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From a TA perspective at the global level, peak impact on new patients entering trials occurred in April (see Figure 4). Cardiovascular and Oncology trials have recovered globally with new patients being added to study-sites at a rate

Frequently discussed topics include telemedicine/decentralization (see FDA Question 19), consent and eConsent (See FDA FAQ 10 & 11), expectations on electronic records/signatures rules (See FDA FAQ 23), and remote monitoring including remote source data veri□cation (rSDV). Note that while the US FDA, UK MHRA, Australia DoH, Health Canada, and Singapore HSA suggest rSDV is possible, the EMA leaves it as an option in very limited circumstances (Section 11 and Annex) and some outright discourage it including Germany and France. Centralized monitoring activities are suggested by most regulators, however.

The regulatory appetite for making COVID □exibilities extend beyond the pandemic is uncertain but there is reason to believe change is possible. For instance, US FDA Commissioner Hahn's June 1 remarks "The COVID-19 Pandemic — Finding Solutions, Applying Lessons Learned" indicated a desire to make some of the changes (i.e. accelerated receptiveness to trial decentralization, master protocols, real world evidence) endure beyond the pandemic.

For additional information on the global regulatory responses to the impact of COVID-19 on clinical studies, visit Medidata's blog here.

Impact to Medidata Customers, Patients and Trials

Real-time and detailed reporting and analytics are critical for sponsors and CROs to assess the day-to-day impact of the pandemic on a trial at the patient, site and country level and so they can quickly implement changes to mitigate the risk of trial failure.

Rapid and safe implementation of protocol amendments is vital to address both site closures and the fact that trial participants no longer receive or have access to the investigational product. Inaccessible sites mean that alternative, remote approaches to drug supply, monitoring study conduct, compliance, patient safety and data quality are needed. The more trials can be safely "virtualized," the more likely they will be able to successfully proceed.

Large pharmaceutical (P□zer, Bristol Myers Squibb and Eli Lilly)[1] and smaller biotechnology companies (Moderna Therapeutics[2], Iveric Bio[3], Aslan[4], Provention Bio[5] and Addex[6]) have announced that they are modifying their R&D plans. Typical modi□cations in certain trials are some form of temporary delay in site activation and/or patient enrollment. The impact of COVID-19 on trial success is already an issue, as evidenced by Aveo Pharmaceuticals Inc., which cited COVID-19 as a reason for the study failure of □clatuzumab in acute myeloid leukemia.[7] These growing examples of trial delays or stoppages by biopharma companies to mitigate the cost and impact of the pandemic dramatically highlight the need for rapid, innovative solutions to help trials successfully start, continue, and □nish.

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The impact of the pandemic on sites was well documented by a survey of over 1,000 clinical site personnel performed by Medidata in late April 2020. Not unexpectedly, the survey results clearly and dramatically show that most sites are feeling the negative impact of the pandemic on current and future trials, speci□cally around delays in patient enrollment and recruitment. They also are concerned about the impact of trial delays and cancellations on their □nancial well-being. Over two-thirds of respondents indicated that they have halted, or will soon halt, patient recruitment for ongoing trials, a third are halting randomization, and about half are now delaying or will be delaying their studies. Sites have shown □exibility and ingenuity in adopting new approaches. Over half of sites are switching site patient visits to virtual ones and/or are using telemedicine to interact with patients. The detailed results of the survey can be reviewed here.

Other COVID-19 clinical trial impact surveys (mostly focused on oncology trials) by the Cancer Research Institute, IQVIA[8] and The American Society of Clinical Oncology[9] demonstrated similar results.

From the patient's perspective, a recent survey of its Phase III patients by a Canadian CRO found that amid the changes COVID-19 has brought to its sites, patients were still committed to continuing their trials. When asked how the CRO could further support its patients, many mentioned medication deliveries and the option to have study visits in traditional, virtual, and hybrid forms, but what was most important was "someone asking us if we are okay."

