Health regulations and essential changes derived from Covid-19

Webinar of the IBA Healthcare and Life Sciences Committee

Tuesday 29 September 2020

15.00 – 16.00 BST

Health regulations and essential changes derived from Covid-19

The webinar is part of a series of webinars, organized by the Healthcare and Life Sciences Committee, that intends to capture the influence of the Covid-19 pandemic on the regulatory approval paths for medicine, medical devices, diagnostics and vaccines; as well as on clinical trials around the world.

Topics to be discussed will include:

- The policy that enabled Uruguay to successfully deal with the pandemic
- Clinical trial in the time of Covid-19
- The response of the regulators to covid-19 drug and vaccine approval
- Insights from the industry

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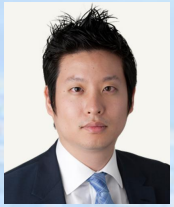
Moderator & Speakers

Sharon Gazit - Goldfarb Seligman & Co. - Israel

Dianne Bourque - Mintz - Boston, Massachusetts

Prof. Henry Cohen - Member, Honorary Scientific Committee - Uruguay

Thomas Lönngren - NDA Group - Upsalla, Sweden



Shohta Ueno - Regeneron - London, UK

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Speaker

Prof. Henry Cohen

Uruguay: a successful experience

Webinar: Health regulations
The essential changes deriving from Covid-19
IBA Healthcare and Life Sciences Committee

Henry Cohen, MD, FACG, AGAF, MWGO
Health Coordinator of the Honorary Scientific Advisory Group (GACH) appointed by the Uruguayan President to address the Covid-19 pandemic

September 29, 2020

GACH

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Uruguay

- 176 000 km^2
- 3 500 000 inhabitants (half in Montevideo)
- “Dry” border with Brazil: 600 km

March 1st, 2020
New government takes office

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March 13th: First cases in Uruguay

MSP - Uruguay
@MSPUruguay

Se confirmaron los primeros 4 casos de Coronavirus Covid-19. Todos procedentes de Milán, habiendo ingresado al país entre el 3 y 6 de marzo. Los pacientes se encuentran estables y en domicilio. Este Ministerio está haciendo el control de trazabilidad de su entorno. (Sigue)

3.589 personas están hablando de esto

Early Government's Decisions

- March 13th: Health emergency declaration, establishment of mandatory quarantine for travellers coming from at-risk countries
- The population was urged to avoid crowded places
- March 14th: Suspension of classes at all levels, public and private

Characteristics of this fase

Transparency

Freedom with responsibility

The most difficult decision: no mandatory lockdown

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The first month in Uruguay

Physical Distancing

- Strong “stay at home” directives from the government
- Massive voluntary response

Tracing, Testing and Isolation

- Initially testing capacity was limited
- Tracing “muscle” had to be developed on the fly
- Isolation: widespread availabilty of home medicine, testing at home

Can we open up? Ask the scientists

April 16th: President Lacalle creates an Honorary Scientific Advisory Group (GACH) that reports directly to the Executive

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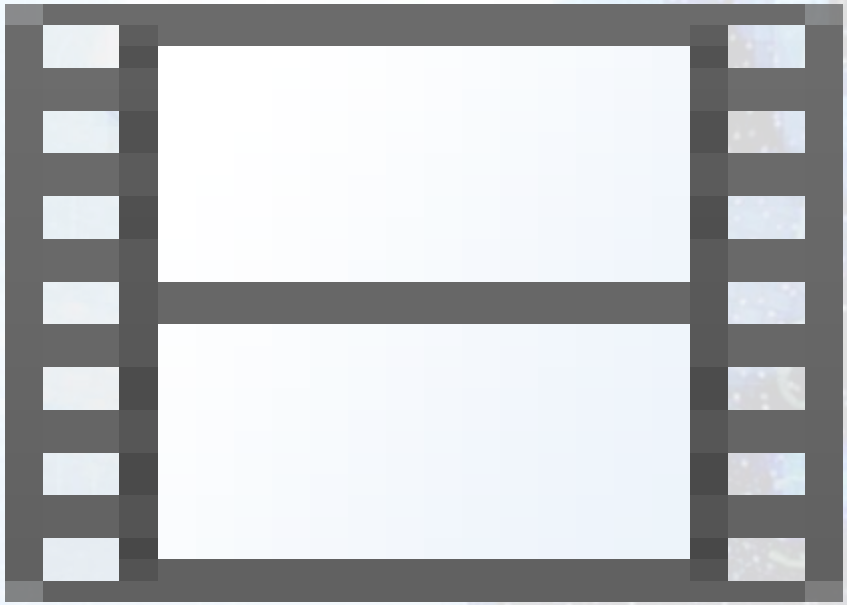
GACH

