificate (NA)	Different	Different	Different	Different
	· Appendices 16.1.9 – Documentation of Pharmacokinetic and Statistical Methods	Different	Different	Different	Different
	· Appendices 16.1.10 – Documentation of Inter-Laboratory Standardization Methods and QA Procedures	Different	Different	Different	Different
	· Appendix 16.1.11 – Publications Based on this Study (NA)	Different	Different	Different	Different
	· Appendix 16.1.12 – Publications Referenced in Report (NA)	Different	Different	Different	Different
	· Protocol #### (continued)	Different	Different	Different	Different
	· Appendix 16.2 – Subject Data Listings	Different	Different	Different	Different
	· Appendix 16.2.1 – Discontinued Subjects (none)	Different	Different	Different	Different
	· Appendix 16.2.2 – Protocol Deviations – Blood Samples	Different	Different	Different	Different
	· Appendix 16.2.3 – Subjects Excluded from Analysis (none)	Different	Different	Different	Different
	· Appendix 16.2.4 – Demographic Data & Baseline Characteristics	Different	Different	Different	Different
	· Appendix 16.2.5 – Drug Concentration Data	Different	Different	Different	Different
	· Appendix 16.2.6 – Individual Data	Different	Different	Different	Different
	· Appendix 16.2.7 – Adverse Event Listings	Different	Different	Different	Different
	· Appendix 16.2.8 – Listing of Individual Lab Measurements	Different	Different	Different	Different
	· Appendix 16.2.9 – Statistical Analysis	Different	Different	Different	Different
	· Appendix 16.3 – Case Report Forms (CRF)	Different	Different	Different	Different
	· Appendix 16.3.1 – CRFs for Deaths, Other Serious Adverse Events, & Withdrawals for AE (none)	Different	Different	Different	Different
	· Appendix 16.3.2 – Other CRFs Submitted (NA)	Different	Different	Different	Different
	· Appendix 16.4 – Individual Subject Data Listings	Different	Different	Different	Different
	· Appendix 16.5 – Analytical Report	Different	Different	Different	Different
	· Appendix 16.6 – Validation Report	Different	Different	Different	Different

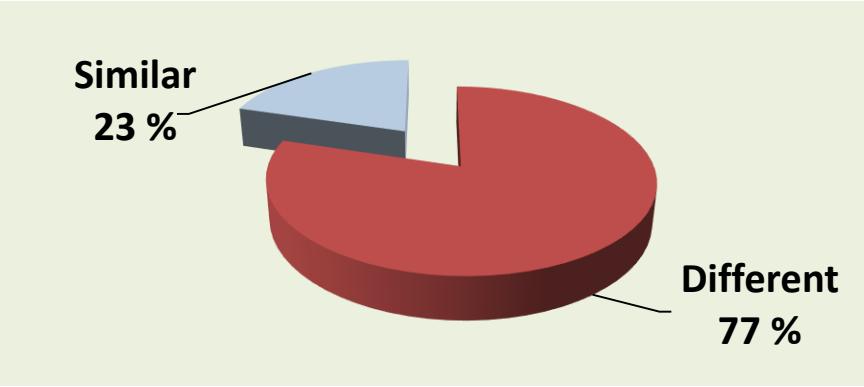
ICH (FDA) REFERENC	ICH (FDA) NAME	PAHO Vs ICH	INDIA Vs ICH	JORDAN Vs ICH	THAILAND Vs ICH
5	MODULE 5 - CLINICAL STUDY REPORTS				
5.3.1.2.2	REFERENCE LISTED DRUG SPONSOR STUDIES	Different	Different	Different	Different
	· FILL IN AS NEEDED: Summary Basis of Approval Review	Different	Different	Different	Different
	· FILL IN AS NEEDED: Summary Basis of Approval Review	Different	Different	Different	Different
	· FILL IN AS NEEDED: Summary Basis of Approval Review	Different	Different	Different	Different
5.3.1.2.3	Published Studies	Different	Different	Different	Different
5.3.1.2.4	Summary	Different	Different	Different	Different
					Different
					Different
					Different
5.3.1.3	In vitro/In vivo Correlation (IV/IVC)	Different	Different	Different	Similar
					Different
					Different
					Different
5.3.1.4	Bioanalytical and Analytical Methods	Different	Different	Different	Similar
					Different
					Different
					Different
5.3.2	Reports of Studies Pertinent to Human PK	Different	Different	Different	Similar
5.3.2.1	Plasma Protein Binding Study Reports	Different	Different	Different	Similar
					Different
					Different
					Different
5.3.2.2	Hepatic Metabolism/Drug Interactions	Different	Different	Different	Similar
					Different
					Different
					Different
5.3.2.3	Studies Using other Human Materials	Different	Different	Different	Similar
					Different
					Different
					Different
				Different	
5.3.3	Reports of Human PK Studies	Different	Different	Similar	Similar
5.3.3.1	Healthy Subject PK and Tolerability	Different	Different	Similar	Similar
					Different
					Different
					Different

ICH (FDA) REFERENC	ICH (FDA) NAME	PAHO Vs ICH	INDIA Vs ICH	JORDAN Vs ICH	THAILAND Vs ICH
5	MODULE 5 - CLINICAL STUDY REPORTS				
5.3.3.2	Patient PK and Initial Tolerability	Different	Different	Similar	Similar
					Different
					Different
					Different
5.3.3.3	Intrinsic Factor PK	Different	Different	Similar	Similar
					Different
					Different
					Different
5.3.3.4	Extrinsic Factor PK	Different	Different	Similar	Similar
					Different
					Different
					Different
5.3.3.5	Population PK	Different	Different	Similar	Similar
					Different
					Different
					Different
5.3.4	Reports of Human PD Studies	Different	Different	Similar	Similar
5.3.4.1	Healthy Subject PD and PK/PD Studies	Different	Different	Similar	Similar
					Different
					Different
					Different
5.3.4.2	Patient PD and PK/PD	Different	Different	Similar	Similar
					Different
					Different
					Different
5.3.5	Reports of Efficacy and Safety Studies	Different	Different	Different	Similar
					Different
5.3.5.1	Controlled Clinical Studies on Indication	Different	Different	Different	Similar
5.3.5.1.A	INDICATION # 1	Different	Different	Different	Different
5.3.5.1.A.1	CLIENT Studies	Different	Different	Different	Different
5.3.5.1.A.2	NDA ##,### Sponsor Studies	Different	Different	Different	Different
5.3.5.1.A.3	Published Studies	Different	Different	Different	Different
5.3.5.1.A.4	Summary	Different	Different	Different	Different
5.3.5.1.B	INDICATION # 2	Different	Different	Different	Different
5.3.5.1.B.1	CLIENT Studies	Different	Different	Different	Different
5.3.5.1.B.2	NDA ##,### Sponsor Studies	Different	Different	Different	Different
5.3.5.1.B.3	Published Studies	Different	Different	Different	Different
5.3.5.1.B.4	Summary	Different	Different	Different	Different
					Different
5.3.5.2	Uncontrolled Clinical Studies	Different	Different	Different	Similar
5.3.5.2.1	CLIENT Studies	Different	Different	Different	Different
5.3.5.2.2	NDA ##,### Sponsor Studies	Different	Different	Different	Different
	• Summary Basis of Approval: Clinical Review	Different	Different	Different	Different
5.3.5.2.3	Published Studies	Different	Different	Different	Different
5.3.5.2.4	Summary	Different	Different	Different	Different
					Different
					Different
					Different

