



QUALIANCE

Integrating the New EMA Requirements on Public Disclosure in the Study Conduct Process DH04

PhUSE Annual Conference, Barcelona

11. October 2016

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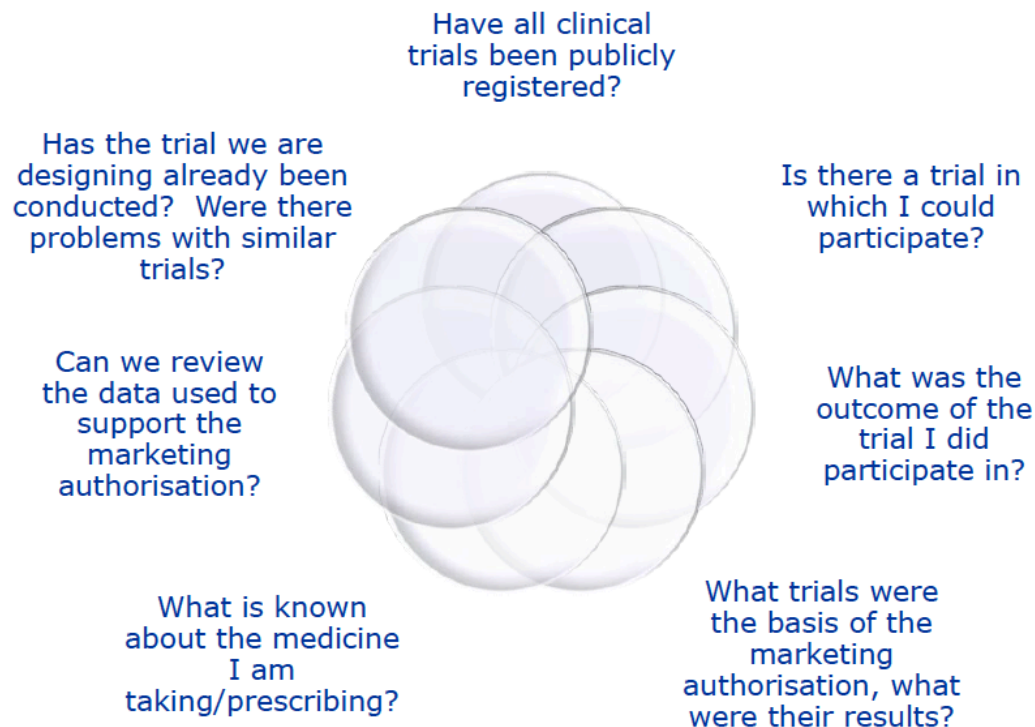
Consultant & Owner

