

# Assessing Uptake of Remote Consent for Clinical Trials: Opportunities to Reduce Patient Burden

January 2023

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## **Executive Summary**

While the COVID-19 public health emergency has caused major disruption to many clinical studies, one positive outgrowth has been the opportunity afforded trials sponsors, investigators, and regulators to implement elements of decentralized trials in on-going clinical studies. Decentralized clinical trials are those in which some or all trial-related procedures and data acquisition take place at locations remote from the investigator, and have been championed as a means of increasing access to clinical trials by reducing travel-related burdens for participants. Guidance documents published by the U.S. Food and Drug Administration and the National Cancer Institute at the outset of the pandemic spelled out protocol modifications that sponsors, institutions, and investigators could utilize to minimize exposure to COVID-19 for study participants and personnel. One such accommodation, remote informed consent, eliminates the need to travel to the study site solely to provide consent to participate in a clinical trial, making it easier and safer for patients to enroll in studies. As part of broader efforts to advance decentralization of clinical trials, LUNgevity Foundation and the National Brain Tumor Society analyzed existing informed consent policies from 16 major academic medical centers to examine uptake of electronic and remote consent practices at these institutions after COVID-19-related flexibilities had been in place for one year. Key findings of the evaluation include a lack of clarity within institutional policies and a lack of consistency across institutional policies concerning definitions and processes for electronic and remote informed consent. The authors highlight noteworthy policies and recommend that institutions adopt explicit, consistent, informed consent policies based on these examples as one meaningful step toward facilitating decentralized clinical trials and reducing burden on trial participants and their caregivers.

## Introduction

The COVID-19 public health emergency has caused major disruption to many clinical studies, requiring sponsors, investigators, and regulators to identify innovative and flexible approaches to conducting therapeutic trials, both to facilitate their continuation and to ensure patient safety. One positive outgrowth has been the opportunity afforded these stakeholders to implement elements of decentralized trials in on-going clinical studies. Decentralized clinical trials (DCTs) are those in which some or all trial-related procedures and data acquisition take place at locations remote from the investigator. DCTs have been championed as one means for increasing patient access to clinical trials by reducing travel-related burdens.<sup>1 2 3</sup>

Guidance documents published by the U.S. Food and Drug Administration (FDA)<sup>4</sup> and the National Cancer Institute (NCI)<sup>5</sup> at the outset of the COVID-19 pandemic spelled out protocol modifications that sponsors, institutions, and investigators could utilize—including shipping of study medicines, use of remote monitoring and assessments, and use of remote informed consent for enrollment and re-consent purposes—to decentralize on-going and planned studies to minimize exposure to COVID-19 for study participants.

## Informed consent

Informed consent is a central tenet of established human research protections governing clinical trials.<sup>6 7</sup>  
<sup>8</sup> The informed consent process requires that participants and study investigators or designated staff

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<sup>1</sup> Apostolaros, M., Babaian, D., Corneli, A., Forrest, A., Hamre, G., Hewett, J., Podolsky, L., Popat, V., & Randall, P. (2020). Legal, Regulatory, and Practical Issues to Consider When Adopting Decentralized Clinical Trials: Recommendations From the Clinical Trials Transformation Initiative. *Therapeutic Innovation & Regulatory Science*, 54(4), 779–787. <https://doi.org/10.1007/s43441-019-00006-4>

<sup>2</sup> Spears, P. (2020). Patient barriers to participation in breast cancer clinical trials. *Breast Cancer Management*. 9. BMT35. 10.2217/bmt-2020-0004.