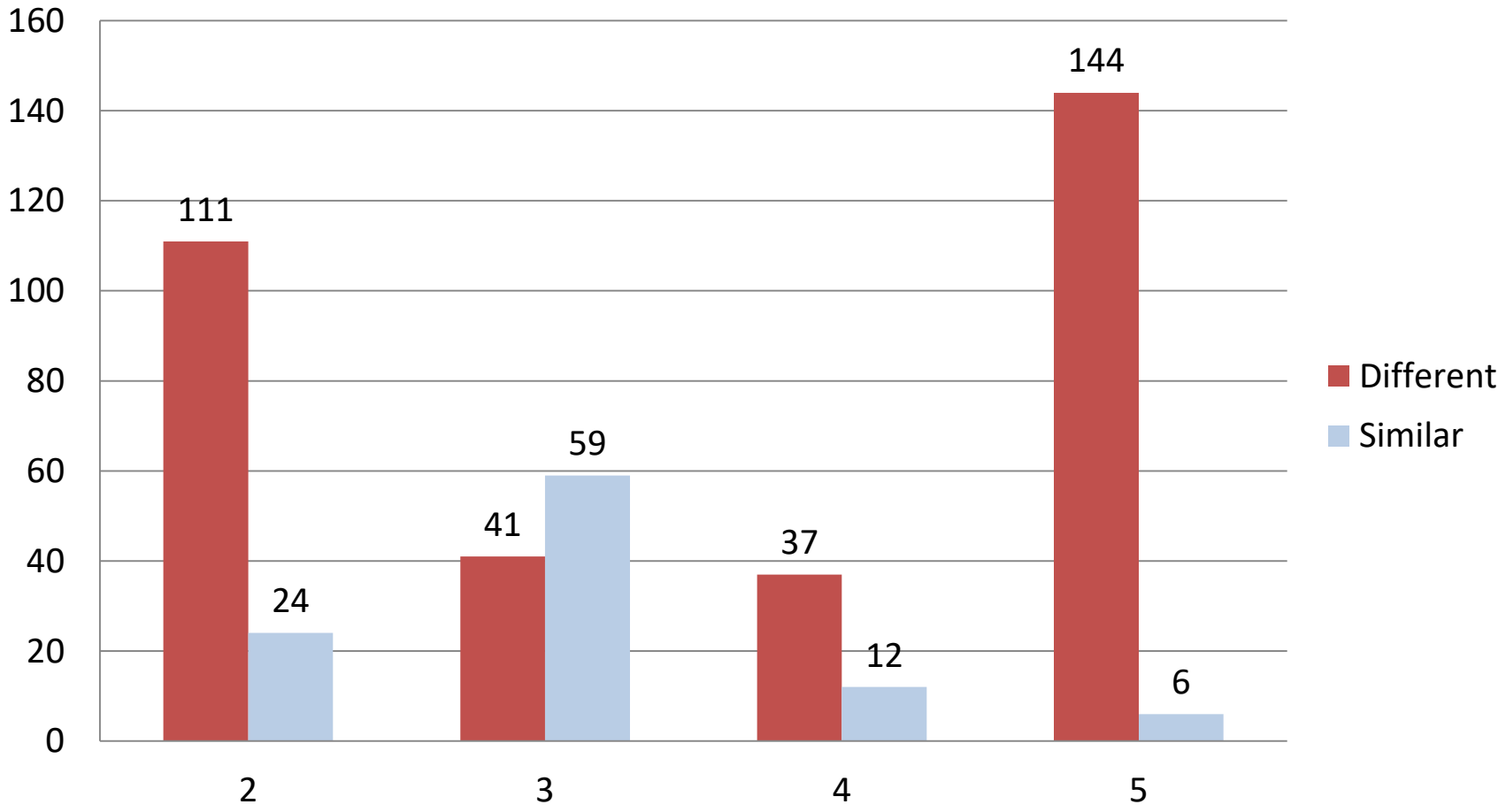
ICH (FDA) REFERENC	ICH (FDA) NAME	PAHO Vs ICH	INDIA Vs ICH	JORDAN Vs ICH	THAILAND Vs ICH
5	MODULE 5 - CLINICAL STUDY REPORTS				
5.3.5.3	Reports of Analyses of Data from More than One Study	Different	Different	Different	Similar
5.3.5.3.1	Integrated Summary of Safety	Different	Different	Different	Different
5.3.5.3.1.A	• INDICATION # 1	Different	Different	Different	Different
5.3.5.3.1.B	• INDICATION # 2	Different	Different	Different	Different
5.3.5.3.2	Integrated Summary of Efficacy	Different	Different	Different	Different
	• INDICATION # 1	Different	Different	Different	Different
	• INDICATION # 2	Different	Different	Different	Different
					Different
					Different
					Different
5.3.5.4	Other Clinical Study Reports	Different	Different	Different	Different
					Different
					Different
					Different
5.3.6	Reports of Post-Marketing Experience	Similar	Similar	Different	Similar
5.3.6.1	Regulatory History of NDA ##,###	Different	Different	Different	Different
5.3.6.2	Generic Approvals	Different	Different	Different	Different
5.3.6.3	Safety Data from Post-Marketing Surveillance	Different	Different	Different	Different
5.3.6.3.1	Foreign Marketing Data in Support of the Original NDA	Different	Different	Different	Different
5.3.6.3.2	US Post-Marketing Surveillance Data	Different	Different	Different	Different
5.3.7	Case Report Forms (CRF)/Individual Patient Listings	Different	Different	Different	Similar
5.3.7.1	Protocol ##### – BE Study	Different	Different	Different	Different
5.3.7.2	Protocol ##### – Food-Effect Study	Different	Different	Different	Different
					Different
					Different
					Different
5.4	Literature References	Similar	Similar	Different	Similar
	Literature References (continued)	Different	Different	Different	Different
			Different		

CTD CONTENT: INDIA, JORDAN, PAHO AND THAILAND Vs. ICH (FDA)
Overall Comparison Modules 2-5

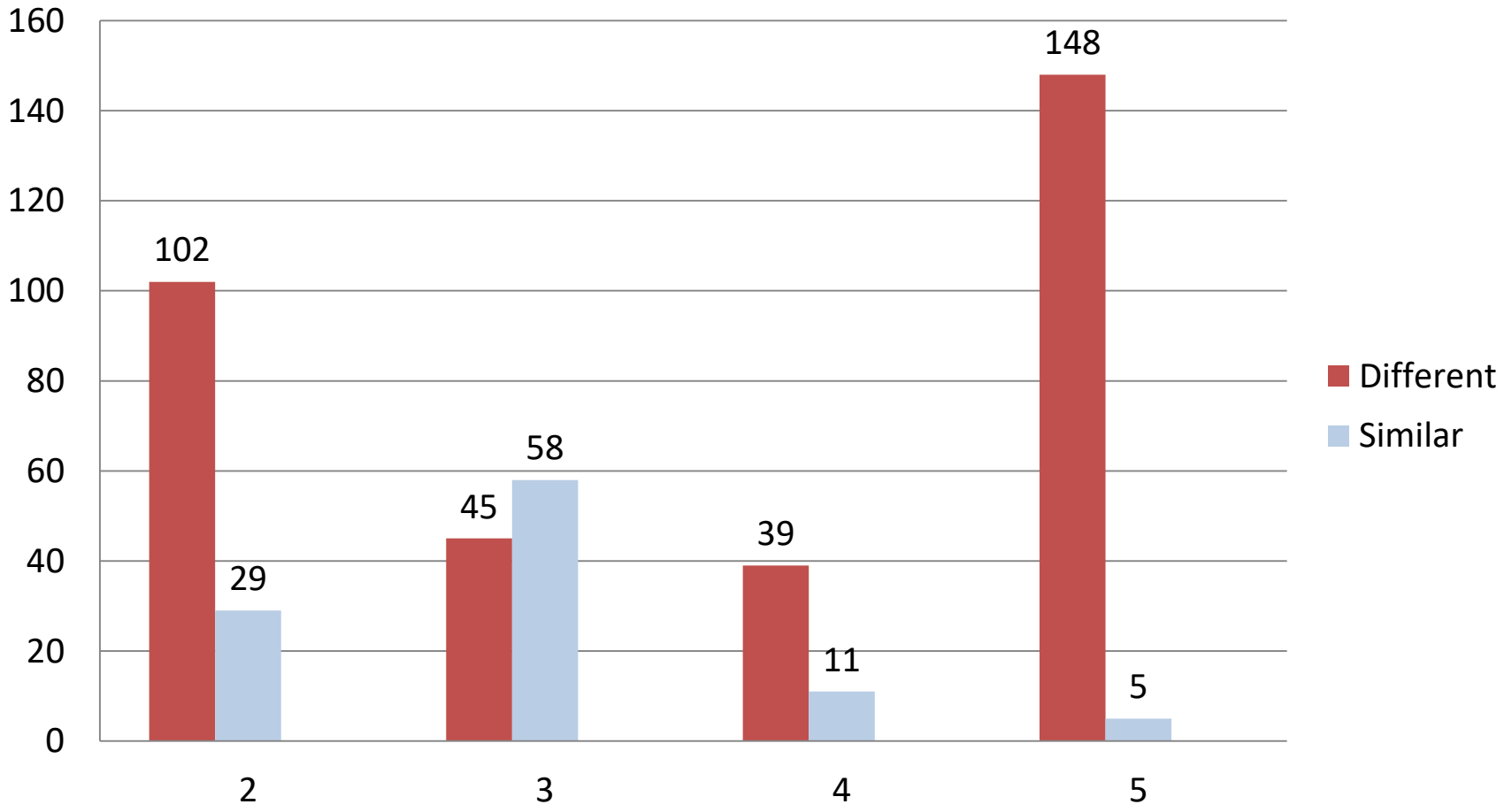
	Number of items PAHO Vs ICH (FDA)	Number of items INDIA Vs ICH (FDA)	Number of items JORDAN Vs ICH (FDA)	Number of items Thailand Vs ICH (FDA)	TOTAL
Different	333	334	308	332	1,307
Similar	101	103	84	108	396
Total	434	437	392	440	1,703
% similarity	23	24	21	25	23
% difference	77	76	79	75	77



