Trials and Tribulations of Electronic Patient Consent: Removing Barriers to eConsent Adoption

With the availability of Complete Consent, IQVIA Technologies continues its leadership in advancing eConsent beyond pilots into wide-scale production.

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Electronic consent (eConsent) technology has existed for nearly 20 years in various iterations. Even so, sponsors overall have taken a cautious approach to using eConsent, piloting it on individual studies but refraining from incorporating it across all pipelines in clinical operations.

The COVID-19 pandemic has shown us, however, that this "decade of dabbling" is over. To put the rapid pace of change in perspective, IQVIA's eConsent solution saw a significant increase in volume—from about 30,000 patient consent transactions per year before the pandemic to up to 50,000 transactions per day at peak times of enrollment for high-profile vaccine trials.

Through this experience, IQVIA Technologies and its clients now know that the only way to capture the benefits of eConsent in site satisfaction, study operations, and sponsor oversight is to commit to widescale adoption across the enterprise and connect it to the broader trial experience. IQVIA Complete Consent is the next generation of eConsent solutions designed to overcome all the major barriers to success.

ECONSENT: FROM TRIAL INNOVATION TO ESSENTIAL TECHNOLOGY

Since its early iterations, eConsent has focused on improving the quality and efficiency of trials. The technology provides a consistent delivery of patient informed consent in a compliant

manner that supports clinical research associate (CRA) review and remote monitoring. eConsent systems automatically generate full audit trails that provide data integrity, oversight, and a pool of data from which to perform analytics.

Positive results were documented pre-pandemic. For example, a biotech company focused in oncology was experiencing consent-related protocol deviations measured at 14% in paper-based informed consent forms (ICFs). Nearly all quality findings were the result of human error and included items as simple as a missing date. The goal of adopting eConsent was to reduce the deviation rate to no greater than 9%, which was calculated as the level at which the system would cover its own cost of implementation.

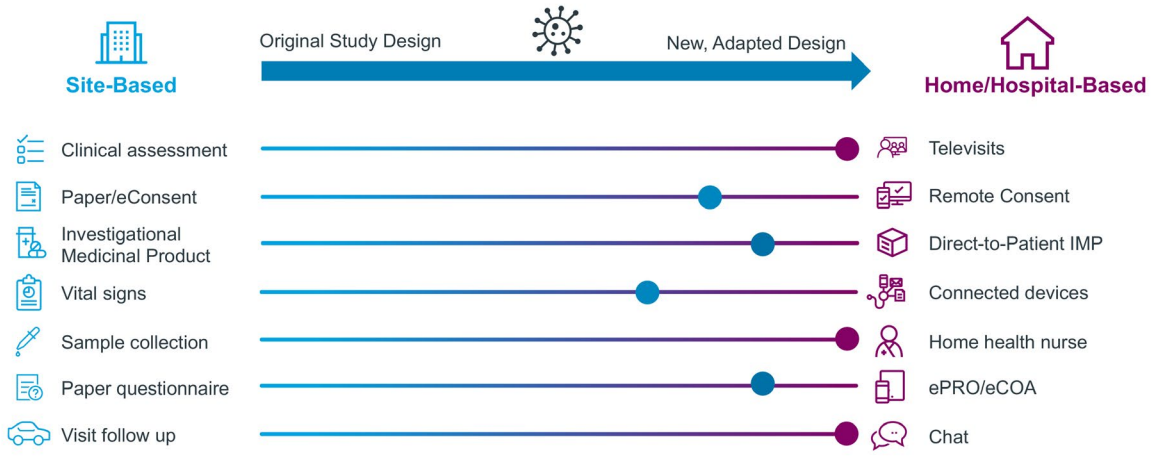
After analyzing results, the eConsent solution was shown to reduce errors to 6% when print-to-sign was employed; and limited errors to 1% where full e-signature could be used. This demonstrates that eConsent can significantly improve compliance and reduce the frustrating efforts and associated costs required to track and resolve consent-related protocol deviations.