EMA Objectives of Transparency

Objectives of transparency



EUROPEAN MEDICINES AGENCY



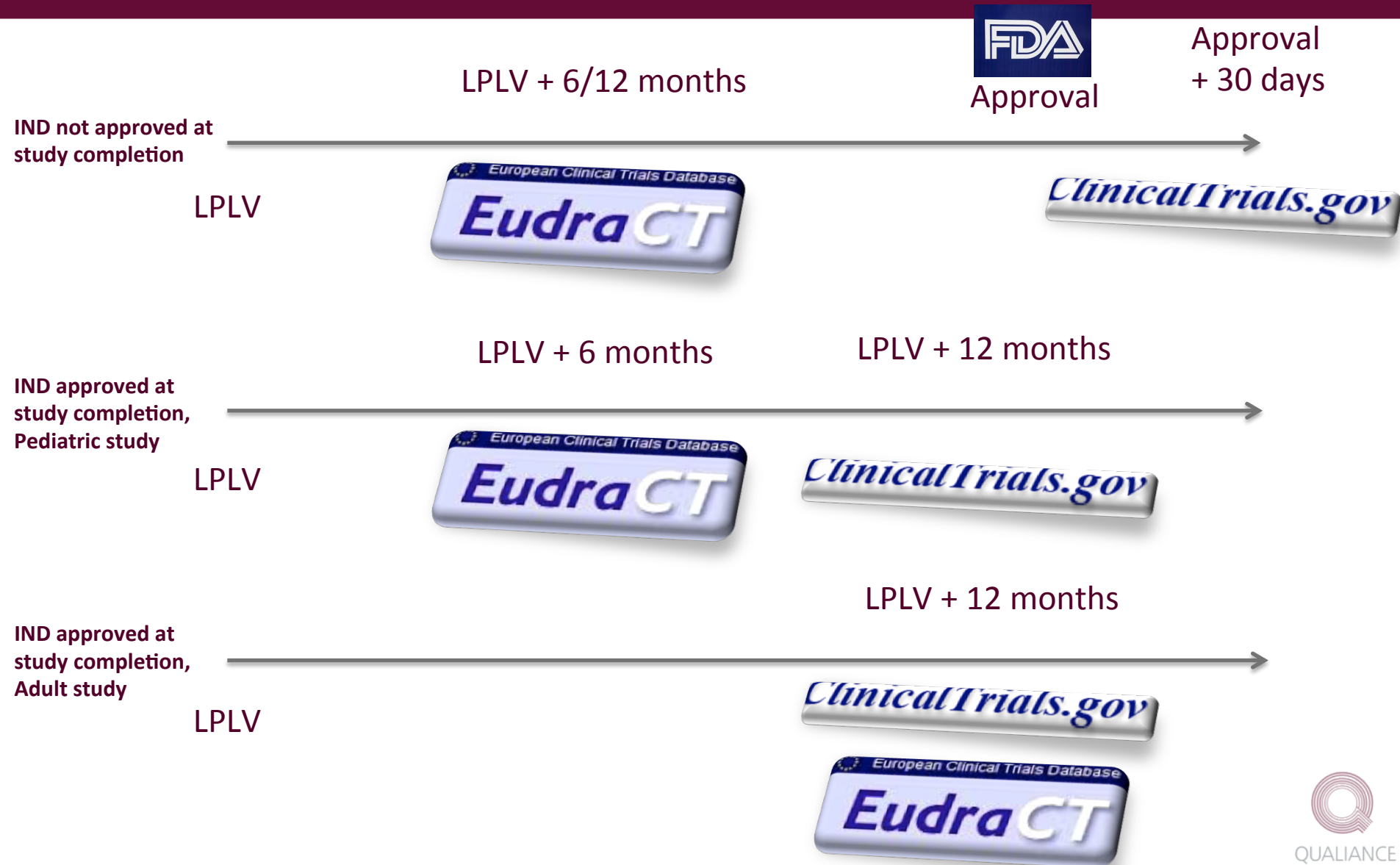
Agenda

- Study Results Public Disclosure Overview
- EudraCT and ClinicalTrials.gov Processes
- Policy 0070 Anonymization Guidance Overview
- Conclusions

Study Results Public Disclosure Overview

 US Public Disclosure Database	 EU Public Disclosure Database	 Policy 0070 Part APart B	
Study Results Effective SEP2008	Study Results Effective 20JUL14	CSR Effective 01JAN15	IPD Effective ???
Any Study part of an approved IND application	Any Study with sites in Europe (EEA) & Studies in Children conducted outside EU but part of a PIP	Any Study part of a Centralized Marketing Authorization application	???
Inform public and trial participants on core Results	Inform public and trial participants on core Results	Understand conclusions	Conduct secondary- purpose analyses, review data or verify results

EudraCT and ClinicalTrials.gov Timelines



EudraCT data on EU Clinical Data Register

The image is a collage of screenshots from the EudraCT (European Clinical Trials Database) website. The screenshots show various sections of the database, including:

- Trial information**: Shows details like Sponsor protocol code, ISRCTN number, US NCT number, WHO universal trial number, Sponsors, Screening details, Period 1, and Scientific contact.
- Subject disposition**: Shows details like Recruitment details, Baseline characteristics reporting, Reporting group title, Reporting group description, Reporting group values, and Number of subjects.
- Recruitment**: Shows details like Allocation method, Blinding used, Roles blinded, Arms, Are arms mutually exclusive, Results analysis stage, Analysis stage, Date of interim/final analysis, Is this the analysis of data?, Primary completion date, Global end of trial date, Global end of trial date, Was the trial ended prematurely?, Pharmaceutical product, Routes of administration, Dosage and administration.
- Baseline characteristics**: Shows details like Baseline characteristics reporting, Reporting group title, Reporting group description, Reporting group values, and Number of subjects.
- Adverse events**: Shows details like Adverse events information, Timeframe for reporting adverse events, Assessment type, More information, Substantial protocol amendment, and Were there any global substantial amendments?
- Results analysis**: Shows details like Results analysis stage, Analysis stage, Date of interim/final analysis, Is this the analysis of data?, Primary completion date, Global end of trial date, Global end of trial date, Was the trial ended prematurely?, Pharmaceutical product, Routes of administration, Dosage and administration.

A central graphic features a blue globe with a green upward-pointing arrow. The EudraCT logo is visible in several screenshots.