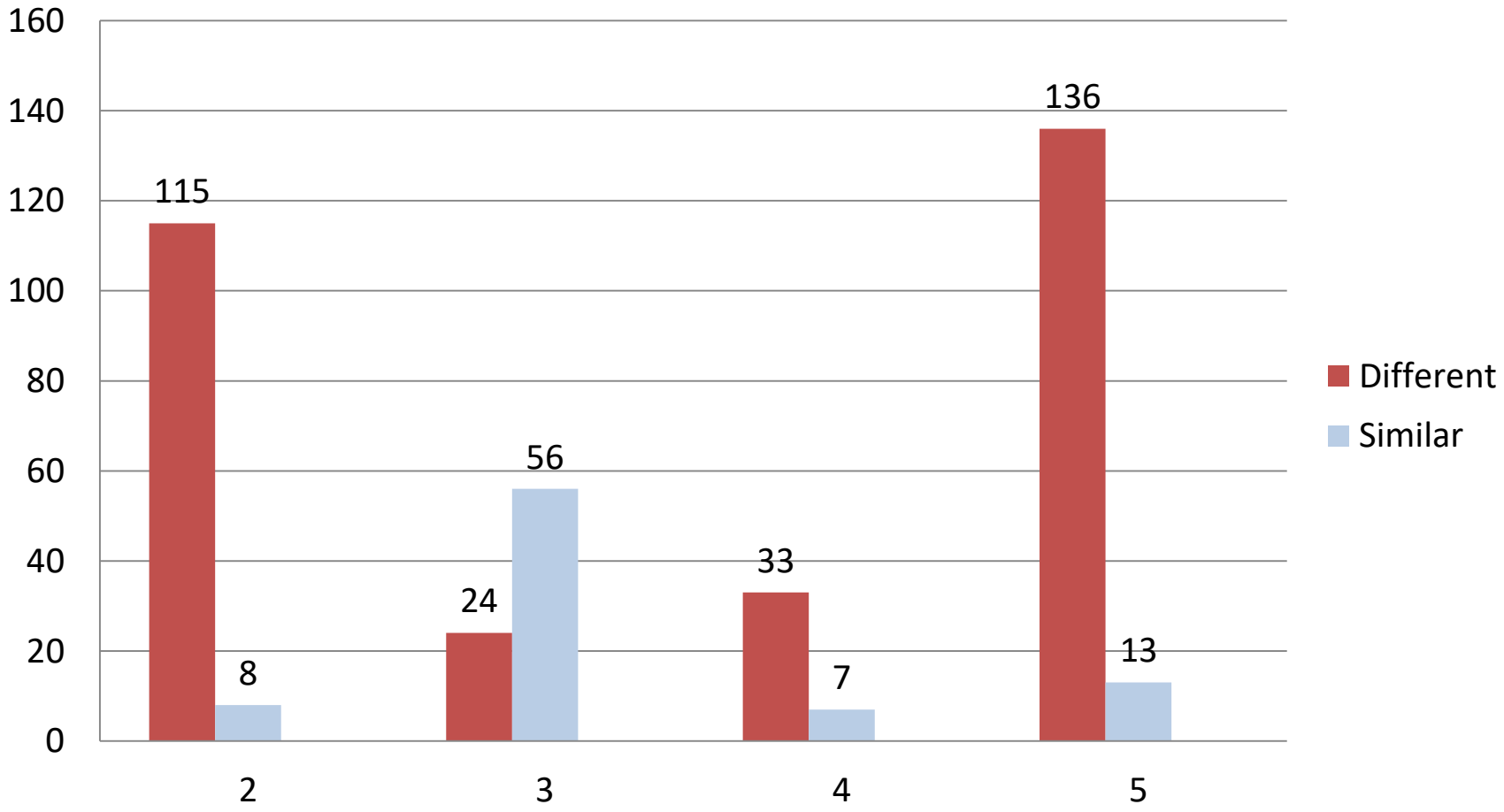
PAHO Vs. ICH (FDA) CONTENT
Comparing Module by Module



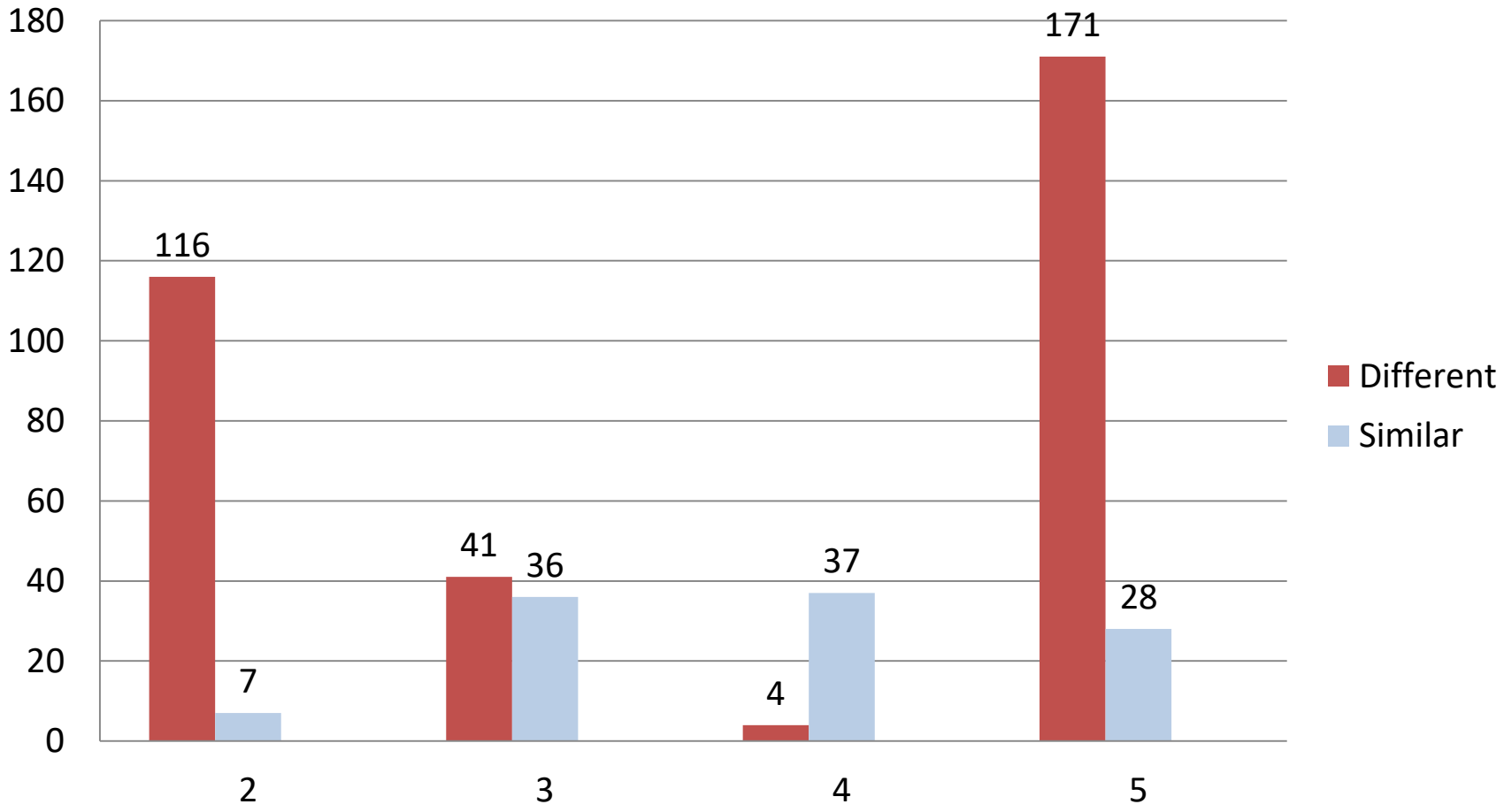
INDIA Vs. ICH (FDA) CONTENT
Comparing Module by Module



JORDAN Vs. ICH (FDA) CONTENT Comparing Module by Module



THAILAND Vs. ICH (FDA) CONTENT Comparing Module by Module



CTD NUMBERING - MODULES 2-5

ASEAN, INDIA, JORDAN, PAHO AND THAILAND Vs. ICH (FDA)

Module	ICH	FDA	PAHO	INDIA	JORDAN	ASEAN	THAILAND
2							
2	2.1	**2.1**	2.1	2.1	2.1		
2	2.2	**2.2**	2.2	2.2	2.2		2.2
2	2.3	**2.3**	2.3	2.3	2.3	Part II - Section B	2.3
2	NA	NA	NA	NA	NA	NA	NA
2	2.3.S	**2.3.S**	2.3.S	2.3.S			
2	2.3.S.1	**2.3.S.1**					
2	2.3.S.2	**2.3.S.2**					
2	2.3.S.3	**2.3.S.3**					
2	2.3.S.4	**2.3.S.4**					
2	2.3.S.5	**2.3.S.5**					
2	2.3.S.6	**2.3.S.6**					
2	2.3.S.7	**2.3.S.7**					
2	2.3.P	**2.3.P**	2.3.P	2.3.P			
2	2.3.P.1	**2.3.P.1**					
2	2.3.P.2	**2.3.P.2**					
2	2.3.P.3	**2.3.P.3**					
2	2.3.P.4	**2.3.P.4**					
2	2.3.P.5	**2.3.P.5**					
2	2.3.P.6	**2.3.P.6**					
2	2.3.P.7	**2.3.P.7**					
2	2.3.P.8	**2.3.P.8**					
2	2.3.A	**2.3.A**		2.3.A			
2	2.3.A.1	**2.3.A.1**					
2	2.3.A.2	**2.3.A.2**					
2	2.3.A.3	**2.3.A.3**					
2	2.3.R	**2.3.R**					
2	2.4	**2.4**	2.4	2.4	2.4	Part III - Section B	2.4
2	NA	**NA**	NA	2.4.1	NA	NA	NA
2		**2.4.1**		2.4.2			
2		**2.4.2**		2.4.3			

Module	ICH	FDA	PAHO	INDIA	JORDAN	ASEAN	THAILAND
2							
2	NA	**NA**	NA	NA	NA	NA	NA
2		**2.4.3**		2.4.4			
2	NA	**NA**	NA	NA	NA	NA	NA
2		**2.4.4**		2.4.5			
2	NA	**NA**	NA	NA	NA	NA	NA
2		**2.4.5**		2.4.6			
2		**2.4.6**		2.4.7			
2	2.5	**2.5**	2.5	2.6	2.5	Part IV - Section B	2.5
2		**2.5.1**					
2		**2.5.2**					
2		**2.5.3**					
2		**NA**	NA	2.6.1	NA	NA	NA
2		**NA**	NA	2.6.2	NA	NA	NA
2		**NA**	2.5.1	2.6.3	NA	NA	NA
2		**NA**	2.5.2	2.6.4	NA	NA	NA
2		**2.5.4**	2.5.4	2.6.5			
2		**2.5.5**	2.5.5	2.6.6			
2		**2.5.6**	2.5.6	2.6.7			
2		**2.5.7**	2.5.7	2.6.8			
2	2.6	**2.6**	2.6	2.5	2.6	Part III - Section C	2.6
2		**NA**	NA	**NA**	NA	1	NA
2	2.6.1	**2.6.1**	2.6.1	2.5.1			
2	2.6.2	**2.6.2**	2.6.2	2.5.2		2	
2		**2.6.2.1**					
2		**2.6.2.2**					
2		**2.6.2.3**					
2		**2.6.2.4**					
2		**2.6.2.5**					
2		**2.6.2.6**					

