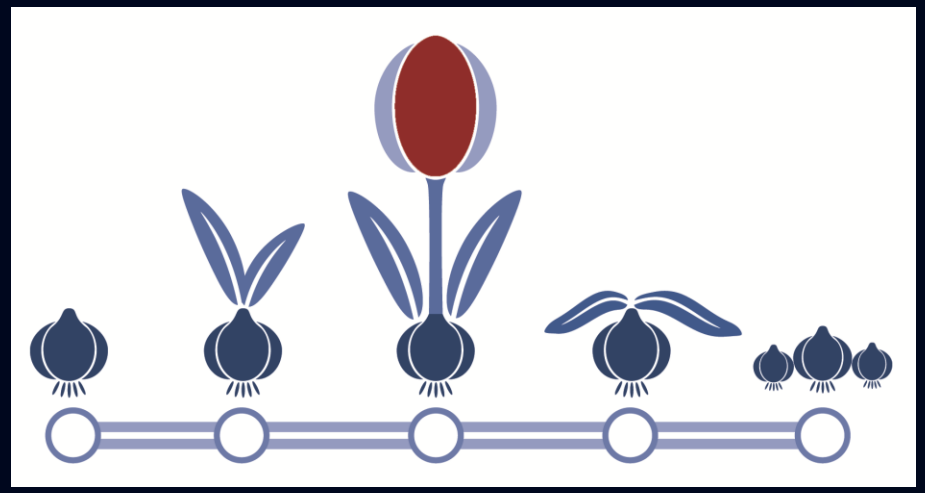
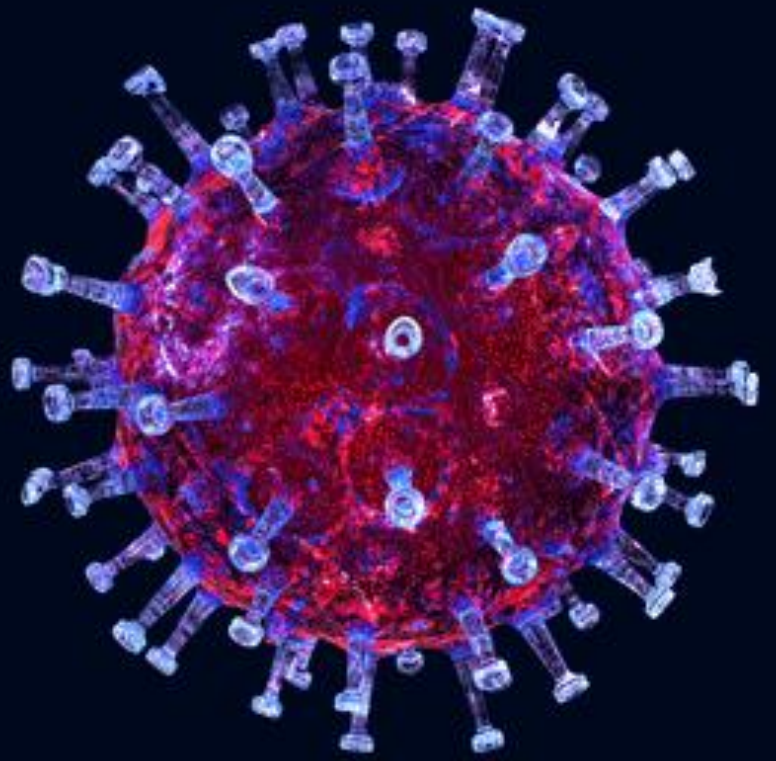




Alliance Project Update 4/1/2020

Joe Lennerz MD PhD

- An update on projects available through the *Alliance*,
- and instructions on how to get involved.

Collaboration

- The Alliance is a regulatory science initiative
- with many contributors
- Free
- Pre-competitive
- Temporary

- **Everyone makes a difference.**
- What have we accomplished?

DPA

COMMERCIAL

TCIA

MORE TO COME…

MDIC

ALLIANCE

TIL-WG

IRAC

WHO

NAME

CAP

NIH

FDA

ACADEMIC MEDICAL CENTERS

BIO-BANKS

ASTHO

Website

- Home Page
- New Navigation

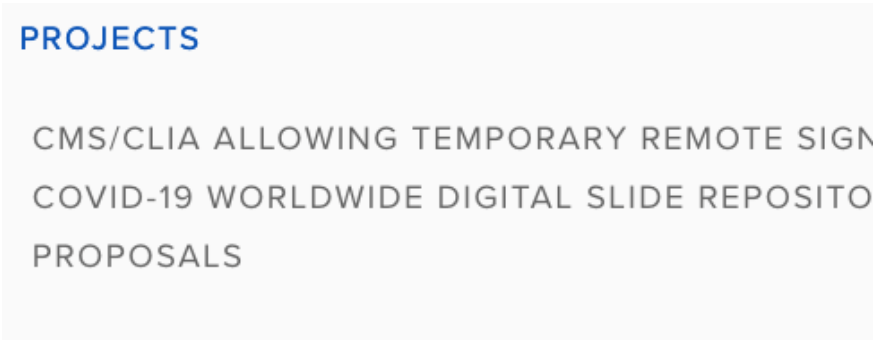
digitalpathologyalliance.org

Digitalpathologyalliance.org

MEETINGS & MEMOS PROJECTS

New! Catalogued meeting information

New! Project-specific pages



Code of Conduct

- Current Progress: https://digitalpathologyalliance.org/code-of-conduct

- Team Lead: JLENNERZ@PARTNERS.ORG

Joe Lennerz, MD, PhD

Center for Integrated Diagnostics
Department of Pathology
Massachusetts General Hospital

The Alliance for Digital Pathology

CODE OF CONDUCT

OUR PLEDGE

We as members, contributors, and leaders pledge to make participation in the Alliance for Digital Pathology, and all applicable sub-committees, a harassment-free experience for everyone, regardless of age, body, size, visible or invisible disability, ethnicity, sex characteristics, gender identity and expression, level of experience, education, socio-economic status, nationality, personal appearance, race, religion, or sexual identity and orientation. We pledge to act and interact in ways that contribute to an open, welcoming diverse, inclusive, and healthy community including.

