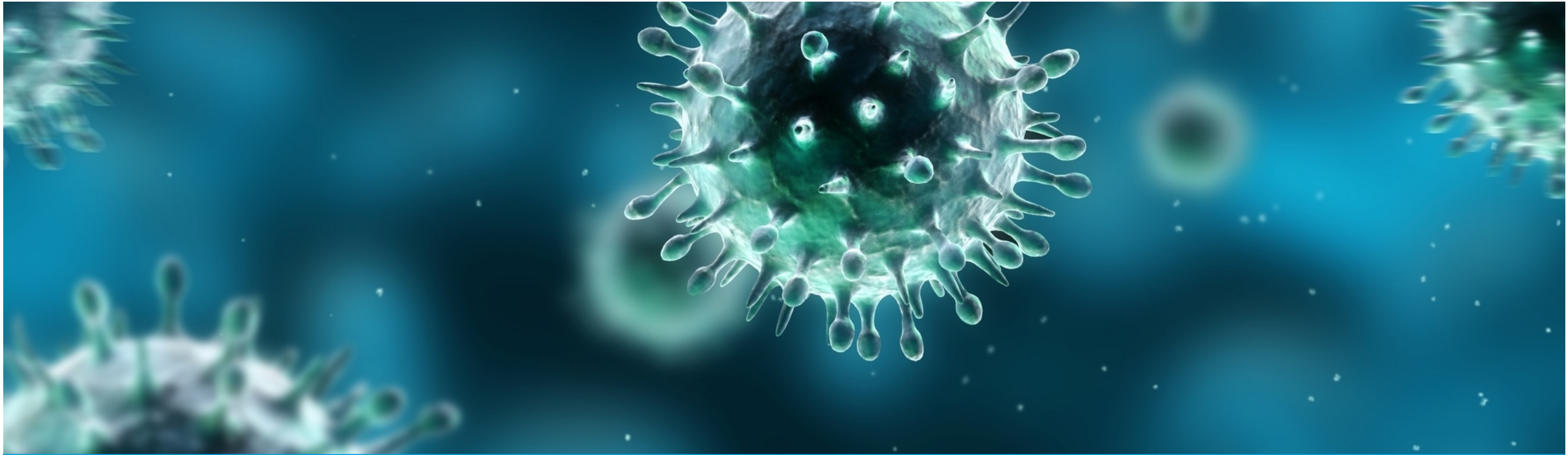




A Case Study: Data Transparency of Clinical Trial Data

PHUSE US Connect 2020

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Data Transparency, Integrated Data Analytics and Reporting
Janssen Pharmaceutical Companies of Johnson & Johnson
10 March 2020

H1N1 influenza virus

A Case Study: Data Transparency of Clinical Trial Data



Disclaimer

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Agenda

Overview of the Data Transparency of Clinical Trial Data

Protocol Registry and Disclosure of the Clinical Trial Summary Results

Submission of Clinical Summary Reports

Sharing of Individual Patient Data for Secondary Analysis and Beyond

Protection of Individual's Patient Data

Plain Language Summaries (or Layperson's Summaries)

Future Requirements of Data Transparency in Clinical Trial Data

Q&A

Agenda

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Q&A

Overview of the Data Transparency of Clinical Trial Data

Regulation requirements:

US HIPAA 1996; effective 14 Apr 2003

US Food and Drug Administration Amendments Act of 2007(FDAAA) regulations of protocol/result disclosure in clinicaltrials.gov; effective 27 Sept 2007

EU Clinical Trials Regulation 536/2014(CTR) for plain language summaries; regulation entered into force on 16 June 2014 with targeted implementation date for early 2022

EudraCT requirements for result disclosure per Directive 2001/20/EC; effective 21 Jul 2014

European Medicine Agent Policy on Publication of Clinical Data for Medicinal Products for Human Use (or, EMA Policy 0070); Phase 1 of Policy 0070 entered into force on 1st Jan 2015. Currently, temporarily suspended since 01 Aug 2018