Despite clear benefits from use cases such as these, eConsent technology had not been widely embraced across clinical operations prior to 2020. Sponsors hesitate to require anything new that may slow site activation, which is a risk when sites are asked to adopt a technology that diverts from their traditional workflow. Additionally, some eConsent rollouts can have complicated regulatory/ethics considerations and multimedia translation requirements that delay study start-up if not planned for and handled appropriately.

THE PANDEMIC PIVOT TO ECONSENT

The onset of the COVID-19 pandemic forced sponsors, contract research organization (CROs), and sites to evolve rapidly to ensure trial continuity. Operational and technological overhauls were necessary, including revising protocols and finding ways to perform study visits when patients were unable or unwilling to travel. FIGURE 1 illustrates the shift from pre-pandemic

Figure 1: Replacing site-based visits with virtual as often and as fast as possible saves studies and lives.



study designs, which center activities around the site, to new, adapted designs that enable home and hospital-based activities.

Although many aspects of trial operation were required to become more flexible, data quality and integrity needed to be maintained. Social distancing made it impossible to huddle around a paper document to perform the essential act of obtaining informed consent.

Existing studies were not the only ones affected. The wave of new COVID-19 vaccine studies presented difficult consent situations for severely ill or intubated patients. These patients, their legally authorized representatives, and their physician/investigator were often in separate rooms or locations. Obtaining consent is a non-negotiable step in trial enrollment, so eConsent solutions specifically designed for remote consenting are needed to accommodate the range of signing scenarios without introducing an onerous and untraceable workflow.

As a result, the adoption of IQVIA eConsent accelerated rapidly over the past year. The solution enabled more patient consents to be completed in 2020/21 than accomplished by the entire industry in all previous years. Through this intense experience, imperatives for the next generation of eConsent solutions were confirmed.

LESSONS LEARNED SO FAR

Lesson 1: eConsent cannot delay site activation. The first major takeaway learned from the 2020/21 COVID-19 pandemic is that eConsent cannot delay site activation for a single minute. This means that the processes that come before a site is activated—before patients are able to begin consent—have to be done in parallel without being a drag on the calendar. Once a situation arises in which all approvals and training are complete, but eConsent needs another day, the site activation is in a failure state. IQVIA has made many changes to both its operations and technology to accommodate processes done in parallel, but partnership from sites and sponsors is still needed to take it to the last step. One dimension of this partnership involves international regulatory concerns.

When designing a trial that will incorporate eConsent, it is imperative to understand the likelihood of an institutional review board (IRB) approving the use of the technology. Experience with and acceptance of eConsent systems varies based on region. FIGURE 2 represents a heatmap of regulatory and ethical acceptance of advanced electronic signature that IQVIA Technology maintains. If eConsent is used in locations with low historical acceptance, then it is vital to have a system that allows a hybrid approach of electronic signatures and print-to-sign. The technology can reach underserved demographics by remotely consenting patients,

Figure 2: International regulatory compliance and privacy.