- The GACH plays an exclusively advisory role: the final decisions are up to the government
- We put together teams including 55 *pro bono* experts in different areas, under two big working fields: health planning and mathematical models and data science
- Main duty: to advise the government:
  - on the management of the pandemic
  - how to transit to the "New Normal". Changing the message: from "Stay home" to "SPD" (Sustained Physical Distancing)

President Lacalle on progressive reopening:

“We will move forward as much as possible, but we will go backwards every time we need, because health is still, the most important”



GACH: Main recommendations

- Resume activities following these criteria: progessiveness,
- regulation, monitoring and evidence-based
- No political interference
- Weekly reports (> 30)
- School opening
- Sustained Physical Distancing (2 m.), wearing masks,
- wash hands, ventilation, concept of time
- Responsible use of public spaces
- Increase tracing, testing and isolation
- New tests: serology, LAMP, sequencing,
- Relations with media

Scientists' contributions

- Local development and manufacturing of excellent quality and quantity PCR tests, with results in 24-48 hs.
- Same for serology (250 000 tests for antibody detection available) and LAMP
- New tests in development (saliva, quick tests)
- Sequencing of viral genomes (molecular epidemiology, 5th in the world)
- Wastewater studies

Current Situation

Coronavirus cases in Latin America, September 11

The region has reported an average of more than 67 000 daily cases in the last seven days, for a total of 8 000 000 cases and 300 000 deaths

Uruguay: current data (September 12th)

- Total cases: 1 780
- Total deaths: 45
  (75% > 65 y.o., 80% men)
- Lethality: 2.53%
- Mortality: 1.28 per 100 000
- Admitted: 18

- ICU: 1
- Active cases: 233; recovered 1 502
- Total tests: 196 892 (5.6% of the total population)
- % of positive tests: 0.9%
- Health care workers: 276 (15.5%), one death

