



General Overview of eCTD

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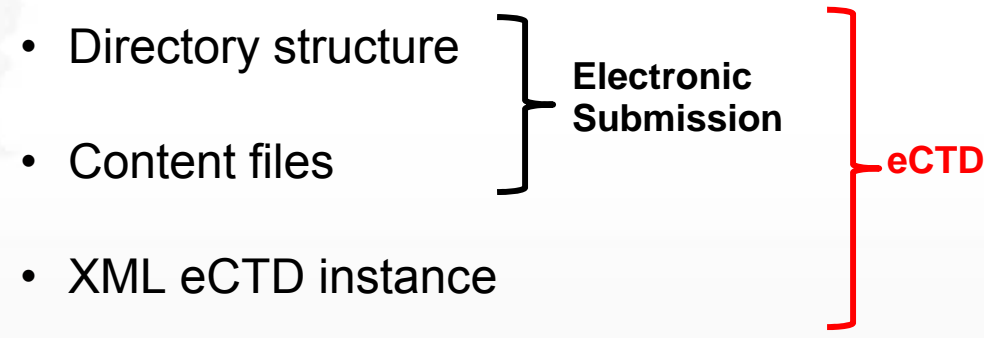
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- **The information within this presentation is based on the presenter's expertise and experience, and represents the views of the presenter for the purposes of a training workshop.**

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What is eCTD?

- **Electronic Common Technical Document**
 - Common Technical Document
 - Common format for Quality, Safety, and Efficacy information
 - Electronic CTD = eCTD
 - An interface for industry to agency transfer of regulatory information
 - Composed of:
 - Directory structure
 - Content files
 - XML eCTD instance
- 

What is eCTD?

