



The Landscape of Standards

Making Sense of the Alphabet Soup

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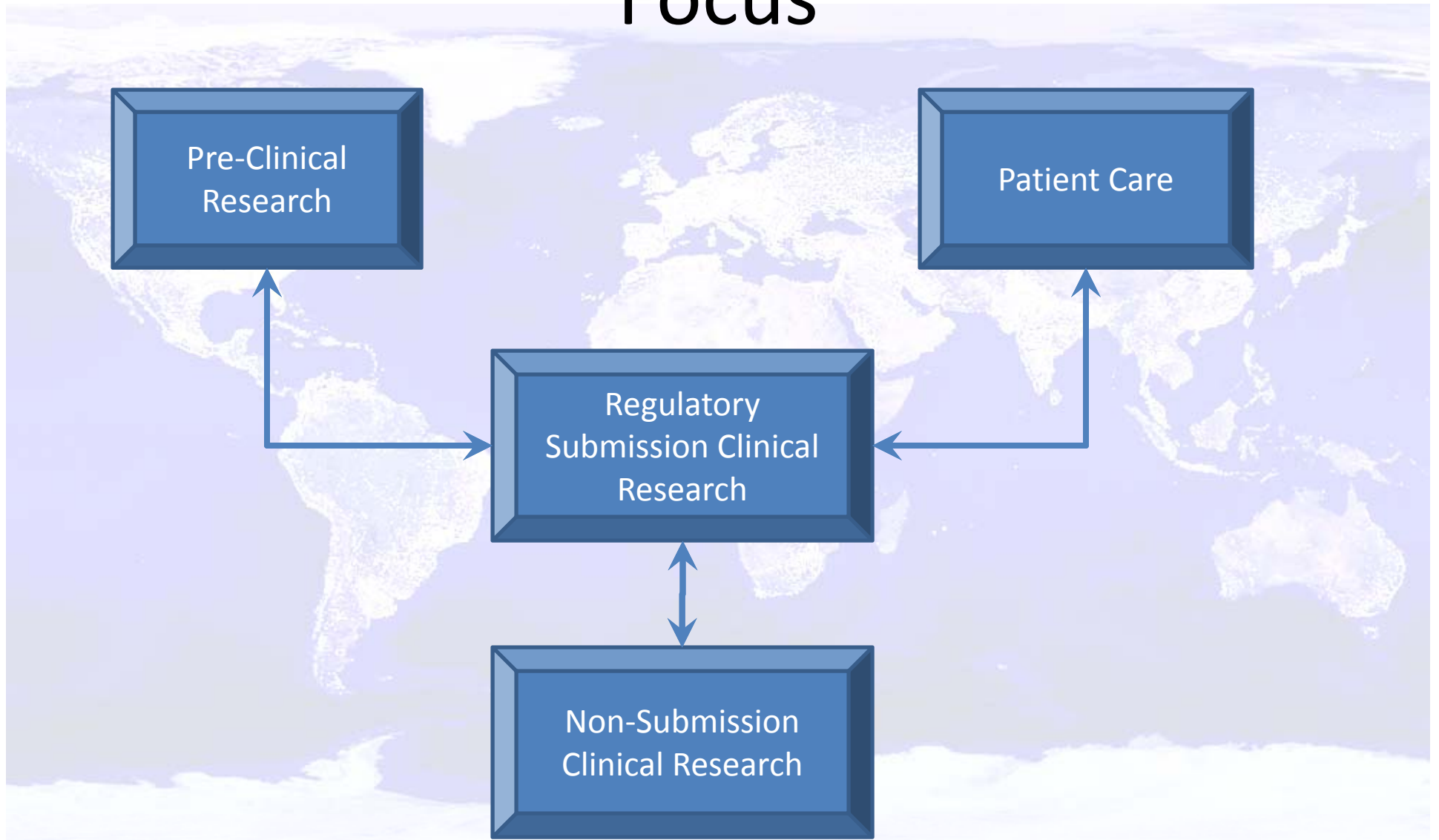




An Over-Used Word...