<sup>3</sup> Steinhubl, S.R., D.L. Wolff-Hughes, W. Nilsen, E. Iturriaga; R.M. Califf. (2019). Digital Clinical Trials: Creating a vision for the future [Internet]. *NPJ digital medicine*. U.S. National Library of Medicine; [cited 2022Apr13]. Available from: <https://pubmed.ncbi.nlm.nih.gov/31872066/>

<sup>4</sup> Center for Drug Evaluation and Research. 2021. *FDA Guidance on Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency: Guidance for Industry, Investigators, and Institutional Review Boards*. U.S. Food and Drug Administration. U.S. Food and Drug Administration [cited 2022Apr13]. Available from: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-guidance-conduct-clinical-trials-medical-products-during-covid-19-public-health-emergency>

<sup>5</sup> Memorandum - ncorp.cancer.gov [Internet]. [cited 2022Apr14]. Available from: <https://ncorp.cancer.gov/d/Memorandum-on-Additional-Guidance-for-Clinical-Trial-Activities-Affected-by-the-Noel-Coronavirus-3-23-2020.pdf?%2F12-things-to-keep-in-mind-when-looking-to-upgrade-your-ctms%2F>

<sup>6</sup> Musmade, P.B., L.P. Nijhawan, N. Udupa, K.L. Bairy, K.M. Bhat, M.D. Janodia, et al. 2013. Informed consent: Issues and challenges. *Journal of Advanced Pharmaceutical Technology & Research*, 4(3):134.

<sup>7</sup> Guide to informed consent [Internet]. U.S. Food and Drug Administration. FDA; [cited 2022Apr13]. Available from: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guide-informed-consent>

<sup>8</sup> ECFR: 45 CFR 46.116 -- general requirements for informed consent. [Internet]. [cited 2022Apr14]. Available from: <https://www.ecfr.gov/current/title-45/subtitle-A/subchapter-A/part-46/subpart-A/section-46.116>

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review the informed consent form and discuss in detail all major aspects of the clinical trial protocol, including potential risks and benefits of study participation.<sup>9</sup>

The informed consent process has traditionally been conducted in-person at the clinical trial site so that study personnel can answer participants' questions about the protocol, assess their comprehension, and document agreement to participate by jointly signing the consent form. However, switching to a remote consent process by utilizing modern technology like video conferencing platforms and encrypted emails has been advocated by patient groups, investigators, and other stakeholders for years as low-hanging fruit for reducing trial-associated travel burdens.<sup>10 11 12</sup>

The term "remote consent" in the context of informed consent for a clinical trial was defined by FDA in 2016 guidance<sup>13</sup> as an occasion "where the subject reviews the consent document in the absence of the investigator." In guidance originally published in March 2020,<sup>14</sup> FDA further stated that "methods of obtaining informed consent other than a face-to-face consent interview may [still] be acceptable if those methods allow for an adequate exchange of information and documentation, and a method to ensure that the signer of the consent form is the person who plans to enroll as a participant in the clinical investigation or is the legally authorized representative of the trial participant." While remote informed consent has been permitted for some time, its use has been sporadic and inconsistent across cancer clinical trials and major clinical trial sites.

With the COVID-19 pandemic renewing emphasis on aspects of DCTs such as remote informed consent and as part of broader efforts to advance the adoption of DCTs for oncologic studies, LUNgevity Foundation (LUNgevity) and the National Brain Tumor Society (NBTS), two leading patient advocacy organizations, partnered to better understand the extent to which academic institutions currently allow remote consent for enrolling participants to clinical trials and their plans to do so when the public health emergency declaration is lifted. This manuscript summarizes their effort to analyze existing and evolving

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<sup>9</sup> Gupta, U.C. 2013. Informed consent in clinical research: Revisiting few concepts and areas. *Perspectives in Clinical Research*, 4(1):26.

<sup>10</sup> Welch, B.M., E. Marshall, S. Qanungo, A. Aziz, M. Laken, L. Lenert, et al. 2016. Teleconsent: A novel approach to obtain informed consent for Research [Internet]. *Contemporary Clinical Trials Communications*. [cited 2022Apr13]. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5096381/>

<sup>11</sup> Strom, L. Clinical trial consent: There is an app for that - food, drugs, healthcare, Life Sciences - United States [Internet]. *Welcome to Mondaq*. Arnold & Porter; 2017 [cited 2022Apr13]. Available from: <https://www.mondaq.com/unitedstates/food-and-drugs-law/580214/clinical-trial-consent-there-is-an-app-for-that>

