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# GI Trials With Novel Services and Technology

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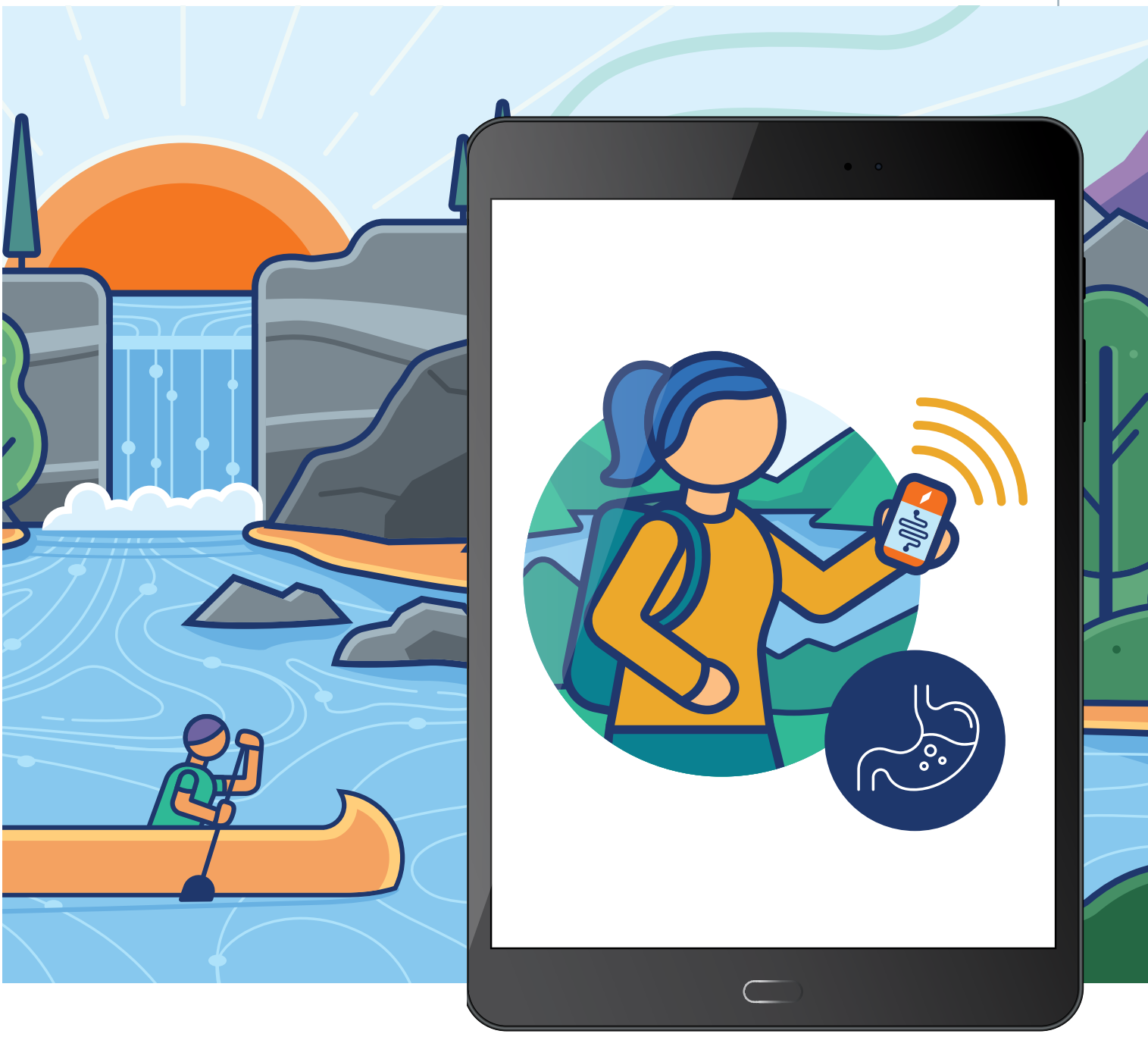

# Introduction

Gastroenterology trials have been growing in number and complexity for years. Current trial solutions rely heavily on electronic clinical outcome assessments (eCOA) including both electronic patient-reported outcomes (ePRO) and clinician-reported outcomes (ClinRO) to improve data quality and integrity. Eligibility decisions based on data from both sources and derived through calculations based on compliance and complex scoring are increasingly common. Further, the accelerating complexity of GI protocols has far outpaced the eCOA industry in simplifying trial solutions for that complexity. Patients are overwhelmed, sites are overburdened, and sponsors are struggling to achieve even modest enhancements in the site and patient experience.