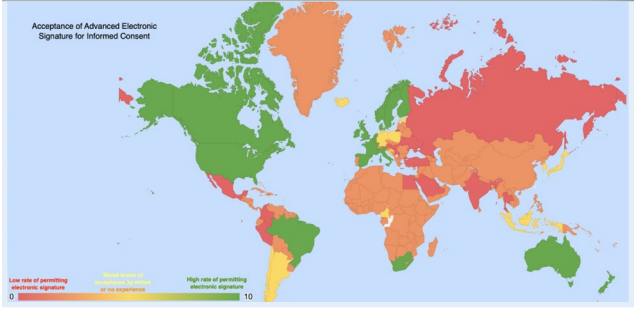
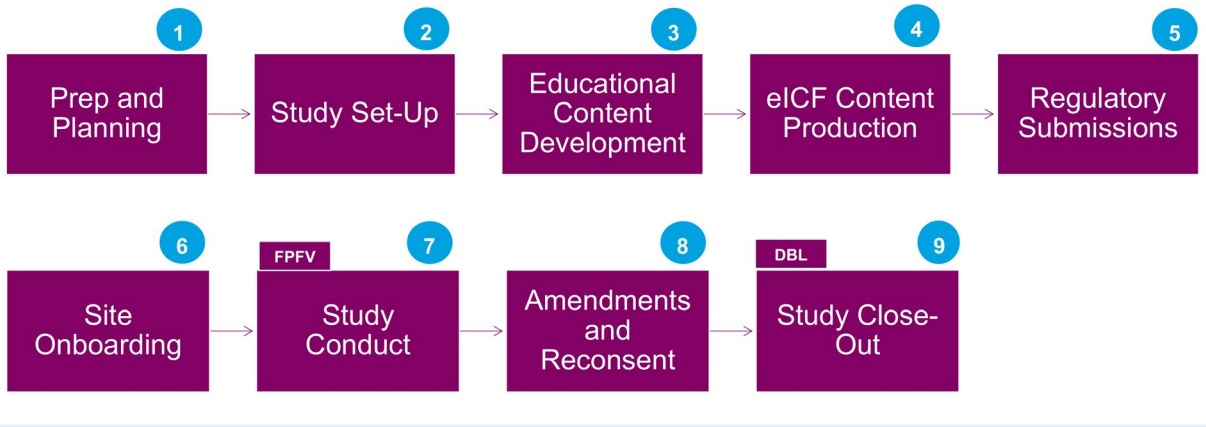


Figure 3: Compressing timelines when needed, from 6-8 weeks to several days for urgent COVID-19 studies.



but tolerance will vary across geographies and should be accounted for in the planning process. The IQVIA Technologies team can drill down into this heatmap to advise clients and support them in advancing regional acceptance of fully implemented eConsent solutions with e-signature capabilities.

It is important to work on internal process efficiency. FIGURE 3 shows a high-level process flow for eConsent implementation in a study. When operating at scale, there are many efficiencies to be gained on repeated work—both in the preparation and planning as well as the definition of the study setup based on technology, standard operating procedures (SOPs), and work instructions.

Regarding educational content development, reusable libraries are an effective strategy for companies in which there is not a large amount of customized material required per study or language. For example, if there is a standard definition for a placebo that can be used in 80% of studies, then the exceptions for the remaining 20% can be managed. This reduces the amount of labor and time needed for content development, quality control, and the submissions process.

Across the industry, the goal is to reduce the complexity of electronic informed consent form content production, as digitizing a consent document is a basic, irreducible amount of work. From there, the selection of sites and central IRBs can play a major role in helping to make eConsent implementation a repeatable process. Central IRBs and geographies, in which eConsent has a known response or a known likelihood of acceptance, is particularly advantageous for speeding approval and onboarding sites into a familiar system.

Lesson 2: eConsent cannot make anyone's job more difficult. This includes the jobs of patients, sites, and sponsors. Often, patients, their families, and caregivers are in high stress, high anxiety situations and are asked to read exceedingly difficult documents, understand them, and make significant decisions—thus, the learning and design principles of the patient experience should be at the core of an eConsent

solution. The same empathy and friendliness should be extended to sites and sponsors.
An eConsent solution that has the following features will ensure trial startup and operations are seamless and keep timelines on track:

