International
CLINICAL TRIALS
Winter 2025

epc European Pharmaceutical Contractor
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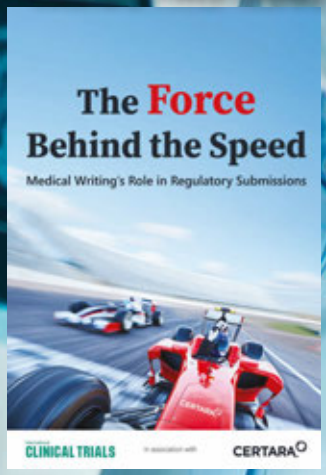


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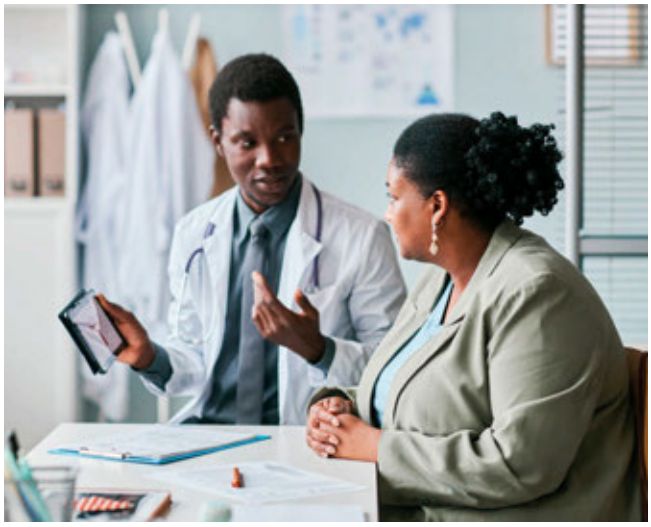

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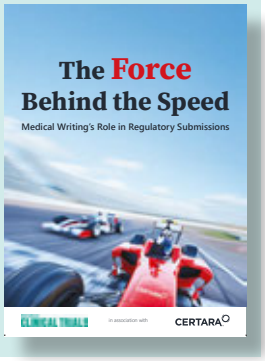

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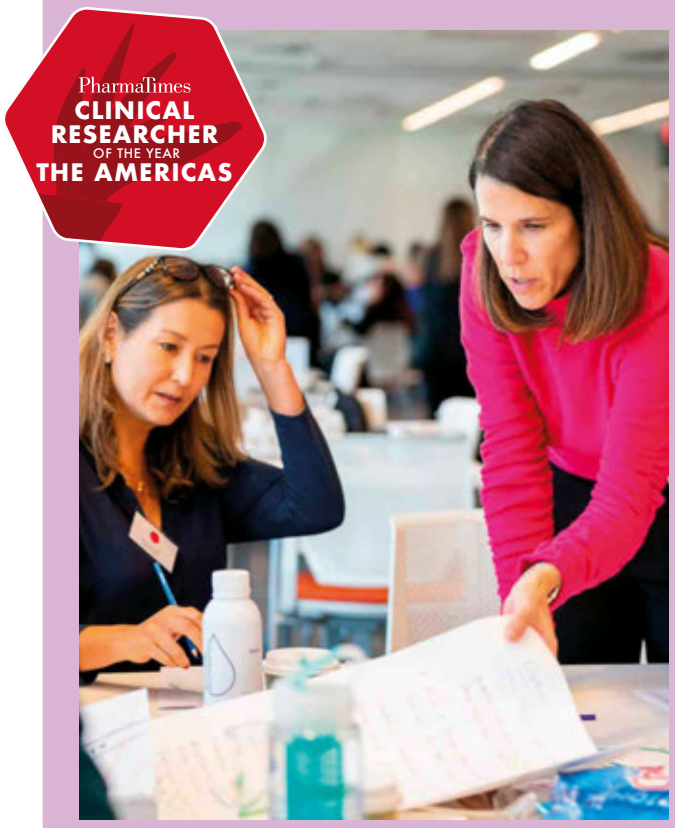

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EDITORIAL DESK

Winter is here, and we're in the middle of a very wet and cold one where inspiration and innovation seem very far away. But key sectors for clinical trials, such as Patient Recruitment and Oncology, can't afford to hunker down and wait for warmer times – fresh ideas are constantly needed to keep pharma R&D progressing.

Even before the clinical research stage, companies look for ways to speed up and improve the patient recruitment process, so trials can start earlier and therapeutics can get to patients faster. However, the trial participant cannot be forgotten in this equation, and in fact must remain a consideration in trial-related decisions throughout the process. Jumo Health discusses the need for a community-based approach to improve diversity, equity and inclusion when recruiting for studies (page 8), while WCG analyses the relationship between trial site and participant (page 12). Innovaderm looks at how contract research organisations and investigative sites can work together to improve the patient experience while ensuring a successful trial (page 16).

Oncology trials are as complex as they are important. There are many elements that need to be planned for and closely monitored so that life-saving treatments reach patients as quickly – and as safely – as possible. PCI Pharma Services looks at the safety requirements for developing and producing highly potent drug products, such as those used in cancer therapies (page 20), and Medidata highlights how imaging, despite its potential risks, can be a helpful tool in tracking the tumours of clinical trial participants (page 29). ANGLE discusses liquid biopsies, another method of tumour tracking (page 24).

For 2025's Medical Writing Supplement, *ICT* has collaborated with Certara on *The Force Behind the Speed: Medical Writing's Role in Regulatory Submissions*. This supplement gives an in-depth look at the processes within medical writing – such as fast-tracking master protocols, strategic clinical study report authoring, and the utilisation of top-down messaging – and how these all come together to ensure accurate documents are produced at speed. Explore the challenges, and their solutions, after page 38.

This edition also showcases another Clinical Outsourcing Group update (page 39). *ICT* is proud to be exclusive media partners for the third year running – come and say hello at our booth at COG UK: London, taking place from 4-5 May.

We hope you enjoy *ICT*'s first edition of 2025, and look forward to welcoming you back in a sunnier May for our Spring edition!

James Spargo

Deputy Editor

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ICON BIOTECH

Whitepaper

Early, precise and efficient; the methods and technologies advancing Alzheimer's and Parkinson's R&D

In this CNS whitepaper, which includes extracts from our survey of over 120 neurodegenerative therapeutic developers, we examine how innovative methodologies and technologies are being implemented to improve the success rate of clinical trials across a range of neurodegenerative disorders.

Download the whitepaper at:
ICONplc.com/CNS-trials

International
CLINICAL TRIALS

Building trust through an authentic community-based approach: strategies to increase diverse representation in clinical research

How can companies utilise community outreach to increase diversity, equity and inclusion in clinical trials?

Kevin Aniskovich at Jumo Health

Despite federal guidance and increasing awareness on the topic, clinical trial diversity continues to be a significant challenge, with underserved communities – especially racial and ethnic minorities – remaining underrepresented in medical research. This representation gap exists even in conditions where minority populations are disproportionately affected, including diabetes, heart disease and cancer.

However, new strategies are emerging to address this imbalance. Targeted healthcare education and community-based approaches in clinical trials are paramount to bridging this gap and paving the way for more inclusive and effective treatment options. These approaches emphasise building long-term relationships with underrepresented communities, which are essential for increasing participation, improving health outcomes and ensuring more equitable representation in medical research.

In examining the critical role that community-based approaches play in advancing health equity, challenges, strategies and recommendations must be explored for improving clinical trial recruitment and retention in underserved populations. By implementing specific solutions and fostering trust through community partnerships, clinical studies can better serve diverse populations, reduce health disparities and, ultimately, improve public health outcomes.

Understanding the problem

Underserved communities, including racial and ethnic minorities, low-income individuals and rural populations face both a disproportionate burden of disease and a lack of access to healthcare. These populations often are also underrepresented in clinical trials. For example, while African Americans represent about 13% of the US population, they make up less than 8% of clinical trial participants.[1,2]

The underrepresentation of diverse populations in clinical research is more than statistics. It means that certain communities may not fully benefit from medical advancements because of a lack of data on how new therapies might affect them. This is particularly concerning for conditions such as heart disease, diabetes, asthma and lupus, where minority communities have higher disease prevalence but lower representation in clinical trials. For instance, lupus is three times more common in African American women than Caucasian women, yet only 14% of lupus clinical trial participants are Black.[3]

The consequences are clear: treatments may not be as effective for all populations if those groups are not adequately represented in research.

Barriers to clinical trial participation among minorities

Many communities, such as Black/African American, Hispanic/Latino, LGBTQ+, American Indian/Alaska Native (AIAN), and Asian American and Pacific Islander (AAPI), face substantial barriers to clinical trial participation.

There are many reasons why underserved communities do not participate in clinical trials, but mistrust of pharmaceutical companies and healthcare providers (HCPs) – driven by historical injustices such as the Tuskegee Syphilis Study – plays a significant role. This mistrust can be compounded by cultural differences, language barriers and the failure to address local needs before asking someone to participate in clinical research.

To rebuild trust with underserved communities and increase representation in clinical trials, pharmaceutical companies must consider:

- Language/dialect
- Cultural nuances
- Education level
- Trusted sources of information
- Relationship with HCPs.

It is imperative to provide culturally relevant, health literacy-focused educational content, tools and

resources that are authentic and comprehensive.

Rebuilding trust is just the first step. It is also important to consider the practical, socioeconomic and logistical barriers these communities often must overcome to participate in a clinical trial. Many minority populations face financial constraints, lack of reliable transportation and limited access to healthcare facilities. In addition, it can be very difficult or impossible to attend appointments during work hours if the site does not offer evening or weekend hours. Additionally, patients with families have the added burden of finding affordable childcare during appointments.

While solutions for transportation, patient payments, decentralised clinical trials (DCTs) and at-home nursing options can help mitigate some of these challenges, sponsors must also consider site accessibility for these communities when the protocol is developed.

The solution

Before discussing solutions to these barriers, it is important first to define the different concepts that play a role in fostering diverse representation in clinical trials. There are a lot of diversity, equity and inclusion (DEI) buzzwords currently in use, however it is important to understand the nuances and differences between each of them:

- ***Diversity:*** refers to the presence of differences within a given setting (eg, race, gender, age, etc)
- ***Equity:*** refers to ensuring fair treatment, access and opportunities by addressing individual needs
- ***Equality:*** means providing the same resources or opportunities to everyone, regardless of their differences
- ***Inclusion:*** creating environments where all individuals feel welcomed, valued and able to participate fully.