Module	ICH	FDA	PAHO	INDIA	JORDAN	ASEAN	THAILAND
2							
2		**2.6.2.7**					
2	2.6.3	**2.6.3**	2.6.3	2.5.3			
2	2.6.4	**2.6.4**	2.6.4	2.5.4		3	
2		**2.6.4.1**					
2		**2.6.4.2**					
2		**2.6.4.3**					
2		**2.6.4.4**					
2		**2.6.4.5**					
2		**2.6.4.6**					
2		**2.6.4.7**					
2		**2.6.4.8**					
2		**2.6.4.9**					
2		**2.6.4.10**					
2	2.6.5	**2.6.5**	2.6.5	2.5.5			
2	2.6.6	**2.6.6**	2.6.6	2.5.6		4	
2		**2.6.6.1**					
2		**2.6.6.2**					
2		**2.6.6.3**					
2		**2.6.6.4**					
2		**2.6.6.5**					
2		**2.6.6.6**					
2		**2.6.6.7**					
2		**2.6.6.8**					
2		**2.6.6.9**					
2		**2.6.6.10**					
2	2.6.7	**2.6.7**	2.6.7	2.5.7			
2	2.7	**2.7**	2.7	2.7	2.7	Part IV - Section C	2.7
2		**NA**	NA	2.7.1	NA	NA	NA
2		**NA**	NA	2.7.2	NA	NA	NA
2		**NA**	2.7.2	2.7.3	NA	NA	NA

Module	ICH	FDA	PAHO	INDIA	JORDAN	ASEAN	THAILAND
2							
2	2.7.1	**2.7.1**				1	
2		**2.7.1.1**					
2		**2.7.1.2**					
2		**2.7.1.3**					
2		**2.7.1.4**					
2	2.7.2	**2.7.2**				2	
2		**2.7.2.1**					
2		**2.7.2.2**					
2		**2.7.2.3**					
2		**2.7.2.4**					
2		**2.7.2.5**					
2	2.7.3	**2.7.3**	2.7.3	2.7.4		3	
2		**2.7.3.1**					
2		**2.7.3.2**					
2		**2.7.3.3**					
2		**2.7.3.3.1**					
2		**2.7.3.3.2**					
2		**2.7.3.3.3**					
2		**2.7.3.4**					
2		**2.7.3.5**					
2		**2.7.3.6**					
2	2.7.4	**2.7.4**	2.7.4	2.7.5		4	
2		**2.7.4.1**					
2		**2.7.4.1.1**					
2		**2.7.4.1.2**					
2		**2.7.4.1.3**					
2		**2.7.4.2**					
2		**2.7.4.2.1**					

Module	ICH	FDA	PAHO	INDIA	JORDAN	ASEAN	THAILAND
2		**2.7.4.2.2**					
2		**2.7.4.2.3**					
2		**2.7.4.2.4**					
2		**2.7.4.3**					
2		**2.7.4.4**					
2		**2.7.4.5**					
2		**2.7.4.5.1**					
2		**2.7.4.5.2**					
2		**2.7.4.5.3**					
2		**2.7.4.5.4**					
2		**2.7.4.5.5**					
2		**2.7.4.5.6**					
2		**2.7.4.5.7**					
2		**2.7.4.5.8**					
2		**2.7.4.6**					
2		**2.7.4.7**					
2	2.7.5	**2.7.5**	2.7.5				
2	2.7.6	**2.7.6**				5	

Mod.	ICH (EU)	ICH (FDA)	PAHO	INDIA	JORDAN	ASEAN	THAILAND
3							
3	3.1	**3.1**	3.1	3.1		Section A	
3	3.2	**NA**	3.2	3.2	NA	Section C	3.2
3	3.2.S	**3.2**	3.2.S	3.2.S	I- 3.2.S		3.2.S
3		**NA**	NA	NA	NA	NA	3.2.S
3	3.2.S.1	**3.2.S.1**	3.2.S.1	3.2.S.1	3.2.S.1		3.2.S.1
3	3.2.S.1.1	**3.2.S.1.1**	3.2.S.1.1	3.2.S.1.1			
3	3.2.S.1.2	**3.2.S.1.2**	3.2.S.1.2	3.2.S.1.2			
3	3.2.S.1.3	**3.2.S.1.3**	3.2.S.1.3	3.2.S.1.3			
3		**NA**	3.2.S.1.4	3.2.S.1.4	NA	NA	NA
3		**NA**	NA	3.2.S.1.4.1	NA	NA	NA
3		**NA**	NA	3.2.S.1.4.2	NA	NA	NA
3		**NA**	NA	3.2.S.1.4.3	NA	NA	NA
3		**NA**	3.2.S.1.5	3.2.S.1.5	NA	NA	NA
3		**NA**	3.2.S.1.6	3.2.S.1.6	NA	NA	NA
3	3.2.S.2	**3.2.S.2**	3.2.S.2	3.2.S.2	3.2.S.2		
3	3.2.S.2.1	**3.2.S.2.1**	3.2.S.2.1	3.2.S.2.1	3.2.S.2.1		3.2.S.2
3	3.2.S.2.2	**3.2.S.2.2**	3.2.S.2.2	3.2.S.2.2	3.2.S.2.2		
3		**NA**	NA	3.2.S.2.3	NA	NA	NA
3		**NA**	NA	3.2.S.2.14	NA	NA	NA
3		**NA**	NA	3.2.S.2.7	NA	NA	NA
3		**NA**	NA	3.2.S.2.8	NA	NA	NA
3		**NA**	NA	3.2.S.2.9	NA	NA	NA
3		**NA**	NA	3.2.S.2.10	NA	NA	NA
3		**NA**	NA	3.2.S.2.11	NA	NA	NA
3		**NA**	NA	3.2.S.2.12	NA	NA	NA
3	3.2.S.2.3	**3.2.S.2.3**	3.2.S.2.3		3.2.S.2.3		
3	3.2.S.2.4	**3.2.S.2.4**	3.2.S.2.4	3.2.S.2.4	3.2.S.2.4		
3		**NA**	NA	3.2.S.2.13	NA	NA	NA
3	3.2.S.2.5	**3.2.S.2.5**	3.2.S.2.5	3.2.S.2.5	3.2.S.2.5		
3	3.2.S.2.6	**NA**	**NA**	3.2.S.2.6	3.2.S.2.6	NA	NA
3	3.2.S.3	**3.2.S.3**	3.2.S.3	3.2.S.3			3.2.S.3
3	3.2.S.3.1	**3.2.S.3.1**		3.2.S.3.1	3.2.S.3.1		
3		**NA**	NA	3.2.S.3.2	NA	NA	NA
3	3.2.S.3.2	**3.2.S.3.2**		3.2.S.3.3	3.2.S.3.2		
3	3.2.S.4	**3.2.S.4**	3.2.S.4	3.2.S.4			3.2.S.4

Mod.	ICH	FDA	PAHO	INDIA	JORDAN	ASEAN	THAILAND
3							
3	3.2.S.4.1	**3.2.S.4.1**	3.2.S.4.1	3.2.S.4.1	3.2.S.4.1		3.2.S.4.1
3	3.2.S.4.2	**3.2.S.4.2**	3.2.S.4.2	3.2.S.4.2	3.2.S.4.2		3.2.S.4.2
3	3.2.S.4.3	**3.2.S.4.3**	3.2.S.4.3	3.2.S.4.3	3.2.S.4.3		3.2.S.4.3
3	3.2.S.4.4	**3.2.S.4.4**	3.2.S.4.4	3.2.S.4.4	3.2.S.4.4		3.2.S.4.4
3	3.2.S.4.5	**3.2.S.4.5**	3.2.S.4.5	3.2.S.4.5	3.2.S.4.5		3.2.S.4.5
3	3.2.S.5	**3.2.S.5**	3.2.S.5	3.2.S.5	3.2.S.5		3.2.S.5
3	3.2.S.6	**3.2.S.6**	3.2.S.6	3.2.S.6	3.2.S.6		3.2.S.6
3		**NA**	NA	3.2.S.6.1	NA	NA	NA
3		**NA**	NA	3.2.S.6.2	NA	NA	NA
3	3.2.S.7	**3.2.S.7**	3.2.S.7	3.2.S.7	3.2.S.7		3.2.S.7
3	3.2.S.7.1	**3.2.S.7.1**	3.2.S.7.1	3.2.S.7.1			
3	3.2.S.7.2	**3.2.S.7.2**	3.2.S.7.2	3.2.S.7.2			
3	3.2.S.7.3	**3.2.S.7.3**	3.2.S.7.3				
3		**NA**	3.2.S.7.4	3.2.S.7.3	NA	NA	NA
3		**NA**	3.2.S.8	NA	NA	NA	NA
3	3.2.P	**3.2.P**	3.2.P	3.2.P	II- 3.2.P		3.2.P
3		**NA**	NA	NA	NA	NA	3.2.P
3	3.2.P.1	**3.2.P.1**	3.2.P.1	3.2.P.1	3.2.P.1		3.2.P.1
3	3.2.P.2	**3.2.P.2**	3.2.P.2	3.2.P.2	3.2.P.2		3.2.P.2
3	3.2.P.2.1	**3.2.P.2.1**			3.2.P.2.1		
3		**NA**	3.2.P.2.1	3.2.P.2.1	3.2.P.2.1.1		NA
3		**NA**	NA	NA	3.2.P.2.1.2	NA	NA
3		**NA**	3.2.P.2.2	3.2.P.2.2	3.2.P.2.2	NA	NA
3	3.2.P.2.2	**3.2.P.2.2**			3.2.P.2.2.1		
3		**NA**	NA	NA	3.2.P.2.2.2	NA	NA
3		**NA**	NA	NA	3.2.P.2.2.3	NA	NA
3	3.2.P.2.3	**3.2.P.2.3**	3.2.P.2.3	3.2.P.2.4	3.2.P.2.3		
3	3.2.P.2.4	**3.2.P.2.4**	3.2.P.2.4	3.2.P.2.5	3.2.P.2.4		
3	3.2.P.2.5	**3.2.P.2.5**			3.2.P.2.5		
3	3.2.P.2.6	**3.2.P.2.6**			3.2.P.2.6		
3		**NA**	3.2.P.2.7	3.2.P.2.3	NA	NA	NA
3	3.2.P.3	**3.2.P.3**	3.2.P.3	3.2.P.3	3.2.P.3		3.2.P.3
3	3.2.P.3.1	**3.2.P.3.1**	3.2.P.3.1	3.2.P.3.1	3.2.P.3.1		