Fortunately, there's a better path. At Clinical Ink, we've spent years aligning our product design tools and service delivery methodologies specifically to a GI-specific technology solution. This technology, which we deploy and customize on demand, is powered by the Lumenis™ technology platform. Our system integrates an ePRO/patient engagement solution for patients at home, a full-service site tablet for ClinROs and PROs collected at visits, and an intuitive and fully customizable reporting portal for remote monitoring and data surveillance.

This paper describes the complexity of GI trials in detail and shows how our solution is designed to overcome their significant, but typical, challenges. Our intimate knowledge of and experience with this therapeutic area enables a better deployment experience and improved trial conduct.

# Typical GI Studies Demand a Considerable Amount of Patient- and Clinician-Reported Outcomes

In GI studies, certain eCOA/ePRO data collection requirements are standard across protocols and sponsors. Knowing these common elements up front allows Clinical Ink's team to advise sponsors on best practices. Data collection for the GI therapeutic area is known to be particularly complex. For example, most protocols require clinicians to complete questionnaires at site visits. They also require patients to complete questionnaires at home and at visits. Further, site staff typically make eligibility decisions based in part on these three types of data, often in relation to additional disparate information. The challenge is to simplify the recording of all this data, ensure patients do what they need to and stay motivated, and make the information easily accessible for all the subsequent decisions that must be made during the course of the trial.

## 1. Patients record data at home

Patient burden is possibly the largest challenge in GI trials. First, patients at home are often faced with two different types of diaries: scheduled and event-driven. Scheduled diary entries must be completed within a specified window of availability. These diaries often include detail about daily GI activity and symptomology and include strict requirements for timely completion. Event-driven or episodic diaries require the patient to record event(s) whenever they occur. This type of diary is used to record specific events, symptom details, and/or medications the patient may have taken related to the event, as required by the given protocol.

The challenge here is that with the high volume and precise scheduling of required entries, patients have a hard time fulfilling the requirements and staying motivated to do so. A full-scale patient engagement strategy is needed.

## 2. Patients report outcomes at site visits

Historical solutions for site-based electronic questionnaire completion required a lot of site intervention to enable patients to get started. Today, solutions for patient-reported outcomes during site visits should focus on reducing the burden for both site staff and patients whenever possible. This means that applications should be designed to be usable with the least possible intervention by site personnel and should be intuitive and clear enough for a subject to complete without extra help.

## 3. Clinicians must review disparate data to complete questionnaires

Some study designs also require clinicians to complete questionnaires. Often, decisions must be made based on review of disparate data, then recorded within a clinician-reported outcome (ClinRO). The challenge in these cases is to ensure the data to be reviewed is easily accessible. Whether it's ePRO data collected at home or at sites, or some other data source, clinicians should not have to search for it. The necessary information should be automatically integrated into the tablet-based ClinRO workflow to simplify the site staff and clinician experience.

## 4. Strict patient compliance is a screening criterion

In many GI trials, ePRO data represents the primary efficacy data. Patient compliance to questionnaire completion in these trials is therefore critical. For this reason, many GI protocols require patients to maintain strict compliance to scheduled diary entries and/or a minimum number of recorded event entries in order to be randomized into the trial.

These screening criteria for compliance can be very elaborate. For instance, a patient may need to complete a minimum of 80% of daily scheduled diaries and/or submit event diaries on 5 out of 7 days to achieve eligibility. Additional qualifying criteria may then apply, such as an event must not be within 30 minutes of another event,

must achieve a 3 or greater average on a 5 point Likert scale for evacuation and/or straining, and must represent a qualifying stool type as defined by a specific diary entry.

Analysis or manual calculation of these qualifications by site staff/clinicians is untenable. A much better scenario is an ePRO solution that automatically reports on the screening criteria and executes calculations.