Each of these concepts must be considered when developing a strategy to increase representation of underserved communities in clinical trials.

Understanding the community-based approach

There are two critical elements of community-based approaches:

- The recognition that one-size-fits-all recruitment strategies are inadequate for reaching underserved populations
- Ongoing, sustained engagement – not just short-term recruitment campaigns – is required to build trust with local communities.

Targeted solutions and long-term partnerships with community organisations are needed to engage underserved populations with culturally appropriate healthcare education, address historical mistrust

in medical research and overcome socioeconomic barriers. Tailoring interventions to community-specific requirements and working with trusted organisations can reduce health disparities and improve awareness about clinical research. A long-term commitment to these strategies can also enhance recruitment and retention rates, improving the representation of diverse populations in clinical trials.

Strategies for implementing community-based approaches

To effectively implement these strategies, pharma sponsors must:

- Pursue relationships with trusted community partners
- Invest in comprehensive, long-term targeted healthcare education programmes
- Contract with community-based sites
- Consider implications of the US Food and Drug Administration (FDA) guidance on Diversity Action Plans (DAPs).

The role of community partners

The first step to implementing a successful community-based approach is to partner with local organisations embedded in the communities that sponsors are trying to reach. These organisations understand the cultural, social and economic challenges that might hinder participation in clinical trials. They also understand the language, context and formats in which people in their community prefer to receive information. While this firsthand insight into the needs and preferences of each unique population is important, the true value of working with a community partner is their ability to foster a safe and trusted environment for discussing sensitive healthcare topics. Their deep ties to their community allow them to truly understand their constituents' concerns about medical research, and overcome these hesitancies in a way that feels authentic and is aligned with the community's best interests.

By partnering with trusted community organisations, sponsors can ensure that they are addressing the specific needs of underrepresented communities, in turn building trust and providing relevant education in a context that feels safe and authentic.

The role of targeted education programmes

One of the most important ways to engage underserved communities is through comprehensive healthcare education. Medical terminology is often complicated and can be overwhelming; educational materials must be culturally relevant, easy to understand and designed to address the unique concerns of these populations.

It is important to develop digital, print, video and interactive media content that speaks to each unique community so they can make informed healthcare decisions. This means ensuring that recruitment materials, patient-facing resources, websites and videos reflect the languages and cultural contexts of the communities. These materials should address common misconceptions about clinical trials, explain the benefits of participation and offer reassurance regarding the consent process.

Just as important as the creation of these educational materials is how they are distributed to members of the community. Hosting informational sessions and micro-workshops in local community centres, churches, beauty salons, barber shops and other trusted venues can help break down the barriers to participation. These events provide an opportunity for individuals to learn about trials in a trusted, pressure-free environment, where they are more likely to be comfortable enough to ask questions and receive answers from experts and community leaders that they trust.

The role of community-based sites

The importance of thoughtful site selection cannot be overstated. Research shows that clinical trial sites are often located far from underserved communities.[4] Selecting community-based trial sites creates significantly improved access to a diverse participant pool.

Often these community-based sites offer the advantage of being in areas

where potential participants already live and work, which makes transportation easier. It is important to consider sites that offer flexible hours, including evening and weekend appointments, to accommodate individuals who might be unable to attend visits during traditional working hours. Another benefit of community-based sites is that often principal investigators and clinical staff at these sites reflect the demographics of the community. This can help to foster trust and increase participant engagement. In addition to selecting community-based sites, it is vital that all clinical sites receive ongoing training on cultural competence and inclusivity. Training should be designed to educate HCPs and site coordinators on the unique needs of diverse populations and how to foster trust with patients. This training can empower site staff to engage with patients from underserved communities. Sites should also receive continuous resources to ensure that recruitment strategies remain inclusive and effective.

The role of federal policy

In recent years, federal policy has played an essential role in encouraging diverse representation in clinical trials. On 26 June 2024, the FDA provided guidance urging pharmaceutical companies and researchers to prioritise diversity with programmes such as DAPs, with the intent being to boost enrolment of participants from historically underserved groups in clinical studies. This approach helps to enrich the data collected about potential users of the therapy, ensuring a more comprehensive understanding of how it affects various patient populations.

In 'Section 4C Measures to Meet Enrollment Goals', the FDA guidance on DAP outlines recommended enrolment and retention strategies that incorporate many aspects of the community-based approach, including:

- Implementing sustained community engagement efforts
- Providing cultural competency training for clinical investigators and research staff
- Improving study participant awareness and education
- Reducing participant burden with flexible appointments, transportation assistance and decentralisation, where possible
- Improving access by selecting community-based sites that serve diverse populations.[5]

Often, community partners and/or service providers can help design the community outreach strategy and help write the corresponding portion of the DAP to ensure the approach aligns with FDA guidance. By following this guidance, pharmaceutical companies can be proactive about their diversity initiatives.

The path forward

If we are to create a healthcare system that truly serves everyone, clinical trials must reflect the diversity of the population. Community-based models are proving to be a powerful tool in achieving this goal, ensuring that medical advancements are informed by those who need them most.

By investing in local engagement, addressing common barriers and building trust, pharmaceutical sponsors can take meaningful steps towards a future where access to clinical trials is truly equitable.

As the industry moves forward, it is imperative that pharmaceutical sponsors, HCPs, community partners, service providers and policymakers continue to prioritise community-based approaches to increase diverse representation in clinical research. When stakeholders collaborate on these initiatives, the industry will see that underserved populations are not only represented but actively engaged in shaping the future of healthcare.

References:

1. *Visit: census.gov/quickfacts/fact/table/US/RHI225222*
2. *Visit: pmc.ncbi.nlm.nih.gov/articles/PMC9133187*
3. *Visit: pubmed.ncbi.nlm.nih.gov/33026693/*
4. *Seidler E M et al (2014), 'Geographic Distribution of Clinical Trials May Lead to Inequities in Access', Clinical Investigation, 4(4), pp373-380*
5. *Visit: fda.gov/regulatory-information/search-fda-guidance-documents/diversity-action-plans-improve-enrollment-participants-underrepresented-populations-clinical-studies*

Kevin Aniskovich is president and CEO of **Jumo Health**. He sets the strategic direction of Jumo Health, playing primary roles in product development and market positioning. A serial entrepreneur, Kevin's career in healthcare started when his mother was diagnosed with a rare disease and faced a dearth of understandable information about her diagnosis and care.

International
CLINICAL TRIALS

Examining patient recruitment and retention from the site and participant perspective

One of the most demanding aspects of clinical trials is the effective recruitment and retention of patients. An examination of both site and participant perspectives is crucial for gaining valuable insights and addressing challenges

Maryia Bonacker and Daniela Popescu at WCG

Clinical trials are indisputably necessary to bring advancement in medicine, and are heavily regulated in terms of safety and conduct. Yet, with both of these core considerations, the enrolment and retention of patients represent long-standing challenges for both sites and participants, impacting trial success.

In clinical trials, the relationship between the study site and the participant experience is crucial in shaping trial outcomes, participant retention and overall study success. While study sites focus on operational efficiency, regulatory compliance and data integrity, participants bring unique perspectives shaped by their personal health journeys, competing motivations and day-to-day trial experiences.

Understanding the junction between these two viewpoints can help optimise trial design, enhance participant engagement and, ultimately, improve the reliability of trial results.

Examining recruitment from the site and participant perspective

It's relevant to recognise that recruitment serves as an 'umbrella' concept that embraces enrolment, involving numerous complex stages from identifying potential subjects to their first office visit. This extensive process includes not only finding and reaching out to candidates but also screening for eligibility, obtaining informed consent and coordinating logistics, like arranging appointments around a participant's schedule but within the trial protocol requirements. Ensuring a seamless transition from identification to recruitment is imperative for the successful execution of a clinical trial.

Site perspective: operational and scientific rigour

Focusing first on the study site perspective, enrolment barriers include a range of factors. Investigators and site staff prioritise participant safety, accurate data collection and adherence to good clinical practice (GCP) standards. From their perspective, a well-run trial is one where recruitment goals are met, protocols are strictly followed and adverse events are properly documented. However, logistical challenges – such as participant retention, protocol complexity and administrative burden – can impact site efficiency and the trial's overall success.

These challenges to enrolment are significantly impacted by the costs associated with staffing and the limited time available to study team members, who must balance both clinical practice and research responsibilities. Additionally, discrepancies between study protocols and prevailing real-world medical practices further complicate enrolment efforts, underscoring the importance of inclusive eligibility criteria.

Participant perspective: motivation; experience; and trust

From the participant's perspective, recruitment is influenced by several common factors that point to the delicate nature of such participation: access to care; treatment expectations; personal motivations, and; potential burdens related to trial participation.

Participants also consider the convenience of site visits, the side effects of investigational treatments, and the clarity of information provided about risks and benefits.

At the start of an engagement with a potential participant, understanding their motivations and taking time to answer their questions is critical because, as a participant, information can translate to empowerment. This includes sharing information effectively regarding the trial itself, potential side effects, anticipated benefits, specific trial steps and procedures, and the time commitment involved.

A well-supported participant experience – characterised by clear communication, flexible scheduling and empathetic interactions – can enhance adherence and engagement.

Conversely, a disconnect between participant expectations and site operations can lead to dropouts and reduced data integrity.

Many societal prejudices about clinical trials exist. A challenge lies in dispelling the misconception that enrolling in a clinical trial equates to participants being treated merely as experimental subjects. This belief can complicate participant recruitment efforts.

It is vitally important to ensure an engaging and thorough interaction during the informed consent process. Complex language and rushed discussions can lead to frustration and someone potentially choosing not to participate. A well-structured, clear and respectful consent procedure that addresses cultural aspects, language barriers and age considerations can eliminate misunderstandings and clarify uncertainties.

There are multiple motivations for the participants, such as the chance to receive new treatments that are not yet accessible to the public and improved medical supervision during the trial. Participants are closely monitored by a dedicated study team and go through regular check-ups for any potential adverse events or to identify other health conditions that might require attention. This is a considerable motivator, as it gives hope for medical advancements that could potentially improve their health conditions or even save their life.

Bridging the gap: aligning priorities

Recognising these intersections can lead to productive actions and subsequent outcomes. For instance, while core factors may influence an individual's motivation to participate, the availability of time required from the site staff may be limited.