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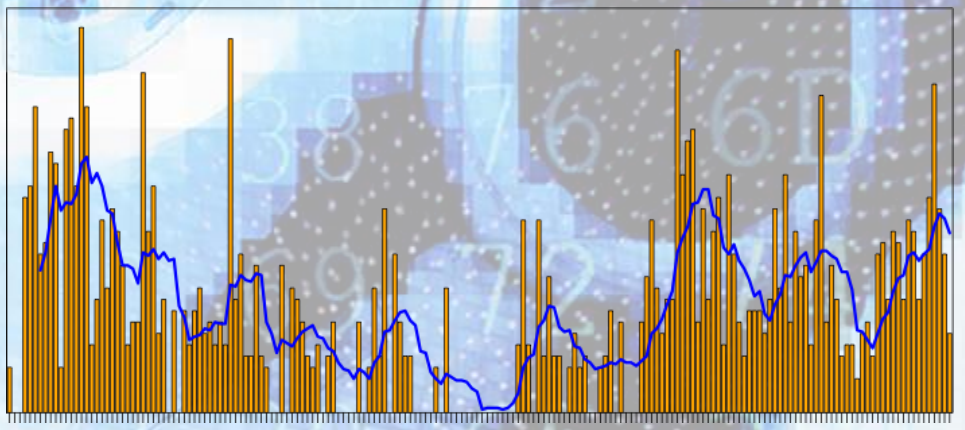
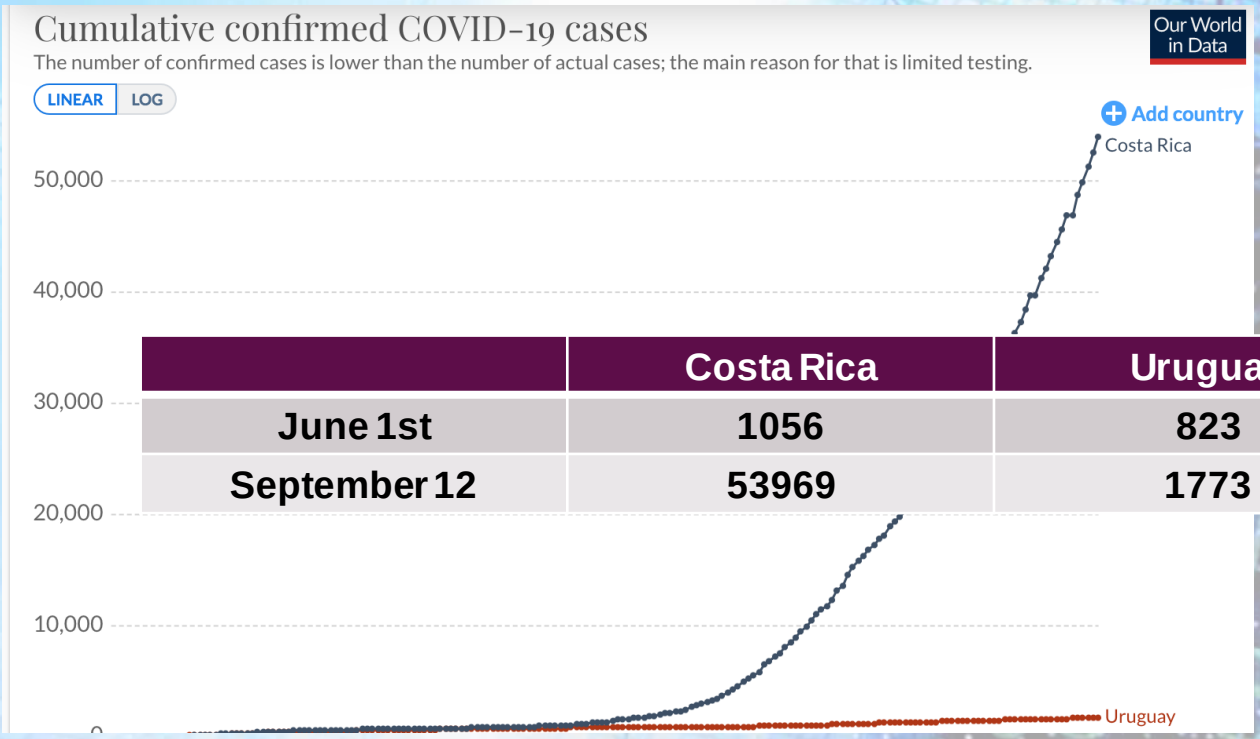
Luckily, we remain "dancing" under control

- We avoided exponential growth, within TTI capacity limits
- New activities are opening, always under distancing protocols
- Threats abound: border, uncontrolled private gatherings…





	Costa Rica	Uruguay
June 1st	1056	823
September 12	53969	1773

But the equilibrium is fragile…

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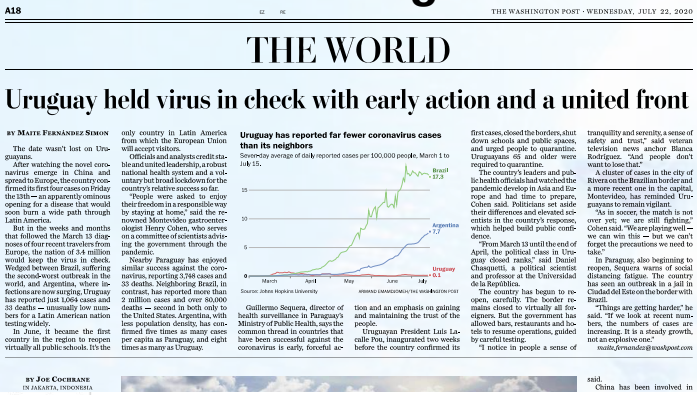
The next few months

- We hope to sustain the current situation: low case and deaths counts, recurrent outbreaks manageable by TTI
- "If not, backsteps may be needed"
- Avoid:
  - Reacting too early: confinement upon each minor outbreak
  - Reacting too late: cases building up beyond TTI capability
- End of the year brings new pressures: summer tourism, mainly from our neighbors. Can we allow it?
- Our future is tied to the rest of Latin America, hopefully improving!