<sup>12</sup> ACSCAN. 2022. *Barriers to Patient Enrollment in Therapeutic Clinical Trials for Cancer* [Internet]. American Cancer Society Cancer Action Network. [cited 2022Apr13]. Available from: <https://www.fightcancer.org/policy-resources/barriers-patient-enrollment-therapeutic-clinical-trials-cancer>

<sup>13</sup> Center for Drug Evaluation and Research. *Use of electronic informed consent – questions and answers* [Internet]. U.S. Food and Drug Administration. FDA [cited 2022Apr13]. Available from: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-electronic-informed-consent-clinical-investigations-questions-and-answers>

<sup>14</sup> Center for Drug Evaluation and Research. 2021. *FDA Guidance on Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency: Guidance for Industry, Investigators, and Institutional Review Boards*. U.S. Food and Drug Administration. U.S. Food and Drug Administration [cited 2022Apr13]. Available from: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-guidance-conduct-clinical-trials-medical-products-during-covid-19-public-health-emergency>

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electronic and remote informed consent policies from 16 major academic medical centers, presents key findings, and suggests best practices for institutions regarding the development of clear, concise remote consent policies.

### **Methods**

In follow-up to separate, multi-stakeholder discussions about ways to remove barriers to clinical trial participation, LUNgevity and NBTS partnered on an initiative to survey a select group of investigators at academic medical centers who regularly conduct clinical studies about their institutions' consent practices. Investigators were chosen based on prominence in their field and experience conducting large, industry-sponsored and/or cooperative group clinical trials. Geographic diversity of institutions was a factor in selecting investigators, with the acknowledgement that there are fewer major academic medical centers in the plains, mountain, and southwestern states compared to the coasts and upper midwest.

A total of 21 clinical investigators at 16 institutions (Appendix A) were individually contacted by personalized email. Each investigator was asked to complete a short survey (Appendix B) about the use of electronic consent (e-consent) for enrolling subjects to interventional clinical trials at his/her institution or, alternatively, to provide the name and contact information of someone at the institution who had the appropriate knowledge (e.g., a clinical operations colleague or IRB member) to respond to the survey. The survey was sent via Survey Monkey link and fillable PDF. Informed consent was not sought from participants however survey participation was optional. The survey was not conducted under a formal IRB-approved protocol as the research meets the criteria for being exempt from human research regulations as per 45 CFR 46.104(d)(2). Retroactive review by the Memorial Sloan Kettering Cancer Center Institutional Review Board also determined that the study did not require its oversight and did not constitute human subjects research.

Survey responses were assessed for similarities, differences, and trends among institutions regarding the existence and extent of e-consent and remote consent policies and practices. Provided electronic and/or remote informed consent policies were analyzed based on a pre-determined set of variables the authors identified as components of a comprehensive policy (Table 1).

**Table 1. Desired Components of Electronic and/or Remote Informed Consent Policies**

<ul style="list-style-type: none"><li>• Policy effective date</li><li>• Definition of electronic and/or remote consent</li><li>• Explicit allowance of electronic and/or remote consent</li><li>• Location of research covered by policy<ul style="list-style-type: none"><li>○ Internal to institution</li><li>○ Partner/network sites</li><li>○ External research for which institution is lead and/or IRB</li></ul></li><li>• Types of non-written consent allowed<ul style="list-style-type: none"><li>○ Electronic, in person</li><li>○ Electronic, remote (e.g., via email)</li><li>○ Verbal, in person</li><li>○ Verbal, remote (e.g., via phone)</li><li>○ Other</li></ul></li></ul>
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- Description of who is allowed to obtain consent
  - Principal investigator
  - Research team member
  - Other trained individual
- Authentication/security measures
- Measures to evaluate participant comprehension for remote consent

## Results

Surveys were received from individuals representing 14 of the 16 institutions included, and electronic informed consent policies were received for 6 of the 16 institutions. A review of survey responses and individual institutions' consent policies yielded information about when remote consent is allowed, at which types of research site locations (i.e., partner/network site, external site), and for which types and phases of trials (i.e., industry-sponsored, cooperative group, investigator-initiated). Ten respondents indicated that e-consent for enrolling patients onto FDA-regulated clinical trials is allowed at their institutions. In many cases, these policies had been put in place or altered due to the COVID-19 public health emergency, although respondents indicated that the policies would likely remain in effect post-pandemic. Web-based searches conducted by the project team identified additional information for several of the institutions, including whether policies had been updated during the pandemic.