In The Netherlands,the User Manual for Toetsing Online states, “This final report will consist of a lay summary and a scientific summary with study results. This has to be submitted via the web portal Toetsing Online.” The public disclosure of study results in the CCMO register applies only to new CTAs submitted as of 15 Dec 2015

EU General Data Protection Regulation (GDPR); effective 25 May 2018

Japan Pharmaceutical Manufacturers Association (JPMA) Information on Japanese Regulatory Affairs; effective in 2018

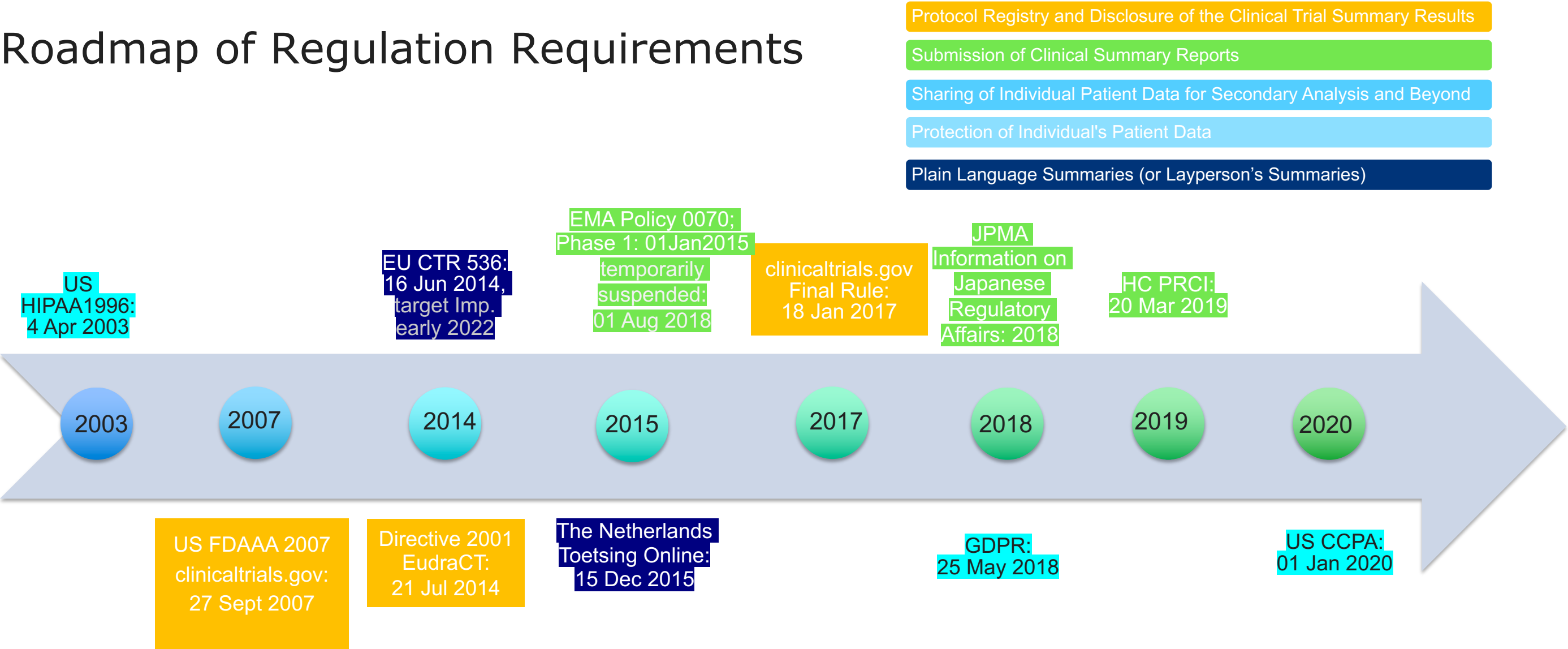
Health Canada's Public Release of Clinical Information (PRCI); effective 20 Mar 2019

The FDA has concluded the Clinical Data Summary Pilot Program and is proposing a new integrated review template in 2019

US California Consumer Privacy Act (CCPA); effective 01 Jan 2020;