Source: <https://www.clinicaltrialsregister.eu/ctr-search/trial/2012-003699-37/results>

Interruptions (globally)

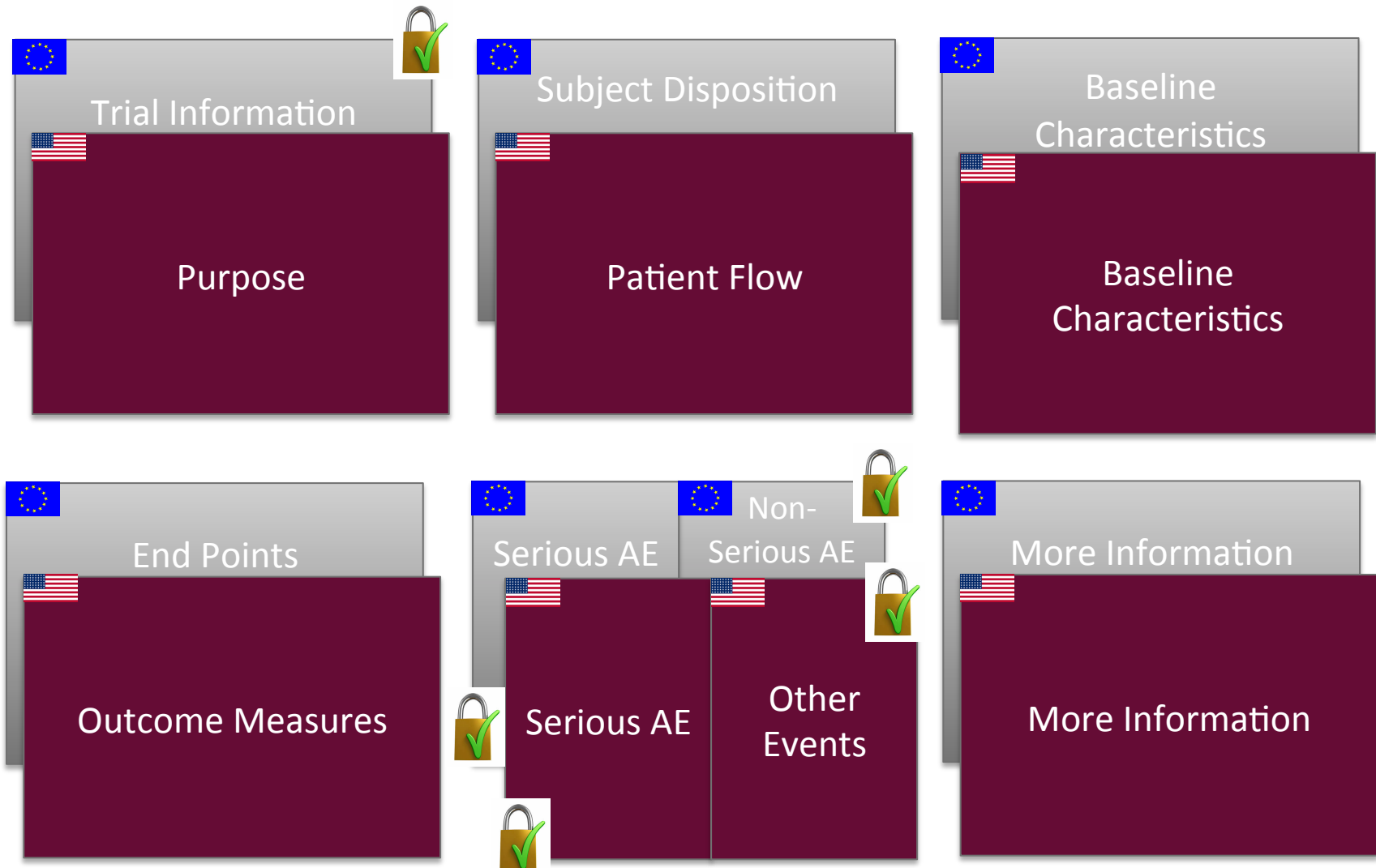
Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