A promising solution involves utilising third-party vendors to assist site staff with study-related tasks, such as recruitment. These professionals can provide the dedicated time that the study team may lack; identifying pools of potentially eligible participants who are not yet visible to the sites and employing strategies such as referral physician networking or community outreach – both of which are often time-intensive. Continuously measuring study needs through data monitoring and adjusting to real-world conditions can also help address study recruitment challenges as they arise. Predicting and managing the inherent uncertainty that clinicians face regarding clinical trials can also significantly aid in the decision-making process. These strategies collectively contribute to overcoming recruitment barriers and enhancing participant involvement in clinical trials.

Examining retention from the site and participant perspective

The successful completion of clinical trials heavily depends on retaining study participants. While recruitment is a key milestone, keeping participants engaged and ensuring adherence throughout the trial is equally important. The intersection between study sites and participants plays a pivotal role in post-recruitment activities, influencing factors such as participant motivation, site engagement and overall trial experience for both parties.

Site perspective: managing burden and enhancing oversight

For many studies, enrolment is the start of the bulk of the work for study

site teams. Once participants are enrolled in a clinical trial, the study site assumes a primary role in guiding, supporting and monitoring participants throughout their journey. Site staff – including investigators, coordinators and nurses – are responsible for ensuring that participants adhere to the protocol while also feeling supported and valued. Recognising signs of participants' non-adherence, such as missed study visits or communication difficulties, is crucial. Interestingly, a significant number of participants drop out directly after consenting to a study, highlighting the need for a dedicated approach by the investigator's team to ensure continued participation from the very beginning.[1]

As study sites frequently run multiple trials, they can be challenged with administrative burdens as each protocol is complex, requiring maximum compliance, adherence to the sponsor's timelines and dedication to strict routines. Participants may experience side effects, doubts about the study or changes in their circumstances that make continued participation difficult. Study site teams are expected to assess well-being at each visit, ensuring that any concerns are acknowledged and addressed.

Furthermore, the responsibilities of a study site related to participant documentation – including data entry and query resolution – are integral components of the overall process. These tasks are not merely byproducts, but essential elements that the site must manage.

Participant perspective: motivation; experience; and trust (again)

For a participant, retention is closely tied to the initial experience at the time of recruitment. The key factors that initially motivated an individual to participate will continue to be the primary considerations that influence their sustained involvement in the study. Gaining insights into participant retention through the lens of the participant is essential for mapping out practical solutions to improve engagement in clinical trials. Challenges participants face can be diverse, and they can impact the willingness to remain in a study if not accounted for. Participants consistently weigh the burden of partaking in a clinical trial against the potential benefits. Upon recruitment, participants often anticipate innovative treatments and sometimes expect quick results. If the trial becomes overly burdensome – due to factors such as frequent visits, invasive procedures or personal inconvenience – participants may lose motivation.

Bridging the gap: reducing complexity

Implementing solutions does not necessitate complexity. Retention strategies adopted by study sites, such as study-specific training, distribution of study materials and sending appointment reminders, have proven to be effective methods. Clear and consistent communication is one of the most effective approaches as it removes the barriers of setting and understanding the expectations, reduces stress and builds trust. Streamlining protocols and offering flexible options makes clinical trials more accessible for participants, and more operational for sites.

Conclusion

In summary, by prioritising participant needs, reducing burdens and fostering meaningful engagement, study sites can enhance retention rates while maintaining the scientific integrity of the study. A collaborative approach that respects both operational efficiency at a site and the participant experience ensures clinical trials not only generate high-quality data from sites, but also build trust in medical research for future participants.

Reference:

1. *Poongothai, S et al (2022), 'Strategies for participant retention in long-term clinical trials: A participant-centric approach', Perspectives in Clinical Research, 14(1), pp3-9*

Maryia Bonacker MBA is a senior country manager at **WCG**. Based in Frankfurt, Germany, Maryia is a seasoned clinical trial professional with an MBA from Fachhochschule für Oekonomie und Management (FOM) in Hamburg, Germany. She leads a team overseeing Recruitment & Retention services in Austria, Croatia, Georgia, Germany, Greece, Netherlands, Russia, Serbia, Switzerland and Ukraine, focusing on accelerating clinical research through efficient enrolment and retention strategies. Fluent in English, German and Russian, Maryia has a strong international background with patient recruitment and retention best practices, and extensive skills in managing clinical trial programmes.

Dr **Daniela Popescu** is a senior country manager at **WCG**, based in Frankfurt, Germany. Originally from Romania, Dr Popescu holds a Pharmacy degree and a PhD in Molecular Biology from the Max Planck Institute for Heart and Lung Research, Germany. Daniela leads a team of country managers overseeing WCG's Recruitment & Retention services in medical institutions across Belgium, France, Israel, Poland, Romania and South Africa, with the aim to provide holistic solutions to optimise site operations and increase patient participation.

The PharmaTimes 2025 Clinical Researcher of the Year – The Americas Awards, is open for entry

With the aim of discovering exceptional talent amongst clinical researchers across the Americas, PharmaTimes Clinical Researcher of the Year – the Americas has established itself as a valuable learning and development opportunity over the past 15 years amongst clinical researchers in pharma, clinical research organisations (CROs) and investigator sites across the globe. The Awards Ceremony is taking place on 27 October 2025 in Raleigh, North Carolina, US.

The competition has 3 stages:

Stage 1: Multiple Choice Questionnaire (MCQ)
Individual entrants complete an online multiple-choice questionnaire, containing questions based on International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), Good Clinical Practice (GCP) and US Food and Drug Administration (FDA) regulatory guidelines. For team entries, you will be required to complete an online application process.

Stage 2: Clinical Challenge (Written Essay)
Individual entrants who score more than 70% at Stage 1 are invited to respond to a short Clinical Challenge which will explore category specific competencies.

Stage 3: The Finals Day
The highest scoring candidates from Stage 2 will be selected to compete in the Finals Day. A unique, fun and challenging learning and development opportunity, the Finals will allow qualifying clinical researchers to complete on-the-day challenges, presenting to judging panels.

The PharmaTimes International Clinical Researcher of the Year Categories can be found on the PharmaTimes website:

croy.pharmatimes.com/categories

For more information on the competition, please contact:

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Setting your sites on successful clinical trials

The selection of sites, and the impact each one has on the overall trial, is not simply a game of chance. How important is nurturing long-standing partnerships with investigative sites, and how can specialist CROs invest time and resources into building their site relationships to ultimately benefit trial sponsors?

Anne Marie Gaulin at Innovaderm Research

Running a clinical trial is riddled with challenges, from patient recruitment and retention to ensuring regulatory compliance and data integrity. Among these, the selection of investigative sites has arguably the biggest influence on the study's success; research sites play a key role in generating robust data and making sure the most appropriate patients are included. These factors impact study timelines and, ultimately, drug approval, with potentially costly ramifications when things go wrong.

Crafting protocols that speak a site's language

Appropriate protocol design is perhaps the primary factor to ensure that the most relevant sites are selected and agree to take part in a clinical trial. Clinicians at these sites rightfully keep their patients at the forefront of this decision, meaning they need to believe not only in the value the tested drug will bring to existing therapeutic options, but also that the design of the study is amenable to their patients. Ideally, these patients should benefit from the experience, even if it's just the chance of relief from a new drug during the study. The study design should therefore take into consideration the number – and intrusiveness – of assessments at every visit, as well as the frequency of those visits. For instance, having multiple blood draws or biopsies, or too many appointments or assessments, is unlikely to attract clinicians or their patients, especially if they are children or elderly. The drug-to-placebo ratio is equally important as it determines a patient's chance of receiving the active drug and possible relief from their condition. Similarly, offering the opportunity for the placebo group to gain access to the drug after a fixed timescale can also be effective. For example, designing a study with a 4:1 ratio of active treatment to placebo, where the placebo cohort can transition to the drug after the primary endpoint has been achieved, is highly appealing and more likely to attract patients.

Some clinical research organisations (CROs) harness in-house research facilities to ensure protocol designs are feasible and attractive for sites and candidates, leaning on experienced staff to review plans in detail. They may also consult with key opinion leaders (KOLs) for their feedback on the design, especially for new indications or determining the feasibility of running sites in specific countries. This is a vital step in patient recruitment, as clinicians will often have patients in mind for a study from the outset, particularly in therapeutic fields with a high prevalence of chronic conditions, such as dermatology and rheumatology. With some patients enrolled from the outset, sponsors will start to notice if there is enough diversity in the clinical trial participants, and whether certain demographics are underrepresented.

Patient diversity is essential to ensure that the findings are applicable to the broadest possible range of individuals who may use the treatment, with regulatory bodies – such as the US Food and Drug Administration (FDA) and European Medicines Agency (EMA) – placing increasing emphasis on representing real-world populations. For example, dermatological studies have traditionally enrolled patients with skin falling between Fitzpatrick types one to four, as it is easier to visualise redness, lesions and other manifestations on lighter skin tones.[1] However, sponsors are now broadening their inclusion criteria to diversify the patient population and, in doing so, they generate more robust data and gain deeper clinical insights.

Exploring international prospects

CROs are increasingly looking further afield to recruit patients meeting the trial's inclusion/exclusion criteria, because it is becoming progressively more difficult to compete for patients in territories such as the US and Canada where so many trials are already underway. Although many sponsors can initially be reluctant to partner with sites in unfamiliar countries, they are quickly convinced when faced with recruitment delays in trials conducted exclusively in North America.

Of course, the challenges of having investigative sites in foreign countries are clear – dealing with different languages as well as addressing the needs of multiple regulatory bodies and reimbursement schemes – but often the advantages far outweigh the drawbacks. The key to overcoming these challenges boils down to identifying countries with experience in running clinical trials in the indication, selecting high-performing sites and establishing relationships with

KOLs in the region for endorsement. It is also vital to understand the therapeutic landscape, prescribing habits of healthcare professionals (HCPs), drug coverage and logistical needs in each country, all of which can only be achieved through experience.

Europe is usually the first preferred expansion region by CROs because it enjoys streamlined regulatory approvals – excluding the UK and other non-EEC states – allowing studies to start and drugs to be marketed simultaneously across countries in the EU. However, it is vital to grasp the intricacies of the varying reimbursement policies, which determine the best locations for a clinical trial. In France, for example, newly approved drugs are quickly added to private and public reimbursement plans to provide widespread – and affordable – access, reducing the incentive for patients to join clinical trials unless the study involves a rare disease or novel mechanism of action. In other EU countries, however, governments often delay reimbursing new drugs, or may limit how many patients can access the new drug in the early years following its approval due to budget constraints. In these cases, clinicians face tough decisions about which patients to treat, and they are far more likely to turn to clinical trials for those who miss out.