Uruguay in the media

The Washington Post



A18 THE WASHINGTON POST · WEDNESDAY, JULY 22, 2020

THE WORLD

Uruguay held virus in check with early action and a united front

BY MAITE FERNÁNDEZ SIMON

The date wasn't lost on Uruguayans.

After watching the novel coronavirus emerge in China and spread to Europe, the country confirmed its first four cases on Friday the 13th — an apparently ominous opening for a disease that would soon burn a wide path through Latin America.

But in the weeks and months that followed the March 13 diagnoses of four recent travelers from Europe, the nation of 3.4 million would keep the virus in check. Wedged between Brazil, suffering the second-worst outbreak in the world, and Argentina, where infections are now surging, Uruguay has reported just 1,064 cases and 33 deaths — unusually low numbers for a Latin American nation testing widely.

In June, it became the first country in the region to reopen virtually all public schools. It's the only country in Latin America from which the European Union will accept visitors.

Officials and analysts credit stable and united leadership, a robust national health system and a voluntary but broad lockdown for the country's relative success so far.

"People were asked to enjoy their freedom in a responsible way by staying at home," said the renowned Montevideo gastroenterologist Henry Cohen, who serves on a committee of scientists advising the government through the pandemic.

Nearby Paraguay has enjoyed similar success against the coronavirus, reporting 3,748 cases and 33 deaths. Neighboring Brazil, in contrast, has reported more than 2 million cases and over 80,000 deaths — second in both only to the United States. Argentina, with less population density, has confirmed five times as many cases per capita as Paraguay, and eight times as many as Uruguay.

Uruguay has reported far fewer coronavirus cases than its neighbors

Seven-day average of daily reported cases per 100,000 people, March 1 to July 15.

Source: Johns Hopkins University

Guillermo Sequera, director of health surveillance in Paraguay's Ministry of Public Health, says the common thread in countries that have been successful against the coronavirus is early, forceful action and an emphasis on gaining and maintaining the trust of the people.

Uruguayan President Luis Lacalle Pou, inaugurated two weeks before the country confirmed its first cases, closed the borders, shut down schools and public spaces, and urged people to quarantine. Uruguayans 65 and older were required to quarantine.

The country's leaders and public health officials had watched the pandemic develop in Asia and Europe and had time to prepare, Cohen said. Politicians set aside their differences and elevated scientists in the country's response, which helped build public confidence.

"From March 13 until the end of April, the political class in Uruguay closed ranks," said Daniel Chasquetti, a political scientist and professor at the Universidad de la República.

The country has begun to reopen, carefully. The border remains closed to virtually all foreigners. But the government has allowed bars, restaurants and hotels to resume operations, guided by careful testing.

"I notice in people a sense of tranquillity and serenity, a sense of safety and trust," said veteran television news anchor Blanca Rodríguez. "And people don't want to lose that."

A cluster of cases in the city of Rivera on the Brazilian border and a more recent one in the capital, Montevideo, has reminded Uruguayans to remain vigilant.

"As in soccer, the match is not over yet; we are still fighting," Cohen said. "We are playing well — we can win this — but we can't forget the precautions we need to take."

In Paraguay, also beginning to reopen, Sequera warns of social distancing fatigue. The country has seen an outbreak in a jail in Ciudad del Este on the border with Brazil.

"Things are getting harder," he said. "If we look at recent numbers, the numbers of cases are increasing. It is a steady growth, not an explosive one."

maite.fernandez@washpost.com

BY JOE COCHRANE
IN JAKARTA, INDONESIA

said.