Be friendly, humble, and patient.

Be considerate. Your work will be used by other people, and you in turn will depend on the work of others. Any decision you take will affect users and colleagues, and you should take those consequences into account when making decisions. Remember that we're a world-wide community, so you might not be communicating in someone else's primary language.

Be respectful. Not all of us will agree all the time, but disagreement is no excuse for poor behavior and poor manners. We might all experience some frustration now and then, but we cannot allow that frustration to turn into a personal attack. It's important to remember that a community where people feel uncomfortable or threatened is not a productive one. Members of the Alliance for Digital Pathology should be respectful when dealing with other members as well as with people outside the Alliance community.

Be careful in the words that you choose. We are a community of professionals, and we conduct ourselves professionally. Be kind to others. Do not insult or put down other participants. Harassment and other exclusionary behavior aren't acceptable.

OUR STANDARDS

Examples of behavior that contributes to a positive environment for our community include:

- Demonstrating empathy and kindness toward other people
- Being respectful of differing opinions, viewpoints, experiences and approaches
- Giving and gracefully accepting constructive feedback

Remote Signout

- Current Progress:
https://digitalpathologyalliance.org/remote-signout

- Team Lead:
sirintrs@mskcc.org

Joe Sirintrapun, MD
Director of Pathology Informatics
Diplomate, Clinical Informatics (ABMS)
Associate Attending
Department of Pathology
Memorial Sloan Kettering Cancer Center

Sending Letters to CMS

- **Many members of the Alliance helped draft multiple pathology society letters to engage CMS to temporarily relax CLIA regulations to enable pathologist to signout remotely.**
  - API
  - DPA
  - CAP

CMS exercises Enforcement Discretion

- **CMS exercises enforcement discretion to ensure pathologists may review pathology slides remotely if certain defined conditions are met during COVID-19 public health emergency**
  - https://www.cms.gov/files/document/qso-20-21-clia.pdf-0

The Alliance analyzes CMS' memorandum

- Part 1: Memo analysis from Dr. Richard Huang
- Part 2: Dr. Richard Huang answers Q&A
  - *"**Fortune favors the prepared.** For those institutions that invested early into establishing an on-site digital pathology signout system now gets to reap all the rewards of their proactive decisions. Their pathologists can fully take advantage of CLIA's enforcement discretion and start signing out remotely from home."*

DEPARTMENT OF HEALTH & HUMAN SERVICES
Centers for Medicare & Medicaid Services
7500 Security Boulevard, Mail Stop C2-21-16
Baltimore, Maryland 21244-1850

Center for Clinical Standards and Quality/Survey & Certification Group

Ref: QSO-20-21-CLIA

DATE: **March 26, 2020**

TO: State Survey Agency Directors

FROM: Director
Quality, Safety & Oversight Group

SUBJECT: Clinical Laboratory Improvement Amendments (CLIA) Laboratory Guidance During COVID-19 Public Health Emergency

Memorandum Summary

- CMS is issuing this memorandum to laboratory surveyors to provide important guidance to surveyors and laboratories during the COVID-19 public health emergency, such as:
  - CMS' Exercise of enforcement discretion to ensure pathologists may review pathology slides remotely if curtained defined conditions are met ,
  - Ensuring that laboratories located in the United States wishing to perform COVID-19 testing that apply for CLIA certification are able to begin testing as quickly as possible during the public health emergency,
  - Highlighting that laboratories within a hospital/University Hospital Campus may hold a single certificate for the laboratory sites within the same physical location or street address,
  - Offering enforcement discretion as to Proficiency Testing (PT) During the duration of the Public Health Emergency,
  - Addressing alternate Specimen Collection Devices, and
  - Addressing Laboratory Developed Tests

- *CMS is committed* to taking critical steps to ensure America's clinical laboratories are prepared to respond to the threat of 2019 Novel Coronavirus (COVID-19) and other respiratory illnesses to ensure reliable testing as well as ensuring patient health and safety.

- All guidance in this memorandum is applicable only during the COVID-19 public health emergency.

- Laboratories that are accredited must follow their accrediting organization (AO) requirments and must follow applicable State laws, which may be more stringent than the CLIA requirements.

- The CLIA program is unable to approve section 1135 waiver requests with respect to waivers of CLIA program requirements. The section 1135 waiver authority is only applicable to specified programs (or penalties) authorized by the Social Security Act (SSA). The CLIA program does not fall into this category of programs.