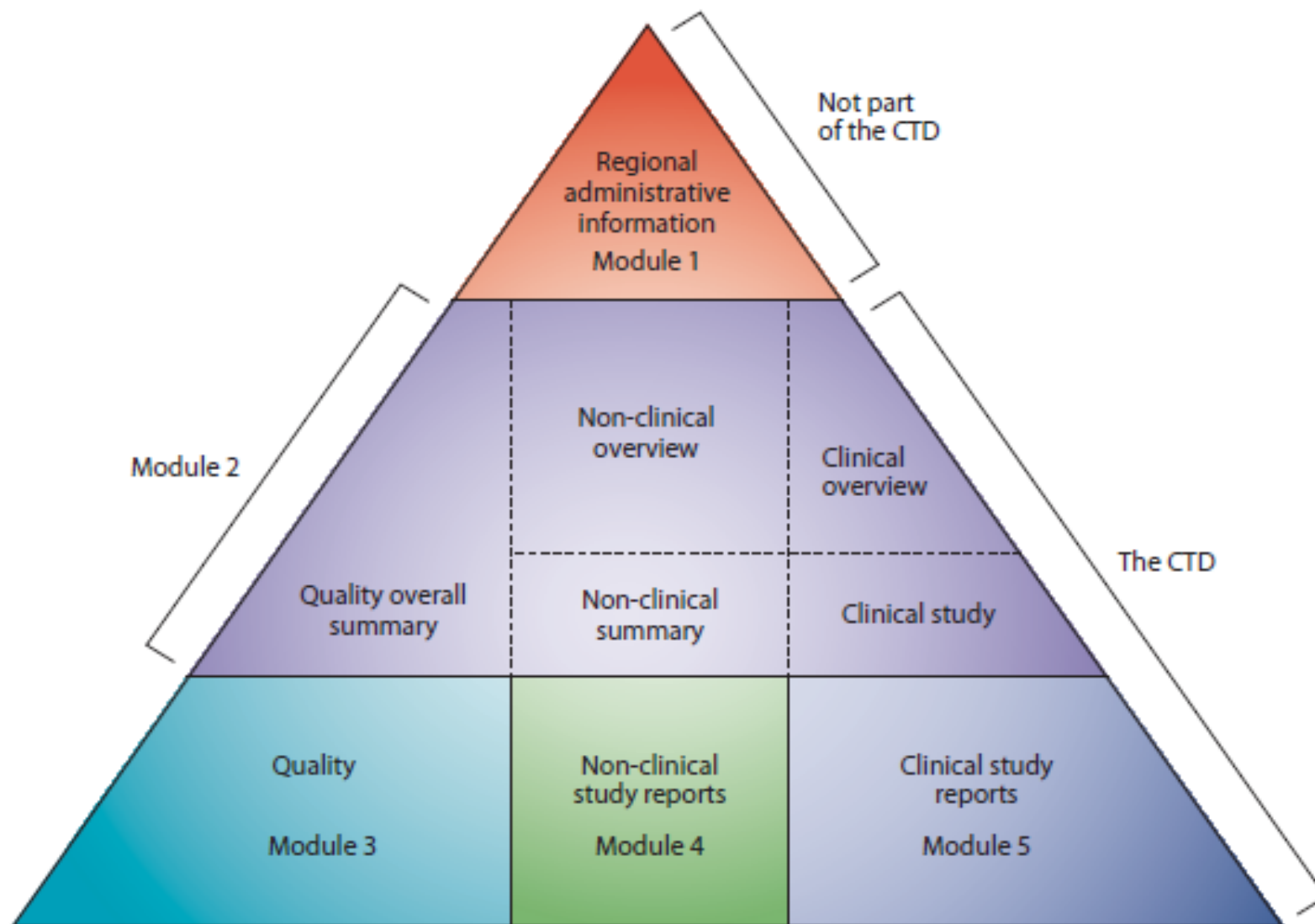
- **Scope of eCTD**

- CTD scope + Module 1

- CTD: Registration applications for new pharmaceuticals (including biotechnology-derived products)
- Module 1: Regional Administrative Information and Prescribing Information

- Regional scope may vary beyond CTD scope

- Investigational New Drug,
- Drug Master File / Active Substance Master File, and etc.



The CTD triangle. The Common Technical Document is organized into five modules. Module 1 is region specific and modules 2, 3, 4 and 5 are intended to be common for all regions.

History

- **Regional reviewer driven**

- 1980s : - Early activities in US in 1980s
- 1990s : - Computer Aided New Drug Application (CANDAs)
 - eNDA Guideline
 - DAMOS in Germany, MANSEV in France

- **Harmonization**

- 1997: - M2 EWG start working closely with M4 (CTD)
- 2003 : - ICH eCTD Guideline v3.0

- **Implementation**

- 2004 : - ICH eCTD Guideline v3.2 → implemented in all ICH regions
- 2008 : - ICH eCTD Guideline v3.2.2
 - All electronic submissions must be in eCTD format in US
- 2010 : - Mandatory eCTD for the Centralised Procedure in EU

Why eCTD?

- **Expectation**
 - High availability
 - Easy view / navigation
 - Fast retrieval
 - Lifecycle support
 - Less paper
- **Results**
 - Expected advantages have been met.
 - Contribute to improvement of:
 - Data quality
 - Reusability
 - Faster access
 - Life cycle management
 - Some challenges found.