China has been involved in

Canal 4, Uruguay

BBC

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Coronavirus en Uruguay: la singular y exitosa estrategia del país para contener la pandemia sin cuarentena obligatoria

Redacción*
BBC News Mundo

29 mayo 2020

Compartir

La Tercera, Chile

LT DOMINGO LT Domingo

Columna de Mario Vargas Llosa: El ejemplo uruguayo

Los fallecidos en Uruguay por obra de la plaga son 23 personas; los contagiados, 826, y los recuperados, 689. Difícil imaginar un balance menos trágico.

Mario Vargas Llosa **6 JUN 2020** 09:13 PM

Why has Uruguay been successful up to now?

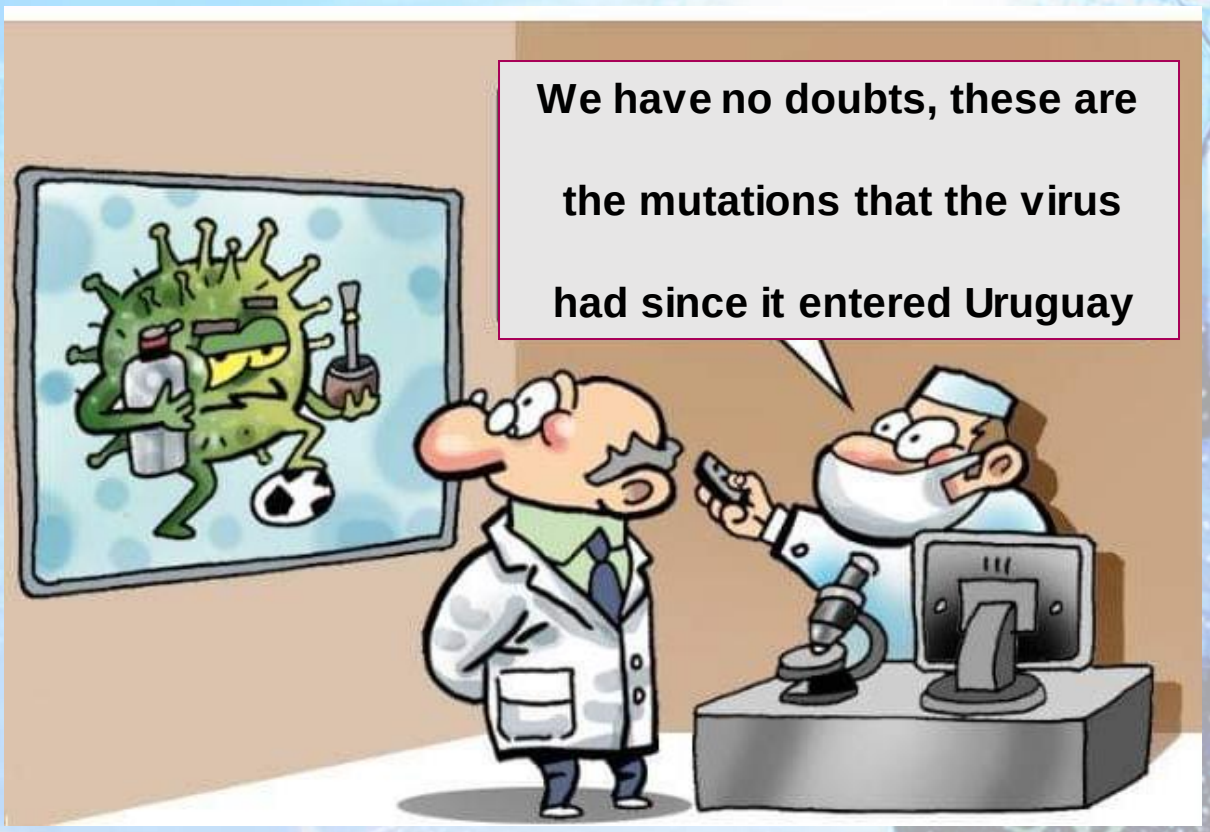
- Relatively small popul… density
- Good literacy rates
- Universal health care … including: strong prim… and good at home ca…
- Excellent scientists

…ate and timely decisions …uguayan government

…between the government …cientific system

…ponse to coronavirus …s

…le citizens' response: personal responsibility and peer pressure-accountability



The real reason!