- **Flexible workflows:** Protocol designs are complex, so eConsent solutions should be flexible enough to accommodate multiple prescreening, screening, and re-consent workflows in the core system without customization. A robust system will also allow users to manage updates without artificial restrictions.
- **Targeted re-consent:** Protocol amendments may require patient re-consent. eConsent solutions should easily display the differences between informed consent form (ICF) versions, reducing the need for the patient to review the entire document again or a coordinator to point out differences.
- **Integrated infrastructure:** Eliminate the siloed, study-level customization of each component by strategically integrating key data points and preventing double data entry.
- **Multimedia libraries:** Informed consent forms have become longer and more complex. Patients and caregivers may be dealing with illnesses and high-anxiety situations, which make reading ICFs difficult. Multimedia presentations of crucial concepts and portions from the consent form are easier to consume and lead to increased comprehension and adherence. Reusable media may also decrease startup timelines and helps sites be activated on time.
- **Socially distant signatures:** The more individuals who handle a device in the same room at the same time, the higher the likelihood that an illness can be spread. Full-function remote consent capabilities maintain the integrity of the consent process without increasing risk.
- **Remote monitoring:** Risk-based monitoring has been gaining momentum for years, but COVID-restricted monitoring visits have made remote monitoring critical for oversight.
- **Single sign-on:** Integrating with single sign-on providers reduces the number of logins a site user must remember and allows efficient switching between applications.
- **Automated training:** Embedded training should deliver and track all training interactions to strengthen compliance. Users should only need to take a single application-level training to learn how to use eConsent.

Once these basics are assured, the focus can shift to the requirements that really make the difference in successful enterprise deployment; namely, global scalability and support.

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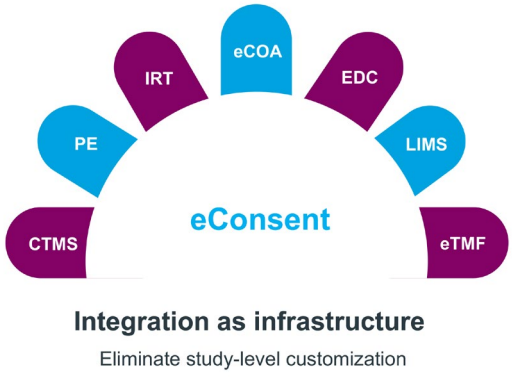
Figure 3: Connecting eConsent to the entire trial experience is critical to site satisfaction, study operations, and sponsor oversight.



Lesson 3: eConsent cannot be an island.
Without integration, eConsent is an island on its own, like a walled garden (see FIGURE 4). Standalone eConsent applications can lead to double data entry, where site users are expected to manually retrieve information—for instance, copy-paste the subject ID from an interactive response technology (IRT) system into the eConsent application. This makes data managers miserable and can only be solved with planning ahead of time.

An important part of this planning involves eliminating data integrations as custom features or requirements per study. Instead of treating them as an infrastructure on their own, clinical systems need an automated way to share information with each other in real time. Enabling eConsent to share information with the clinical trial management system (CTMS), electronic clinical outcomes assessment (eCOA) solutions, IRT system, patient engagement (PE) platforms, and others is crucial to avoid any drag on study timelines. This then eliminates double data entry and quality problems that result from one-off pilots or situations in which sponsors continue to test out various eConsent systems for extended periods of time.

Lesson 4: Remote consent needs a plan.
The last lesson involves remote consent. Much of the work done during the COVID-19 pandemic was remote consent as an emergency contingency, which was absolutely the right move for those studies at the time. Subsequently, there needs to be a proactive plan for what remote consent looks like moving forward.

Remote consent should be thought of as an SOP, meaning it should be used when needed for particular study designs. Rather than reaching for it at the last minute, it should be planned for and include upfront training.

Integrating remote consent with telemedicine and decentralized trial platforms can help alleviate many structural problems associated with traditional clinical trials, opening up new regions and demographics to recruitment efforts. To increase patient diversity in clinical trials, sponsors need to provide the capability to do remote consent with the same ease of use and auditability as face-to-face, onsite consent.

IQVIA COMPLETE CONSENT: THE NEXT-GENERATION OF ECONSENT
Patient centricity has been the focus of IQVIA's eConsent platform for many years. As mobile technology and communications have advanced, the platform has incorporated multimedia and the ability to respond to the subject's interaction with the information presented. IQVIA Complete Consent delivers

AWS creates a secure, redundant, and scalable platform for the application to run on.

a solution that meets the needs of all stakeholders. A decade of feedback from sponsors, sites, and patients (pre- and post-pandemic) informed the design of Complete Consent. As it anticipates and removes the significant barriers to eConsent adoption, the ultimate result is improved protocol compliance and subject retention.