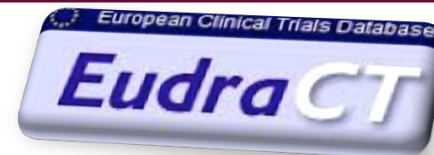
None reported

EudraCT vs. ClinicalTrials.gov



Serious Adverse Event Data Elements

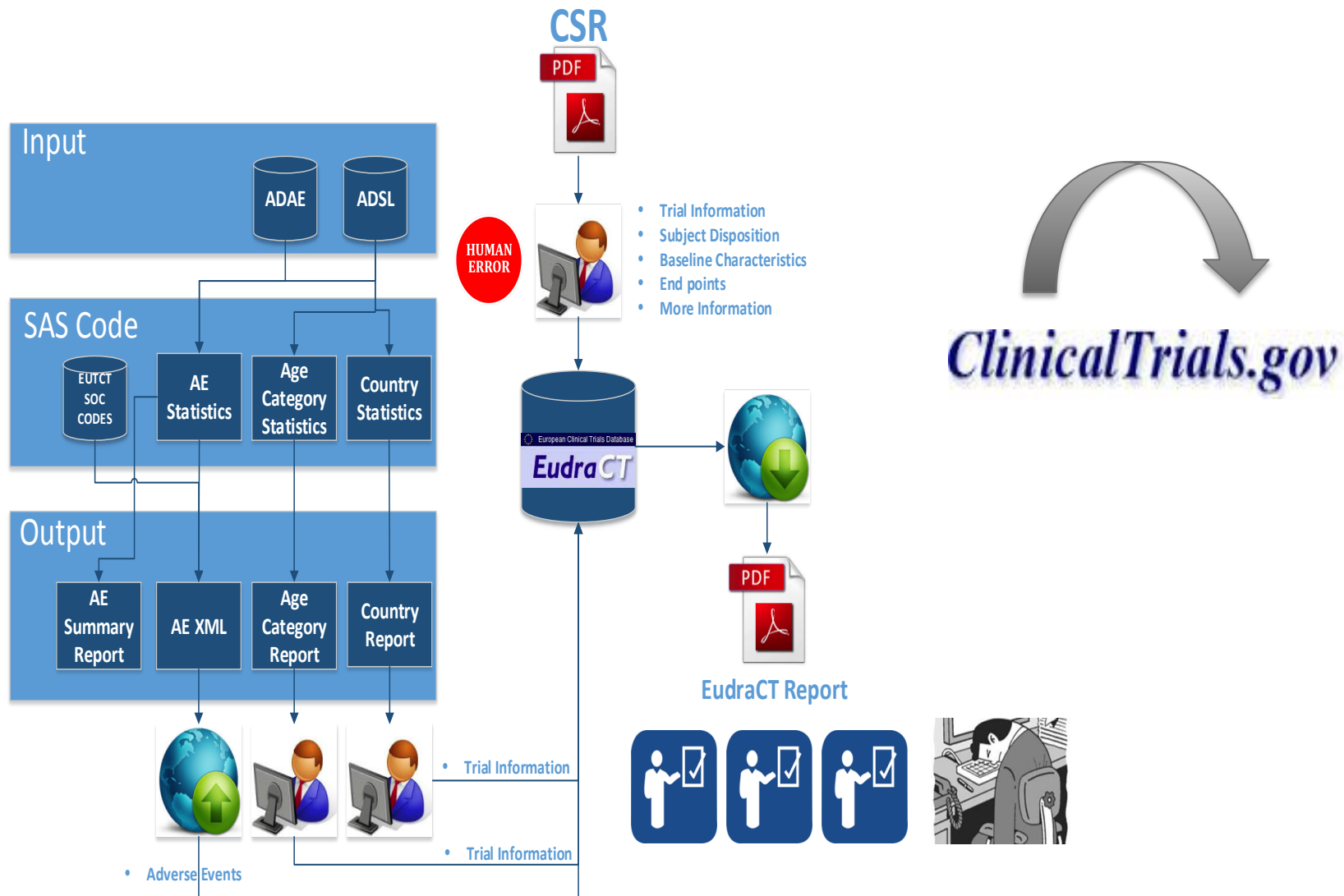
ClinicalTrials.gov



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Current Public Disclosure Process



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Endpoint Statistical Analysis

Statistical analysis title	Comparison of Proportion of Patients With Complete
Statistical analysis description	The null hypothesis (H0) was stated as: • H0 : CR 0-24 hr palonosetron - CR 0-24 hr ondansetron <~10% The alternative hypothesis (H1) was stated as: • H1 : CR 0-24 hr palonosetron - CR 0-24 hr ondansetron >~10% A power of 80% was used for sample size computation.
Comparison groups	Palonosetron and Placebo to Ondansetron v Ondansetron and Placebo to Palonosetron
Number of subjects included in analysis	661
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[1]
Method	
Parameter type	Risk difference (RD)
Point estimate	-4.4
Confidence interval	
level	95%
sides	2-sided
lower limit	-10.5
upper limit	1.7