These trials provide patients with access to innovative therapies, offering a potential source of relief for those who are excluded from, or are unable to afford, the latest medications.

More than just a site

It is clear that understanding not only how investigative sites operate, but also the goals and ambitions of the clinicians, is essential to gaining their interest in a clinical trial. To this end, a well-respected CRO should treat investigative sites as a key stakeholder, just as it does its sponsors, and recognise – as well as deliver on – the benefits of trials to the HCPs working there. Above all, clinical trials offer a chance for clinicians to be at the forefront of medical advances, providing access to new

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> *...well-established CROs operating in niche fields go one step further by offering additional training to investigators, helping them to optimise the study to generate high-quality data, as well as standardising assessments*

medications for patients who have failed or are no longer responsive to standard treatments, and might otherwise lack therapeutic options.

This ability to address unmet patient need – especially in complex cases – is critical to clinical practice, helping to improve patient outcomes while improving trust and satisfaction. While financial compensation can be a factor, it's rarely the primary driver, especially in teaching hospitals where a good proportion of the funds from clinical activities benefits the institution. For academic centres, the prestige associated with clinical trials also plays its part, providing an opportunity to publish findings and build a research profile. Finally, clinical trials introduce new opportunities and variety to medical practice, especially in fields like dermatology and rheumatology where patient cases concentrate on key common indications. Clinicians therefore appreciate the diversity that research introduces to their practice, as well as the chance to work with patients on a different level.

There is little doubt that strengthening the CRO-investigative site relationship in these ways builds trust and fosters future collaborations. But well-established CROs operating in niche fields go one step further by offering additional training to investigators, helping them to optimise the study to generate high-quality data, as well as standardising assessments. This training is crucial for aligning the site staff with the protocol requirements, regulatory guidelines and the study's specific objectives, especially for less experienced sites.

The art of collaboration

Initiatives such as this underscore the key advantages of partnering with specialist CROs: their profound expertise in the chosen field and the strong relationships they have cultivated with key stakeholders over time. Concentrating on the same field means that specialist CROs have a wealth of disease-specific knowledge, ensuring they are instantaneously on the same wavelength as the sponsor. Importantly, it also means they have an acute awareness of what's happening in the industry, and know who and where to turn for each indication. Experienced CROs should be able to quickly assess the quality of each investigative site, taking into account a variety of factors including indication experience, patient recruitment capability, ability to adhere to protocols and timelines, and other logistical and competency-related aspects, which ultimately saves time at study start up.

With established relationships in place, the best CROs also know the clinicians who have access to the relevant patient population, as well as the KOLs most likely to become advocates for the medication once launched.

Conclusion

The choice of investigative sites is certainly a vital factor in determining the outcome of a clinical trial. Taking a data-driven and collaborative approach to site selection – as well as developing patient-centred protocols, fostering diversity in patient demographics and harnessing expertise in navigating global regulatory landscapes – is the key to success. This often hinges on the expertise of the CRO that can add immense value through established partnerships and knowledge of international regulations. CROs should focus on aligning sponsors, investigators and patients towards a shared goal, forming partnerships that strengthen trust, accelerate timelines and, ultimately, lay the foundation for future breakthroughs in medicine.

Reference:

1. *Visit: uhd.nhs.uk/uploads/about/docs/our_publications/patient_information_leaflets/dermatology/The-Fitzpatrick-Skin-Type-Chart.pdf*

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Safety first

Considerations for the development and manufacture of highly potent drug products, particularly in oncology treatments

David O'Connell at PCI Pharma Services

As biopharmaceutical companies continue to invest in precision oncology treatments, the development and manufacture of drug products containing highly potent active pharmaceutical ingredients (HPAPIs) remain in high demand. These versatile compounds deliver therapeutic benefits at low doses with less toxicity than conventional cancer treatments. HPAPIs can be used as stand-alone therapies, as part of antibody drug conjugates (ADCs), or in immuno-oncology agents.[1] According to one report, about 60% of oncology drugs contain HPAPIs.[2]

Scientific and technical advances have enabled the development of HPAPIs that were previously limited due to safety and toxicity challenges. However, safety remains the primary concern to protect not only patients but also facility staff from overexposure to potentially harmful substances.

A rigorous containment strategy, validated cleaning protocols and an established track record in handling HPAPIs are critical for any contract development and manufacturing organisation (CDMO) responsible for developing and/or manufacturing such therapies. Experience in the development and manufacturing of drug products containing HPAPIs is essential, as it enables successful translation of highly potent drug substances into safe, effective therapies for patients who urgently need them.

Trends in highly potent oncology APIs

Because of their ability to target diseased cells at low doses, HPAPIs are well suited to oncology in a range of dosage forms. The more traditional oral solid dosage (OSD) forms (tablets and capsules) remain a strong driver for growth. A Research and Markets report states that the global OSD market is expected to exceed $72bn by 2030, registering a compound annual growth rate (CAGR) of around 8.6%.[3] There is also a growing interest in antibody-drug conjugates (ADCs), which use extremely potent and effective antineoplastic payloads linked to a monoclonal antibody. Roots Analysis has estimated that the ADC contract manufacturing market will hit around $7bn by 2035, registering a CAGR of about 13%.[4]

HPAPIs require special handling, however, due to their toxic potential to cells. A strict containment strategy is therefore essential for patient and worker safety. Because of the toxic nature of HPAPIs, traditional open processing methods for handling a non-potent API are insufficient. Among other differences, formulators and manufacturing personnel must rely on data from processing machines rather than information obtained first-hand. HPAPI drug products are generally manufactured at smaller production scales due to the low doses required to initiate advantageous pharmacological effects. This means production facilities must have both small-scale operations as well as an ability to scale up to large-scale clinical and commercial operations if demand is high. Because of the strict handling protocols, iterative data-driven processes, and specialised equipment and personnel required to develop HPAPIs, success and speed-to-market can hinge on CDMO selection.

A proactive approach to highly potent OSD manufacturing

Pharmaceutical companies and their CDMOs classify APIs based on occupational exposure limits (OEL). OEL assessments are used to measure the acceptable concentration of API in workplace air; the lower the limit, the higher the toxicity. HPAPIs typically fall into the toxic or extremely toxic categories, with an OEL at or below 10µg/m.[5]

To ensure drug substance exposure to the workforce remains at or below defined limits, an experienced CDMO will practice robust new product introduction (NPI) processes. NPI starts with proof-of-concept testing to assess whether the product and processes achieve the desired result. Once this benchmark is met, the CDMO can expand production to the predetermined clinical or commercial scale.

Other protocols CDMOs must use during NPI include:

- Performing the required activities in a contained facility, using totally enclosed process equipment
- Producing suitable data (eg, torque, tablet hardness, compaction) for risk assessments, since the product cannot be observed during processing
- Preventing cross-contamination and exposure in all circumstances.

CDMO partners with HPAPI experience use validated, automated clean-in-place or wash-in-place systems for equipment. Cleaning processes are notoriously difficult from an exposure protection perspective, as the introduction of huge amounts of cleaning solutions using pressurised systems can stress the containment design of the equipment, potentially resulting in exposure leaks.

In addition, compounds must be treated so they do not contaminate the water

supply. In all, CDMO facilities must build multiple levels of containment into their design – a prerequisite for the development, clinical production and commercial supply of products with an OEL down to 0.01µg/m^3.

Dispensing for OSD products is performed within either rigid-walled isolators or flexible isolators. Here, CDMOs use various methods to safely transfer HPAPI with excipients to the sieving equipment or next stage in the process. Split butterfly valves and flexible containment bags mitigate risk during product transfer.

Granulation, milling, blending, encapsulation, tabletting and film coating use enclosed processing design techniques such as isolator units, negative pressure processing and enclosed movement of powdered product from one process to another – again, to minimise exposure. The ISPE Standard Methodology for the Evaluation of Pharma Airborne Particle Emissions from Containment Systems Good Practice Guide is used to determine OELs.[6]

ADCs: a different approach for a novel technology

HPAPIs previously deemed too potent for administration are moving through clinical trials as ADCs – to date, the US Food and Drug Administration (FDA) has approved 15 ADCs.[7] Due to their ability to selectively deliver antineoplastic payloads to target cells, ADCs are a promising area of cancer treatment.[8] Because of their composition – typically a monoclonal antibody (mAb) covalently attached to a cytotoxic drug via a chemical linker – careful selection of target antigen, antibody, payload, linker and conjugation methods are critical to achieve safety and efficacy.[9]

CDMOs tend to specialise in either bioanalytical services or later-stage services, such as fill-finish and lyophilisation for ADCs. Concerning the latter, operator safety remains paramount, though the processes differ from conventional methods. Instead of using positive pressure to protect the product in fill-finish, ADCs require negative pressure isolator technology to handle some formulation and compounding aspects of the liquid and mixing. The drug product is fed into a positive-pressured aseptic filling zone to ensure sterility, then filled into glass vials and capped. To ensure that potential exposure risk is reduced, vials should be fed into a further negative pressure isolator for a final outer-vial clean.

Lyophilisation requires a hybrid isolator that begins with positive pressure to protect the product, followed by negative pressure to ensure containment during vial exterior cleaning. This prevents HPAPI from adhering to the glass, mitigating cross-contamination.

Quality considerations

A robust quality management system (QMS) is an essential requirement for successful development and regulatory approval of any product. For products using HPAPIs, OEL, risk assessment and other product data must be acquired early to ensure safe, efficient development

and manufacturing that meets good manufacturing practice (GMP) quality and purity standards.

When developing and manufacturing drug products containing HPAPIs, quality assurance (QA) and quality control (QC) are intertwined. QA functions include, but are not limited to, ensuring that no cross-contamination between equipment has occurred, that operators have suitable protection and that the facility uses negative-pressure equipment systems.

Tests that relate to QC, such as Karl Fischer titration (a common test for moisture), will need to be modified to protect analysts when handling highly potent drug products. Analysts grinding up tablets or pooling capsules require the same level of exposure protection as manufacturing operators.