Validating Whole Slide Imaging (WSI) for Diagnostic Purposes in Pathology Guideline[1]

Summary of Recommendations

Guideline Statements

1. *Expert consensus opinion:* All pathology laboratories implementing WSI technology for clinical diagnostic purposes should carry out their own validation studies.
2. *Recommendation:* Validation should be appropriate for and applicable to the intended clinical use and clinical setting of the application in which WSI will be employed. Validation of WSI systems should involve specimen preparation types relevant to intended use (eg, formalin-fixed paraffin-embedded tissue, frozen tissue, immunohistochemical stains, cytology slides, hematology blood smears).
   Note: If a new intended use for WSI is contemplated, and this new use differs materially from the previously validated use, a separate validation for the new use should be performed.
3. *Recommendation:* The validation study should closely emulate the real-world clinical environment in which the technology will be used.
4. *Recommendation:* The validation study should encompass the entire WSI system.
   Note: It is not necessary to validate separately each individual component (eg, computer hardware, monitor, network, scanner) of the system nor the individual steps of the digital imaging process.
5. *Expert consensus opinion:* Revalidation is required whenever a significant change is made to any component of the WSI system.
6. *Recommendation:* A pathologist(s) adequately trained to use the WSI system must be involved in the validation process.
7. *Recommendation:* The validation process should include a sample set of at least 60 cases for one application (eg, H&E stained sections of fixed tissue, frozen sections, cytology, hematology) that reflects the spectrum and complexity of specimen types and diagnoses likely to be encountered during routine practice.
   Note: The validation process should include another 20 cases for each additional application (eg, immunohistochemistry, special stains).
8. *Suggestion:* The validation study should establish diagnostic concordance between digital and glass slides for the same observer (ie, intraobserver variability).
9. *Recommendation:* Digital and glass slides can be evaluated in random or nonrandom order (as to which is examined first and second) during the validation process.
10. *Recommendation:* A washout period of at least 2 weeks should occur between viewing digital and glass slides.
11. *Expert consensus opinion:* The validation process should confirm that all of the material present on a glass slide to be scanned is included in the digital image.
12. *Expert consensus opinion:* Documentation should be maintained recording the method, measurements, and final approval of validation for the WSI system to be used in the clinical laboratory.

[1]Pantanowitz L, Sinard JH, Henricks WH, et al. Validating whole slide imaging for diagnostic purposes in pathology: Guideline from the College of American Pathologists (CAP) Pathology and Laboratory Quality Center. *Arch Pathol Lab Med*. doi: 10.5858/arpa. 2013-0093-CP. Effective date: May 1, 2013.

Validation Approach Outline

- Current Progress:

https://digitalpathologyalliance.org/

- Team Lead:

RHUANG6@mgh.harvard.edu

Richard Huang, MD

Clinical Informatics Fellow
Department of Pathology
Massachusetts General Hospital

cap

Validating Whole Slide Imaging (WSI) for Diagnostic Purposes in Pathology Guideline[1]

Summary of Recommendations

https://webapps.cap.org/apps/docs/membership/wsi_validation_summary.pdf

There are other ways to validate your system.

Validation approach is ultimately at the discretion of the lab's medical director and applicable laws and regulations.

From QSO-20-21-CLIA:
"Laboratories that are accredited must follow their accrediting organization (AO) requirements and must follow applicable State laws, which may be more stringent than the CLIA requirements."

- Current Progress:

https://digitalpathologyalliance.org/covid19

- Team Leads:

MDHERRMANN@PARTNERS.ORG
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Department of Pathology
Massachusetts General Hospital

Matt@Lumea.org
Matt Leavitt
Pathologist
Chief Medical Officer
Lumea

ALO@visiopharm.com
Amanda Lowe
Managing Director, Americas
Visiopharm Corporation

The Alliance sent out an e-mail to everyone on the mailing list about this effort. Please check your inbox (including spam folder).

I WANT TO HELP. WHAT CAN I DO RIGHT NOW?

Thank you! This is a rapidly evolving environment and your patience and support as a collaborator are greatly appreciated. To get started please,

- Answer this short Questionnaire >> CLICK HERE. It will take less than 2-minutes.

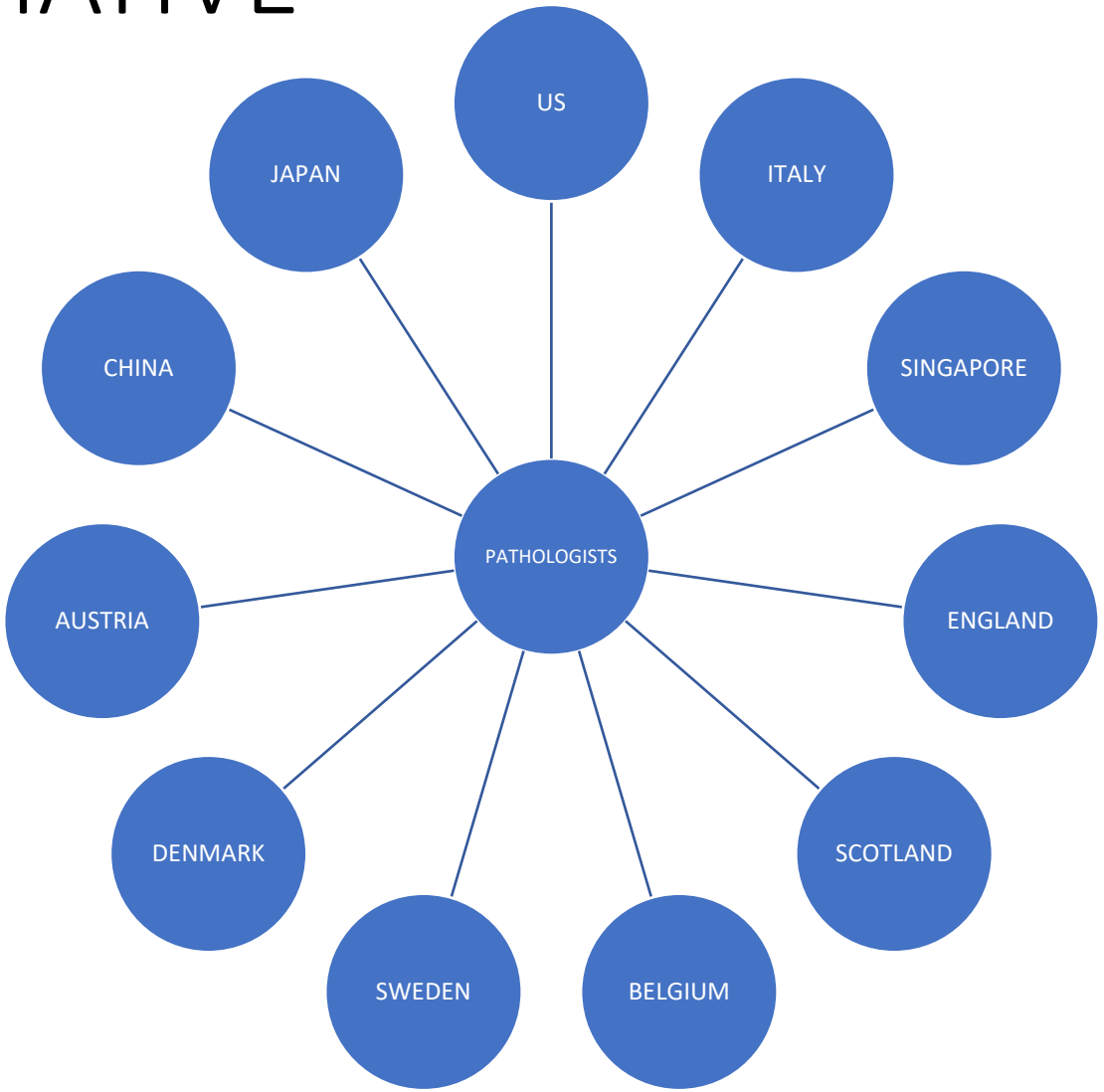
  Questionnaire Link:
  https://forms.office.com/Pages/ResponsePage.aspx?id=0XsL3p61F0aFaiWhO9m69d9QWI1ILdlPmIRUnz1tCr9UMkJDWEIxSVMzTU9NTzgyVU1RWjEzMzhCTC4u