- 'Standards' has many meanings
 - Diagnostic and treatment rules (heart failure)
 - Service agreements (car repair)
 - Classification methods (Dewey Decimal System)
 - Manufacturing (metal purity)
- In the data manager's world...
 - Terminology (dictionaries of terms and/or codes)
 - Technical requirements (database structures)
 - Reporting programs (listings, tabulations)
 - Common processes (SOPs)

Focus



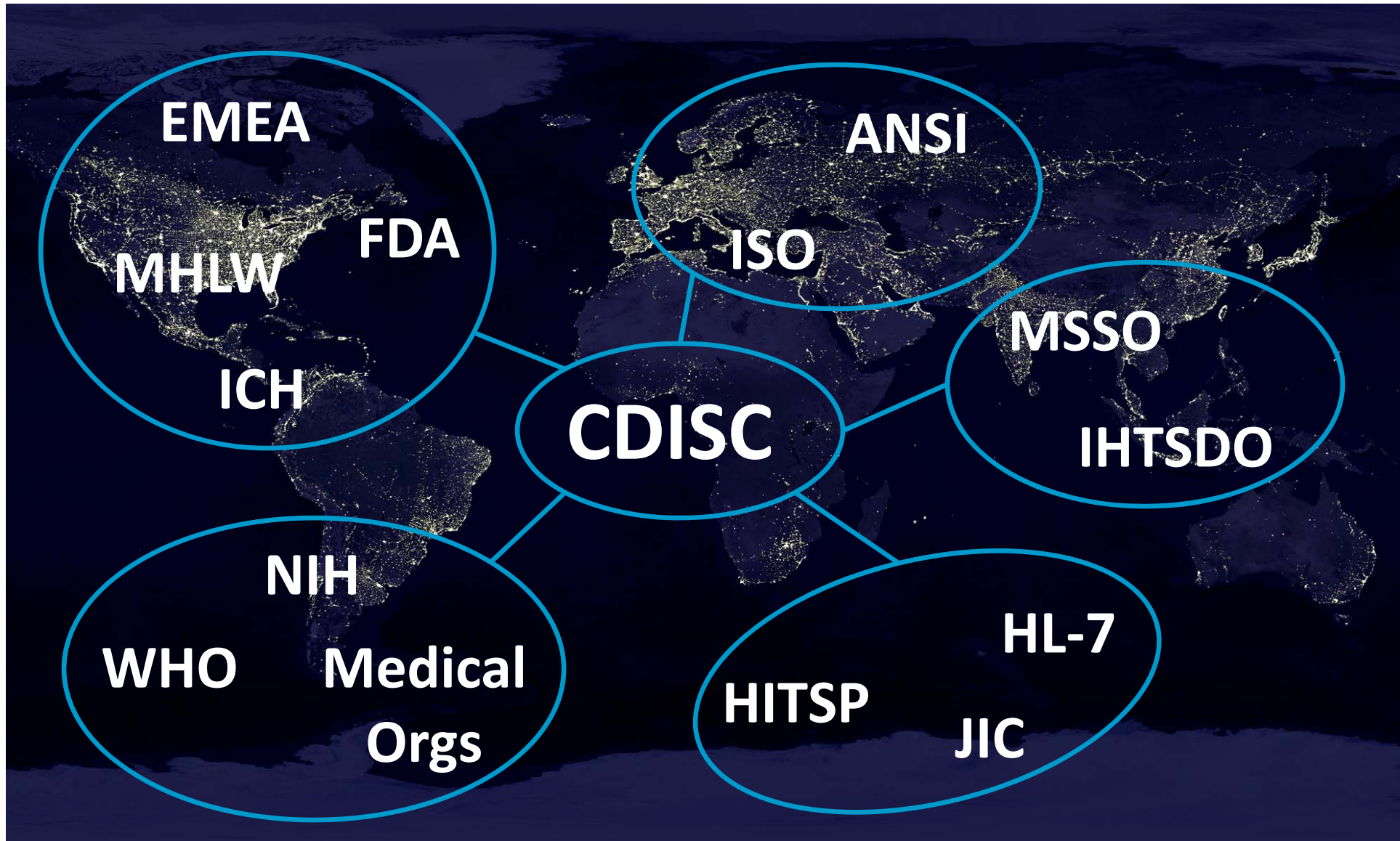
Drivers of Standardization

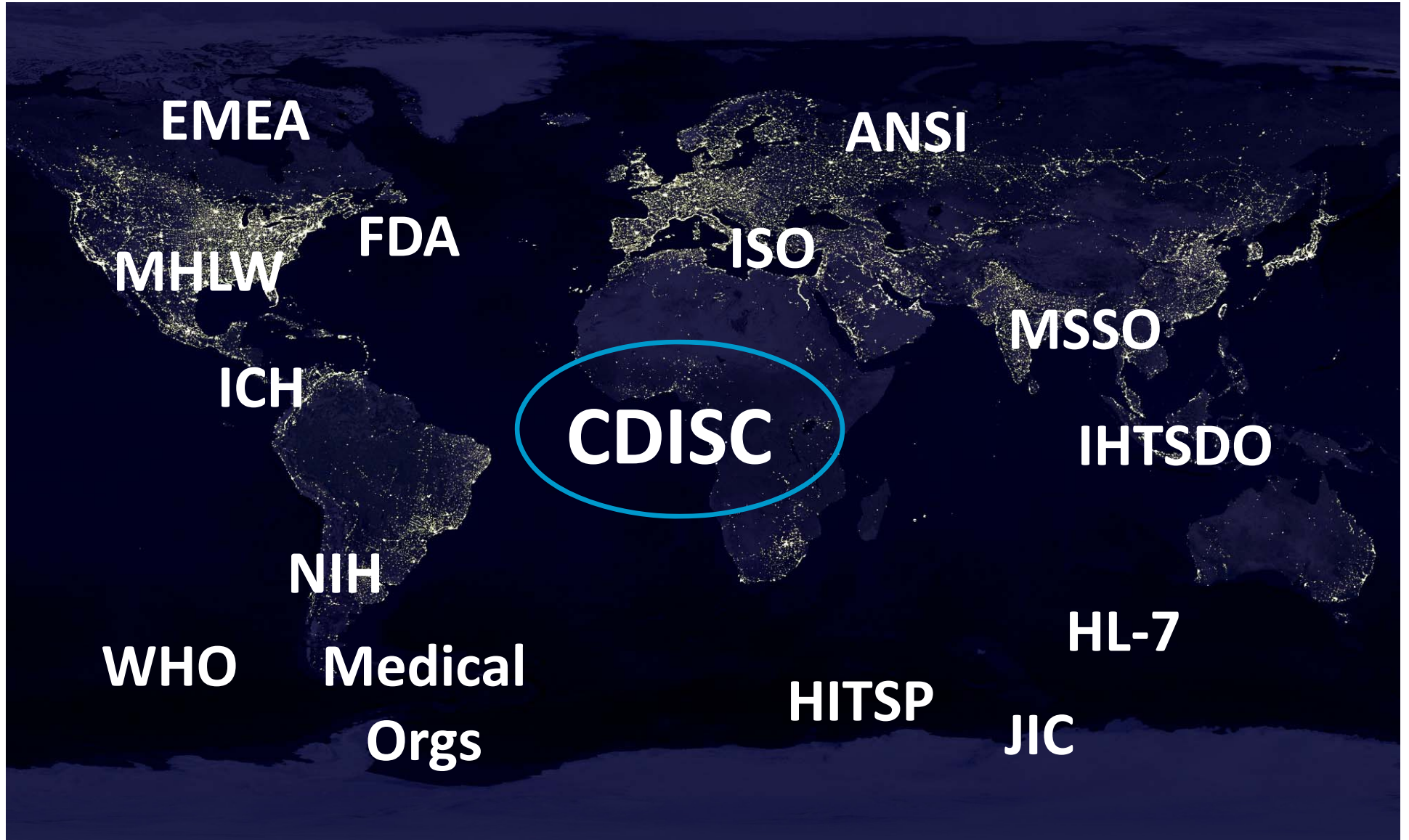
- Scientific Breakthroughs
 - Sharing and pooling data allows for additional research and discoveries without patient exposure
 - Inability to pool data keeps information insular and prevents full cross-functional collaboration
- Ethics
 - Resources used for duplicating research slows progress, exposes additional patients to potentially ineffective or unsafe treatments and results in fewer patients receiving effective treatments
 - Inability to share healthcare records hinders the delivery of appropriate medical care
- Cost
 - Reinventing the wheel is expensive
 - Increasing pressure on research funding, healthcare costs & drug development costs prohibit continuing with the current model

Flavors of Standards



- Categories
 - Exchange
 - Terminology
 - Common terms
 - Dictionaries/code lists
 - Templates
 - Models
 - Documents
 - Programs
 - Content
- Attributes
 - **Open** / proprietary
 - **Consensus** / arbitrary
 - **Voluntary** / mandatory