Before eCTD

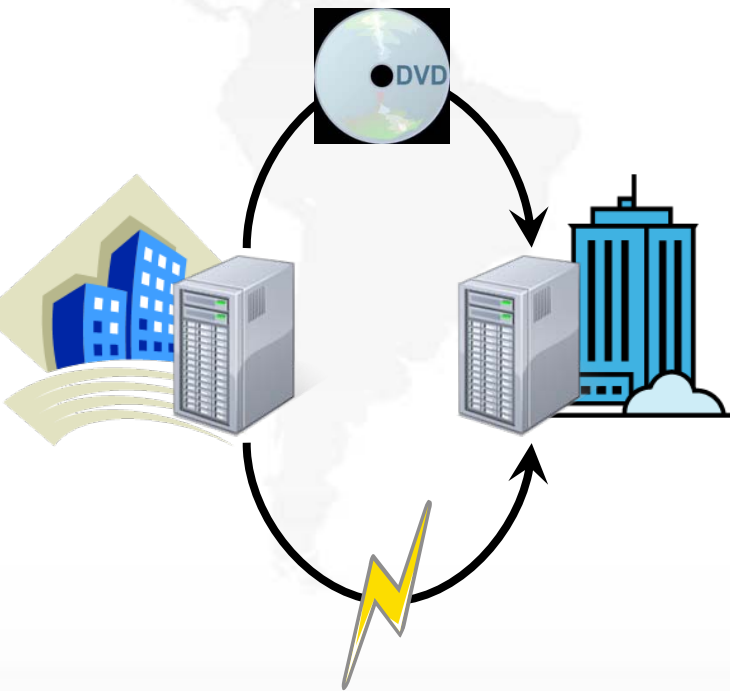


CTD dossier in bookrack



Reviewer's desk

After eCTD



CTD dossier in server

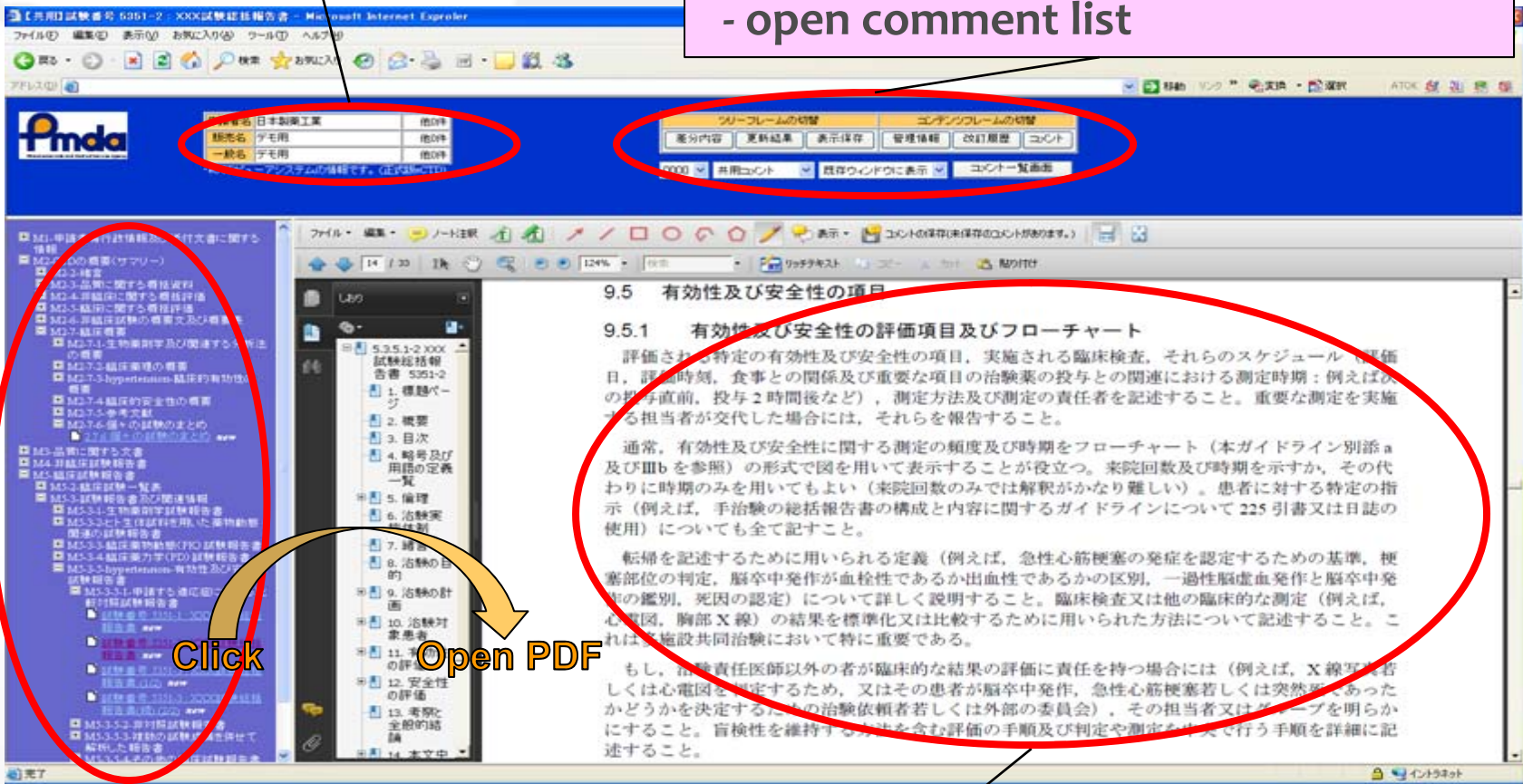


Reviewer's desk

Administrative Information

Switches

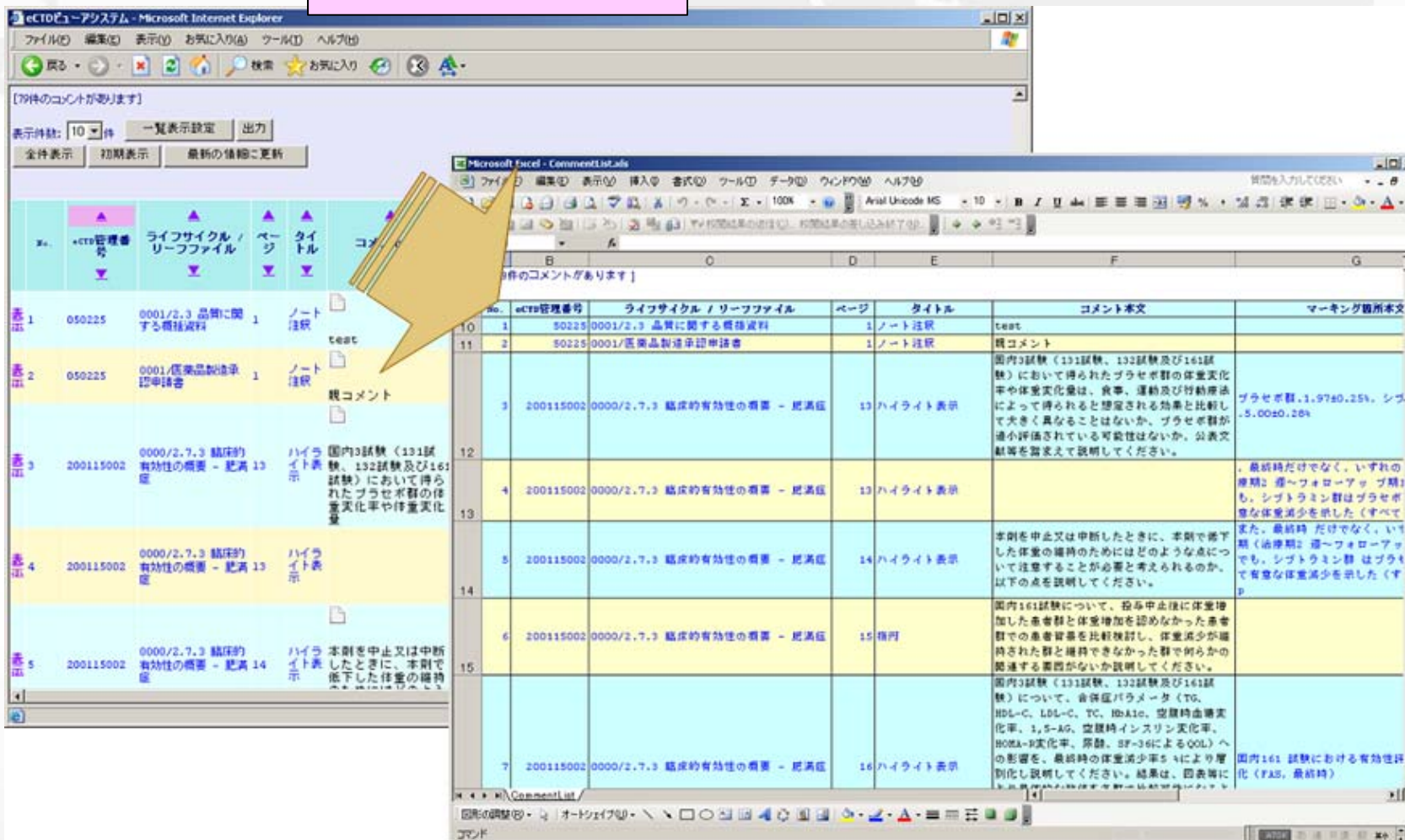
- sequence number (0000, 0001...)
- view / review (comment)
- open in new window
- open comment list



CTD Tree

Annotation, underline, highlight, insert memo, etc. for himself/herself or for sharing with review team

Comment list



The screenshot shows the eCTD system interface in Microsoft Internet Explorer. The main window displays a list of comments with columns for No., eCTD management number, lifecycle/revision file, page, title, and comment text. A yellow arrow points from this list to a Microsoft Excel spreadsheet window titled 'CommentList.xls'. The spreadsheet contains the same data as the web browser, including detailed comment text and marketing text.