Mod.	ICH (EU)	ICH (FDA)	PAHO	INDIA	JORDAN	ASEAN	THAILAND
3							
3	3.2.P.3.2	**3.2.P.3.2**	3.2.P.3.2	3.2.P.3.2	3.2.P.3.2		
3	3.2.P.3.3	**3.2.P.3.3**	3.2.P.3.3	3.2.P.3.3	3.2.P.3.3		
3	3.2.P.3.4	**3.2.P.3.4**	3.2.P.3.4	3.2.P.3.4	3.2.P.3.4		
3	3.2.P.3.5	**3.2.P.3.5**	3.2.P.3.5	3.2.P.3.5	3.2.P.3.5		
3		**NA**	3.2.P.3.6	3.2.P.3.6	NA	NA	NA
3	3.2.P.4	**3.2.P.4**	3.2.P.4	3.2.P.4	3.2.P.4		3.2.P.4
3		**NA**	NA	NA	NA	NA	3.2.P.4
3	3.2.P.4.1	**3.2.P.4.1**	3.2.P.4.1	3.2.P.4.1	3.2.P.4.1		
3	3.2.P.4.2	**3.2.P.4.2**	3.2.P.4.2	3.2.P.4.2	3.2.P.4.2		
3	3.2.P.4.3	**3.2.P.4.3**	3.2.P.4.3	3.2.P.4.3	3.2.P.4.3		
3	3.2.P.4.4	**3.2.P.4.4**	3.2.P.4.4	3.2.P.4.4	3.2.P.4.4		
3	3.2.P.4.5	**3.2.P.4.5**	3.2.P.4.5	3.2.P.4.5	3.2.P.4.5		
3	3.2.P.4.6	**3.2.P.4.6**	3.2.P.4.6	3.2.P.4.6	3.2.P.4.6		
3	3.2.P.5	**3.2.P.5**	3.2.P.5	3.2.P.5	3.2.P.5		3.2.P.5
3	3.2.P.5.1	**3.2.P.5.1**	3.2.P.5.1	3.2.P.5.1	3.2.P.5.1		3.2.P.5.1
3	3.2.P.5.2	**3.2.P.5.2**	3.2.P.5.2	3.2.P.5.2	3.2.P.5.2		3.2.P.5.2
3	3.2.P.5.3	**3.2.P.5.3**	3.2.P.5.3	3.2.P.5.4	3.2.P.5.3		3.2.P.5.3
3	3.2.P.5.4	**3.2.P.5.4**	3.2.P.5.4	3.2.P.5.5	3.2.P.5.4		3.2.P.5.4
3	3.2.P.5.5	**3.2.P.5.5**	3.2.P.5.5	3.2.P.5.6	3.2.P.5.5		3.2.P.5.5
3	3.2.P.5.6	**3.2.P.5.6**	3.2.P.5.6	3.2.P.5.7	3.2.P.5.6		3.2.P.5.6
3		**NA**	3.2.P.5.7	3.2.P.5.3	NA	NA	NA
3	3.2.P.6	**3.2.P.6**	3.2.P.6	3.2.P.6	3.2.P.6		3.2.P.6
3	3.2.P.7	**3.2.P.7**	3.2.P.7	3.2.P.7	3.2.P.7		3.2.P.7
3		**NA**	NA	3.2.P.7.1	NA	NA	NA
3		**NA**	NA	3.2.P.7.2	NA	NA	NA
3	3.2.P.8	**3.2.P.8**	3.2.P.8	3.2.P.8	3.2.P.8		3.2.P.8
3	3.2.P.8.1	**3.2.P.8.1**	3.2.P.8.1	3.2.P.8.1	3.2.P.8.1		
3		**NA**	NA	3.2.P.8.2	NA	NA	NA
3		**NA**	NA	NA	NA	NA	NA
3	3.2.P.8.2	**3.2.P.8.2**	3.2.P.8.2	3.2.P.8.3	3.2.P.8.2		
3	3.2.P.8.3	**3.2.P.8.3**	3.2.P.8.3		3.2.P.8.3		
3		**NA**	3.2.P.8.4	3.2.P.8.4	NA	NA	NA
3	3.2.A	**3.2.A**	3.2.A	3.2.A			3.2.A
3	3.2.A.1	**3.2.A.1**	3.2.A.1	3.2.A.1			3.2.A.1
3	3.2.A.2	**3.2.A.2**	3.2.A.2	3.2.A.2			3.2.A.2
3	3.2.A.3	**3.2.A.3**					3.2.A.3
3	3.2.R	**3.2.R**					3.2.R
3		**3.2.R.1**					

Mod.	ICH	FDA	PAHO	INDIA	JORDAN	ASEAN	THAILAND
3							
3		**NA**	NA	NA	NA	NA	NA
3		**NA**	NA	NA	NA	NA	NA
3		**3.2.R.2**					
3	3.3	**3.3**	3.3	3.3			3.3

Mod.	ICH (EU)	ICH (FDA)	PAHO	INDIA	JORDAN	ASEAN	THAILAND
4							
4		**NA**	NA	NA	A.	NA	NA
4		**NA**	NA	NA	B.	NA	NA
4	4.1	**4.1**	4.1	4.1	4.1	Part III - Section A	
4	4.2	**4.2**	4.2	4.2	4.2	Part III - Section D	4.2
4		**NA**	NA	NA	NA	1	NA
4	4.2.1	**4.2.1**	4.2.1	4.2.1	4.2.1	2	4.2.1
4	4.2.1.1	**4.2.1.1**	4.2.1.1	4.2.1.1			4.2.1.1
4	4.2.1.2	**4.2.1.2**	4.2.1.2	4.2.1.2			4.2.1.2
4	4.2.1.3	**4.2.1.3**					4.2.1.3
4	4.2.1.4	**4.2.1.4**					4.2.1.4
4	4.2.2	**4.2.2**	4.2.2	4.2.2	4.2.2	3	4.2.2
4	4.2.2.1	**4.2.2.1**	4.2.2.1	4.2.2.1			4.2.2.1
4	4.2.2.2	**4.2.2.2**					4.2.2.2
4	4.2.2.3	**4.2.2.3**					4.2.2.3
4	4.2.2.4	**4.2.2.4**					4.2.2.4
4	4.2.2.5	**4.2.2.5**					4.2.2.5
4	4.2.2.6	**4.2.2.6**					4.2.2.6
4	4.2.2.7	**4.2.2.7**					4.2.2.7
4	4.2.3	**4.2.3**	4.2.3	4.2.3	4.2.3	4	4.2.3
4		**NA**	4.2.3.1	4.2.3.1	NA	NA	NA
4		**NA**	NA	NA	NA	NA	NA
4		**NA**	NA	NA	NA	NA	NA
4	4.2.3.1	**4.2.3.1**					4.2.3.1
4	4.2.3.2	**4.2.3.2**					4.2.3.2
4		**NA**	NA	NA	NA	NA	NA
4		**NA**	NA	NA	NA	NA	NA
4		**NA**	4.2.3.2	4.2.3.2	NA	NA	NA
4		**NA**	NA	NA	NA	NA	NA
4		**NA**	NA	NA	NA	NA	NA
4	4.2.3.3	**4.2.3.3**					4.2.3.3
4	4.2.3.3.1	**4.2.3.3.1**					4.2.3.3.1
4	4.2.3.3.2	**4.2.3.3.2**					4.2.3.3.2
4		NA	4.2.3.3	4.2.3.3	NA	NA	NA
4	4.2.3.4	**4.2.3.4**					4.2.3.4
4	4.2.3.4.1	**NA**	**NA**	**NA**	**NA**	**NA**	4.2.3.4.1
4	4.2.3.4.2	**NA**	**NA**	**NA**	**NA**	**NA**	4.2.3.4.2

Mod.	ICH	FDA	PAHO	INDIA	JORDAN	ASEAN	THAILAND
4							
4	4.2.3.4.3	**NA**	**NA**	**NA**	**NA**	**NA**	4.2.3.4.3
4	4.2.3.5	**4.2.3.5**					4.2.3.5
4	4.2.3.5.1	**4.2.3.5.1**					4.2.3.5.1
4	4.2.3.5.2	**4.2.3.5.2**					4.2.3.5.2
4	4.2.3.5.3	**4.2.3.5.3**					4.2.3.5.3
4	4.2.3.5.4	**4.2.3.5.4**					4.2.3.5.4
4	4.2.3.6	**4.2.3.6**					4.2.3.6
4	4.2.3.7	**4.2.3.7**					4.2.3.7
4	4.2.3.7.1	**4.2.3.7.1**					4.2.3.7.1
4	4.2.3.7.2	**4.2.3.7.2**					4.2.3.7.2
4	4.2.3.7.3	**4.2.3.7.3**					4.2.3.7.3
4	4.2.3.7.4	**4.2.3.7.4**					4.2.3.7.4
4	4.2.3.7.5	**4.2.3.7.5**					4.2.3.7.5
4	4.2.3.7.6	**4.2.3.7.6**					4.2.3.7.6
4	4.2.3.7.7	**4.2.3.7.7**					4.2.3.7.7
4		**NA**	NA	4.2.4.2	NA	NA	NA
4		**NA**	4.2.4	4.2.4	NA	NA	NA
4		**NA**	4.2.4.1	4.2.4.1	NA	NA	NA
4	4.3	**4.3**	4.3	4.3	4.3		4.3