- If you have access to COVID-19 tissue samples, and the ability to digitize samples in form of WSI, please contact us immediately at

  data-repository@digitalpathologyalliance.org.

- Spread the word! Forward this email, engage others on social media, and let your colleagues around the world know about this effort.

GLOBAL INITIATIVE



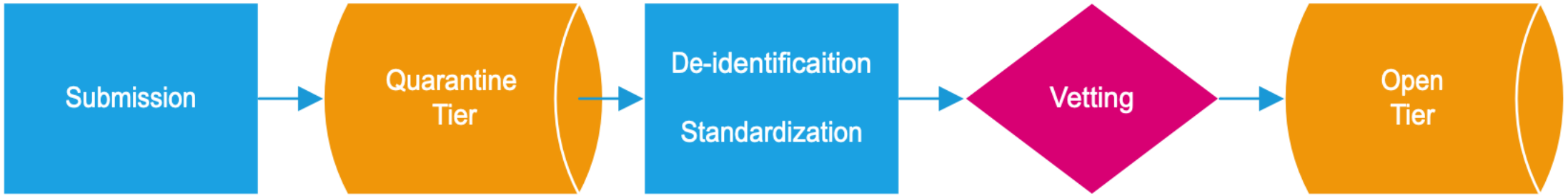
MORE TO COME..

Data Management, De-identification and Curation

Public, international data repository

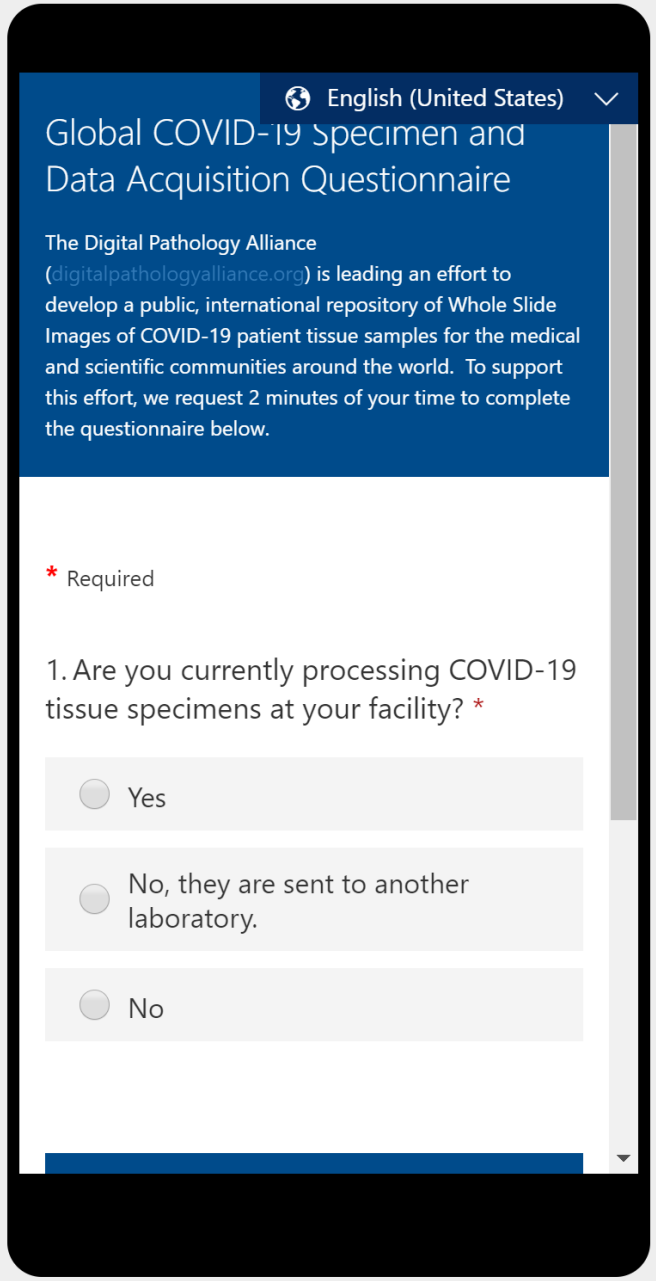
- Public domain
- Free of charge
- Open source license (Creative Commons)
- Harmonized
- Fully de-identified in compliance with applicable rules and regulations (HIPAA, GPPR)
- Open, standard, vendor-neutral format (DICOM)

Two-tier data management



COLLABORATION GROWTH

Please distribute and advocate for our very brief survey!



https://www.fda.gov/emergency-preparedness-and-response/counterterrorism-and-emerging-threats/coronavirus-disease-2019-covid-19

New mailboxes in the FDA.

