APPENDIX B. **STANDARDS SITUATION IN THREE COUNTRIES RELATED TO COVID-19**

Category	Standards			Global Collaborative Opportunities
	Spain	**Italy**	**U.S.**	
Test Kits **A** **Blocks 2.2, 2.3**	In Spain the Ministry of health has the capacity of validation and authorization of testing and test kit validation	In Italy the tests are validated by the Public Health Institute (Istituto Superiore di Sanità) the scientific branch of the Ministry of Health	In the U.S. test kit validation and approval is the responsibility of the FDA CDRH (Center for Devices and Radiological Health).	• Expansion of testing • Faster tests and test results • More accurate tests • Standard definitions of which test data are to be combined, contrasted, compared and reported.
Laboratories **B** **Block 4**	The Carlos III Health Institute (ISCIII), under the ministry of health in coordination with the Ministry of Science and Innovation has the capacity to validate laboratories and universities to perform testing	The diagnostic PCR tests should be analyzed only in public and certified laboratories. The immunodiagnostic tests for COVID-19 (blood samples or point-of-care) are not considered as diagnostic tests, rather only for epidemiologic purposes and can be analysed by accredited laboratories (public and private).	In the U.S. clinical laboratories are certified through CLIA (Clinical Laboratory Improvement Amendments), a CMS responsibility. For Covid-19, U.S. HHS has announced reporting requirements for laboratory data from test results (4 June 2020)	• Tests conducted more rapidly by more laboratories that are licensed and certified • Standards for collecting and reporting laboratory results should be harmonized with existing standards for healthcare and research.
Contact Tracing **C** **Block 2.2**	Spain was initially involved in the Pan-European Privacy-Preserving Proximity Tracing (PEPP-PT) uncloaked on April 1, calling for developers of contact tracing apps to standardize approaches to processing smartphone use across borders and reduce the risk of overly intrusive location-tracking; Asturias region is conducting a pilot using a bluetooth app (not phones)	The Italian government promoted a call for proposal for a contact tracing app. A company with smartphone app originally called **Immuni** won the call (name will likely change). Due to privacy problems the app had to change the original methodology. The efficacy remains in dispute and evidence of efficacy is lacking.	A variety of methods and apps are being used and/or developed in the U.S., some including GPS coordinates (e.g. via mobile phones). Some cell phone vendors appear to be unwilling to share data with health officials. Other groups (e.g. MIT) are exploring bluetooth methodology. Others are relying on manual methods (i.e. phone calls).	• This area is ripe for standardization and new methods, especially those that address the key issues related to the appropriate management of privacy and personal health information, the ability to safely and securely provide this information to appropriate health officials to support decisions and attention to compliance of citizens with respect to sharing necessary contact information.
EHRs/Real World Evidence (e.g. Observational Research) and Epidemiology **D** **Blocks 2.2 - 2.6**	HL7 is the generally accepted standard in Spain, although this is not national policy. Common Data Models in use include OHDSI/OMOP and i2b2/ACT.	In Italy, digital health initiatives currently concern the following aspects: • Single Reservation Center (CUP) • Electronic Health Record (ESF) • Electronic disease certificates • ePrescription (electronic medical prescription) • Telemedicine	EHR data acquisition and storage models still vary by vendor and by implementation, necessitating use of Common Data Models for cross-EHR queries. Currently, various networks (PCORNet, OHDSI/OMOP, i2b2/ACT, Sentinel) conduct distributed studies using their own 'common data models' (CDM).	• Sharing data globally with one standard CDM would be optimal. • U.S. National COVID Cohort Collaborative (N3C) is trying to harmonize across networks using OMOP v5 as their common model. • NCATS and FDA Evidence Accelerator have done mapping across all CDMs and with CDISC and HL7 FHIR to support N3C. • HL7 V2 is still widely used for exchanging EHR data although FHIR use for a U.S. CORE dataset is now being required through HHS/ONC • Additional FHIR 'resources' would expand usefulness of FHIR for research.
Test Kits **A** **Blocks 2.2, 2.3**	In Spain the Ministry of health has the capacity of validation and authorization of testing and test kit validation	In Italy the tests are validated by the Public Health Institute (Istituto Superiore di Sanità) the scientific branch of the Ministry of Health	In the U.S. test kit validation and approval is the responsibility of the FDA CDRH (Center for Devices and Radiological Health).	• Expansion of testing • Faster tests and test results • More accurate tests • Standard definitions of which test data are to be combined, contrasted, compared and reported.

Category	Standards			Opportunities
	Spain	**Italy**	**U.S.**	
Regulated Clinical Research Studies (e.g. vaccines and treatments) **E** **Blocks 2.5, 2.6, 4**	EMA does not require that raw data be submitted for approvals of new therapies, but CDISC standards are acceptable AEMPS (Spanish Medicinal Products and Medical Devices Agency) is the public organization in charge to approve the different steps of the process	EMA does not require that raw data be submitted for approvals of new therapies, but CDISC standards are acceptable	CDISC standards are required for eSubmissions of data in support of new therapies and vaccines.	• CDISC global clinical research standards (SDTM, ADaM and define.xml) are required by the U.S. FDA and Japan's PMDA (and are endorsed by Europe, China) to submit data in support of new treatment and vaccine approvals. Collection of data using CDISC standards (CDASH) is strongly encouraged to minimize 'back-end' mapping and to enable direct cross-study comparisons of clinical trial results. • Standard controlled terminology complements the CDISC standards and is hosted by the NIH/NCI Enterprise Vocabulary Services. • A COVID-19 CDISC TA standard user guide has been published. The WHO/ISARIC/IDDO data collection forms have been annotated with CDISC elements and are in use by ~40 countries. • Master protocols can standardize research studies to simultaneously compare multiple therapies. These are being encouraged.
Clinical Trial Registration **F** **Blocks 2.5, 3, 4**	EMA's EudraCT and WHO International Clinical Trial Registry Platform (ICTRP)	EMA's EudraCT and WHO International Clinical Trial Registry Platform (ICTRP)	Clinicaltrials.gov; possibly also WHO International Clinical Trial Registry Platform (ICTRP)	• One standard can populate three international registries WHO ICTRP, EudraCT, ct.gov); all clinical trials in progress for new therapies and/or vaccines should be registered in at least one of these registries.
Public Health **G** **Blocks 2.2 – 2.6**	WHO/ISARIC Data Tool (case report form) available; annotated with CDISC standards	WHO/ISARIC Data Tool (case report form) available; annotated with CDISC standards	WHO/ISARIC Data Tool (case report form) available; annotated with CDISC standards	• Annotated case report form and mapping spreadsheet developed by CDISC are based on the 'data tool' developed by WHO/ISARIC/IDDO, which is in use by ~40 countries for COVID-19 research studies.
Adverse Events and Safety Surveillance **H** **Block 4**	Ministry of health In cooperation with health regions has a national strategy for adverse events (2015)	The National Scientific Health Committee and the high commissioner of civil protection in charge for the pandemic can suggests to the government the measures needed.	The OHDSI/OMOP data model and the U.S. Sentinel Network common data model have been used for this purpose.	• For pre-approval submissions, adverse events data submitted to FDA or Japan's PMDA, CDISC AE standards apply. • For safety surveillance, OMOP appears to be a global standard (although the Sentinel network uses a different CDM in the U.S.)