CDISC

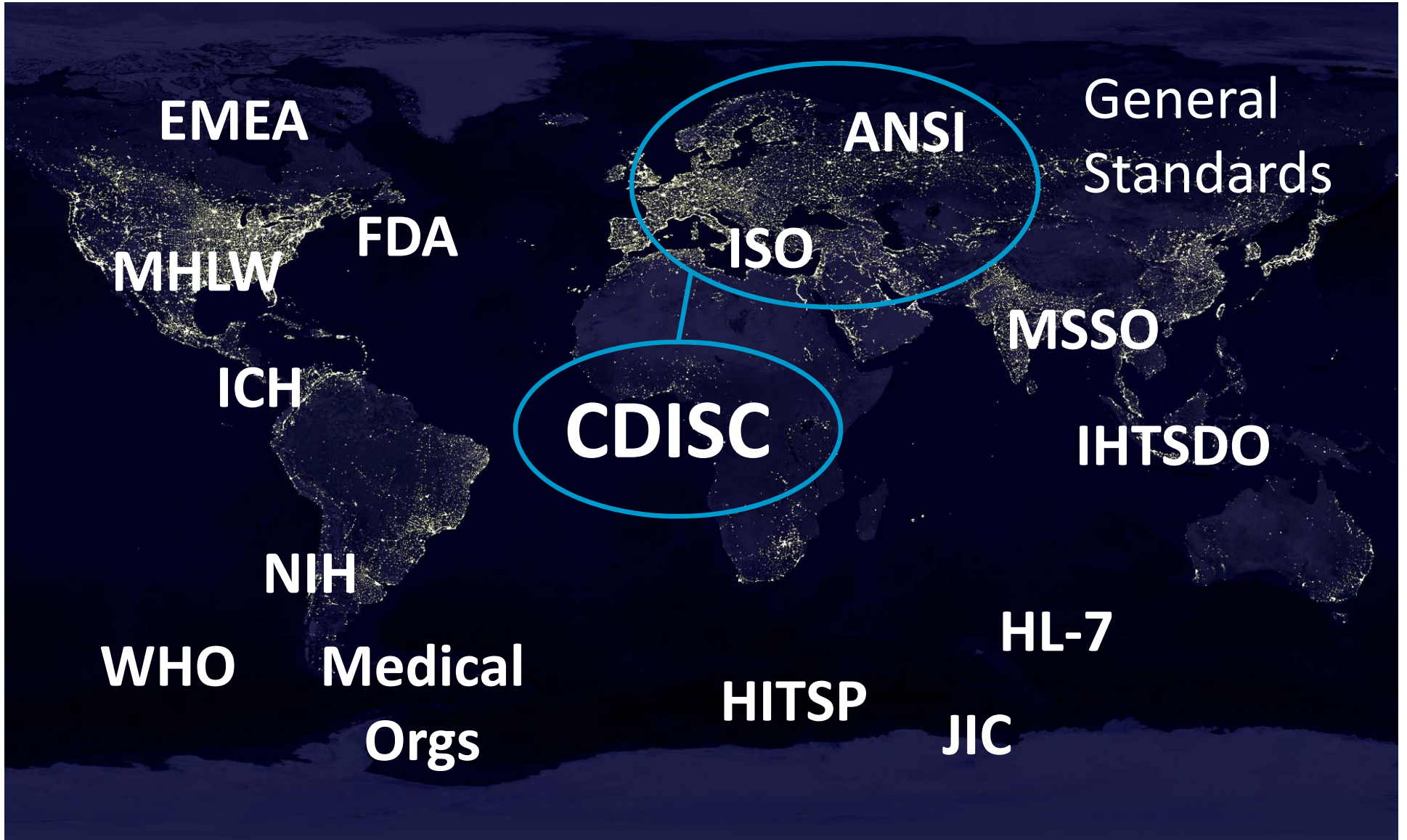
- Clinical Data Interchange Standards Consortium
- Develop data standards for (industry-sponsored) clinical research
- Primary focus is exchange of clinical research information intended for regulatory submissions
- Includes exchange, terminology and templates

CDISC Groups

- SDTM
 - Study Data Tabulation Model
 - Structure and content of patient data in electronic regulatory submissions files
- CDASH
 - Clinical Data Acquisition Standards Harmonization
 - Data capture definitions
- ADaM
 - Analysis Data Model
 - Structure of analysis datasets for submission
- BRIDG
 - Biomedical Research Integrated Domain Group Model
 - Framework for linking and harmonizing the other standards

CDISC Groups

- ODM
 - Operational Data Model
 - XML model for describing & managing CRF-based data
- LAB
 - Laboratory
 - Content standard for defining lab data
- SEND
 - Standard for the Exchange of Non-clinical Data
 - Pre-clinical data exchange definitions
- TDM
 - Trial Design Model
 - Model for describing the protocol's treatment plan
- Terminology
 - Defining code lists/controlled terminology for CDISC variables
 - NCI's Enterprise Vocabulary Enterprises will provide controlled versioned management