## Real-World Example of a Complex GI Workflow Demanding Analysis of Disparate Data Types

This example demonstrates the complex requirements GI investigative site staff, clinicians, and patients grapple with. Consider a Crohn's disease trial leveraging the Crohn's Disease Activity Index (CDAI) and an at-home event diary of bowel movements and detailed stool data. Typically, the CDAI will support decisions for patient eligibility after a screening period in which patients collect and record data at home. Patient-sourced data in this activity forms one portion of the CDAI calculation, which also includes clinician-entered data and lab detail. For this example, we'll assume this patient data is collected via a smartphone-enabled, home-based diary with the CDAI itself being completed via a tablet-enabled, site-based questionnaire.

At the randomization visit following the screening period, clinicians will need to evaluate the following patient-reported data:

- Total number of soft/liquid stools in the last 7 days
- General well-being (average daily rating over past 7 days: generally well/slightly well/slightly under par/poor/very poor/terrible)
- Abdominal pain (average daily rating over past 7 days: none/mild/moderate/severe)
- Anti-diarrheal drug use

Once the data is evaluated and entered into the CDAI, the clinician will need to calculate the composite CDAI score to determine whether that patient can be randomized into the trial. It goes without saying that this makes for both a stressful and risky randomization visit for sponsor, site staff, and patient. Deployment of efficient eCOA/ePRO technology can help the clinician and the patient while saving a lot of time.

## Data Access in Real Time Allows Clinicians and Sponsors to Monitor and Support

While it is important that the above eligibility scores are correctly calculated within the ePRO application, it is even more vital that site users, clinicians, and sponsors have access to this data in near real time for monitoring and support. To this end, eligibility reporting should include key criteria and summary outputs for sites. Qualifying event criteria are also typically leveraged for eligibility. In this case, site staff should be able to view eligibility reporting through summary outputs online that detail whether patients meet criteria.

Scoring is often included. In this case, each parameter, such as average daily pain, has an eligibility cutoff value. Reporting for all criteria should be summarized into a single, simple report. This eliminates the need to seek out disparate sources to make randomization decisions related to ePRO criteria. These reports should also be customizable so sponsors may elect to show sites all the details or just provide them with a determination of eligibility.

## Real-Time Alerts Notify Staff and Prompt Patients

Beyond reporting, summary alerts inform site and study staff when patients exceed acceptable thresholds for compliance. The conciseness of these alerts ensures signal over noise for recipients. Alerts should be deployed as part of an outreach strategy for site and study monitors to support patients at risk in the screening phase, when applicable. This approach can improve subject compliance, increasing the chances that subjects will not become ineligible due to the stringent compliance requirements so common in this therapeutic area.

## Enhanced Functionality Reduces Build Times and Improves Site and Patient User Experiences

With an authoring tool that supports an agile design and a collaborative requirements process, lengthy build times and review cycles — commonplace for GI trials — can become a thing of the past. Using our custom-built, proprietary ePRO/eCOA authoring tool, Lumenis brings the patient and site user experience to the forefront of the design process, rather than leaving them as afterthoughts. By focusing on the patient and site experience at the beginning, Clinical Ink simplifies the identification of functional requirements, allowing the sponsor to experience rather than conceptualize what patients will do in the application. This prototype-driven design allows Clinical Ink project managers (PMs) and study design consultants to rapidly advance ideas to prototypes that sponsor study teams can load and review on their own iOS and/or Android smartphones in hours and days, rather than weeks and months. Doing so improves the patient experience and significantly reduces build times.

This approach has downstream implications for user acceptance testing (UAT) as well. It shifts the UAT focus from initial review of questionnaire requirements and workflow on the device, based on decisions made on paper months prior, to a simple end-to-end confirmation of everything already approved through detailed and regular prototype reviews. This approach greatly reduces stress on sponsor study teams, as they can focus on testing important back-end data items, such as eligibility calculations or custom reporting. They can then confirm their expected experience in its totality and gain confidence in overall study success.

## A Robust Patient Engagement Strategy Is Key

Even with a great design and implementation model in place, it is still important to keep the study patients engaged, adherent to their visit schedules, and compliant with their questionnaires. To this end, a solid patient engagement strategy should be deployed. Since the patient-generated data in these trials is critical to study success, noncompliant patients are often removed from the study. The Clinical Ink solution delivers both capability and a strategy for study success through robust patient engagement.