During formulation development, experts typically devise a suitable Design of Experiment (DoE)/Quality by Design (QbD) approach at early stages in a product's life cycle. DoE is statistical and systematic, with the goal of optimising the product and process by understanding the relationship between various input and output variables.[10] This method helps identify the most influential factors, determine their optimal levels, and establishes robust and efficient processes while minimising the number of experimental runs.

Future outlook for HPAPIs in oncology

While drug products containing HPAPIs are beneficial to a range of therapeutic areas – including neurology, autoimmune disorders and women's health – oncology is currently a major driver. The versatility of HPAPIs to target disease cells at low doses makes them attractive for oral solids, immunotherapies and hybrid therapies such as ADCs. Additionally, from an OSD perspective, highly targeted, non-injectable drug products are easier to administer and are therefore more patient-centric. CDMOs with dedicated facilities, engineered containment technologies, and deep scientific knowledge and experience with HPAPIs are most likely to possess the containment strategies necessary to deliver safe, quality products with the least amount of risk. Those with broad, end-to-end capabilities reduce risk further while potentially accelerating speed to market.

As the global oncology landscape evolves, it is imperative for CDMOs to refine their containment strategies to accommodate emerging products such as combination therapies and ADCs. They must also have the flexibility to manufacture not only smaller clinical batch sizes, but commercial batch sizes in the hundreds of kilograms range based on commercial success and demand.

Large biopharma companies, as well as emerging biotech start-ups, are exploring oncology therapies containing HPAPIs. Meeting the needs of both types of customers requires both extensive scientific expertise as well as enabling technologies. By offering both from early development through to commercialisation, a CDMO can develop and test prototypes and then scale up to clinical trials and beyond, all while reducing the number of technical transfers. CDMOs that can provide integrated services for clients will ensure the development of safe, effective and personalised oncology therapies for patients facing life-altering diseases.

References:

1. *Visit: themedicinemaker.com/discovery-development/getting-a-handle-on-high-potency*
2. *Visit: rootsanalysis.com/reports/hpapi-and-cytotoxic-drugs-manufacturing/299.html*
3. *Visit: researchandmarkets.com/report/oral-solid-dosage-contract-manufacturing*
4. *Visit: rootsanalysis.com/reports/adc-contract-manufacturing-market/218.html*
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7. *Visit: adc.bocsci.com/resource/review-and-formulation-analysis-of-14-antibody-drug-conjugates-adcs-approved-by-fda-up-to-2022.html*
8. *Tsuchikama K et al (2024), 'Exploring the next generation of antibody-drug conjugates', Nat Rev Clin Oncol, 21(3), pp203-223*
9. *Fu Z et al (2022), 'Antibody drug conjugate: the "biological missile" for targeted cancer therapy', Signal Transduct Target Ther, 7(1), p93*
10. *Visit: pci.com/resources/cdmo-insights-high-potent-formulation-development-in-oncology*

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From blood to breakthroughs: how multi-analyte liquid biopsies can transform precision oncology, drug development and clinical trials

Addressing key oncology drug development challenges through multi-analyte liquid biopsy approaches

Karen Miller and Sydney Barrell at ANGLE plc

Multi-analyte and multi-omic liquid biopsy is a minimally invasive procedure that analyses multiple tumour-derived components (analytes) in body fluids (generally blood) to provide a real-time, comprehensive view of a patient's cancer. Such multi-omic analysis is transforming oncology drug development by addressing key challenges that pharmaceutical companies face in early drug development and clinical trials. Multi-analyte liquid biopsy analysis provides a cost-effective means to stratify patient cohorts, track clonal evolution and tumour heterogeneity, detect resistance mutations early, and identify minimal residual disease (MRD). As such, liquid biopsy provides real-time insights that can enhance clinical trial outcomes.

The complexity of cancer biology presents significant challenges for the pharmaceutical industry, particularly in developing effective, targeted treatments. While valuable for initial diagnostics, traditional tissue biopsies are invasive and impractical for repeat monitoring of patients. Liquid biopsy offers a transformative, minimally invasive solution for analysing multiple biomarkers circulating in the bloodstream.[1] By incorporating multi-analyte and multi-omic data, liquid biopsy can address some of the key challenges in oncology drug development and clinical trials, from patient stratification and monitoring tumour dynamics to enhancing patient safety and trial efficiency (**Figure 1**).

The multi-analyte approach

Liquid biopsy analytes, primarily circulating tumour DNA (ctDNA) and circulating tumour cells (CTCs) provide complementary insights into the tumour landscape. ctDNA – the most established analyte in liquid biopsy due to straightforward sample collection, molecular analysis and significant investment – consists of fragmented DNA released predominantly from dying cancer cells through necrosis or apoptosis.[1,2] Through analysis of ctDNA, researchers can identify mutation status and track genetic changes associated with resistance or disease progression.[1] This information can also be obtained by analysing genomic DNA (gDNA) derived from CTCs – intact, viable tumour cells that spread the cancer, often referred to as the 'seeds of metastasis'.[3] CTCs are the closest proxy to solid tissue biopsy.[4] They not only carry gDNA but also a wealth of information in their proteome, transcriptome and metabolome (multi-omic data).[4,5] By analysing proteins, RNA and metabolites within CTCs and CTC clusters, researchers can gain additional insights into tumour aggressiveness, metastatic potential and altered metabolic pathways.[1,5] Other liquid biopsy analytes include exosomes (extracellular vesicles [EVs]), circulating free RNA (cfRNA), specific proteins and metabolites that potentially offer additional clues about immune evasion and intercellular signalling.[5]

The dual analysis of ctDNA and CTCs is gaining traction and provides valuable complementary insights into tumour dynamics, enabling real-time, adaptive responses to cancer's complex behaviours.[2,6]

Some key challenges faced in oncology drug development and clinical trials

Challenge: need for real-time monitoring

Traditional biopsies are invasive, costly and unsuitable for repeat sampling, and may only be repeated once more from a metastatic site.[1,7] The unsuitability of tissue for real-time monitoring to detect changes in tumour

Figure 1: Use of liquid biopsy in the patient care pathway

dynamics prevents timely and effective treatment decisions. Multi-analyte liquid biopsy provides an ideal solution by enabling repeat sampling to provide a real-time view of tumour evolution. Through regular analysis of ctDNA, CTCs and other analytes, researchers gain continuous insights into tumour progression, mutation patterns and cell behaviour, capturing changes that could otherwise go unnoticed.[6,8] Lustberg *et al* discuss the value of this approach, highlighting the potential of monitoring liquid biopsy analytes to provide insights into tumour evolution and resistance mechanisms.[7] One study found that HER2 status changed in 37% of breast cancer recurrences, underscoring the importance of re-evaluating tumour biomarkers to optimise drug treatment.[9] Furthermore, multiple papers describe how liquid biopsy is effective in detecting minimal residual disease, often providing early indication of relapse before traditional imaging methods reveal progression.[10,11,12] In one case, CTC enumeration indicated the presence of MRD four years before clinically detectable metastatic disease, offering early insights for therapeutic management.[13] In clinical trials, real-time molecular data from liquid biopsies could prove invaluable by providing up-to-date insights into tumour dynamics. This has the potential to improve clinical trials by enabling pharmaceutical teams to monitor treatment efficacy more rapidly, evaluate biomarker changes over time and make data-driven adjustments to trial strategies, thereby minimising uncertainties, optimising patient care and ensuring that emerging disease changes are not overlooked.

Challenge: tumour heterogeneity and drug resistance monitoring

Cancer's inherent variability presents a major obstacle in oncology, as both interpatient heterogeneity (differences

across patients) and intrapatient heterogeneity (differences within a single patient) make treatment selection and efficacy difficult to predict.[14,15] Tumours evolve dynamically, with cancer cell populations mutating in response to therapies, often leading to treatment resistance.[1,14] Therefore, to develop effective treatment strategies, pharmaceutical companies need a clear understanding of the tumour and the ability to monitor its evolution.

Multi-analyte liquid biopsy tackles tumour heterogeneity and drug resistance by providing a comprehensive, real-time molecular profile that captures a tumour's evolution.[2,6] By integrating data from ctDNA, CTCs and other analytes, liquid biopsy enables researchers to track the emergence of specific mutations or adaptive characteristics as they arise.[5,6,15] A study in melanoma by Sementsov *et al* used a multi-analyte approach, and demonstrated that CTC analysis provided additional genomic information to ctDNA in 68.8% of the samples, identifying mutations in key melanoma pathways related to metastasis and therapeutic resistance, such as BRAF, NRAS, CTNNB1 and MAP2K1.[8] These findings exemplify how CTCs deliver unique and complementary insights into tumour evolution and resistance mechanisms.

This dynamic tracking is crucial in clinical trials, where treatment resistance is a frequent cause of trial failure. By detecting resistance mutations early and observing changes in tumour cell characteristics, liquid biopsy allows R&D teams to make timely, data-driven decisions. Early prediction of treatment failure may enable trials to 'fail fast', by providing an early endpoint when signs of resistance arise, and help to reduce costly later-stage failure. It may also help identify patient cohorts with a specific

biomarker profile who are either likely or unlikely to benefit from the study drug, and can therefore be included or excluded from subsequent studies.

The LIQUID IMPACT trial highlights the potential of multi-analyte liquid biopsy for addressing tumour heterogeneity and resistance in advanced cancers.[16] By measuring protein expression changes, such as EGFR and mTOR overexpression, the study demonstrated an ability to monitor key tumour characteristics.[16] This capability is valuable for pharmaceutical companies seeking to stay informed about dynamic changes in a patient's cancer.

Challenge: patient stratification for precision medicine

Accurate patient stratification is critical for targeted treatment and ensuring positive clinical trial outcomes. Selecting patients whose tumour profiles align with investigational drugs may enhance trial success rates, reduce trial costs, increase pricing and reimbursement coverage, and accelerate drug development. Multi-analyte liquid biopsy offers a comprehensive and non-invasive approach for revealing relevant genetic, transcriptomic and proteomic changes essential for targeted patient selection.

The ELIMA project exemplifies this approach by analysing CTCs, EVs and ctDNA from a single blood sample.[17] This method enabled the identification of patients who may benefit from specific therapies, such as the PIK3CA inhibitor Alpelisib, which has been approved for metastatic breast cancer patients with PIK3CA mutations detected in ctDNA.[17] Another clinical trial demonstrates that proteomics from CTCs can significantly enhance patient stratification by identifying patients most likely to benefit from advanced targeted therapies, such as antibody drug conjugates (ADCs).[18] By enabling the selection of patients with the highest likelihood of response, stratification ensures trials are both cost-effective and positioned for regulatory and commercial success, avoiding the risks associated with low response rates.