Use the following emails:

- CDRH-EUA-Templates@fda.hhs.gov for diagnostic enquiries and EUAs
- CDRH-NondiagnosticEUA-Templates@fda.hhs.gov for non diagnostic enquiries and EUAs
- DeviceShortages@fda.hhs.gov is the industry hotline for shortages
- COVIDManufacturing@fda.hhs.gov for any manufacturing/ 3D printing/ testing and specifications etc

https://www.fda.gov/emergency-preparedness-and-response/counterterrorism-and-emerging-threats/coronavirus-disease-2019-covid-19

FDA-ARGOS SARS-CoV-2 Reference Grade Sequence Data

Share | Tweet | Linkedin | Email | Print

On March 11, 2020, the World Health Organization declared COVID-19 a pandemic. The President of the United States declared a national emergency on March 13, 2020, in response to the COVID-19 outbreak in the United States. This public health emergency has led to an unprecedented number of Emergency Use Authorizations (EUAs) for COVID-19 diagnostic tests.

https://argos.igs.umaryland.edu/

Update on COVID19 serologic testing at MGH

Results from head-to-head validation of available ELISAs and Point of Care Tests to detect SARS-CoV-2 antibodies

Thursday, April 2nd, 2:00 PM

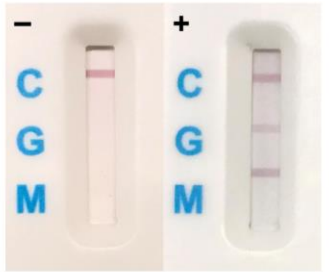
https://partners.zoom.us/j/441173684

Outline validation strategies for serology assays

IgM, IgA, and IgG antibodies during pandemic.

COVID-19 antibody status useful for:

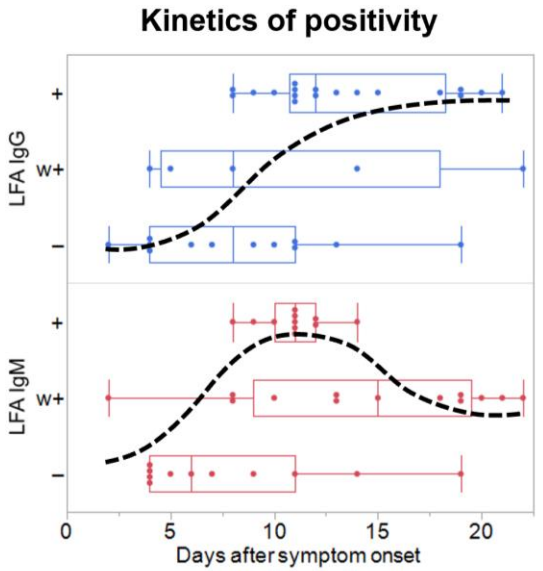
- Prevalence of disease exposure in population
- Potentially identifying individuals with immunity
- Return-to-work criteria
- State of disease response in individuals
- Identifying high-titer donors for therapeutic plasma



10 min
Sensitivity of detection

Symptoms	IgM+	IgG+	IgG+ or IgM+
≤7 days	**13%** (1/8)	**25%** (2/8)	**38%** (3/8)
>7 days	**85%** (23/27)	**78%** (21/27)	**89%** (24/27)

Specificity = 100% (0/30)



Presented by:
John Iafrate MD, PHD
Tyler E. Miller, MD, PhD
Wilfredo Garcia Beltran, MD, PhD

MASSACHUSETTS GENERAL HOSPITAL PATHOLOGY

Advancing Diagnosis and Discovery

HARVARD MEDICAL SCHOOL

“RuleOut” COVID19

Current Progress:

ruleout.org

Monica.deBaca.MD@ruleout.org

COVID-19 Decentralized Testing Proposal

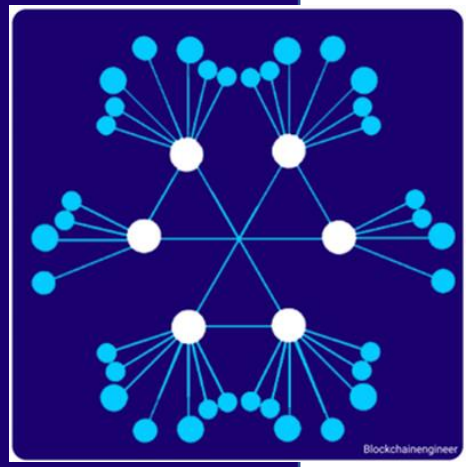
“We propose a ‘Rule-Out’ Lab Developed Test (LDT) and regulatory framework which is readily implementable”