Mod.	ICH (EU)	ICH (FDA)	PAHO	INDIA	JORDAN	ASEAN	THAILAND
5							
5		**NA**	NA	NA	B.	NA	NA
5	5.1	**5.1**	5.1	5.1		Section A	
5	5.2	**5.2**	5.2	5.2		Section D	5.2
5		**5.2.1**					
5		**5.2.2**					
5		**NA**	NA	5.2.1	NA	NA	NA
5		**NA**	NA	5.2.2	NA	NA	NA
5		**NA**	NA	5.2.3	NA	NA	NA
5		**NA**	NA	5.2.3.1	NA	NA	NA
5		**NA**	NA	5.2.4	NA	NA	NA
5		**NA**	NA	5.2.5	NA	NA	NA
5		**NA**	NA	5.2.7	NA	NA	NA
5		**NA**	NA	5.2.8	NA	NA	NA
5		**NA**	NA	5.2.9	NA	NA	NA
5	5.3	**5.3**	5.3		B.2	Section E	5.3
5	5.3.1	**5.3.1**					5.3.1
5	5.3.1.1	**5.3.1.1**			B.1		5.3.1.1
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**5.3.1.1.1**					
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**5.3.1.1.2**					
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**5.3.1.1.3**			B.3		
5		**5.3.1.1.4**					
5		**NA**	NA	NA	B.4	NA	NA
5		**NA**	NA	NA	B.5	NA	NA
5		**NA**	NA	NA	A.	NA	NA
5		**NA**	NA	NA	A.2	NA	NA
5	5.3.1.2	**5.3.1.2**			A.1		5.3.1.2
5		**5.3.1.2.1**					
5		**NA**					

Mod.	ICH	FDA	PAHO	INDIA	JORDAN	ASEAN	THAILAND
5							
5		**NA**					
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Mod.	ICH (EU)	ICH (FDA)	PAHO	INDIA	JORDAN	ASEAN	THAILAND
5							
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5		**NA**					
5		**5.3.1.2.2**					
5		**NA**					
5		**NA**					
5		**NA**					
5		**5.3.1.2.3**					
5		**5.3.1.2.4**					
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5	5.3.1.3	**5.3.1.3**					5.3.1.3
5		**NA**	NA	NA	NA	NA	NA

Mod.	ICH	FDA	PAHO	INDIA	JORDAN	ASEAN	THAILAND
5							
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5	5.3.1.4	**5.3.1.4**					5.3.1.4
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5	5.3.2	**5.3.2**					5.3.2
5	5.3.2.1	**5.3.2.1**					5.3.2.1
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5	5.3.2.2	**5.3.2.2**					5.3.2.2
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5	5.3.2.3	**5.3.2.3**					5.3.2.3
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	A.4	NA	NA
5	5.3.3	**5.3.3**			A.4.3.1		5.3.3
5	5.3.3.1	**5.3.3.1**			A.4.3.1.1		5.3.3.1
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5	5.3.3.2	**5.3.3.2**			A.4.3.1.2		5.3.3.2
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5	5.3.3.3	**5.3.3.3**			A.4.3.1.3		5.3.3.3
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5	5.3.3.4	**5.3.3.4**			A.4.3.1.4		5.3.3.4
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5	5.3.3.5	**5.3.3.5**			A.4.3.1.5		5.3.3.5

Mod.	ICH (EU)	ICH (FDA)	PAHO	INDIA	JORDAN	ASEAN	THAILAND
5							
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5	5.3.4	**5.3.4**			A.4.3.2		5.3.4
5	5.3.4.1	**5.3.4.1**			A.4.3.2.1		5.3.4.1
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5	5.3.4.2	**5.3.4.2**			A.4.3.2.2		5.3.4.2
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5	5.3.5	**5.3.5**			A.3		5.3.5
5		**NA**	NA	NA	NA	NA	5.3.5
5	5.3.5.1	**5.3.5.1**					5.3.5.1
5		**5.3.5.1.A**					
5		**5.3.5.1.A.1**					
5		**5.3.5.1.A.2**					
5		**5.3.5.1.A.3**					
5		**5.3.5.1.A.4**					
5		**5.3.5.1.B**					
5		**5.3.5.1.B.1**					
5		**5.3.5.1.B.2**					
5		**5.3.5.1.B.3**					
5		**5.3.5.1.B.4**					
5		**NA**	NA	NA	NA	NA	
5	5.3.5.2	**5.3.5.2**					5.3.5.2
5		**5.3.5.2.1**					
5		**5.3.5.2.2**					
5		**NA**	NA	NA	NA	NA	NA
5		**5.3.5.2.3**					
5		**5.3.5.2.4**					
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5	5.3.5.3	**5.3.5.3**					5.3.5.3
5		**5.3.5.3.1**					
5		**5.3.5.3.1.A**					

Mod.	ICH	FDA	PAHO	INDIA	JORDAN	ASEAN	THAILAND
5							
5		**5.3.5.3.1.B**					
5		**5.3.5.3.2**					
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5	5.3.5.4	**5.3.5.4**					5.3.5.4
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5	5.3.6	**5.3.6**	5.3.6	5.2.6			5.3.6
5		**5.3.6.1**					
5		**5.3.6.2**					
5		**5.3.6.3**					
5		**5.3.6.3.1**					
5		**5.3.6.3.2**					
5	5.3.7	**5.3.7**					5.3.7
5		**5.3.7.1**					
5		**5.3.7.2**					
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA
5	5.4	**5.4**	5.4	5.3		Section F	5.4
5		**NA**	NA	NA	NA	NA	NA
5		**NA**	NA	NA	NA	NA	NA

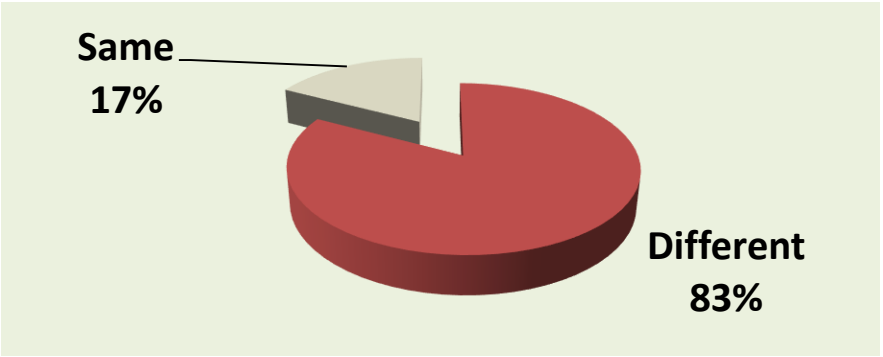
Legend

Same
Similar
Different

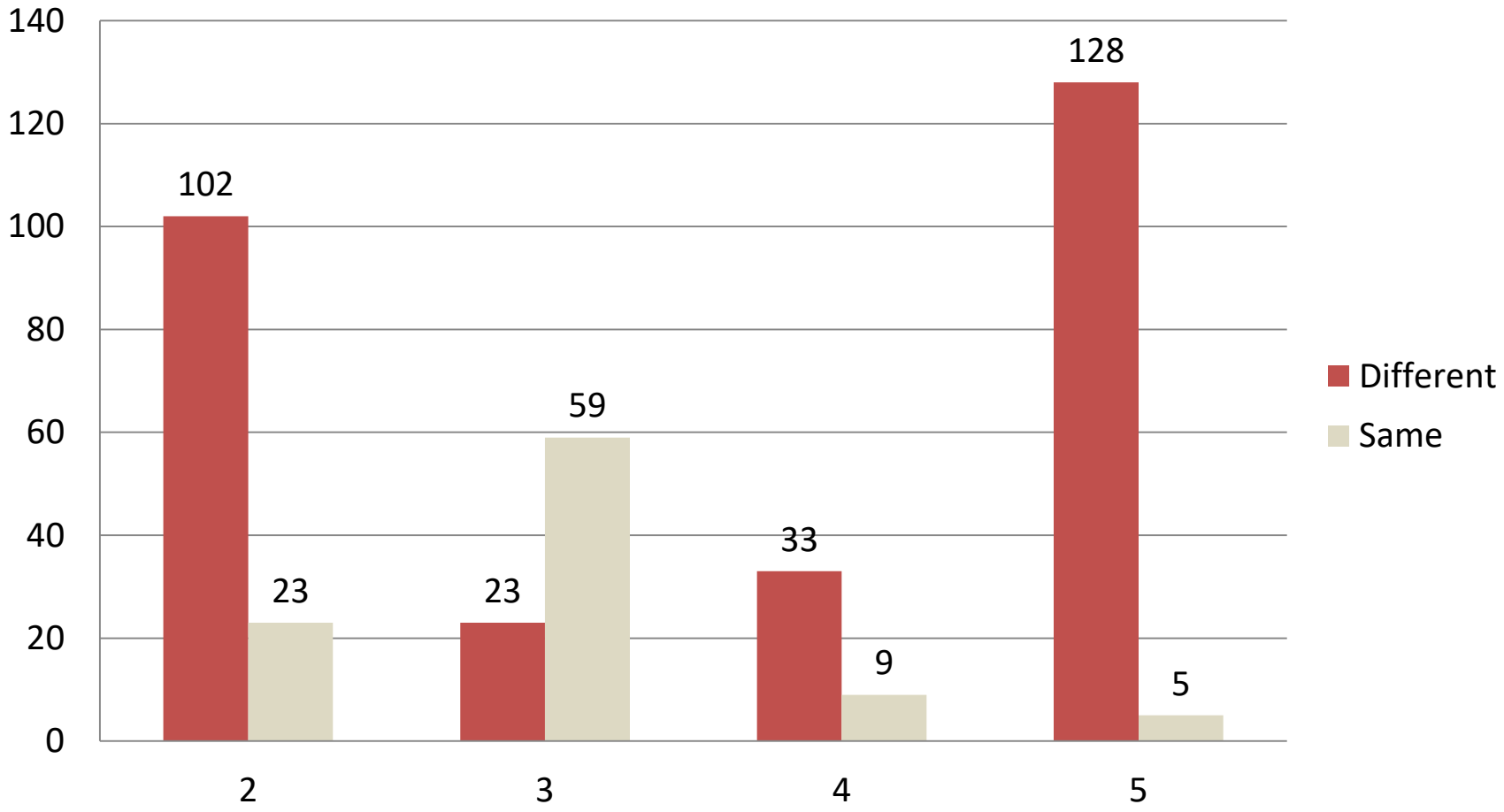
CTD NUMBERING: ASEAN, INDIA, JORDAN, PAHO AND THAILAND Vs. ICH (FDA) Comparing All Modules 2-5