No.	eCTD管理番号	ライフサイクル / リーフファイル	ページ	タイトル	コメント本文	マーキング箇所本文
10	50225	0001/2.3 品質に関する概括資料	1	ノート注釈	test	
11	50225	0001/医薬品製造承認申請書	1	ノート注釈	親コメント	
12	200115002	0000/2.7.3 臨床的有効性の概要 - 肥満症	13	ハイライト表示	国内3試験（131試験、132試験及び161試験）において得られたプラセボ群の体変化率や体変化量は、食事、運動及び付随療法によって得られると想定される効果と比較して大きく異なることはないか、プラセボ群が過小評価されている可能性はないか、公表文獻等を踏まえて説明してください。	プラセボ群、1.9740、25%、シブ -5.00±0.26%
13	200115002	0000/2.7.3 臨床的有効性の概要 - 肥満症	13	ハイライト表示		、最終期だけでなく、いずれの 期間2 期〜フォローアップ 期1 も、シブトラミン群はプラセボ 意な体変化減少を示した（すべて また、最終期 だけでなく、い 期（治療期2 期〜フォローアッ でも、シブトラミン群はプラセ で有意な体変化減少を示した（すべて
14	200115002	0000/2.7.3 臨床的有効性の概要 - 肥満症	14	ハイライト表示	本剤を中止又は中断したときに、本剤で低下した体重の維持のためにはどのような点について注意することが必要と考えられるのか、以下の点を説明してください。	
15	200115002	0000/2.7.3 臨床的有効性の概要 - 肥満症	15	横切り	国内161試験について、投与中止後に体重増加した患者群と体重増加を認めなかった患者群での患者背景を比較検討し、体重減少が維持された群と維持できなかった群で何らかの関連する要因がないか説明してください。	
16	200115002	0000/2.7.3 臨床的有効性の概要 - 肥満症	16	ハイライト表示	国内3試験（131試験、132試験及び161試験）について、合併症パラメータ（TG、HDL-C、LDL-C、TC、HbA1c、空腹時血糖実化率、1.5-Ag、空腹時インスリン実化率、HOMA-R実化率、尿酸、SF-36）によるQOLへの影響を、最終時の体重減少率5%により層別化し説明してください。結果は、四表等に	国内161 試験における有効性評 化（FAS、最終時）