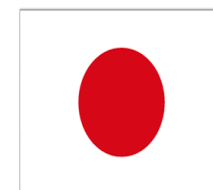
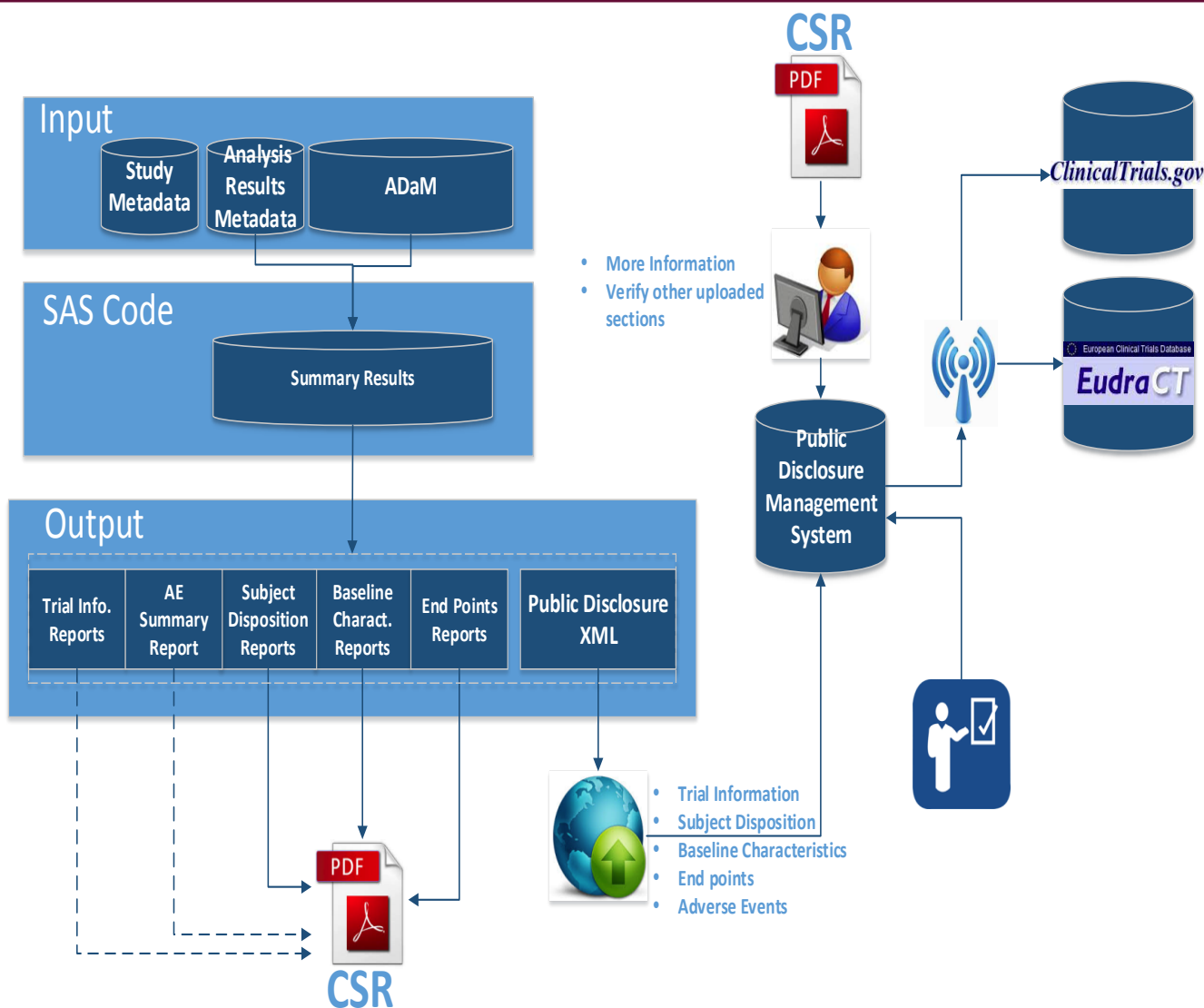
Notes

[1] - For the primary efficacy analysis, the confidence interval (CI) was built on the FAS using the stratum adjust correction of continuity. The non-inferiority margin was -10%.