Of the six policies reviewed, four explicitly address use of remote consent, which is defined in three of the policies. Only two policies lay out detailed processes for conducting and documenting informed consent remotely. Due to the complexity and variability concerning content and terminology of the policies received, and inconsistencies between respondents from the same institution regarding their institution's informed consent practices and policies, it was concluded that a quantitative analysis of the data received would be unfeasible.

Qualitatively, several institutional policies stood out for having positive attributes. For example, the University of Colorado policy,<sup>15</sup> which has been in place since 2019, includes a specific definition of e-consent: "the use of an electronic system to obtain and document a research subject's informed consent for research, instead of relying on a paper process," and provides direction for how e-consent or remote consent can be included in an application to the Institutional Review Board (IRB). MD Anderson Cancer Center (MDACC) clearly states how its electronic consent policy applies to patients consented at MDACC, at external sites (if data is to be collected and analyzed by an MDACC investigator), and in cases when MDACC is the lead site of multi-site study.<sup>16</sup> University of California San Francisco's IRB COVID-19 FAQs & Resources<sup>17</sup> contains a helpful chart explicitly noting that remote consent is allowed but requires prior approval from the IRB if there is a switch from more traditional consent to remote consent. UT

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<sup>15</sup> COMIRB: IRB for the University of Colorado Denver: Anschutz Medical Campus and Affiliates. 2019. *New: Guidance for e-Consent*. [cited 2022Apr13]. Available from: <https://research.ucdenver.edu/comirb/home/comirb-announcements/new-guidance-for-e-consent>

<sup>16</sup> Human Research Protection Program [Internet]. MD Anderson Cancer Center. [cited 2022Apr13]. Available from: <https://www.mdanderson.org/research/research-resources/office-of-clinical-research-administration/human-research-protection-program.html>

<sup>17</sup> IRB COVID-19 FAQs & Resources [Internet]. Human Research Protection Program (HRPP). [cited 2022Apr13]. Available from: <https://irb.ucsf.edu/irb-covid-19-faqs-resources>

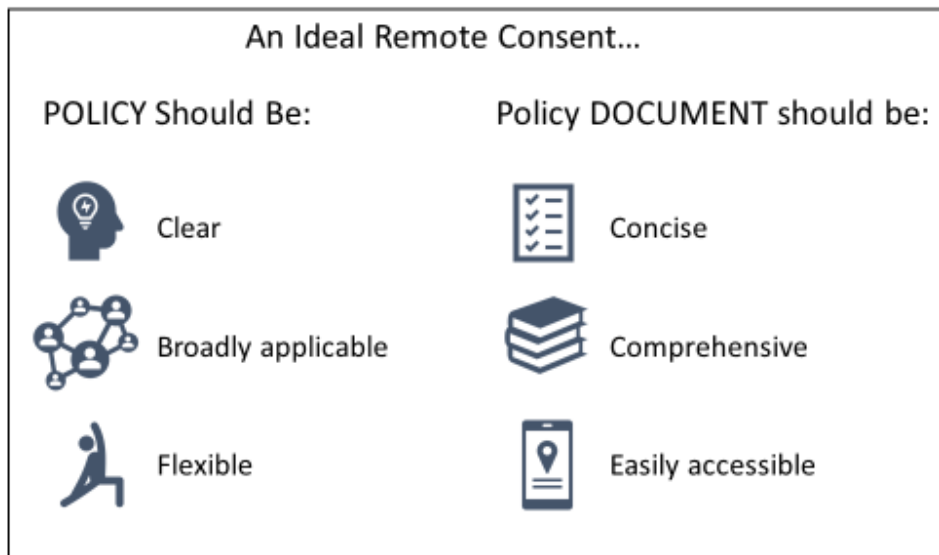
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Southwestern added a concise “Remote Consent and Documentation” guidance document<sup>18</sup> to its HRP Program webpage in April 2020, which includes important terms, references, and options for conducting the whole informed consent process remotely, all within four pages.