There were a variety of different ways patients wanted to stay engaged – updates on COVID-19, updates on their research trial, opportunities to ask questions about their trial, opportunities to discuss dif□culties they are facing, etc. What was most important to them was "being informed, I can make better decisions" and "more awareness always is good – it provides hope."[10]

The Race for a Vaccine

The future of global public health is dependent on the scienti□c and medical communities' ability to develop readily

Figure 5: The 21 COVID-19 Vaccines in Clinical Development

Platform	Type of Candidate Vaccine	Developer	Current stage of clinical evaluation/regulatory status - Coronavirus candidate
Inactivated	Inactivated + alum	Sinovac	Phase 3 NCT04456595 Phase 1/2 NCT04383574 NCT04352608
Non-Replicating Viral Vector	ChAdOx1-S	University of Oxford/AstraZeneca	Phase 3 ISRCTN89951424 Phase2b/3 2020-001228-32 Phase 1/2 PACTR202006922165132 2020-001072-15
Non-Replicating Viral Vector	Adenovirus Type 5 Vector	CanSino Biological Inc./ Beijing Institute of Biotechnology	Phase 2 ChiCTR2000031781 Phase 1 ChiCTR2000030906
RNA	LNP-encapsulated mRNA	Moderna/NIAID	Phase 2 NCT04405076 Phase 1 NCT04283461
DNA	DNA plasmid vaccine with electroporation	Inovio Pharmaceuticals/ International Vaccine Institute	Phase 1/2 NCT04447781 NCT04336410
DNA	DNA plasmid vaccine	Cadila Healthcare Limited	Phase 1/2 CTRI/2020/07/026352 (not yet recruiting)
Inactivated	Inactivated	Wuhan Institute of Biological Products/Sinopharm	Phase 1/2 ChiCTR2000031809
Inactivated	Inactivated	Beijing Institute of Biological Products/Sinopharm	Phase 1/2 ChiCTR2000032459

Figure 6: Graphical Summary of COVID-19 Vaccine Candidates by Phase

Medidata Solutions to Assist Sponsors/Partners, Patients and Trials

Medidata has solutions that can be immediately leveraged by our customers to both better understand the impact of the pandemic on their trials, and to mitigate the challenges of patients unable to visit sites for their drugs and protocol-directed clinical and patient-reported data capture.

There are **four** main categories of challenges facing clinical trials. The following is a high level summary of these challenges and the solutions that Medidata is prepared and ready to provide:

N 1: N N IN IN I I N

Solutions:

- Study/sponsor level metrics and dashboards to understand impact on enrollment, patient visits, data collection, query response rates, and additional metrics to help diagnose risk areas
- Industry-wide dashboards and analysis to understand trends globally and areas of greater or lesser disruption

N 2: N I IN I I N N

Solutions:

- Shift to more virtualization – reduce patient visits; minimize site burden
- Shift site mix to lower-impacted countries/regions
- Consider synthetic controls to reduce patient enrollment needs

N 3: IN ININ I N

Solutions:

- Centralize data oversight and monitoring activities, bringing identi□cation of patient anomalies earlier in the process and away from onsite identi□cation
- Closely monitor patient volume and drug supply to minimize supply disruptions

N 4: IN

Solutions:

- Sponsors focused on developing vaccines against, and treatments for COVID-19, must safely and effectively accelerate study start up times through faster investigator budgeting, so cures and treatments can get to market faster

Details on New and Adapted Medidata Solutions

The following tables provide details about the Medidata's solutions available now to assist with your trial challenges. Since some aspects of the four challenges are not mutually exclusive, some solutions may be applicable to more than one challenge.

N 1: N N IN IN I I N

Acorn AI Intelligent Trials

CHALLENGE	SOLUTION

N 2: N I IN I I N N

Rave eCOA

CHALLENGE	SOLUTION
Provide ways for missed or risked visit forms to be remotely □lled out by patients on existing studies.	Medidata's eCOA solution can be used to convert site-based data forms to remote data forms. If study modi□cations are made to accommodate this approach, patients can download the patient cloud app from the app store and provide urgent data forms as needed for missed visits. Any Rave EDC study using eCOA can have additional data forms pulled into the eCOA app and made available to patients. Any Rave EDC studies not using eCOA can add eCOA to the project and immediately begin converting forms to remote-enabled forms.

myMedidata/ Rave Virtual Trials

CHALLENGE	SOLUTION
Quantify the impact of trial participants with COVID-19 symptoms on ongoing research studies. ***New Medidata Solution**	In late April, Medidata and 3DS launched the **COVID-19 Symptom Tracker*** as part of **myMedidata*** (the Medidata Patient Portal), which will be used as a remote patient symptom tracker. This Tracker will function as a registry (in an MVP version) and will allow sites to remotely monitor and report symptoms of patients in their trials. Learn more about myMedidata and the COVID-19 Symptom Tracker here.