Examples for this being integrated in best practice include AstraZeneca's application of a multi-omic strategy. By integrating genomics, transcriptomics, proteomics and metabolomics data across its oncology pipeline, AstraZeneca enhances trial participant selection by focusing on specific tumour pathways, improving the accuracy of treatment response predictions.[19]

Challenge: rising costs, regulatory pressures and drug pricing

The financial and regulatory demands in oncology drug development are considerable, and developing a new drug requires substantial resources to meet strict regulatory standards for safety, efficacy and cost-effectiveness. High failure rates, especially in later phase trials, further burden budgets and delay patient access to new treatments. Multi-analyte liquid biopsy offers a strategic advantage by providing real-time molecular insights that support early trial adaptations, reduce costly late-stage failures and alleviate the financial pressures of precision oncology trials. For instance, a lung cancer trial at the University of Arkansas for Medical Sciences (UAMS), US, utilises liquid biopsy for longitudinal monitoring. This approach aims to improve efficiency by enabling earlier detection of recurrence and tailoring interventions, potentially reducing trial costs through streamlined processes and minimising the need for invasive procedures.[20]

Pantel and Alix-Panabières, in *Nature Reviews Clinical Oncology*, highlight the cost-saving potential of liquid biopsy in oncology trials, noting that monitoring CTCs and ctDNA may serve as early surrogate endpoints for clinical outcomes.[11] This approach could shorten follow-up and reduce costs, allowing pharmaceutical companies to make faster, cost-effective decisions in evaluating adjuvant therapies.

Conclusion

Multi-analyte and multi-omic liquid biopsy continues to demonstrate its potential in overcoming key challenges in the oncology space. The integration of liquid biopsy into clinical trials may pave the way for faster, more cost-effective drug development and improved regulatory compliance. By delivering precise, real-time molecular insights, liquid biopsy can enhance patient stratification, treatment monitoring and clinical trial efficiency, ultimately accelerating the development of effective precision cancer therapies. Current clinical trials are evaluating dual CTC and ctDNA analysis across multiple cancer types to stratify patients, monitor treatment response and enhance sensitivity in disease monitoring as compared to standard practice.[2]

> *The integration of liquid biopsy into clinical trials may pave the way for faster, more cost-effective drug development and improved regulatory compliance*

Once approved, targeted drugs such as ADCs, DNA damage response (DDR) inhibitors and immuno-oncology drugs require targeted treatment selection through a companion diagnostic. Utilising liquid biopsy solutions will be critical to enable real-time, repeatable biomarker assessment to support regulatory clearance and reimbursement.

References:

1. *Alix-Panabières C et al (2021), 'Liquid Biopsy: From Discovery to Clinical Application', Cancer Discov 11, pp858-873*
2. *Wishart G et al (2024), 'Molecular Profiling of Circulating Tumour Cells and Circulating Tumour DNA: Complementary Insights from a Single Blood Sample Utilising the Parsortix® System', Curr Issues Mol Biol 46, p773*
3. *Gupta S et al (2017), 'Whole Genomic Copy Number Alterations in Circulating Tumor Cells from Men with Abiraterone or Enzalutamide-Resistant Metastatic Castration-Resistant Prostate Cancer', Clin Cancer Res 23, pp1346-1357*
4. *Zhang C et al (2016), 'Tumor heterogeneity and circulating tumor cells', Cancer Lett 374, pp216-223*
5. *Yu W et al (2021), 'Exosome-based liquid biopsies in cancer: opportunities and challenges', Ann Oncol 32, pp466-477*
6. *Ntzifa A et al (2021), 'Detection of EGFR Mutations in Plasma cfDNA and Paired CTCs of NSCLC Patients before and after Osimertinib Therapy Using Crystal Digital PCR', Cancers 13, p2736*
7. *Lustberg M B et al (2018), 'Implementing liquid biopsies in clinical trials: State of affairs, opportunities and challenges', Cancer J. Sudbury Mass 24, p61*
8. *Sementsov M et al (2024), 'Mutation analysis in individual circulating tumor cells depicts intratumor heterogeneity in melanoma', EMBO Mol Med 16, pp1560-1578*
9. *Bergeron A et al (2023), 'Anticipating changes in the HER2 status of breast tumours with disease progression – towards better treatment decisions in the new era of HER2-low breast cancers', Br J Cancer 129, pp122-134*
10. *Nikanjam M et al (2022), 'Liquid biopsy: current technology and clinical applications', J Hematol Oncol 15, p131*
11. *Pantel K et al (2019), 'Liquid biopsy and minimal residual disease – latest advances and implications for cure', Nat Rev Clin Oncol 16, pp409-424*
12. *Anandappa G et al (2021), 'Minimal residual disease (MRD) detection with circulating tumor DNA (ctDNA) from personalized assays in stage II-III colorectal cancer patients in a U.K. multicenter prospective study (TRACC)', J Clin Oncol 39, pp102*
13. *Stergiopoulou D et al (2023), 'Comprehensive liquid biopsy analysis as a tool for the early detection of minimal residual disease in breast cancer', Sci Rep 13, p1258*
14. *McGranahan N et al (2017), 'Clonal Heterogeneity and Tumor Evolution: Past, Present, and the Future', Cell 168, pp613-628*
15. *Gilson P et al (2022), 'Deciphering Tumour Heterogeneity: From Tissue to Liquid Biopsy', Cancers 14, p1384*
16. *Visit: doi.org/10.1101/2021.12.23.21268152*
17. *Visit: magazine.eacr.org/multi-analyte-multi-omic-liquid-biopsy-testing-for-therapy-management-of-breast-cancer-patients*
18. *Fehm T et al (2024), 'Efficacy of Lapatinib in Patients with HER2-Negative Metastatic Breast Cancer and HER2-Positive Circulating Tumor Cells-The DETECT III Clinical Trial', Clin Chem 70, pp307-318*
19. *Visit: astrazeneca.com/what-science-can-do/topics/disease-understanding/new-era-multi-omic-data-analysis-oncology.html*
20. *Visit: onclive.com/view/partner-perspectives-uams-winthrop-p-rockefeller-cancer-institute-pushes-liquid-biospy-research-forward*

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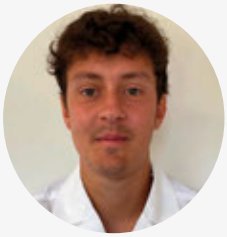


Sydney Barrell is a medical writer at **ANGLE plc**. Sydney holds a Master's degree in Genetics from the University of Sussex, UK, where his research focused on genome maintenance, replication fork proteins and chemotherapy resistance. His work contributed to projects at the Genome Damage and Stability Centre, developing a deeper understanding of mechanisms critical to cancer biology and treatment.

Understanding the role of imaging in streamlining oncology trials and improving the patient experience

The demands and risks of imaging technologies pose challenges to patients and practitioners in oncology trials, but they have the potential to improve patient experiences, transform the work of imaging scientists and streamline clinical trial management

Sarah Westall at Medidata Solutions

Imaging is necessary in the vast majority of solid tumour and lymphoma oncology trials to assess drug efficacy, and is often used to support a primary or secondary endpoint. Imaging technologies such as MRI, CT and PET scans are the primary applications practitioners use to identify tumours and monitor how they are affected by new therapies. Last year alone, 35 oncology US Food and Drug Administration (FDA) drug approvals for solid cancer tumours relied on data gathered from imaging as a primary endpoint, highlighting the important role imaging plays in oncology trial outcomes.[1]

Patient experiences

At the centre of oncology trials are patients, who can face significant challenges when participating in studies involving imaging because of the anxiety and health risks associated with undergoing scans. Despite the importance of imaging technologies, many cancer patients find experiences of scans invasive and uncomfortable due to the duration of the scanning process or the nature of the equipment involved. Oncology patients are also vulnerable to further health complications caused by repeated and long-term exposure to radiation and strong magnetic fields if they are required to undergo many scans repeatedly.

In response to these challenges, imaging scientists and clinical trial providers should work to optimise how imaging data is shared and treated across different clinical trial sites. This could ensure that patients don't have to undergo repeated scans unnecessarily. At the moment, patient data remains highly siloed, and participants do not always receive access to their scans once they have been uploaded and used by clinical trial managers. This often leaves patients feeling disengaged from the clinical trial process, as they are denied the opportunity to actually see the data that can contribute to their own treatment plans and health records. Therefore, imaging scientists should take measures to return data to patients, which can also minimise the need for patients to undergo further scans should they be visiting another clinical trial site or doctor as imaging data can be repurposed.

In addition, patients often need to travel to the imaging centre at a designated enrolling site, which can often be far away from their home. As oncology patients are often very unwell, reducing the physical, logistical and health burden of travelling to multiple sites to participate in imaging scans is paramount for improving the patient experience in oncology trials. As well as this, imaging scientists can work to improve how the context and significance of imaging data in oncology trials is communicated to participants, such as by keeping patients informed of trial outcomes, key endpoints and drug developments that have been achieved as a result of their contributions.

Challenges facing CROs and sponsors

As well as the challenges facing patients, many of the burdens of imaging in oncology trials fall on contract research organisations (CROs) and sponsors. Compared to other diagnostic technologies, clinical management of imaging has lagged behind wider developments in the diagnostic healthcare sector. This is largely because managing imaging in the clinical trials process requires a synergy of various trial processes, from data capture and de-identification, to system upload and image sharing. Introducing integrated platforms for managing and sharing imaging data can help to mitigate existing difficulties CROs face in reconciling data queries, thereby reducing their workload and speeding up processes.

Sponsors and CROs can also work towards enhancing data reproducibility, so that standardised results can be produced consistently across different trial sites and studies. As imaging technologies continue to evolve and play a pivotal role in oncology trials, it is also becoming increasingly important for researchers and imagining scientists to enhance their understanding of data integrity and good

> *...focusing on the role of imaging in oncology trials can help to shine light on the strengths and limitations of clinical trial management, data processing and patient engagement as they currently stand today*

clinical practice (GCP) principles in the acquisition and treatment of imaging data, ensuring oncology trials protect patient privacy and uphold regulatory standards.