### Discussion

It is clear from the LUNgevity-NBTS initiative that routine use of remote informed consent to enroll patients on interventional clinical trials, although expanded during the COVID-19 pandemic, has not reached all academic medical centers. Even among a curated and limited set of academic institutions, there is significant variability among policies related to the use of electronic and remote consent for clinical trials. Variability in content, terminology, specificity, and clarity within institutional policies makes it difficult to evaluate the extent to which remote consent is available as an option for patients at these sites.

Patients, patient advocacy organizations, investigators, IRBs, and sponsors would all benefit from consistency across definitions of and explicit policy language on use of electronic and remote consent. The authors strongly recommend that every institution conducting clinical trials should adopt a clear, explicit policy allowing and defining terms for utilizing remote consent (Figure 1).



**Figure 1. Best Practices for Developing and Communicating Institutional Remote Informed Consent Policies**

Ideally, policies should extend to all clinical research studies for which the institutional IRB has oversight; any exceptions should be noted. Moreover, policies should be flexible, with straightforward avenues for accommodating switches of mode of consent (e.g., in-person to remote) or addition of research not initially covered with minimal administrative burden. Communication of the remote consent policy should be succinct yet comprehensive, laying out how each step of the informed consent process can be conducted remotely. Additionally, the policies should be readily accessible to investigators and the

<sup>18</sup> News [Internet]. UT Southwestern Medical Center. [cited 2022Apr13]. Available from: <https://www.utsouthwestern.edu/research/hrpp/news/>



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public—that is, available and clearly marked in a logical, online location. Based on the factors we evaluated (Table 1), the authors consider the UT Southwestern remote consent policy document<sup>19</sup> to represent a best practice and model for other institutions to refine and adopt.

Institutional remote consent policies should be written in clear, transparent language such that it is apparent that the institution allows, or does not allow, remote consenting of research participants and under what circumstances. Including definitions for both electronic and remote informed consent is helpful to prevent misinterpretations of the scope of the policy and permitted processes. Anticipating changing circumstances for the use and acceptability of remote informed consent and outlining standard procedures for whom and when to contact are additional best practices. Policy documents should be as brief as possible while still providing all necessary information for conducting and documenting the remote informed consent process; outline and/or Q&A formats are useful. Finally, remote consent policy documents should be easily available in a logical, online location, without the need for multiple clicks or extensive scrolling to locate the policy within another document.

Once standardized policies are in place, there will be a need to educate investigators, clinical operations staff, and trial sponsors about the existence and proper implementation of these institutional policies. Additionally, it is important to promote awareness among patient advocacy organizations and professional societies about the availability of remote consent for clinical trial enrollment so that they can subsequently educate patients and caregivers on their options. The goal for all of these actions is to ease and enhance clinical trial participation, especially among patients who live far from an academic medical center and/or for whom travel poses a substantial barrier to trial enrollment.

In discussions about remote consent, the terms “virtual consent” and “e-consent” are often used interchangeably. While “virtual consent” can be considered synonymous with “remote consent,” “e-consent” generally refers to the process by which the informed consent form is read and/or signed by the participant, using an electronic device rather than pen and paper. Unlike remote (or virtual) consent, e-consent can and often does occur while the patient is physically at the clinical trial site. Inaccurate usage and/or improper conflation of these three terms can lead to confusion about what is actually being discussed, which is one potential limitation of this effort. Despite these terms not being explicitly distinguished in the LUNgevity-NBTS survey, it produced useful information including the main takeaways: 1) that remote informed consent has not been adopted by many major academic medical centers despite being called out as acceptable in guidance by FDA and NCI and that institutions, investigators; and 2) that patients would benefit from more consistency among institutional electronic and remote consent policies.