Overview of the Data Transparency of Clinical Trial Data

Roadmap of Regulation Requirements



Agenda

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Protocol Registry and Disclosure of the Clinical Trial Summary Results

US: FDAAA / ClinicalTrials.gov, effective since 27 Sept 2007



- Applicable Clinical Trials
 - Controlled clinical trial (placebo or active comparator)
 - Initiated or ongoing as of 27 Sept 2007, and completed after/on 26 Dec 2007
 - Phase II to IV
- Protocol Registry
 - Submit within 21 days after the first patient is enrolled
- Result Disclosure
 - Post results within 1 year of Primary Completion Date (PCD)
 - If new approval: 30 days to report results for completed trials > 1 year from PCD
- Final Rule, effective 18 Jan 2017
 - Applicable clinical trials includes for non-licensed products
 - Disclose the full protocol, SAP, and all amendments (with redaction, as required)
 - Major changes in result disclosure: Baseline Characteristics, AE, and outcome measures:
 - Primary Complete Date on or after 18 Jan 2017: **FINAL RULE**
 - Primary Completion Date before 18 Jan 2017: **STATUTE**

Protocol Registry and Disclosure of the Clinical Trial Summary Results

EU: Directive 2001/20/EC, EU Clinical Trials Register / EudraCT

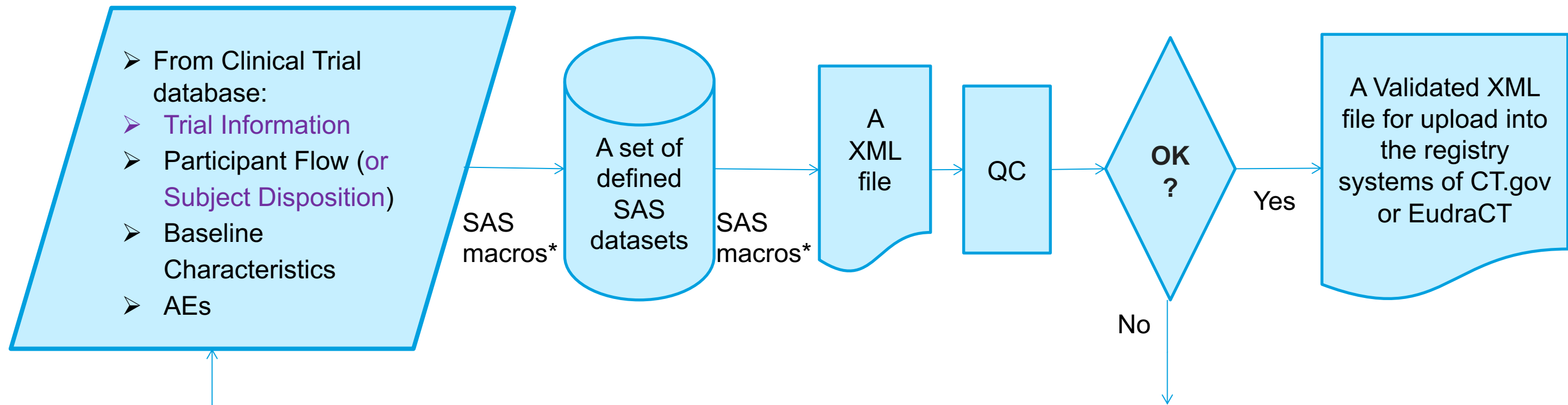


- Applicable Clinical Trials
 - Interventional clinical trials
 - Started after 01 May 2004
 - Phase I to IV
- Protocol Registry
 - ≤ one month after either the EMA decision agreeing a Paediatric Investigation Plan (PIP), or the first approval/positive opinion of the trial by a ‘third country’ competent authority and/or ‘third country’ ethics committee, whichever is the latest
- Result Disclosure, effective 21 Jul 2014
 - For trials that ended on or after 21 Jul 2014
 - Submit result within 12 months after Last Patient Last Visit (LPLV) for Adult trials
 - Submit result within 6 months after Last Patient Last Visit (LPLV) for Pediatric trials
 - For trials that ended before 21 Jul 2014
 - sponsors to submit the results retrospectively, in accordance with the specific timeframe in the EU guideline

Janssen's Automation Method for Result Disclosure



Data Flow of the Automation Process



* SAS macros are developed in two sets of macros: one set is based on the requirement of ClinicalTrials.gov (CT.gov); the other set is based on the requirement of EudraCT.