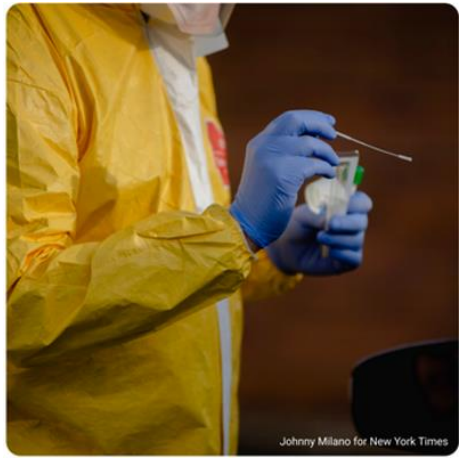
The Problem: Conventional Testing Doesn’t Scale

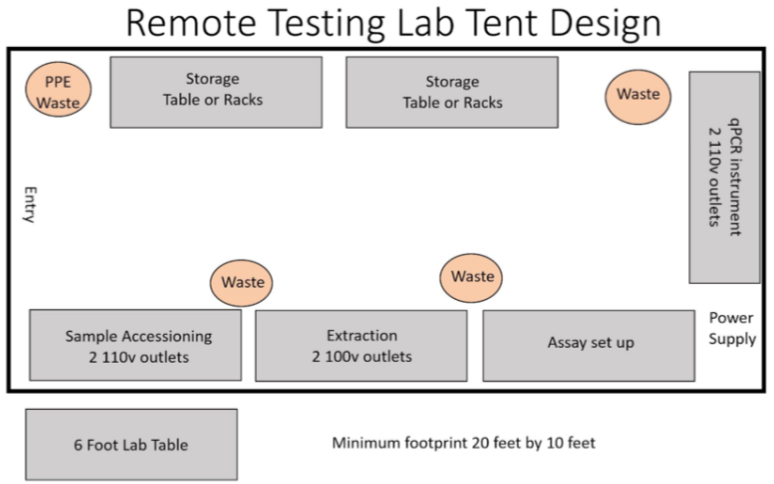
- Crucial testing shortage
- Conventional testing = “Rule-in”
- Massive backlogs

The Solution: a “Rule-Out” LDT with Regulatory Framework

- Decentralized “Rule-out” testing
- Exponential increase in testing capacity
- Conservation of critical supplies







World Health Organization

A COORDINATED GLOBAL RESEARCH ROADMAP: 2019 NOVEL CORONAVIRUS

MARCH 2020

There is broad consensus on the need for research to: focus on actions that can save lives now; facilitate actions so that those affected are promptly diagnosed and receive optimal care; and catalyse the full integration of all innovations within each research area.

Moreover, there is an imperative to support research priorities in a way that leads to the development of sustainable global research platforms pre-prepared for the next disease X epidemic. This will allow for accelerated research, innovative solutions and R&D of diagnostics, therapeutics and vaccines, as well as the timely and equitable access to these life-saving tools for those at highest risk.

R&DBlueprint
Powering research to prevent epidemics

https://www.who.int/blueprint/priority-diseases/key-action/novel-coronavirus/en/

COVID-19 Public Health Emergency of International Concern (PHEIC)

Global research and innovation forum: towards a research roadmap

On 30 January 2020, following the recommendations of the Emergency Committee, the WHO Director-General declared that the outbreak constitutes a Public Health Emergency of International Concern (PHEIC).

World scientists on COVID-19 met at the World Health Organization's Geneva headquarters from 11 to 12 February 2020 to assess the current level of knowledge about the new virus, agree on critical research questions that need to be answered urgently, and ways to work together to accelerate and fund priority research that can contribute to curtail this outbreak and prepare for future outbreaks.

- 2019 Novel Coronavirus: Global Research and Innovation Forum: Towards a Research Roadmap/report
  pdf, 431kb
- 2019 Novel Coronavirus: Overview of the state of the art and outline of key knowledge gaps/slides
  pdf, 3.89Mb
- A coordinated Global Research Roadmap
  pdf, 800kb

Latest reports

Vaccines

- Draft landscape of COVID-19 candidate v
  pdf, 595kb
  26 March 2020
- COVID-19 Phase IIb/III Vaccine Trial Syn
  pdf, 667kb
  February 2020
- Informal consultation on prioritization of c
  novel coronavirus 2019 infection
  pdf, 645kb
  30 January 2020

2019 NOVEL CORONAVIRUS GLOBAL RESEARCH AND INNOVATION FORUM: TOWARDS A RESEARCH ROADMAP

About this document

On 11-12 February 2020, WHO, in collaboration with the Global Research Collaboration for Infectious Disease Preparedness and Response (GLOPID-R) – an international network of funders to facilitate coordination and information sharing, organized a Global Forum on research and innovation for COVID-19 ('Global Research Forum').

COVID-19 EVIDENCE ACCELERATOR

FRIEND OF CANCER RESEARCH

=PATIENT ADVOCACY GROUP

Working with the FDA

1) Establish a common set of core data elements to embed into existing data collection efforts;

2) Identify an initial set of immediate questions regarding the therapeutic interventions, treatment settings, and associated outcomes that could be the initial focus of COVID-19 data aggregation efforts.

Team Lead

jallen@focr.org

Jeff Allen, PhD

President & CEO

Payor Approaches

- Current Progress:

https://digitalpathologyalliance.org/feb-2020

- Team Leads:

esther.abels@pathai.com

Esther Abels

VP Regulatory Affairs, Clinical Affairs,
Strategic Business Development
PathAI

JLENNERZ@PARTNERS.ORG

Joe Lennerz, MD, PhD

Center for Integrated Diagnostics
Department of Pathology
Massachusetts General Hospital

During the Alliance 2020 workshop we had two goals:

Develop an overview of all entities and stakeholders involved in reimbursement for Digital Pathology (DP)

Kick off the development of a whitepaper.

An overview of stakeholders will be one of the key inputs for the whitepaper.