EMEA

MHLW

FDA

ICH

NIH

WHO

Medical
Orgs

ANSI

ISO

CDISC

MSSO

IHTSDO

General
Standards

HL-7

HITSP

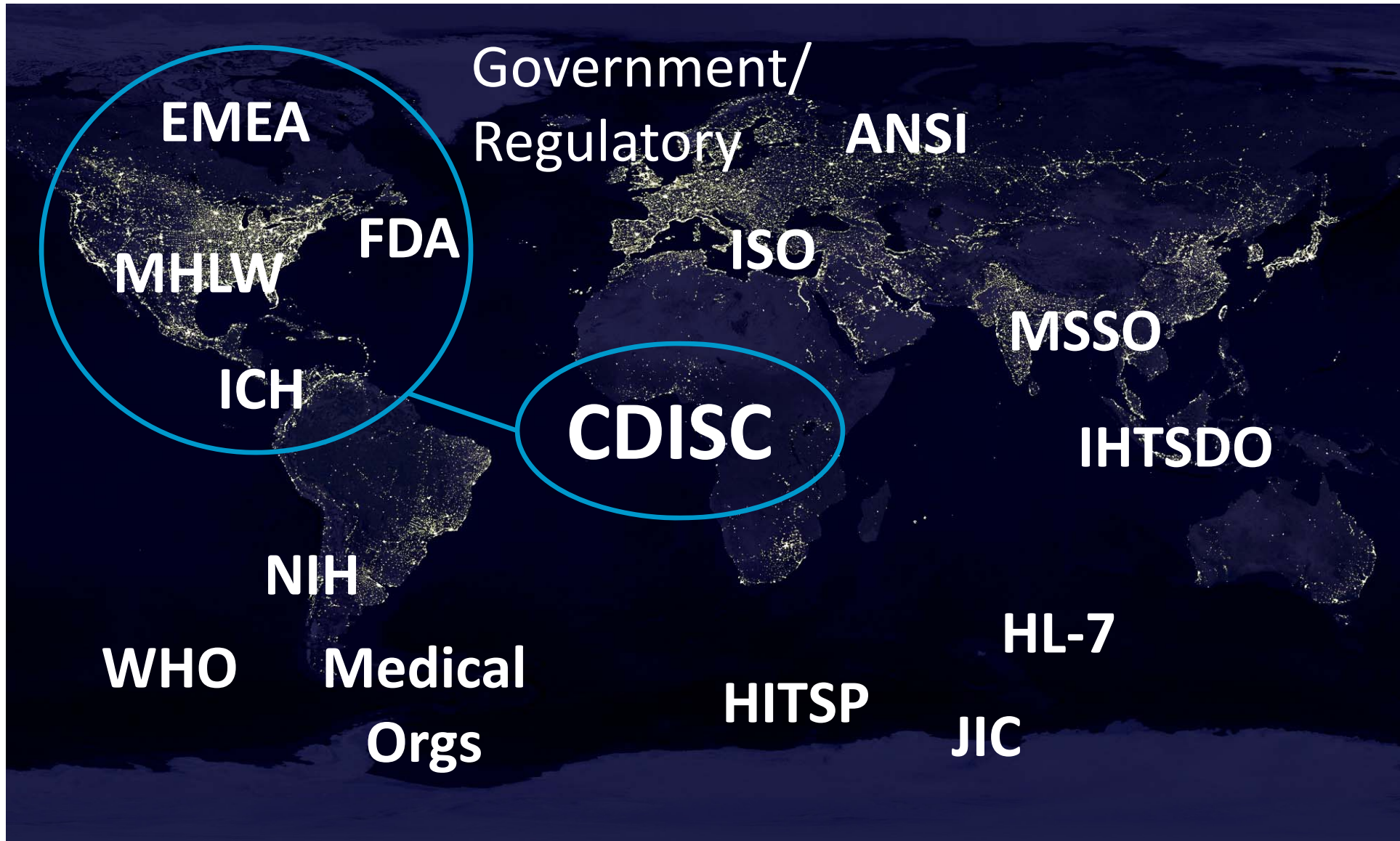
JIC

General Standards Organizations

- ISO
 - International Standards Organization
 - Combination of governmental & non-governmental organizations representing 157 countries
 - Develops a very wide variety of standards
 - Graphical symbols for maps
 - Guide for radiation dosimetry for sterile insects release programs
 - Calculation of load capacity of spur and helical gears
 - Specification of the design, dimensions, material and requirements of tablet glass bottles
 - ISO 8601: Data elements and interchange formats -- Information interchange -- Representation of dates and times

General Standards Organizations

- ISO (cont.)
 - CDISC is a Liaison A status to ISO TC 215 (healthcare standards)
 - Possible because CDISC process conforms to ISO standards
 - Allows CDISC to skip some initial steps in ISO approval process
- ANSI
 - American National Standards Institute
 - The US representative to ISO
 - CDISC standards developed with HL-7 can be ANSI-accredited