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    • H1 : CR 0-24 hr palonosetron - CR 0-24 hr ondansetron >~10%~#xD;
    A power of 80% was used for sample size computation.
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Future Public Disclosure Process



Recent Initiatives on Harmonization

EU portal and database – Data standardisation



WHO

WHO ICTRP standard will be fully met, and data provided to the ICTRP by the EU database

NIH

(clinicaltrials.gov)

Collaboration and discussion on the anticipated changes to the data model (focusing on protocol / results) to ensure convergence and alignment where the same elements are used in both US and EU systems

CDISC

Collaboration on clinical trial registration including study design data model, and in due course on results model

Source: EMA Update, Sweeney & Alteri, CDISC European Interchange, Vienna, 27 April 2016

Industry Standards Being Developed

- **CDISC CTR-XML Specification, version 1.0 released on 28MAR2016**
 - Clinical Trial registry submissions to WHO, EudraCT registry and ClinicalTrials.GOV



Protocol Representation Implementation Model

- Protocol schema that can be implemented in Software
- Harmonization with **TransCelerate protocol work**



Clinical Trial Registration & Results 2

- Summary results data elements
- Collaboration with the **PhUSE RDF Working Group**

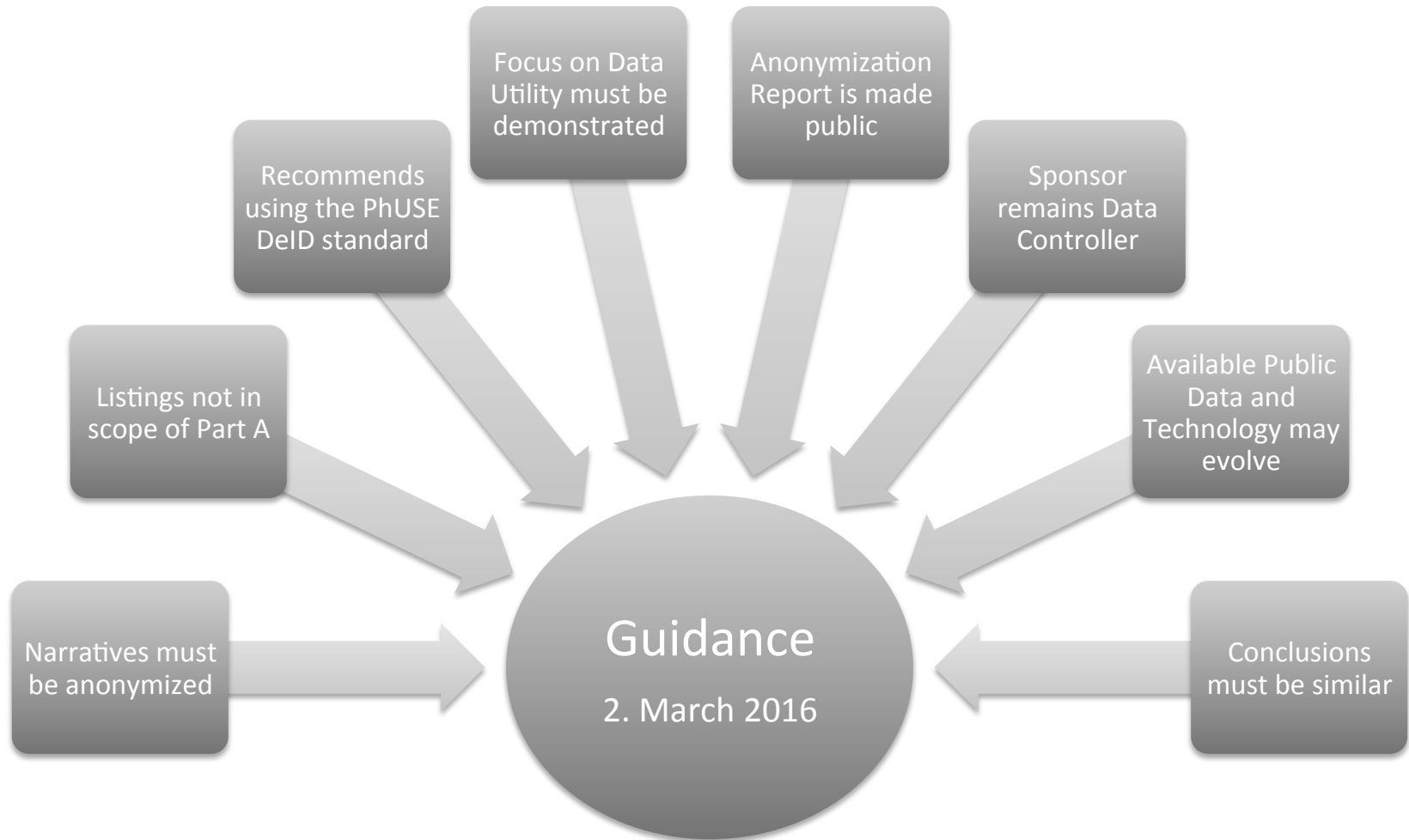
Source: CTR Update, Paul Houston, CDISC European Interchange, Vienna, 28 April 2016

Policy 0070 Part A & Part B, Data Transparency and more...