Agenda

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Q&A

Submission of Clinical Summary Reports

- EMA Policy 0070, effective 01 Jan 2015
 - Two Phases:
 - Phase 1, effective 01 Jan 2015: publishing of CSR with redacted package
 - Phase 2, later stage: publishing of individual patient data (IPD)
 - Encouraged Re-identification risk threshold: 9%
 - EMA temporarily suspended since 01 Aug 2018 per EMA's business continuity plan:
 - Continue to publish clinical data submitted by the end of Jul 2018
 - No new data package will be processed until further notice
- Health Canada Public Release of Clinical Information (PRCI), effective 29 Mar 2019
 - Anonymized CSR package
 - Re-identification risk threshold: 9%
 - Accept documents prepared for EMA Policy 0070
- JPMIA Information on Japanese Regulatory Affairs, 2018
 - Redacted/anonymized CSR per request

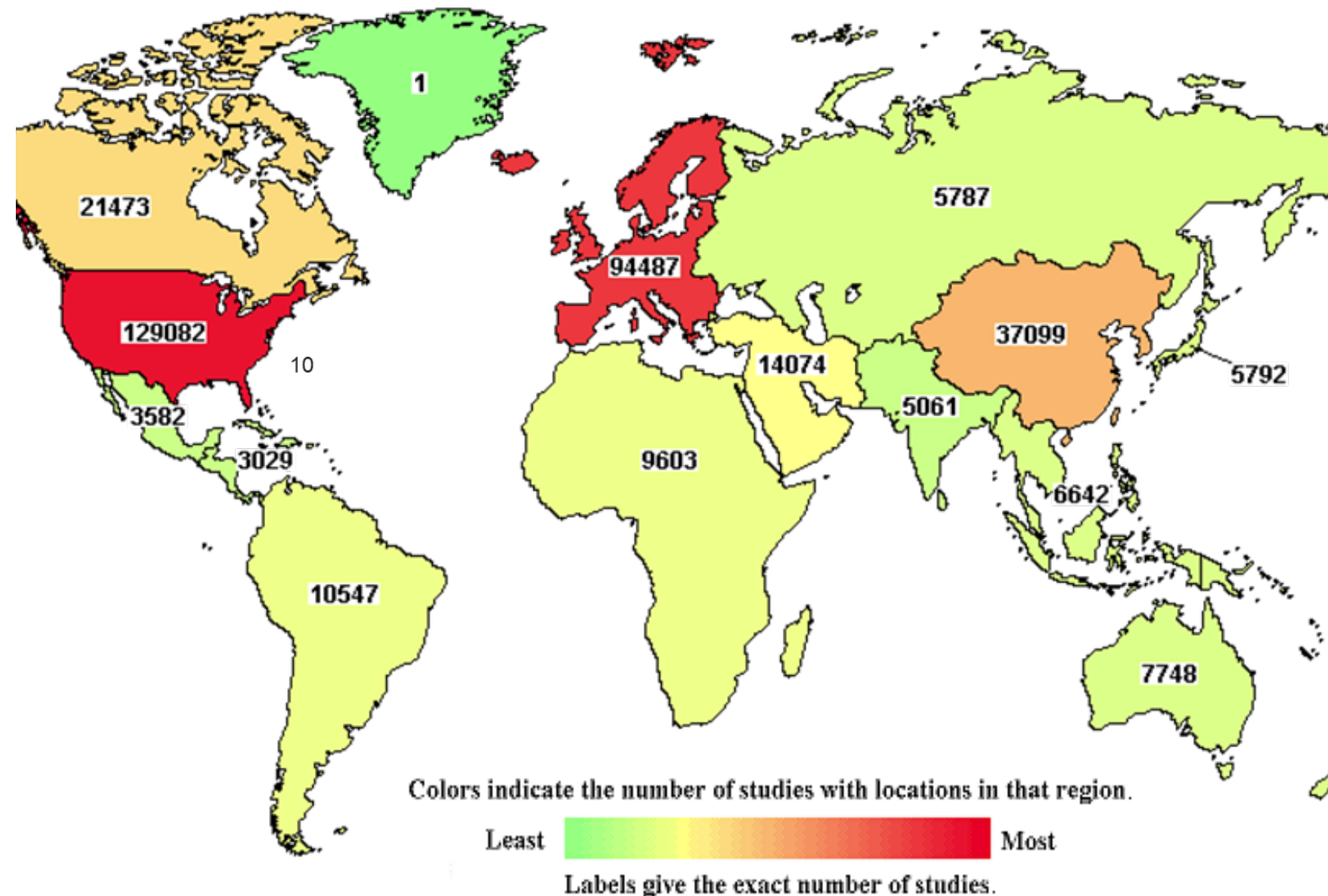
Submission of Clinical Summary Reports

Janssen's Method: Consistent Reporting

- Apply common requirements across anonymization package starting 2019

Adopt re-identification threshold: 9%

- Reduce potential data leakage
- Gain efficacy in different submissions across globe



Source: ClinicalTrials.gov, accessed on 22 Feb 2020

Agenda

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Sharing of Individual Patient Data for Secondary Analysis and Beyond

Both HIPAA and EMA Policy 0070 Phase 2 requires:
data de-identification/anonymization of Individual Patient Data (IPD)

IPD is in high demand in research communities

Janssen shares data with research communities:

- Yale Open Data Access (YODA) Project
- Project Data Sphere
- TransCelerate / DataCelerate Data Sharing Project
- Vivli, IMI, ..

Janssen provides anonymization data package:

- Anonymized IPD datasets
- Anonymized data report
- Anonymized CSR
- aCRF



Sharing of Individual Patient Data for Secondary Analysis and Beyond

- Janssen's Responsible Data Sharing

- Balance between data privacy and data utilities

- Maximize data utility: consistency between anonymized CSR and anonymized IPD, such as same anonymized Subject ID

- Data privacy: adopt the same re-identification risk threshold (9%)