EMEA

Government/
Regulatory

ANSI

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Regulatory Bodies



- EMEA
 - European Medicines Agency
 - The European Union's FDA
- MHLW
 - Ministry of Health, Labor & Welfare
 - Japan's FDA
- FDA
 - Food & Drug Agency
 - Part of US Dept of Health & Human Services

ICH

- International Conference for Harmonisation
 - Collaboration by EMEA, MHLW and FDA, and industry
 - Developed guidelines to enable one product submission to be acceptable to all participants
 - Four categories of documents
 - Q: Quality, primarily manufacturing
 - S: Safety, meaning pre-clinical
 - E: Efficacy, covering clinical
 - M: Multidisciplinary, documents that cover multiple areas

ICH

- Effectively established standards, e.g.,
 - E2A & B: Expedited Safety Reporting
 - E3: Clinical Study Report outline
 - E15: Genomics-related Terminology Definitions
 - M1: MedDRA
 - M4: Common Technical Document
- ICH documents provide content & structure for CDISC standards

FDA

- Food and Drug Agency
 - Includes CDER, CBER and CDRH
 - Each division has its own practices, though there is a lot of commonality
 - Policy is that standards in one division apply to all
 - FDA receives the clinical data portions of electronic regulatory submissions in CDISC's SDTM format with ADaM analysis datasets and (eventually) CDASH CRF data
 - CDER has taken the lead with CDISC

FDA Data Standards Council

- Oversees standards across all centers
- FDA collaborates with many organizations
 - Structured Product Labeling (HL-7)
 - Regulated Product Submission (HL-7)
 - CDISC Data Standards (CDISC)
 - Substance Registration System - Unique Ingredient Identifier (FDA/US Pharmacopeia)
 - FDA Terminology hosted by NCI EVS (NIH)
- JANUS
 - Vision for the ultimate data warehouse
 - Will be SDTM-friendly



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Healthcare

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WHO

- World Health Organization
- Directing and coordinating authority for health within the United Nations
- Provides leadership on global health matters
 - shaping the health research agenda
 - setting norms and standards
 - monitoring and assessing health trends
- They own WHO-Drug Dictionary
- Huge potential for data sharing

NIH



- National Institutes of Health
- US government body that conducts the vast majority of health research in US
- 27 institutes & centers
- Has a larger budget than many 3rd world countries
- NIH Roadmap \approx FDA Critical Path Initiative
- Huge potential for data sharing

NIH

- NIH Roadmap:
 - “Each institute sponsoring clinical research should develop a central clinical investigations database that maintains all data specified to be collected in the clinical study (either intervention or natural history).”
- Each Institute charged with developing therapy-specific data standards
- Clinical Trials Center is available to help, but each institute is working largely independently