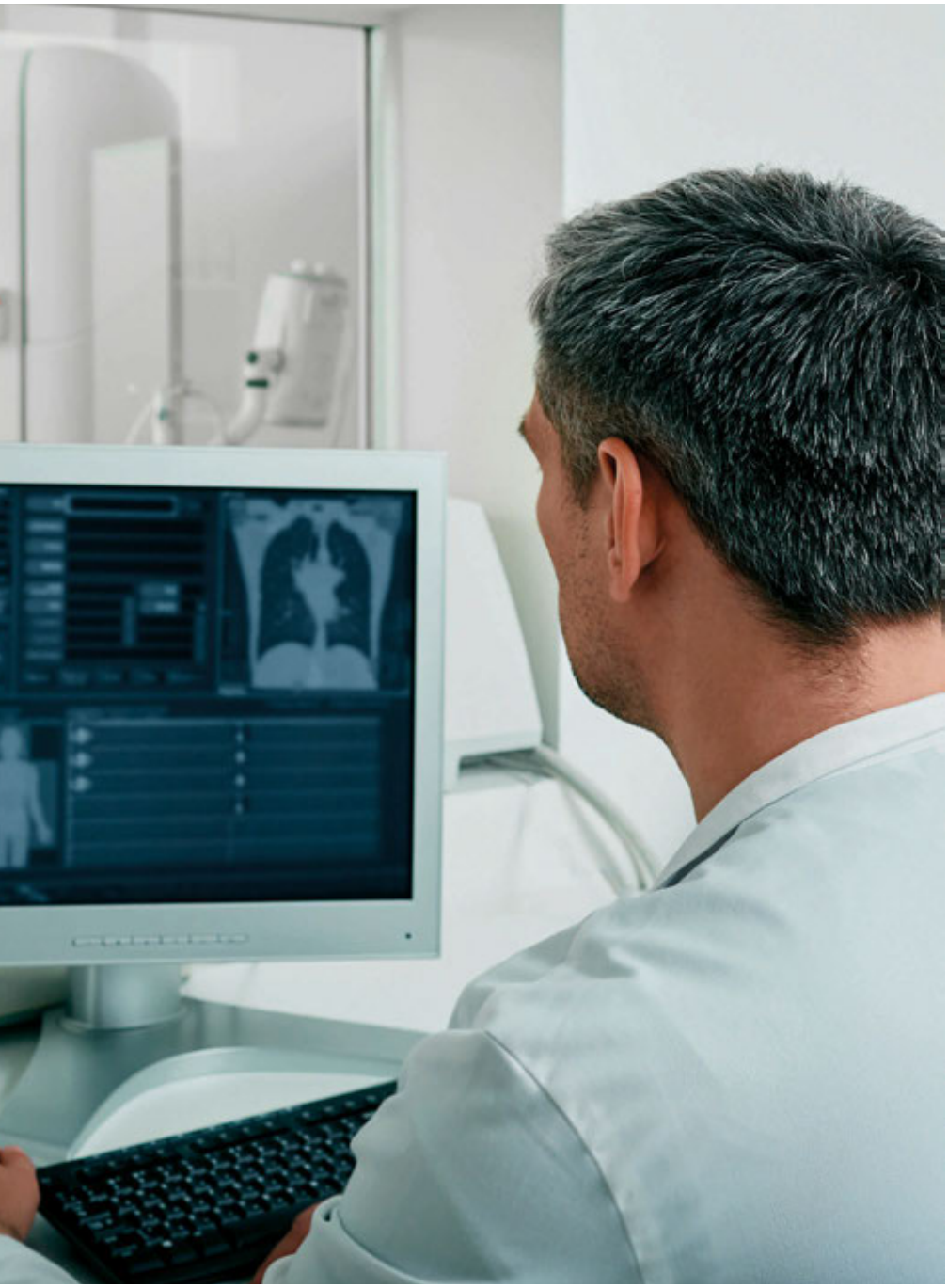
The role of AI

Innovations in artificial intelligence (AI) can play a vital role in assisting, rather than replacing, the responsibilities of radiologists and imaging scientists in oncology trials. By leveraging AI as an assistive tool, practitioners can reduce errors, improve the early detection of cancer tumours and spot subtle tumour growths or regressions quicker than the human eye.

In clinical trial management, AI can also be used to streamline processes, relieving radiologists who suffer from 'reader fatigue', as they are often overburdened with performing blinded independent clinical trial reads after their full-time clinic work. For example, AI models can be used to confirm uploads of images, remove personal health data for de-identification and provide automatic lesion detections in pre-annotated images for radiologists to confirm. The latter point is particularly significant for reducing reader variability in image readings between different practitioners and clinical sites, improving how efficiently imaging data is managed whilst ensuring it remains standardised and consistent across different sites. The use of AI models can also be leveraged to improve patient experiences and outcomes during oncology trials, as images can be treated and re-shared in a standardised, high quality format that may reduce the need for patients to undergo additional scans.

Future trajectories

Alongside the technical innovations that promise to transform oncology trials, the future of imaging in trials is highly dependent on boosting collaboration between oncologists and radiologists – who work on delivering treatment plans for patients – and imaging scientists, who review imaging data and provide insights on therapies and patient responses for clinical trials. Despite their different roles, co-ordinating workflows and improving communication between these two groups can ensure that imaging scientists communicate quicker with physicians to effectively support trial outcomes. More standardised communication and processes can also help to ensure that oncology trials are increasingly mobile and accessible for patients. For instance, if imaging data were made more shareable and reproducible, patients could potentially visit any clinical trial site to participate in a study, reducing the need to travel beyond their local hospital or clinic, or interrupt their holiday schedules. As sponsors and CROs invest a lot of time and resources into delivering imaging scans for patients, there are wider benefits to better utilising imaging data once it has been collected.



Currently, images tend to be 'single-use' for application on trials only. If this data could instead be stored and repurposed, CROs and sponsors could use it to identify where certain patients may benefit from participating in other oncology trials.

Therefore, focusing on the role of imaging in oncology trials can help to shine light on the strengths and limitations of clinical trial management, data processing and patient engagement as they currently stand today. CROs, sponsors, oncologists and imaging scientists will need to work more collaboratively to better synthesise the various processes of oncology trials with the promising applications of imaging technology. Only by doing so will oncology trials be able to fully leverage the potential of imaging technology to enhance early detection, diagnostic accuracy and patient-centred engagement.

Reference:

1. *Visit: fda.gov/media/175253/download?attachment*

Sarah Westall is a connected data team lead at **Medidata Solutions**. Sarah works across various therapeutic areas to provide clinical trial managers with faster, cheaper and lower-risk cloud-based medical imaging systems to simplify trial processes for labs, sponsors and trial sites. Before joining Medidata in January 2022, Sarah spent over fifteen years working in sales for a range of clinical software providers that created digital solutions for adverse events collection, laboratory information and database management.

International
CLINICAL TRIALS

Why data monitoring committees are crucial in multi-regional oncology trials

In multi-regional oncology clinical trials, the inherent complexity of trial design and execution is amplified by the diverse cultural, genetic and health practice variabilities across global regions. Such diversity necessitates robust mechanisms to safeguard both data integrity and patient safety

Barbara Schneider at Advarra

In February 2022, the US Food and Drug Administration (FDA) highlighted its concerns over the relevance of trial data to US patients when the FDA's Oncologic Drugs Advisory Committee (ODAC) rejected approval of the PD-1 inhibitor sintilimab (Eli Lilly and Company and Innovent Biologics) for non-small cell lung cancer (NSCLC).[1]

Among other concerns, the main trial – ORIENT-11 – was conducted entirely in Innovent's home country of China, and the ODAC said the trial did not reflect the broad genetic diversity of patients in the US.[2,3] Treatment received by ORIENT's control arm – chemotherapy instead of another PD-1 blocker – also fell short of the current US standard of care. ODAC asked for additional studies to prove the value of the agent in a US-based population, but more than two-and-a-half years later, sintilimab remains unapproved.

The FDA said in a press release that it has been seeing decreasing proportions of US participants in oncology multi-regional clinical trials (MRCTs).[4] But, in fact, the rate of adult cancer treatment trial participation has seemingly increased from 2-3% in the 1990s and early 2000s, to 5% in the 2010s, and with the current estimates now being 7.1%.[5] Unfortunately, the participation rates are proven fallacy when considering the jump in the number of oncology trials overall, with the number having nearly quadrupled since 2000 from 421 trials to 1,489 trials in 2021, showing that participation rates have not kept pace.[6]

The decreasing proportion of US participants in recent oncology MRCTs limits the Agency's ability to assess whether treatment outcomes in the US reflect those observed globally. In response, the FDA issued new draft guidance titled *Considerations for Generating Clinical Evidence from Oncology Multiregional Clinical Development Programs* in September 2024.[7] The guidance expands on current principles of MRCTs and emphasises the importance of generating clinical evidence that's both inclusive and representative, particularly when it comes to US cancer patients.

This recent guidance underscores a transformative approach in regulatory expectations, particularly highlighting a commitment to inclusion and representation for heterogeneous patient populations within the US.

Implications of FDA guidance on cancer MRCTs

Recognising that most drug development is global, the guidance explains how drug developers should address requirements for ensuring oncology MRCTs include populations that enable interpretability and relevance of the results to US patients. The guidance also clarifies the FDA's position on the use of foreign data to support marketing applications for cancer therapies in the US, with the FDA's draft guidance on MRCTs emphasising that oncology trials should adequately represent the US population, and ensure that trial results are generalisable and interpretable in the context of US medical practice.

A major shift in this guidance is the FDA's insistence that clinical trials conducted in a single country or region will no longer be sufficient to support a

marketing application in the US since this data will not enable understanding of any differences in treatment effect for the diverse US population. While FDA regulations allow for the use of foreign data to support a marketing application, the regulations – along with the guidance focused on ensuring diversity in clinical trials – state that foreign data is acceptable only if the patient population is representative in terms of criteria such as demographics and disease characteristics. This places additional responsibility on sponsors to ensure that their trial designs and populations are globally representative, with sufficient US participation.

With the new draft guidance (note: comments were accepted until 18 November 2024), the FDA is taking a more aggressive position on the importance of generating clinical evidence that is applicable to diverse populations, particularly US patients, and consistent with US oncological practice. When finalised later this year, the guidance will provide additional recommendations to improve the planning, design, design, conduct and analysis of future oncology MRCTs.