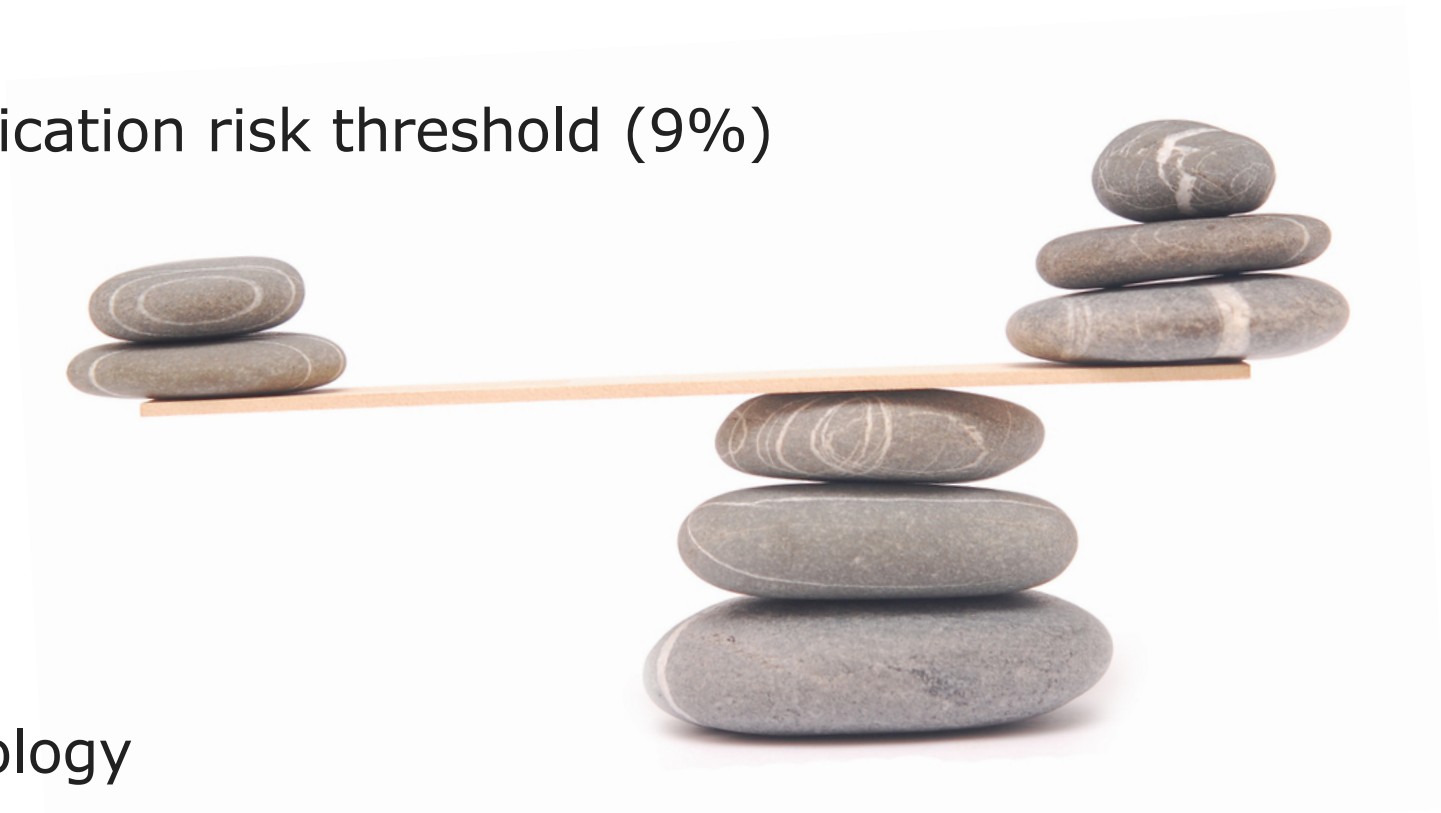
- Methodology improvement

- De-identified / Anonymized Data

- Synthetic Data

- System testing

- Development of new data-driven technology



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Q&A

Protection of Individual's Patient Data

- Regulations to Protect Data Privacy
 - US HIPAA Privacy Rule 1996
effective 14 Apr 2003
 - Data should be de-identified for Protected Health Information (PHI)
 - EU General Data Protection Regulation (GDPR), effective 25 May 2018
 - Individuals'/study participants' data rights, "Right to be forgotten"
 - Sponsors to provide well defined purpose for data collection and use

The 18 identifiers of HIPAA PHI are:

- Names
- Dates, except year
- Telephone numbers
- Geographic data
- FAX numbers
- Social Security numbers
- Email addresses
- Medical record numbers
- Account numbers
- Health plan beneficiary numbers
- Certificate/license numbers
- Vehicle identifiers and serial numbers including license plates
- Web URLs
- Device identifiers and serial numbers
- Internet protocol addresses
- Full face photos and comparable images
- Biometric identifiers (i.e. retinal scan, fingerprints)
- Any unique identifying number or code