SPONSOR OVERSIGHT

The pandemic exposed how clinical trials were dependent upon in-person activities. Complete Consent system settings allow for the monitoring structure to easily be switched between remote or on-site paradigms, including appropriate blinding restrictions automatically enabled depending on the model.

Verifying a patient's identity is difficult when consenting a patient remotely because site staff, patients, and auxiliary signatories may not be in the same room. Complete Consent builds identity verification into the application and supports use on a phone, desktop, or tablet. The information viewable by all parties is identical and standardizes the verification process with a high level of confidence.

RAPID DEPLOYMENT AND AMENDMENTS

IQVIA's collaboration with enterprise-level clients has validated the use of multimedia and training material libraries. Content can easily be used across multiple programs and studies to reduce startup timelines and increase the return on investment.

Protocol amendments are a standard part of operating trials, and managing ICF versions, approvals, and patients qualifying for re-consent are critical activities. The Complete Consent system tracks these items with audit trail-level transparency. Re-consented patients are prompted to review differences from previous versions only, which saves time and frustration for sites, subjects, and caregivers. IQVIA uses site activation managers to oversee the implementation with sites. The Complete Consent application can be implemented quickly, even for sites with little or no eConsent experience.

ROBUST TECHNOLOGICAL INFRASTRUCTURE

IQVIA's eConsent solution leverages the Amazon Web Services (AWS) infrastructure. AWS creates a secure, redundant, and scalable platform for the application to run on. AWS's regionalization also ensures that personally identifiable information data is not moved across borders from where it is collected, a critical component of privacy regulation compliance.

The system also supports single sign-on capabilities, allowing site users to effortlessly move between Complete Consent, electronic data capture, IRT, and any other technologies using the same service. Single sign-on solutions are 21 *Code of Federal Regulations* Part 11 compliant and increase efficiency and reduce frustration without increasing risk.

A PROVEN PROCESS TO HELP SPONSORS BRING ECONSENT IN-HOUSE

Bringing SaaS technologies in-house successfully has been a challenge in the clinical trials industry. When deploying solutions from IQVIA Technologies, sponsors can choose the business model that best supports their goals, from full-service to SaaS, and take advantage of just the right support services.

With IQVIA Complete Consent, the management of study and site settings, user access, and training flows have been simplified and streamlined, which allows sponsors to have more control over the eConsent process. Complex protocols can also be managed with core system functionality, even when managing cohort-based or follow-up studies.

The Complete Consent team has deep experience and a proven process to help its clients create their own center of expertise as they deploy SaaS eConsent across their organization. IQVIA's team works with clients to:

- **Strategize:** Set goals and plan the eConsent process
- **Analyze:** A client playbook is developed based on the strategy identified
- **Pilot:** Collaboration on pilot studies proves the concept and identifies areas for improvement
- **Adopt:** Widescale rollout of a SaaS program built on successful planning and proof of concept
- **Adjust:** Partnership designed to measure progress and adapt the process for increased efficiency and ease of use.

SUMMARY

The COVID-19 pandemic accelerated the adoption of eConsent by pushing sponsors to confront the barriers that have historically resulted in sporadic implementations. IQVIA Complete Consent is strategically positioned to help sponsors, CROs, and sites navigate this process. By leveraging more than a decade of experience, including the intensity of the operational demands created by the pandemic, IQVIA has created a product and organization that overcomes traditional obstacles and is leading the industry into wide-scale eConsent adoption, integration, and interoperability.

About the Author

Peter Hassett has worked in the area of patient informed consent for more than 20 years, from the very first FDA grant for an electronic consent (eConsent) pilot to enterprise-level activation of tens of thousands of patients to meet the demands of COVID-19 trials. In that time, Peter has kept patient centricity at the heart of eConsent products while navigating changing international regulatory and privacy landscapes. From implementation and operations to compliance and analytics, Peter has hands-on experience in every corner of eConsent.

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