	Number of items PAHO Vs ICH (FDA)	Number of items INDIA Vs ICH (FDA)	Number of items JORDAN Vs ICH (FDA)	Number of items ASEAN Vs ICH (FDA)	Number of items THAILAND Vs ICH (FDA)	Total
Different	286	346	313	366	269	1580
Same	96	69	63	0	102	330
Total	382	415	376	366	371	1910
% similarity	25	17	17	0	27	17
% difference	75	83	83	100	73	83

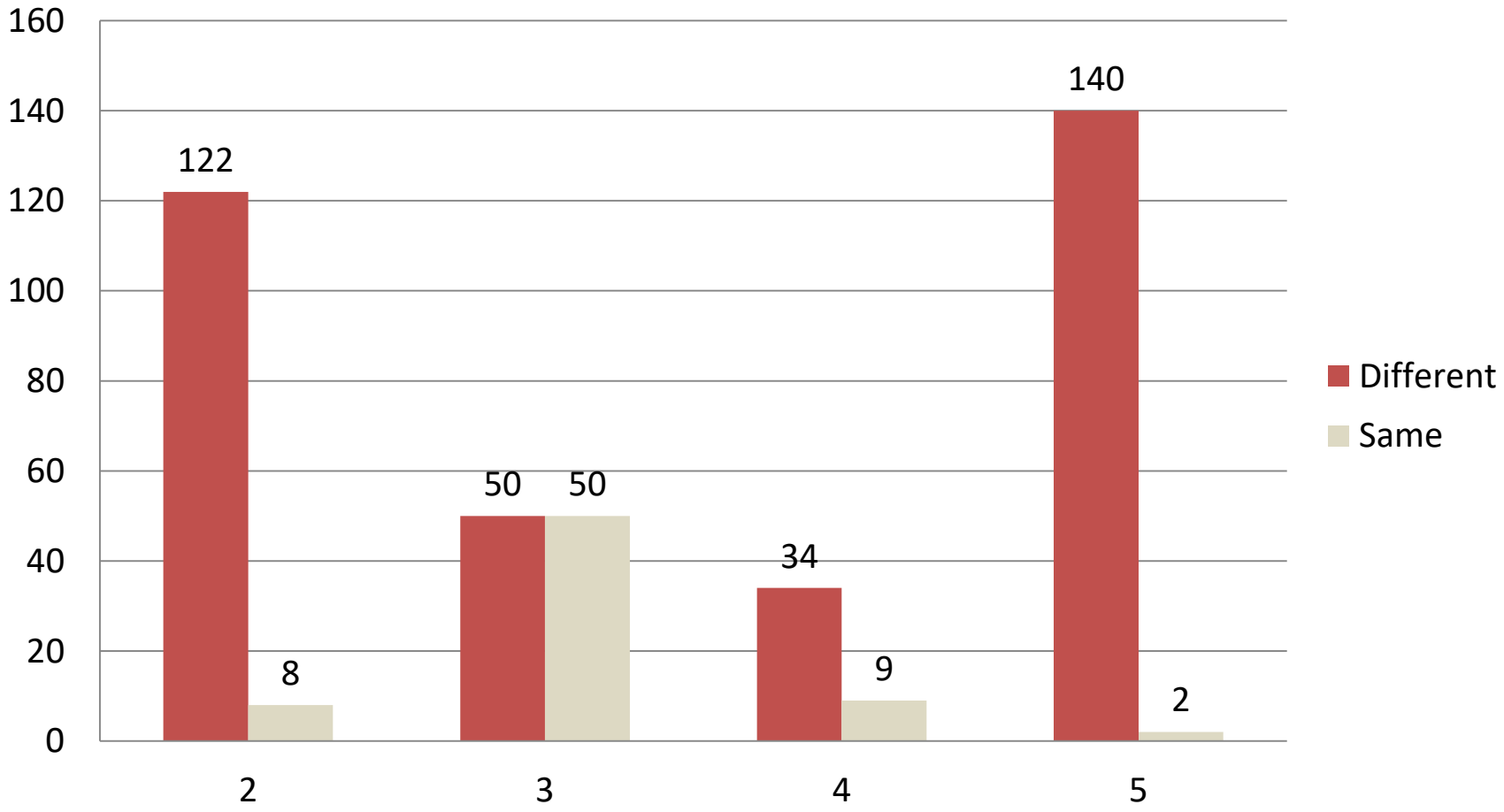
CTDs in different countries/regions of the world differ even more in terms of numbering, particularly the ASEAN CTD has a completely different structure and numbering to the ICH CTD



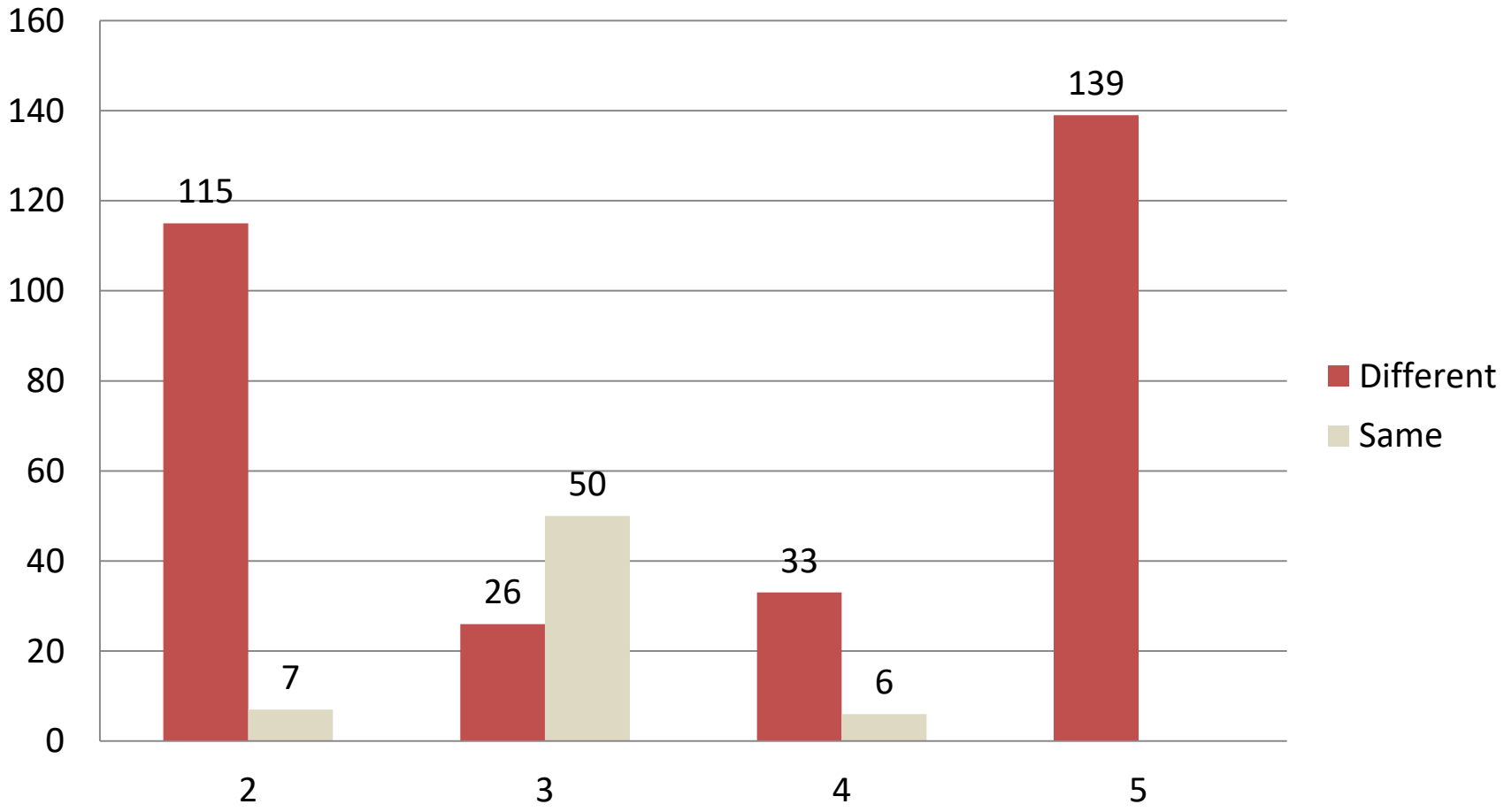
PAHO Vs. ICH (FDA) NUMBERING Comparing Module by Module