Protection of Individual's Patient Data

- Regulations to Protect Data Privacy (cont.)
 - US, the California Consumer Privacy Act (CCPA) 2018, effective 01 Jan 2020
 - ❑ Any California consumers have rights of their personal information
 - ❑ Personal information” includes:
 - Identifiers such as a real name, alias, postal address, unique personal identifier, online identifier IP address, email address, account name, Social Security number, driver’s license number, passport number, or other similar identifiers
 - Characteristics of protected classifications under California or federal law
 - Commercial information including records of personal property, products or services purchased, obtained or considered, or other purchasing or consuming histories or tendencies
 - Biometric information
 - Internet or other electronic network activity information including, but not limited to, browsing history, search history and information regarding a consumer’s interaction with a website, application or advertisement
 - Geolocation data
 - Audio, electronic, visual, thermal, olfactory or similar information
 - Professional or employment-related information
 - Education information, defined as information that is not publicly available personally identifiable information (PII) as defined in the Family Educational Rights and Privacy Act (20 U.S.C. section 1232g, 34 C.F.R. Part 99)
 - Inferences drawn from any of the information identified in this subdivision to create a profile about a consumer reflecting the consumer’s preferences, characteristics, psychological trends, preferences, predispositions, behavior, attitudes, intelligence, abilities and aptitudes
 - An amendment, AB 874, currently awaiting the governor's signature would exempt publicly available, deidentified and aggregate consumer information from being classified as PII.
 - An amendment, AB713, currently introducing the exceptions from the CCPA, such as de-identified information according to the HIPAA rule, personal information that is collected for, or used in, used in biomedical researches.....

Protection of Individual's Patient Data

Janssen's Solutions

- Standard Process
 - Systematic Tracking of GDPR Requests
 - Implementation of GDPR Requests at Study Level
- A Standard ICF Template with Well-Defined Data Use Language Based on the Input from Members across Different Functions:
 - Data Transparency
 - Legal Group
 - Clinical Development
 - Global Clinical Operations

Agenda

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Plain Language Summaries (Layperson's Summaries)

- EU Clinical Trial Regulation (EU CTR)
 - Regulation No 536/2014
 - Planned implementation target date: Early 2022
 - Requires Plain Language Summary (PLS):
 - For all Phase I – Phase IV interventional studies conducted in EU
 - Timeline follows the same timeline for trial result disclosure in EudraCT
 - Planning of PLS should begin before the study starts
 - Should be communicated to study participants via ICF
 - Require to be written in a manner that the trial participants can understand
 - At a minimum, be provided in the local language of each of the EU countries where the trial took place
- The Netherlands Requires a Public Summary
 - Toetsing Online states “This final report will consist of a lay summary and a scientific summary with study results. This has to be submitted via the web portal Toetsing Online”

Plain Language Summaries

Janssen's Plan

- Proactively started a PLS initiative to develop:
 - ❑ Standard Process
 - Safeguards participant's privacy
 - Ensures a clear understanding of the various published results, including result disclosure
 - ❑ Standard Template
 - Apply for all studies across Phase I to Phase IV
 - Maintain efficiency and consistency
 - ❑ A Volume Forecast of Studies with Planned PLS
 - Resource planning
 - Budget planning

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Future Requirements

- New Regulatory Programs Across the Globe
 - FDA's Clinical Data Summary Pilot Program
 - FDA's Integrated Review Template
 - The Ministry of Health of Ukraine's Draft Order:
"PROCEDURE for the Access to the Results of Nonclinical Studies and Clinical Trials of Medicinal Products (Reports on Nonclinical Studies and Clinical Trials)"
 - More to come