Output to spreadsheet

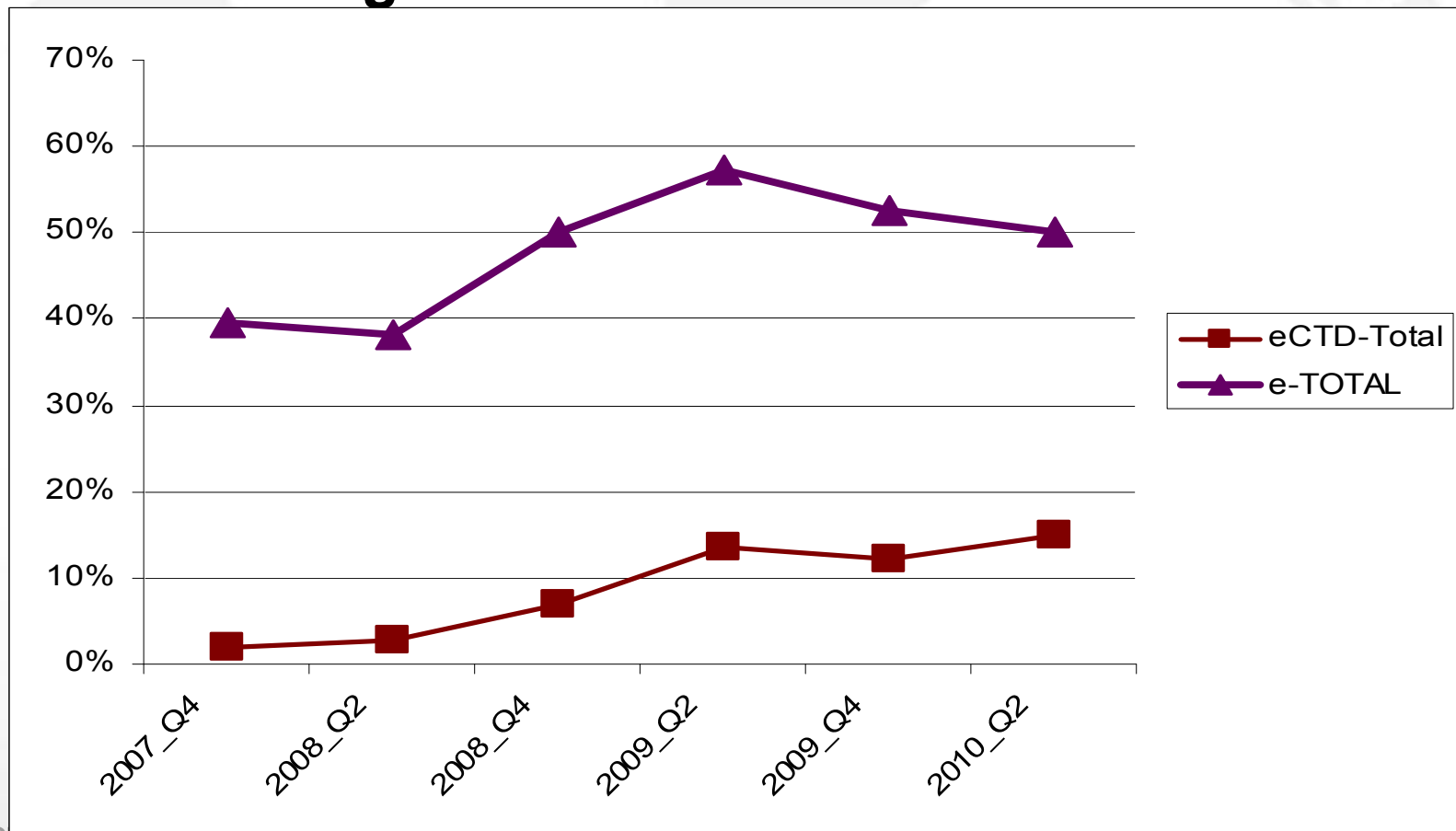
eCTD Growth

- **US**

	FY2005	FY2006	FY2007	FY2008	FY2009	FY2010
NDA Total	22,252	21,217	23,310	22,308	22,148	22,443
NDA Electronic	4,341	5,689	8,771	11,272	13,297	15,497
NDA Electronic %	19.51%	26.81%	37.63%	50.53%	60.04%	69.05%
NDA eCTD	521	2,225	2,085	7,410	11,146	14,007
NDA eCTD % of Total	2.34%	10.49%	8.94%	33.22%	50.33%	62.41%
NDA eCTD % of Electronic	12.00%	39.11%	23.77%	65.74%	83.82%	90.39%

eCTD Growth

- **EU: Percentage of eCTD**



eCTD Growth

- **EU: Percentage of eCTD**

EU	2009	2010	Δ%
Total New applications	28484	49876	43%
Total Variations	370491	361365	-3%
Total Renewals	29336	25529	-15%
Total Submissions	428311	436770	2%
Total eSubmissions	219537	213125	-3%
%eSubmissions	51%	49%	-2%
Total eCTD	29954	32834	9%
%eCTD of total	7%	8%	1%
%eCTD of electronic	14%	15%	1%

eCTD Growth

- **JP**

	2004	2005	2006	2007	2008	2009	2010	Total
Original	0	1	3	5	2	26	48	85
Reference	1	9	24	32	37	25	16	144
Total	1	10	27	37	39	51	64	229

- Original :
 - eCTD is official dossier
- Reference:
 - Paper dossier is official and eCTD is for reviewer's reference (and industry can practice eCTD submission)

Challenges

- **Advantages sometimes perceived as disadvantages**
 - Granularity
 - PDFs
 - Hyperlinks
- **Requires tools and trained technical experts**
- **Different implementation approach**
- **Regional rules vary**
- **Changes in way of working**
- **Last minute changes not easy**