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Dianne Bourque

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Clinical Trials in the Time of COVID-19

Dianne J. Bourque, Member

September 29, 2020

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Agenda

- Introduction on Current State of Clinical Trials During the Pandemic
- Current Regulatory Accommodations for Clinical Trials
- Regulatory Considerations for Initiating a Clinical Trial Related to COVID-19
- Practical Legal and Regulatory Considerations for Sponsors and Sites
- Perspectives on Clinical Trials in 2021 and Beyond
- Discussion and Q&A

Introduction on Current State of Clinical Trials During the Pandemic

Review of Regulatory Accommodations for Clinical Trials

FDA Guidance for Clinical Trials During the Pandemic

Key points from the guidance:

1. **Assess new risks to subjects and the study itself in light of circumstances, including**
   - the type of investigational product,
   - ability to conduct safety monitoring,
   - supply chain,
   - nature of the subjects' condition
2. **Develop appropriate measures that mitigate risks to subjects**
3. **Document all deviations and mitigations!**

FDA Guidance for Clinical Trials During the Pandemic

The Q&A appendix at the end of the guidance provides more detailed information on acceptable mitigations that comply with FDA regulations

- **FDA regularly updates the Q&A based on major issues and inquiries sent to Clinicaltrialconduct-COVID19@fda.hhs.gov**

Major topics include:

- **Performing remote "clinic visits" or site monitoring**
- **Conducting clinical outcome assessments remotely**
- **Options for obtaining informed consent**
- **Shipping investigational products to HCPs**
- **Using alternative laboratories or imaging centers**

FDA has made its COVID MyStudies app available as an option for obtaining informed consent electronically

FDA Policy on Remote Monitoring Devices Support Expanded Use of Telehealth

Applies to specifically named devices, which may be connected to a wireless network to transmit data to HCPs:

- ***E.g.*, Clinical electronic thermometer, ECG, cardiac monitor, pulse oximeter, non-invasive blood pressure meters, respiratory rate monitors**

FDA states that it does not intend to bring enforcement action for limited modifications to such devices, such as:

- **Including claims or functionality relating to monitoring of COVID-19 patients**
- **Changing indication to include home use**
- **Hardware or software changes to increase remote monitoring capabilities**

Any modifications must not create "undue risk" to patients!

Other Federal Agency Accommodations

Federal agencies modified policies to blunt the impact of COVID-19 on clinical trial sponsors, sites, and human subjects:

- **OHRP issued guidance relating to the Common Rule and is directing researchers and sponsors to FDA resources**
- **CTEP & NCORP issued interim guidance for patients in clinical trials**
- **OCR relaxed enforcement of HIPAA Privacy Rule requirements for teleconferencing platforms**

All interim polices emphasize that patient safety is the primary consideration when implementing any mitigation relating to COVID-19

Accommodations for NIH Grants and the Common Rule

The Office of Human Research Protections (OHRP) is offering flexibility to researchers and encouraging a "safety first" approach

Per OHPR's April 8, 2020 Guidance on COVID-19:

- **"the research community is encouraged to prioritize public health and safety"**
- **"OHRP will take into account the specific circumstances that institutions and investigators are experiencing, and use available flexibility in its decision making"**
- **"investigators may implement changes to approved research prior to IRB review and approval if the changes are necessary to eliminate apparent, immediate hazards to subjects"**
  - Note that such deviations for participant safety are already permitted under the Common Rule

Accommodations for NIH Grants and the Common Rule

On March 12, NIH published a Notice announcing flexibility for applicants and recipients of federal funding. https://grants.nih.gov/grants/guide/notice-files/NOT-OD-20-086.html

- "NIH will be doing our part to help you continue your research"

On March 16, NIH published guidance for NIH-funded clinical trials affected by COVID-19

- "Recipients will likely encounter delays to ongoing research based on the effects of COVID-19. … recipients may submit late financial and progress reports, if research is delayed due to COVID-19, and may carryover unobligated balances on active grants without requesting prior approval."