Future Requirements

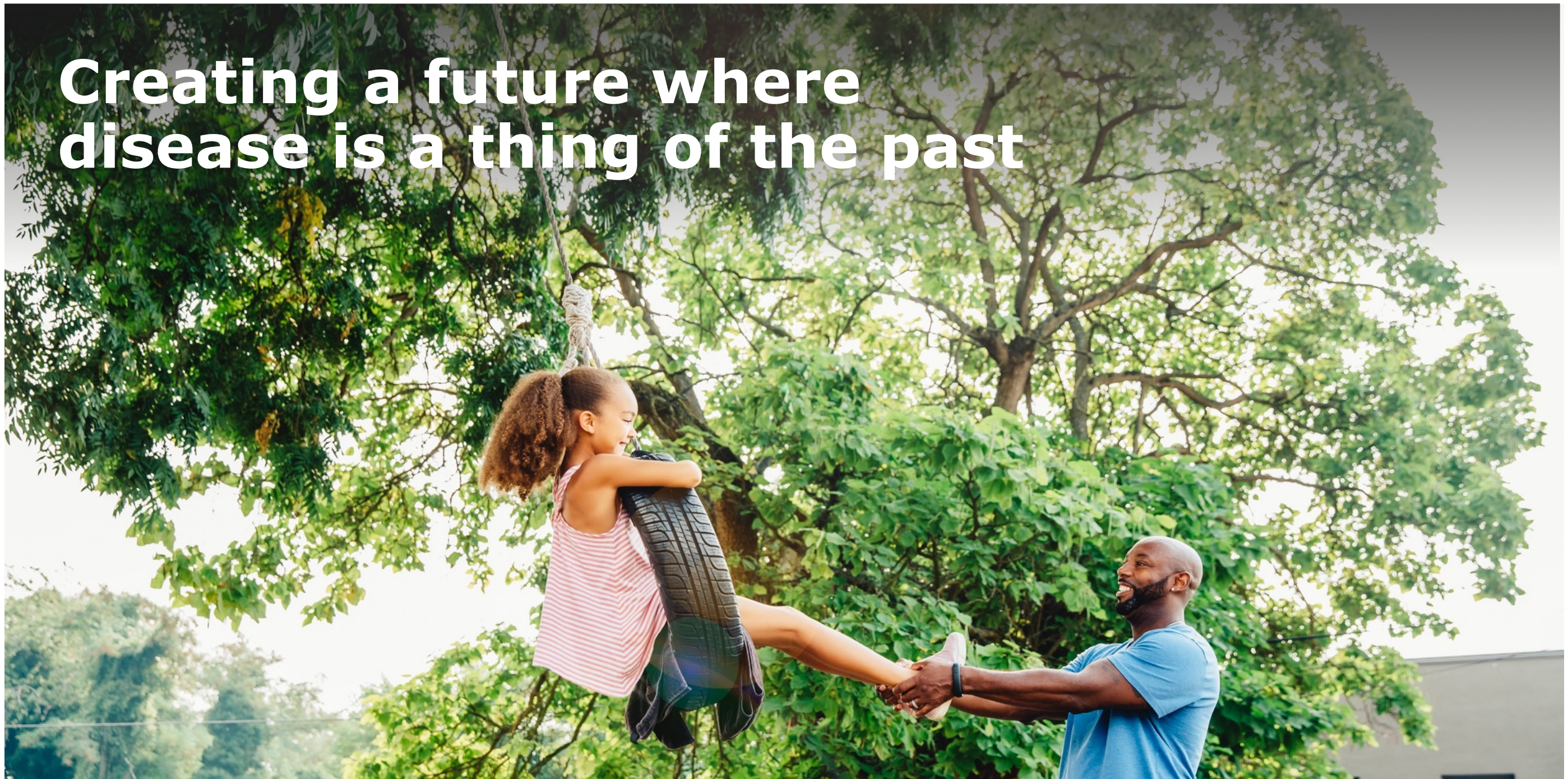
Janssen's Solutions: Prepare for the Future

Actively Participate in Health Authorities and Industry Initiatives:

- FDA's Clinical Data Summary Pilot Program
- Review of the Ministry of Health of Ukraine's Draft Order: "PROCEDURE for the Access to the Results of Nonclinical Studies and Clinical Trials of Medicinal Products (Reports on Nonclinical Studies and Clinical Trials)"
- Review of FDA's Proposal for Integrated Review Template
- Development of PHUSE De-identification Standard for CDISC SDTM 3.2
- Publication of PHUSE Clinical Trial Transparency and Disclosure: A Global View
- Contribution to PHUSE A Global View of the Clinical Transparency Landscape – Best Practice Guide
- Participation in EFGCP-EFPIA Roadmap Initiative to Good Lay Summary Practice

Conclusion

- Data Transparency of Clinical Trial Data
 - The Complexity of Regulatory Requirements
 - Responsible Data Sharing
 - Balancing between Data Privacy and Data Utility
 - Consistency and Efficiency
 - Innovative Value-added Solutions
 - Our Ultimate Goal: Our Patients
 - Protect our Patients' Privacy
 - Benefit our Patients with Valuable Data



**Creating a future where
disease is a thing of the past**

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Q&A