Acorn AI Synthetic Control Database / Trial Design

CHALLENGE	SOLUTION
Improving understanding of safety in experimental treatments (e.g., chloroquine) that are now under review for cross-indication use.	Support research by providing aggregated data, e.g., Synthetic Control Database (SCD) to support understanding of expected and unexpected AEs for products being studied for COVID-19. These drugs are already marketed with a mature safety pro□le, but an SCD might improve the analyses above what published literature can provide. In addition, historical trial data can be compared against real-world data from claims or EMRs to provide con□dence and validation in trial design, better understand inclusivity of patients populations to better re□ect real world clinical practice, and potentially decrease sample size requirements for event-driven trials.
Closing out on-going studies given barriers completing visits.	Leveraging historical clinical trial data to augment or replace control arms of trials that are in danger of high dropout or unful□lled enrollment due to COVID-19; reduce scienti□c uncertainty to advance to the next phase, reduce patient enrollment burden or increase statistical power.

CHALLENGE	SOLUTION
Restrictions of access to sites by staff and patients has affected the investigators' ability to maintain medical oversight. This has impacted, among other key processes, completion of trial assessments, completion of trial visits, and the provision of Investigational Medicinal Products (IMPs).	

Medidata Remote Source Review*

CHALLENGE	SOLUTION
As a result of global restrictions, sponsors are experiencing an inability to adequately monitor their active studies on site, and may not be able to manage critical document acquisition and source document review (SDR) activities. Some have turned to less secure, antiquated, risky tools to manage these critical documents such as fax, email, video and file sharing software. **Without the ability to securely manage these documents, patient safety and data integrity are at risk and studies may not progress.** **Regulatory guidance allows for sponsors to find ways to perform critical document management and SDR remotely via a secure cloud-based viewing portal in certain regions, excluding EMEA.** ***New Medidata Solution**	Following FDA Guidance, Medidata has tailored its Rave imaging workflow tool to enable clients to rapidly and remotely deploy a method to assist monitors in their critical document acquisition, workflows, and Source Document Review. **Medidata Remote Source Review*** is a streamlined and quick-to-implement solution (2 weeks go-live) that helps fill the gap when studies have critical timelines and no secure option to collect, de-identify, manage, review and verify critical study documents. Easy to get started with no software to download, is available at no cost to the sites, and can be used as a primary solution or alternative for sites **Medidata Remote Source Review:** • Acquires documents, via secure browser-based uploads, routes and manages document workflows to support source document review and verification remotely • Is a 21 CFR Part 11 compliant system that includes the ability to de-identify and redact Personally Identifiable Information (PII) and Protected Health Information (PHI) • Mitigates risk due to site monitoring and patient visit disruption for some studies with no secure option to manage critical documents

Rave EDC and Rave RTSM

CHALLENGE	SOLUTION
Patients can't get to the site for dispensation - sites are open but do not have supply for dispensation. ***New Medidata Solution**	**Direct to Patient Supply Management*** Rave RTSM can now be configured to send investigative product directly from the Depot to the patient's home. Upon registering a dispensing visit, Rave RTSM sends a shipment request notification to the depot including the SubjectID, and the depot can send the dispensed items straight to the subject's home or office.
Patients can't get to the site for dispensation but the site is open.	Sites can process dispensation through Rave EDC as a visit and send the drug to the subject via a courier. Rave EDC could be updated to store the courier tracking number (collected as text data). Adding a new field would require a migration in Rave EDC.

CHALLENGE	SOLUTION
Sites are closed and patients need a dispensation.	Subjects may be transferred to sites that are open, or if site users are able to work remotely

CHALLENGE

With COVID-19 investigator-initiated studies, there are budget negotiation delays due to the gap between the site's and sponsor's individual cost benchmarks. Disparate data sources for clinical procedure activities and other direct costs at the investigator and site-level can undermine decision-making. There is a need for an independent industry benchmark.

SOLUTION

Rave Grants Manager COVID IIS enables Sponsors to negotiate investigator-initiated studies