NCI

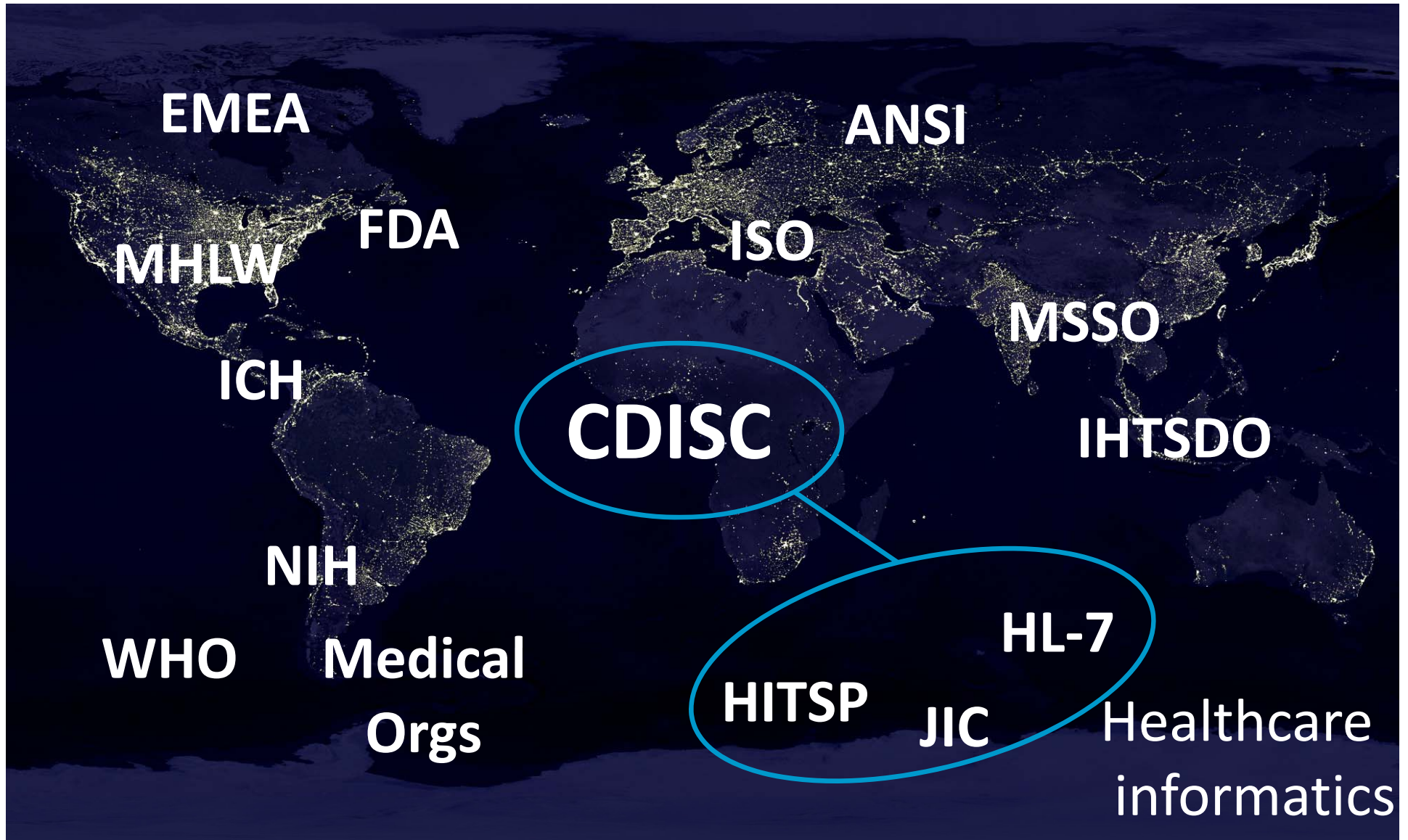
- National Cancer Institute sponsors caBIG (**cancer Bioinformatics Grid**)
- Most familiar to industry world, and probably farthest ahead
- Defining core & administrative data elements and cancer-specific elements
- Map to CDISC
- Enterprise Vocabulary Services (NCI EVS)
 - Publishing/managing CDISC Terminology

NINDS

- National Institute of Neurological Disorders & Stroke Common Data Elements project
- Defining core & administrative data elements
- Defining common neurological and stroke data, e.g.,
 - HamD
 - Beck Depression
 - Mini Mental State Exam
 - NIH Stroke Scale
 - Genetics elements
 - PDQ39 (QOL scale)

Medical Organizations

- Many medical specialties and therapy areas have professional organizations, e.g.,
 - American Heart Association/American College of Cardiology
- Develop diagnostic, treatment, outcomes and quality guidelines and recommendations
- These can provide the content for therapy-specific standards
- CDISC coordinating TB standards development



HL-7

- Health Level 7
- “A protocol for formatting, transmitting and receiving data in a healthcare environment”
 - i.e., Define the envelope for transmission, not the content, e.g.,
 - Lab data: ordering, specimen collection, specimen tracking, chain of custody, and results reporting
- Primary focus is exchange of health care info
- CDISC is a member organization
- Several HL-7 standards are being developed in collaboration with CDISC