Critical to this strategy is keeping patients connected by placing information they tend to look for in a place where it's easy to find. As patients are already utilizing the application to answer required study questionnaires, the application itself is the most intuitive place for this. This means making the ePRO solution something more. At Clinical Ink we've developed a completely unified patient engagement and ePRO experience through our native application. Wherever possible, the solution can be deployed not just through provisioned devices (ePRO on provided smartphones), but also on a patient's personal smartphone, a bring-your-own-device (BYOD) approach. An added benefit is that we have seen that a BYOD approach improves how often patients access their ePRO applications and how much time they spend in them.

Our patient engagement solution is designed to be mobile-optimized, content-rich, graphical in nature, and targeted to drive the key behaviors sponsors need patients to maintain in order to keep up with their study requirements. Further, content is educational, informational, and timely: It provides details about the study, indication, and site the patient might benefit from, it provides necessary study detail and site information, and it's delivered when it matters and when it's relevant for the patient.

Sponsor, Site, and Patient Burden Summary

| Key GI ePRO/eCOA Study Challenges | | |
|---|---|---|
| Sponsors | Sites | Patients |
| Lengthy/Complex Requirements | Patient Training | Daily Questionnaires |
| Confusing UAT | Complex Eligibility | Event/Episodic Questionnaires |
| Time to Go-Live | Compliance Monitoring | Event Criteria |
| Reporting | Inventory | Event History |
| Data Delivery | Reporting | Visit Schedule |
| Data Quality | Data Quality | Visit Activity |

## Lumenis: A Better Experience for Patients, for Sponsors, and for Clinicians

Delivering the complete patient engagement strategy described above alongside patient questionnaires, and directing patients to the ePRO application to learn more about the trial and keep up with the trial requirements, will change the GI trial paradigm. We believe this approach will deliver better patient experiences, and in turn, better data quality by driving compliance and keeping the trial top of mind for the patients enrolled. Dynamic reminders support patients in performing the tasks they need to for the diaries they're expected to complete, the visits they're supposed to attend, and the dosing they're required to maintain. The Lumenis platform reminder model for patients, as referenced above, targets only those who need it. Reminders in the form of smartphone push notifications for questionnaires only fire when patients haven't completed diaries and will not pester those patients who remembered to complete the questionnaires when they were supposed to. For those subjects who need an extra nudge, the reminders can persist at predetermined intervals, until the patient completes the task.

While the above-described functionality should be a given when choosing an ePRO/eCOA provider for your GI trial, at Clinical Ink we've also invested in the design and deployment technology required to implement them. And further, our service-first methodology focuses on the key support sponsors need: project management, shipping and logistics planning, license procurement and translation, help desk and full-service training, as well as outcome solution support and subject matter expertise for the life of the trial. From the moment the protocol is received for scoping a fit-to-purpose ePRO and engagement solution to the moment the archive request is received, you will feel confident that you are supported by a team that understands your GI study needs and that the technology deployed for it is custom-fit for your protocol.

## A GI Trial Where Work Streams and Data Flows

Conducting trials in the same way over and over simply because it's the way it's been done before doesn't work for ePRO/eCOA solutions within an indication as complex as GI. At Clinical Ink, innovation lies at the heart of all our solutions. Our GI-specific technology solution powered by our Lumenis platform and our service-first methodology represent breakthrough innovations and complete dedication to service excellence in the ePRO/eCOA space. These innovations are built on years of experience and our service methodology addresses what sponsors are looking to improve on. Through our GI-specific technology solution and customized services, we are enhancing site staff and patient experiences as well as overall data quality and solution delivery.

Clinical Ink supports these solutions in the full range and breadth of complexity they require without overwhelming the study team, confusing the patient, or overburdening the site. **Imagine a GI trial where work streams and data flows. Now make it a reality with Clinical Ink.**

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## Direct Data Capture | eCOA | ePRO | eConsent

Clinical Ink, a global clinical technology company, offers data certainty from source to submission. Our eSource clinical technology and configurable ePRO and eCOA modules — a suite of solutions for capturing and integrating electronic data from sites, clinicians, and patients at its source — naturally enhance your clinical trial workflow by reducing manual labor, providing anytime, anywhere data access, and saving resources as your trials progress. Accelerate the completion of key clinical development milestones in your study and confidently manage your trial's critical decisions with our flexible menu of collaborative services, remote monitoring support, and a complete, real-time view of your trial.


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