The whitepaper will outline:

- Current reimbursement landscape
- Concerns from users
- Value proposition
- Areas of focus for getting DP reimbursed

Payor Whitepaper status and progress

- Engaged interactive discussion with over 15 participants from different entities
- Outline of whitepaper has been agreed upon:
  - **Objective:** provide guidance to broader digital pathology community to how to build buy in for adoption of these technologies (industry, pathologists)
  - **Introduction:** current status of reimbursement in DP, stakeholders, why its needed for adoption (ROI)
  - **Potential Sources of Value of Digital Pathology:** Workflow efficiency, accuracy/precision (reduction in intra-pathology scoring/interperson), and novel information., make clear need both clinical and economic arguments
  - **Need for evidence:** establish limitations of current care paradigm , what outcomes do we measure,, build towards patient care about outcomes
  - **Reimbursement:** need new CPT codes for digital techniques (indication specific), move from cost to value, re-examination of value of pathology services beyond slide reading into integration of complex services and time, novel information provides could get PLAs, consider parallel review FDA+CMS
  - **Approaches:** suggest next steps and identify key use cases, clinical utility and approaches to new codes / PLA, and / or need for policy changes
- First draft is being developed. Expected timeline and Journal TBD-ed

AIDA

- Current Progress:

https://medtech4health.se/en/aida-en-2/

- Team Lead:

Joel Hedlund, PhD

CIO/Data director
CMIV/AIDA

Medtech 4 Health

Analytic Imaging Diagnostics Arena, AIDA

AIDA is a Swedish arena for research and innovation on artificial intelligence, AI, for medical image analysis. Here, academia, healthcare and industry meet to translate technical advances in AI technology into patient benefit in the form of clinically useful tools. AIDA is an initiative within the Strategic innovation program Medtech4Health, jointly supported by VINNOVA, Formas and the Swedish Energy Agency.

Opportunities for Funding

Several support opportunities are available for efforts within the AIDA area. Both in the form of funding and as unique prerequisites for method and knowledge development. AIDA is now accepting applications for new innovation projects with a time span of up to two years, Apply

Truthing Project

- Current Progress:
  - https://ncihub.org/groups/eedapstudies/wiki/HighThroughputTruthingYear3
- Team Lead:
  - Brandon.gallas@fda.hhs.gov
  - Brandon D. Gallas, PhD
  - Division of Imaging, Diagnostics, and Software Reliability, OSEL, CDRH, FDA

Data-collection information webinar
- Feb. 19, 2020
- Recording and slides available

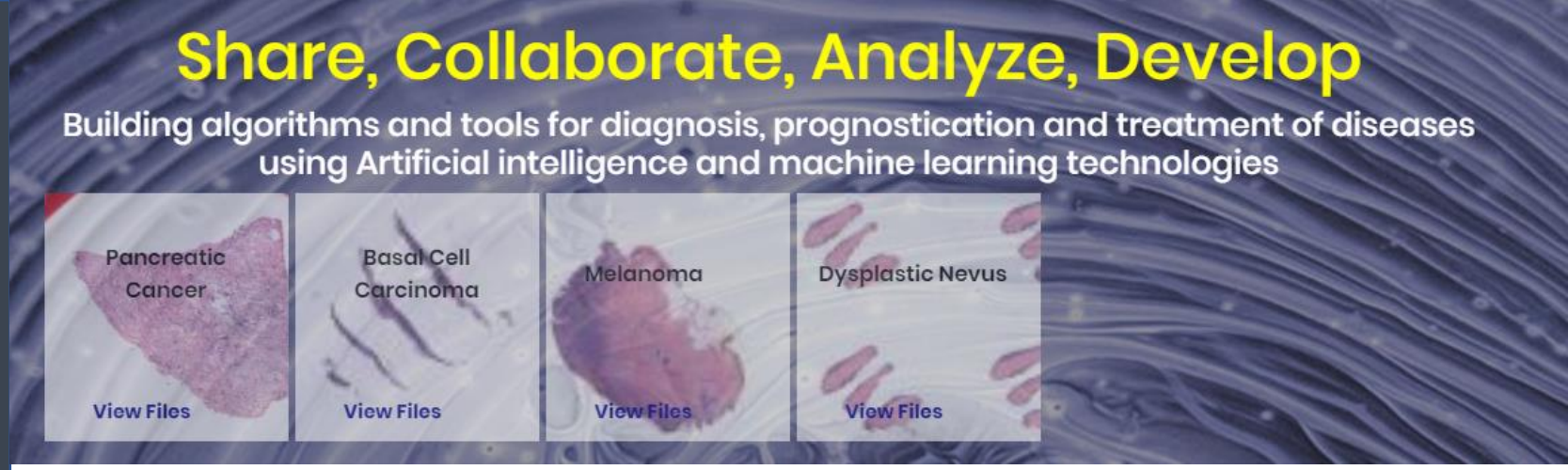
Data-collection event
- Feb. 28, 2020: Coordinated with Alliance meeting pre-USCAP in LA

Data-collection progress
- Building APIs and scripts to monitor data collection
- Building scripts to clean the data
- Building scripts to explore the data

- Planning live data-collection events put on hold
  - Road trips and equipment shipping
- Focus on digital data collection
  - Remind participants to finish. Recruit more participants.