NIH COVID-19 resources page: https://grants.nih.gov/policy/natural-disasters/corona-virus.htm

OLAW has published information for institutional animal care and use programs coping with the pandemic: https://olaw.nih.gov/covid-19.htm

Considerations for Initiating a Clinical Trial Related to COVID-19

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Considerations for Sponsors

While many non-COVID clinical trials have paused, the number of clinical trials studying COVID-19 and possible treatments continue to grow:

- Clinicaltrials.gov shows 2,200+ COVID-related trials
- WIRB-Copernicus Group reports there are 1,700+ clinical trials underway worldwide for potential COVID-19 treatments and vaccines

There are massive populations of patients who could benefit from investigational COVID-19 treatments or vaccines

Consider subject risks and safety issues beforehand:

- Informed consent process
- Logistics of administering an investigational product
- Conducting safety assessments
- Study monitoring process

Considerations for Sites

Considerations for taking on clinical trial responsibilities revolve around ensuring the safety of patients and HCPs

- Benefits and risks of investigational product
- Status of institution's IRB
- Subject assessment and safety monitoring
- Institution and investigator capacity to perform clinical trial
- Protecting investigators

Implement policies and procedures for engaging in and conducting new clinical trials

- Make sure that the sponsor accepts safety procedures and that the protocol is compatible with them

Overview of Legal and Regulatory Considerations for Sponsors and Sites

Legal and Regulatory Considerations for Sponsors

Sponsors should continue to:

- Assess ongoing trials and determine (1) potential/actual risks and (2) necessary mitigations
- Engage with sites and CROs to prevent exercise of early termination rights
- Consider suspension as an option to termination
- Establish and assess procedures for protecting study subjects and adjusting trial processes to account for COVID-19 disruptions
- Determine whether usable data can still be collected
- Document COVID-related disruption to your study, contingency measures, how human subject participation was affected and – most importantly – measures that have been taken to keep participants safe

Legal and Regulatory Considerations for Sites

Sites should continue to:

- **Communicate with sponsors/CROs and responsible IRBs to discuss COVID-19 impacts on a trial and necessary deviations or modifications**
- **Discuss all protocol and process changes with study subjects and make sure to obtain informed consent for any modifications requiring new or revised consent**
- **Evaluate any alternatives that are implemented**
- **Assess actual risks to study subjects and research personnel and consider terminating, if necessary**

Perspectives on Clinical Trials in 2021 and Beyond

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THANK YOU!

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For ongoing coverage, visit Mintz's COVID-19 Insight Center at:
https://www.mintz.com/insights-center/coronavirus

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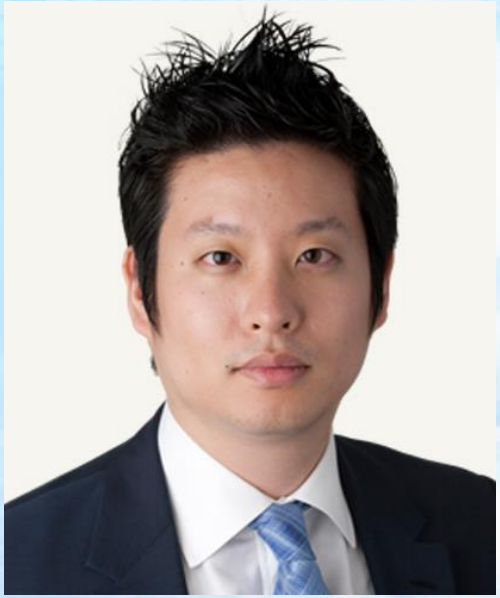

Shohta Ueno

Q&A session

Any questions?

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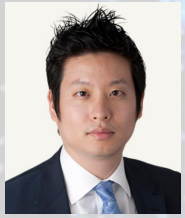

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