HL-7 Terms

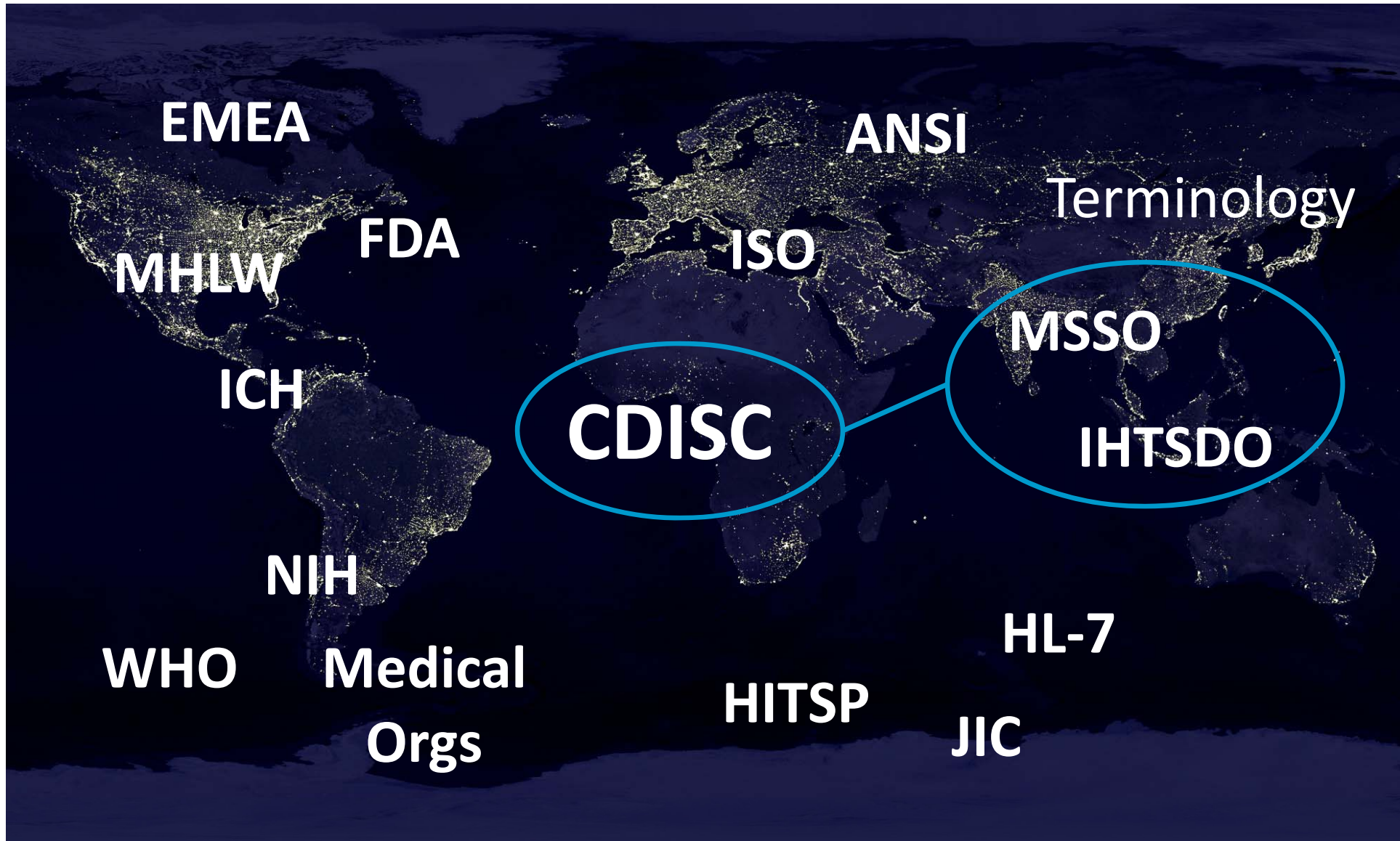
- RCRIM – Regulated Clinical Research Information Management technical committee (CDISC is a founder)
- RIM – Reference Information Model
- CDA – Clinical Document Architecture
- SPL – Structured Product Label
- Protocol Representation (collaborative w/ CDISC)
- EHR-S FM – Electronic Health Record System Functional Model

HITSP

- Healthcare Information Technology Standards Panel
- Managed by ANSI, which is a member of HIMSS, the Healthcare Information and Management Systems Society
- Primary driver for full Electronic Health Record (EHR) interoperability
- Enormous potential for integrating clinical research into patient care, and drawing patient data directly into research databases
- CDISC is a member organization of HITSP, and is on the HITSP Board
- CDISC participates in HIMSS Interoperability Showcase

JIC

- Joint Initiative Council
- Formal collaboration between ISO, HL-7 and CEN (European Committee for Standardization)
- Established in August 2007
- Goal is to harmonize healthcare informatics standards
- In late Feb 2008 CDISC was invited to be the first new member



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Dictionaries / Terminology

- IHTSDO
 - International Health Terminology Standards Development Organization
 - National Library of Medicine licenses SNOMED from them for general use
- MSSO
 - Maintenance and Support Services Organization
 - Run by Northrup Grummond
 - Maintains MedDRA
- Regenstrief Institute
 - Manages LOINC

Standards By Type

Terminology

WHO-DD
MedDRA
SNOMED
LOINC
CDISC
Terminology

Transmission

SPL
TDM
CDA
eCTD
ODM

Content

LAB
SEND
SDTM
CDASH
E2A/B
ADaM
NIH Activities

Diagnosis &
Treatment
Guidelines

Template

E3 CSR
Protocol Representation
SAP template

Take-home Message

- There are many standards that may impact our work
- It's necessary to think broadly and long-term when considering standards
- Before developing a new standard...

CHECK TO SEE WHAT IS ALREADY AVAILABLE!

THE GUY WHO INVENTED THE
WHEEL



P. Christ

References & Contact Info

- Many thanks to Becky Kush, CDISC, for assistance with content and review
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- www.ich.org
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