DATA COLLECTION PROGRESS	PathP (digital platform)	Camicro (digital platform)	Eedap (microscope platform)
nReaders	4	8	7
nObs USCAP	850	300	440
nObs since USCAP	0	451	0
nObs Total	850	751	440

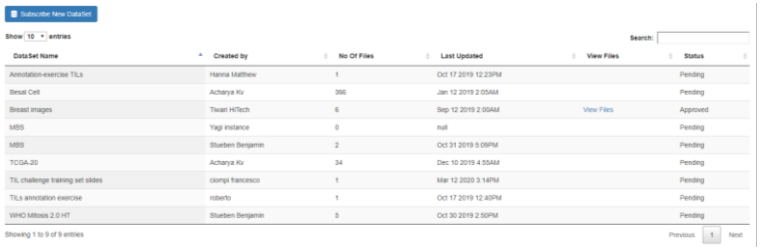
PathPresenter



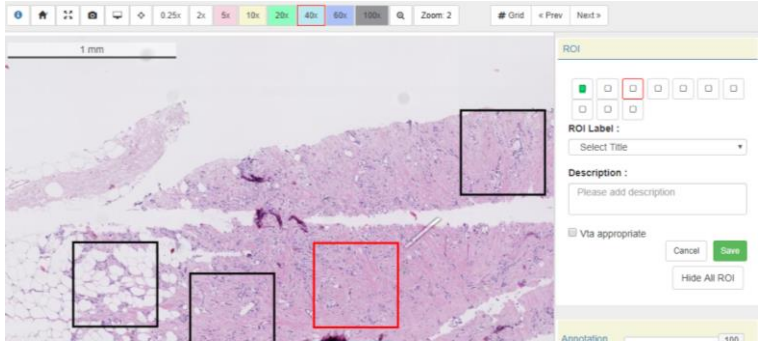
- Current Progress:
https://pathpresenter.net/#/login

- Team Lead:
skinpathology@gmail.com

Rajendra Singh, MD
Professor
Director, Immunodermatology
Associate Director, Dermatopathology Section
Dermatopathology Fellowship Program Director
Dept. Of Pathology and Dermatology
Mt. Sinai School of Medicine



Share, Subscribe and Control Image Database Access



Annotate Images

Collaborate, Share and Educate

IC3R

International Agency Research on Cancer

World Health Organization

- Current Progress:

https://journals.sagepub.com/doi/full/10.1177/1010428320907544

- Team Lead:

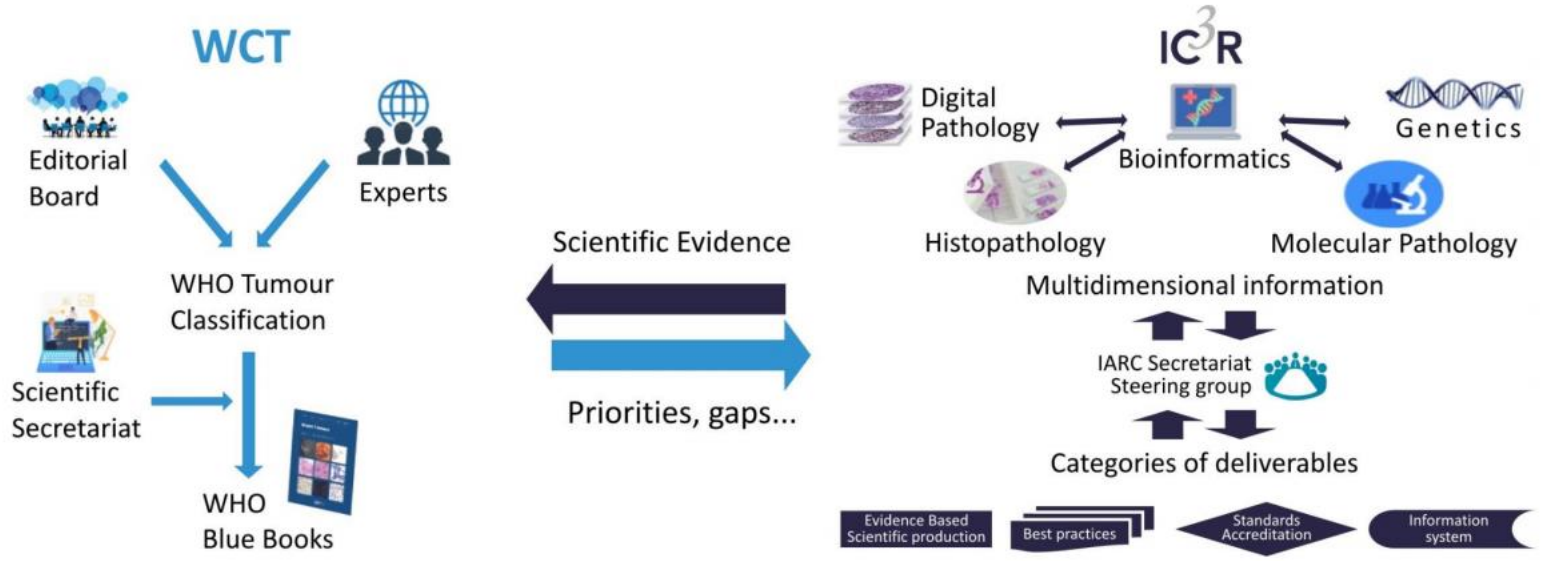
https://www.iarc.fr/staff_member/blanca-indave-ruiz/

Iciar Indave

Systematic Reviewer
Group on Classification of Tumours Series
International Agency for Research on Cancer
World Health Organization

The International Collaboration for Cancer Classification and Research (IC3R) is a forum for high-quality research, and for coordinating evidence generation, synthesis, and evaluation, for tumor classification.

Member institutions coordinate the provision of evidence and the promotion of universal standards underpinning WHO Classification of Tumours.



Become an Alliance Member

Join the Alliance

https://digitalpathologyalliance.org/

The benefits of membership:

- Contribute to the latest Alliance projects
- Direct e-mail updates from the Alliance
- View all previous presentations and meeting summaries