The LUNgevity-NBTS project represents an important start to an effort that should be undertaken by clinical trial sites and all stakeholders in the clinical trial ecosystem. There is an opportunity to substantially advance efforts to decentralize clinical trials by allowing remote consent for enrolling patients, one among many flexibilities in trial protocols specifically allowed by regulatory bodies that have the potential to reduce burdens on patients.

Future work to be considered includes conducting additional discussions with trial investigators and with members of IRBs to ascertain how the arc of the informed consent process—from drafting and approving the informed consent document to conducting and documenting the consent process with

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<sup>19</sup> IRB COVID-19 FAQs & Resources [Internet]. Human Research Protection Program (HRPP). [cited 2022Apr13]. Available from: <https://irb.ucsf.edu/irb-covid-19-faqs-resources>

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patients—works in practice, regardless of what is and is not written in institutions’ policies. Additionally, a more detailed analysis of existing policies across all major academic medical centers as well as community cancer centers could allow a quantitative assessment of the current consent policy landscape, which was not possible through this pilot project. Finally, it would be instructive to engage sponsors and clinical research organizations directly to understand their role in facilitating and promoting remote consent opportunities.

### **Acknowledgments**

The authors would like to thank those who responded to the survey for their time and insights. Dylan Ashley, previously with LUNgevity Foundation, assisted with the policy analysis.

## Appendix A. Institutions Invited to Participate in E-consent Survey.

Institutional representation of investigators invited to answer questions about electronic and remote informed consent policies. Not all investigators responded.

Institution	Brain Contact	Lung Contact
Columbia University	X	
Dana-Farber Cancer Institute	X	
Johns Hopkins School of Medicine	X	X
Mayo Clinic	X	
MD Anderson Cancer Center	X	X
Memorial Sloan Kettering Cancer Center	X	X
Moffitt Cancer Center	X	X
Mt. Sinai	X	
NYU Langone Health	X	
Stanford University	X	
UCLA	X	X
UCSF	X	
University of Chicago		X
University of Colorado		X
UT Southwestern		X
Vanderbilt University		X

## Appendix B. LUNGeivity-NBTS Survey Regarding Electronic and Remote Consent Policies.

Survey questions on institutional electronic and remote consent policies, and compiled responses. The definition of electronic informed consent was taken from the 2016 Guidance by the US Food and Drug Administration,<sup>20</sup> and was included in the survey background.

1. Does your institution currently recognize electronic consent (e-consent) as a means for patients to enroll onto clinical trials?
2. If Yes to #1, to which categories of trials does the e-consent policy apply? (check all that apply)
  - a. Investigator initiated studies.
  - b. Cooperative group studies
  - c. Sponsored studies
  - d. Phase 1, 2 and 3 Studies
  - e. Other (please specify)
3. What restrictions, if any, does your institution place on a patient's ability to use electronic or virtual consent to enroll onto clinical trials?
4. Was your institution's e-consent policy put in place or altered because of the COVID-19 pandemic?
5. If Yes to #4, could you describe significant changes from the previous policy?"
6. If this policy was implemented or altered due to COVID, will your institution maintain the changes once the public health emergency has ended?
7. If the answer to #6 is no, why not?
8. To support efforts by LUNGeivity Foundation & the National Brain Tumor Society (NBTS) to evaluate the current landscape for e-consent, we kindly request a copy of your institution's e-consent policy or a detailed summary. The landscape analysis will be purely informative, comparing and contrasting policies' various elements. No identifying information will be included. Would you be able to provide this information?

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<sup>20</sup> Center for Drug Evaluation and Research. Use of electronic informed consent – questions and answers [Internet]. U.S. Food and Drug Administration. FDA; [cited 2022Apr13]. Available from: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-electronic-informed-consent-clinical-investigations-questions-and-answers>