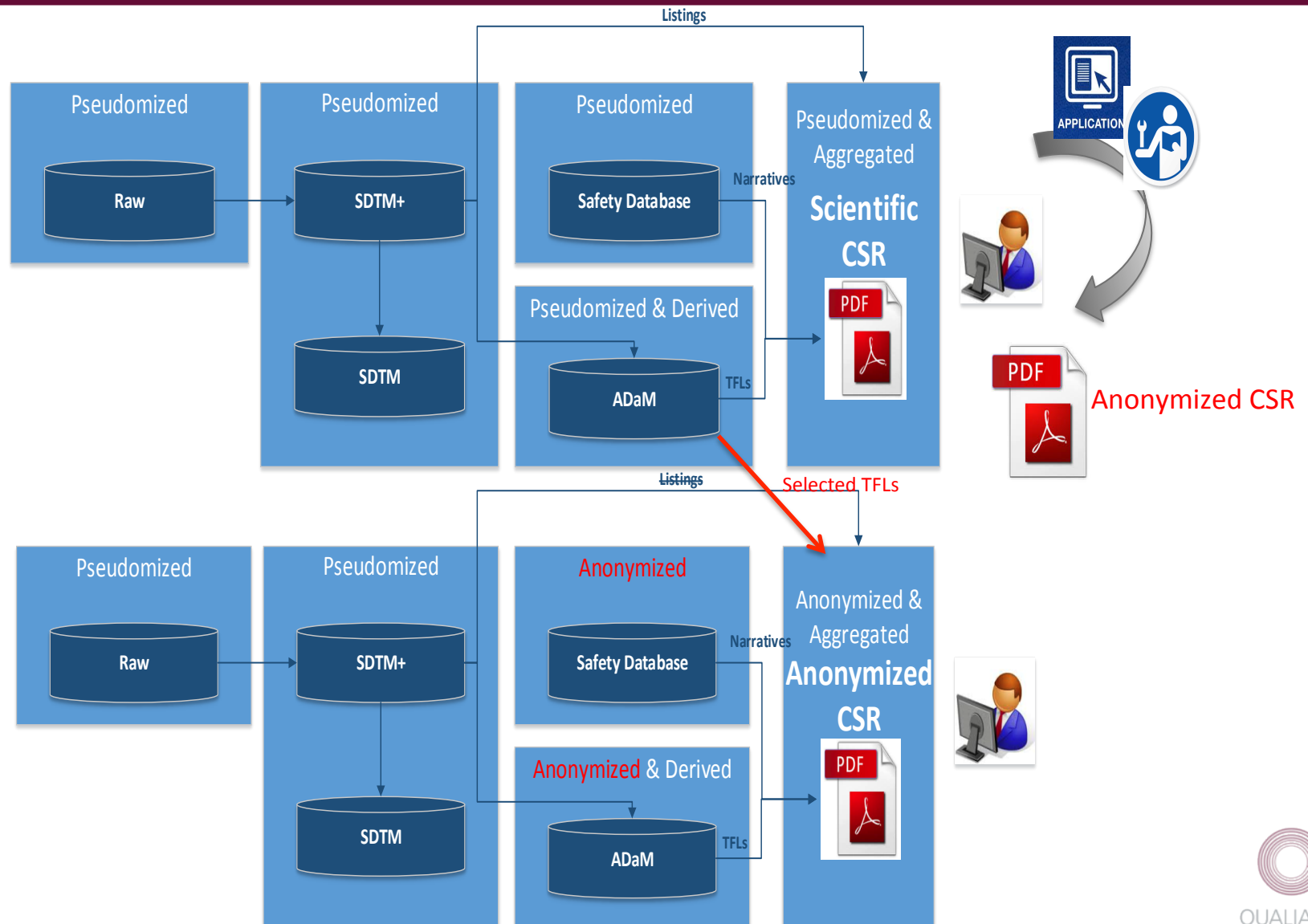
Sponsors Publications	Sponsors Data Transparency Initiatives	 Policy 0070 Part A Part B	
Based on Pseudomized IPD Forever...	Anonymized IPD Started in 2013 with GSK	Anonymized CSR Portal go-live SEP2016	Anonymized IPD <i>Effective ???</i>
Sponsors' choice	Any Study related to an approved application in EU & US	Any Study part of a Centralized Marketing Authorization application	???
No Anonymization	Safe-Harbor or Average Risk Metrics	Qualitative or Maximum Risk Metrics	Average or <i>Maximum Risk Metrics?</i>
Public Domain	May result in Publications available in Public Domain	Semi-Public Domain	<i>Public Domain or Controlled?</i> Publications available in Public Domain