Future

- **eCTD v4.0**

- Development by SDO process (HL7 → ISO/CEN → ICH)
- Plan
 - Step 2 in 2013
 - Development depends on schedule of SDOs (HL7, ISO, CEN)
- Specification
 - HL7 RPS (Regulated Product Submission) will be used for message exchange
 - ICH M4 CTD and Granularity Document will remain as dossier structure
 - PDF will remain as major document format

eCTD v4.0

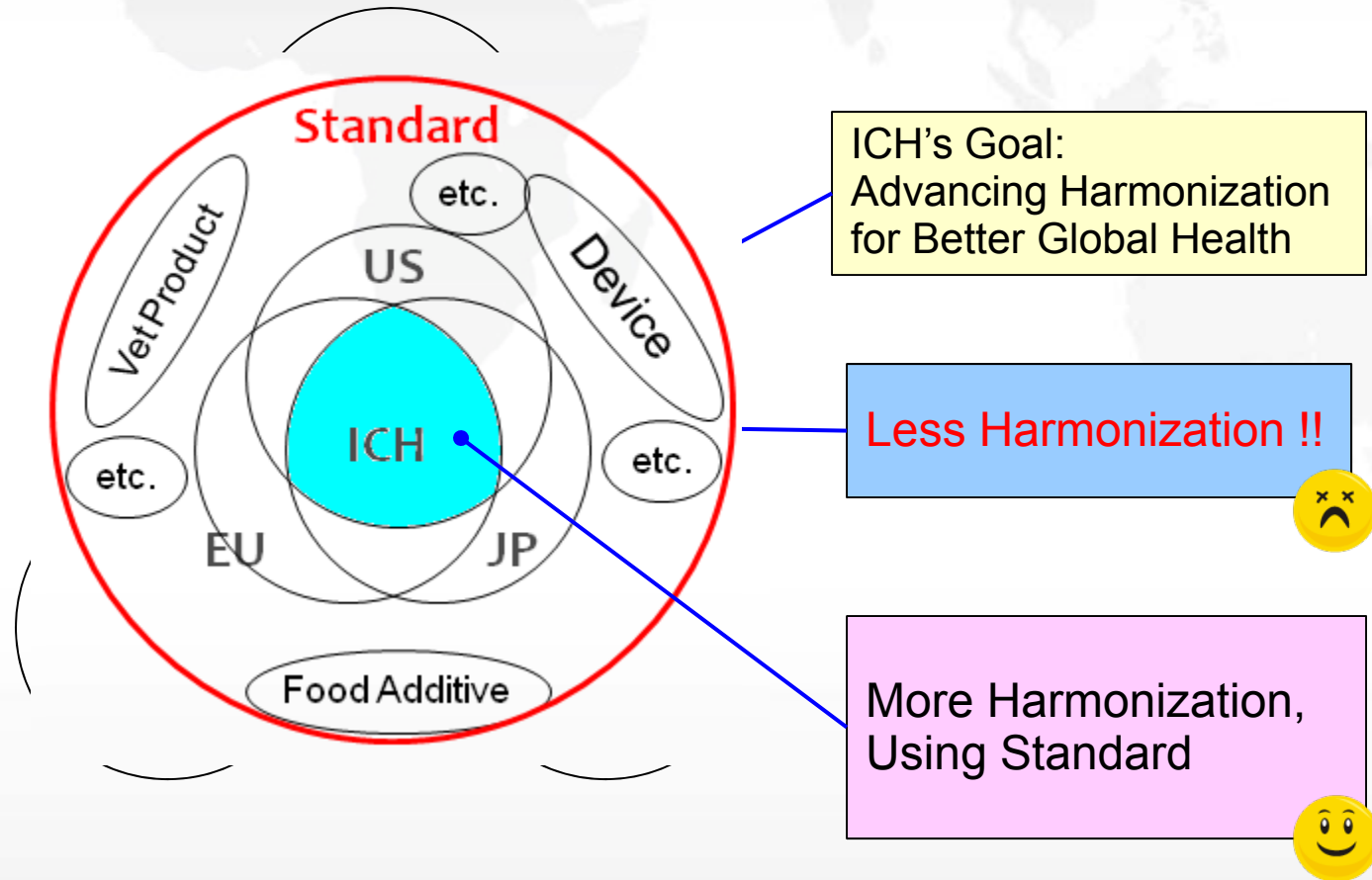
- **Benefits**

- Broader scope and standardization
- Interoperability

- **Challenges**

- Need to understand HL7 process / methodology
- Will require new tools
- Regional requirements in the scope of SDO standardization

ICH Objective in SDO process





Thank You!