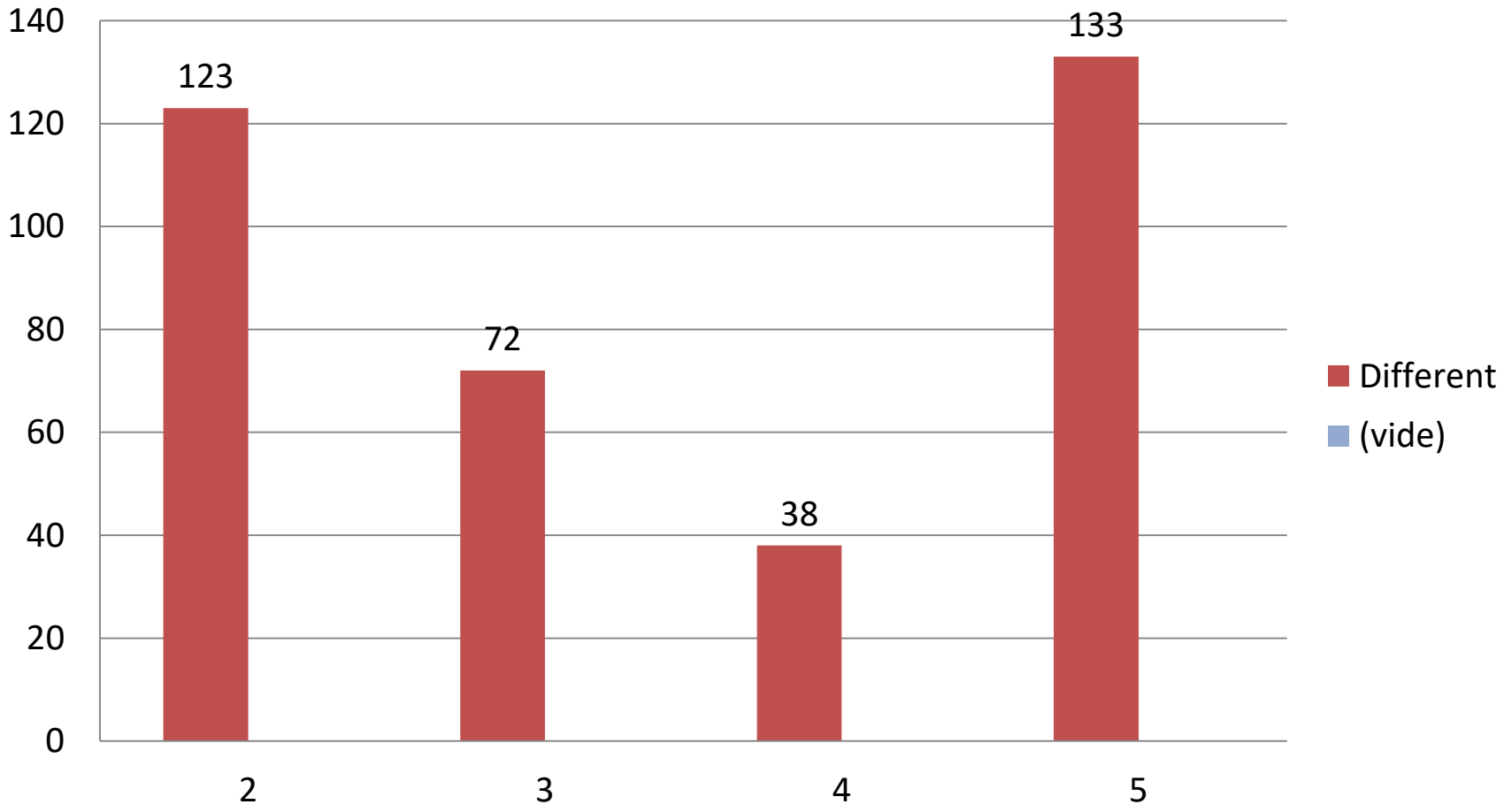
INDIA Vs. ICH (FDA) NUMBERING
Comparing Module by Module



JORDAN Vs. ICH (FDA) NUMBERING
Comparing Module by Module

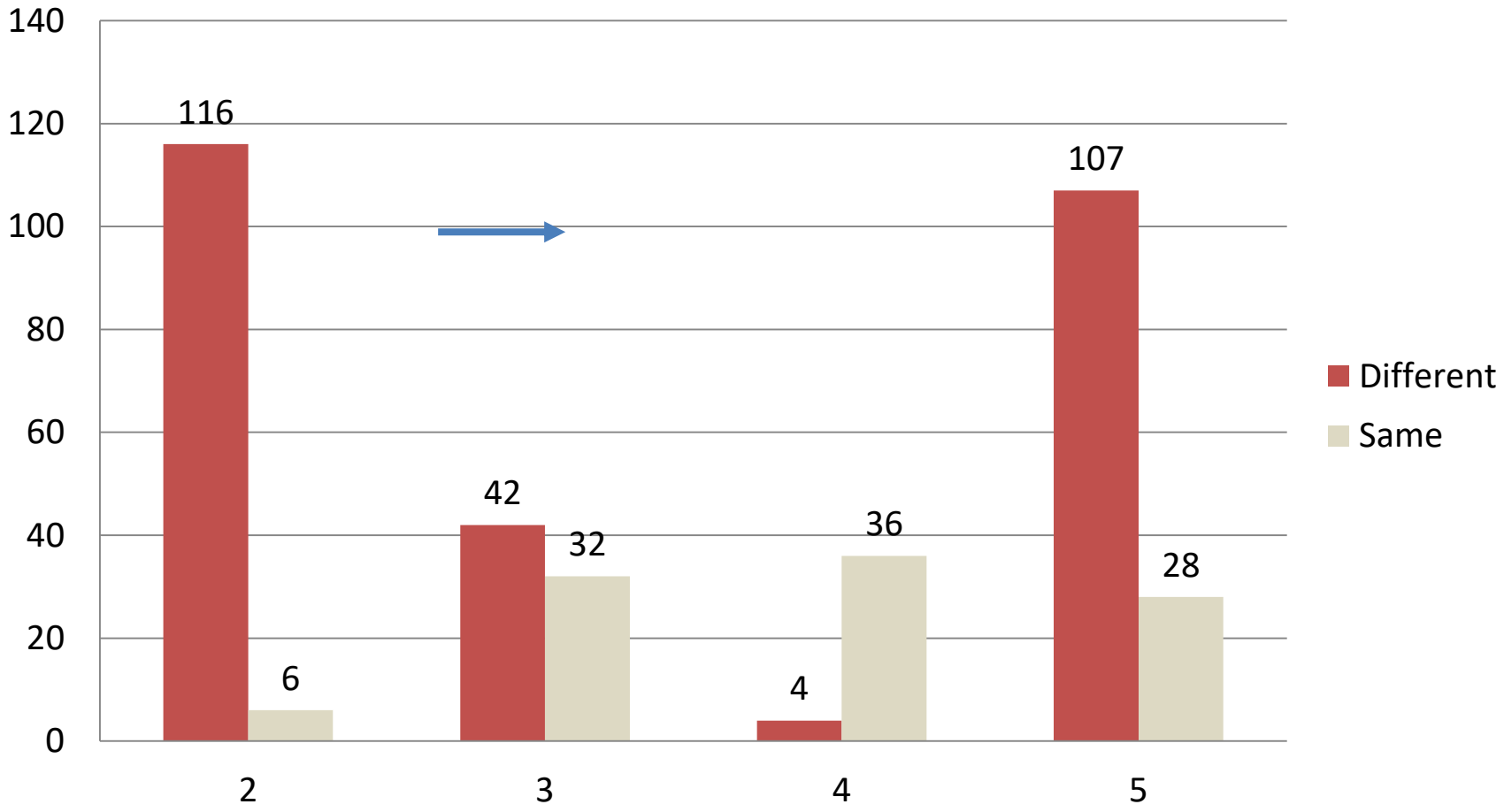


ASEAN Vs. ICH (FDA) NUMBERING Comparing Module by Module



Organization (structure of ASEAN CTD is completely different from ICH CTD

THAILAND Vs. ICH (FDA) NUMBERING Comparing Module by Module



Relevance of the difference

- CTDs from different countries/regions differ substantially in contents (77%) except for the ASEAN and ICH CTDs which are quite similar (93%)
- The difference is greater in the numbering system with an average difference of 83 %, and a 100% difference between the ASEAN and the ICH CTD due to their completely different structure
- One may argue that differences in numbering are trivial, while differences in content are important

Relevance of the difference (2)

- Differences in numbering are more important than it may seem at first sight, since all the information, even if identical has to be organized to fit the exact numbering required by each target country, hence representing a huge workload to regulatory affairs staff for no added value, and leading to delays in vaccine availability
- Strong advocacy by manufacturers and vaccine stakeholders and an effort by regulators towards alignment should enable
  - faster dossier preparation by manufacturers,
  - faster and easier review work by NRAs,
  - Increased work and information sharing opportunities among NRAs (they would all talk in the same language)
  - And lastly but not least, quicker access to medicines in countries, which is the end goal

Acknowledgements

Working Group Members: Mary Allin (Pfizer), Abdulaziz M.M Almotiri (Arabio), Paula Barbosa (IFPMA), Nirav Amitkumar Chokshi (Zydus Cadila), Monique Collaço de Moraes Stávale (Bio-Manguinhos), Samir Desai (Zydus Cadila), Shubhangi Ghadge (Serum Institute of India), Tarek Ibrahim (Arabio), Seon Gyeong Jeong (LG Chem). Matthew Marsden (Pfizer), Mic McGoldrick (Merck), YIJIE Qu (CNBG), Christophe Saillez (former GSK), Mira Uton (Biofarma), Qiaoruo Xiong (CNBG), Nora Dellepiane (Consultant), Paula Barbosa (Secretariat IFPMA), Sonia Pagliusi and Ching Chia Ting (Secretariat DCVMN)

THANK YOU