Policy 0070 Part A

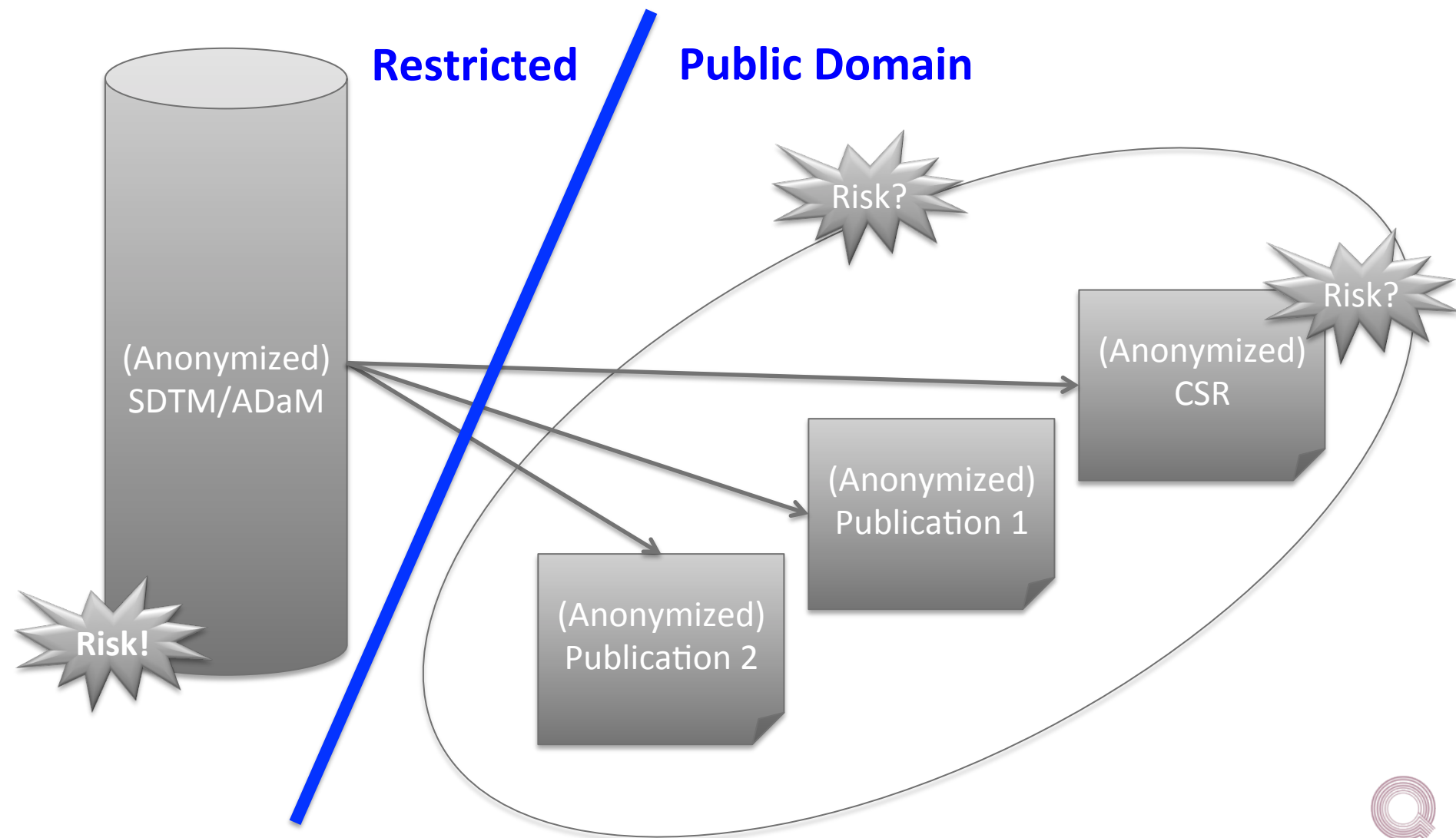
EMA CSR Anonymization Guidance



Current & Possible Future Process



Where to Measure the Risk?



Conclusions

- Can we expect Regulatory Agencies to align or even integrate such requirements?
 - Probably not fully...but to some extent yes...
 - Different legal environments
 - Large difference in resources
- Global data models for protocol and results summary will be required to ensure interoperability and reuse
- EMA CSR Anonymization Guidance is still being interpreted by a number of industry groups and companies and a number of solutions should emerge in the coming year...

Thanks!

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