The indispensable role of DMCs in oncology MRCTs

In February 2024, the FDA issued draft guidance, *Use of Data Monitoring Committees in Clinical Trials*, to guide clinical trial sponsors in determining when a data monitoring committee (DMC) would be useful for trial monitoring, and what procedures and practices would help when guiding their operation.[8] A DMC is an independent body that oversees patient safety, trial conduct and the quality of data in clinical trials. The new guidance is an update to the FDA's 2006 guidance to address changes that have occurred in the structure and practice of DMCs, also known as Data Safety Monitoring Committees (DSMCs), Data Safety Monitoring Boards (DSMBs) and Independent Data Monitoring Committees (IDMCs). Some of the key changes include:

- An increase in the use of DMCs in clinical trials of modest size
- A trend for DMC charters to become longer and more detailed
- An increased use of DMCs to implement certain adaptive clinical trial designs
- An increased use of some DMCs to oversee an entire clinical development programme rather than a single clinical trial
- The potential for expansion of functions of a DMC; for example, for review of aggregate data for safety reporting for trials under an investigational new drug application (IND)
- An increased globalisation of medical product development and use of multi-regional trials with DMCs.

In the context of oncology MRCTs, the diversity in regional practices, treatment responses and patient characteristics makes it critical for a DMC to closely monitor ongoing trial data. Its role becomes even more significant in oncology, where trial participants are often vulnerable patients with aggressive diseases, and safety risks can emerge unexpectedly across different regions.

The complexity of oncology MRCTs underscores the need to deploy an independent DMC to ensure patient safety, data integrity and population representation in trials that stretch across borders. Further, DMCs must ensure that US subsets of trial participants are adequately monitored, and that any potential discrepancies in outcomes between regions are promptly identified. Because regulators in each region will require that the clinical study population is representative of that region, companies with global oncology development plans must expect to meet region-specific and population-specific requirements for all countries in scope.

> *The complexity of oncology MRCTs underscores the need to deploy an independent DMC to ensure patient safety, data integrity and population representation in trials that stretch across borders*

Diverse DMC membership with multinational representation can help here, as sponsors may have to consider a 'blended' approach to development with several trials – ie, conduct an MRCT that will enrol a substantial proportion of participants in a single foreign geographical region, but also have one or more additional pivotal trials that will enrol a population that is representative of the US population. Further, sponsor companies developing therapies for oncology indications that have already conducted their clinical trials in a single country or geographical region may have to conduct additional trials to ensure their clinical programme is representative of the target US patient population. Key responsibilities of MRCT DMCs include:

- ***Ensuring uniform safety standards across regions:*** Given the variability of regional treatment practices and patient responses highlighted in the FDA's guidance, it is essential that DMCs ensure the uniform application of safety standards across all regions. This includes identifying and addressing regional variations in adverse events that could otherwise be overlooked if evaluated solely on a global scale
- ***Monitoring regional differences in efficacy:*** The FDA now stresses the importance of ensuring that oncology MRCTs generate data applicable to US patients. DMCs are tasked with monitoring whether the drug's efficacy is consistent across regions, ensuring that any regional differences do not compromise the trial's overall validity. This includes assessing variations in response rates that might arise due to different genetic, environmental or healthcare factors in diverse populations
- ***Interpreting interim data:*** Oncology trials often rely on interim data to make decisions about continuing or stopping a trial, especially when early evidence points to overwhelming benefits or risks. A DMC plays a critical role in interpreting such data, making unbiased recommendations on whether a trial should continue as planned, be modified or be terminated early for safety reasons.

Challenges specific to oncology MRCTs

Oncology trials present unique challenges that reinforce the need for a DMC:

- ***Disease variability across regions:*** Differences in cancer prevalence, genetic mutations and disease progression across regions can impact trial results. DMCs must account for these variations, ensuring that regional differences do not obscure meaningful treatment effects or introduce biases into the trial's findings
- ***Emerging therapies with high risk:*** Many oncology trials involve cutting-edge therapies like CAR T-cells and immunotherapies, which carry significant risks. The FDA has underscored the importance of DMCs in closely monitoring such high-risk trials, especially given the potential for rare but severe side effects across different populations
- ***Ethical considerations:*** With vulnerable cancer patients participating in these trials, it is critical that DMCs uphold the highest ethical standards, ensuring that participants are not exposed to unnecessary risks, and that trials are halted or modified if safety concerns arise.

What's next?

Technology will play an increasingly important role in DMC reviews in multi-regional clinical trials, specifically artificial intelligence (AI)-fuelled platforms. AI will help improve efficiency and quality by automatically de-identifying patient data, among other capabilities. Next-generation safety oversight activation and reporting (SOAR) platform technology, for instance, includes modern eDSMB and eAdjudication functionality combined with independent DMC review services from a global network of medical experts. Systems like SOAR enable all DMC members across regions to operate within a secure, HIPAA-compliant environment, minimising risks associated with data sharing and access.

The shifting regulatory landscape amplifies the need for robust oversight mechanisms like DMCs, supported by advanced technology. By ensuring safety, addressing regional differences in efficacy, and guiding decision-making through the careful interpretation of interim data, DMCs play a pivotal role in maintaining the scientific and ethical integrity of these complex trials. As the global nature of oncology drug development grows, the role of DMCs will only become more essential in ensuring that clinical trial outcomes are applicable to diverse populations, particularly within the US. In addition to oncology trials, DMCs are increasingly important to ensure the validity and safety of all complex novel trials, including cell and gene therapies and mental health trials.

While the FDA is initially focusing its guidance on oncology MRCTs – likely due to their prevalence and unique complexities – all therapeutic and disease areas should have the same rigour and DMC review to ensure the best clinical outcomes for all populations.

References:

1. *Visit: medscape.com/viewarticle/968320?form=fpf*
2. *Visit: pubmed.ncbi.nlm.nih.gov/35917647/*
3. *Visit: fda.gov/advisory-committees/advisory-committee-calendar/february-10-2022-meeting-oncologic-drugs-advisory-committee-meeting-announcement-02102022*
4. *Visit: fda.gov/news-events/press-announcements/fda-issues-draft-guidance-conducting-multiregional-clinical-trials-oncology*
5. *Visit: ascopubs.org/doi/10.1200/JCO.23.01030*
6. *Visit: centerwatch.com/articles/25599-oncology-trials-outpacing-rest-of-the-field-in-complexity-and-duration-study-shows*
7. *Visit: federalregister.gov/documents/2024/09/17/2024-20995/considerations-for-generating-clinical-evidence-from-oncology-multiregional-clinical-development*
8. *Visit: federalregister.gov/documents/2024/02/13/2024-02849/use-of-data-monitoring-committees-in-clinical-trials-draft-guidance-for-industry-availability-agency*

Barbara Schneider is executive director of Biostatistical Services at **Advarra**. She heads Advarra's independent data monitoring committee and endpoint adjudication services, which provide trusted safety oversight for hundreds of clinical trials around the world. Prior to acquisition by Advarra in 2021, Schneider was the founder and CEO of Watermark Research Partners. Watermark was the first company to provide independent data safety monitoring board services and endpoint adjudication to the clinical trial industry.

International
CLINICAL TRIALS

A likely adoption path of AI in clinical research

While artificial intelligence is often presented as a panacea for the pharmaceutical industry, many see it as one more challenge and pushback. What does the past tell us about how the adoption of new technologies is likely to proceed, and how will all companies, large and small, benefit in the near future?

Rob Nichols at Coronado Research

A lot has been written about the impact artificial intelligence (AI) will have – and is having – on clinical research, and there is undoubtably huge potential for an industry desperate to increase efficiency and decrease costs. Big pharma has invested heavily in AI to drive its drug discovery programmes, and this resource is now being pointed at the clinical research teams, and beyond, to see what value can be achieved.

For smaller organisations, however, this feels like a distant world. The term AI can often close down a conversation as the assumed challenges come to mind: we don't have AI experts in-house; AI hallucinates cannot be trusted; we have no historical data to feed the algorithms; we are too small to get any value; and many other understandable preconceptions.

A trip back in time

For more than 25 years, technology has had an ever-increasing impact on the conduct of clinical research. It's unthinkable today that a study would be conducted without a framework of technology underpinning it, making the capture of data faster and more accurate, and driving the standardisation of key operational processes. The benefits of this evolution are real and continue to accumulate.

Those first-wave technologies are now well established and can today randomise and consent patients, process patient data in near real time at the clinic, capture patient data outside the clinic and ensure that drugs are at sites when required. These technologies also provide a flow of reliable data on study progress to the project team and manage study documents, so they are available for regulatory and other purposes.

Recent history

More recently, the art of the possible with technology in clinical research has benefitted from significantly enhanced computing capabilities and access to increasingly complex data from many

different sources (such as wearables and sensors). Much of this data is now available in real time via the cloud. In parallel, driven by the COVID-19 pandemic when there was little choice but to adapt quickly, it has been shown that, with the right mindset, barriers that delay the adoption of technology can be overcome.

New use cases within this landscape include solutions to support patient recruitment and screening, protocol adherence, and patient retention. Once the data is collated in more sophisticated data repositories, risk-based quality management (RBQM) approaches also become viable. These are powered by advanced analytics and provide near-real-time reports. In parallel, the use of standards for data formats has moved forward (with the caveat that much still needs to be done), and these data structures have allowed exciting developments. One example is the movement of structured data directly from electronic health records (EHR) into electronic data capture (EDC) systems, which has a significant impact on site workloads.

Finally, the recent wave of technologies has nearly all been cloud-based, allowing researchers to start running aspects of clinical trials away from the traditional brick sites. This has, in turn, helped to increase the diversity of patients entering trials.

Hurdles to technology adoption

The market demand for the solutions outlined above is now sufficient that most are provided by a broad ecosystem of vendors, with over 100 companies estimated to provide EDC alone.[1] At least some of these vendors provide entry-level pricing that, in theory, makes access to technology possible for all. Hurdles to adoption of established technology often stem from the internal effort involved for quality and operational change management. This includes well-thought-out and managed processes to ensure the new solutions are fit for purpose and implemented successfully, and making sure all functionality is utilised so that advantages are realised. In many cases, where appropriate resources are not already in-house, there is a need to hire and/or equip teams with the correct training.

Another barrier to adoption is that technologies often do not play well together, with interoperability being absent across solutions, even when these are from a single vendor. From the user's perspective, these solutions (even those solving the same problem) all operate differently and require training. In addition, the holy grail of a single sign-on (SSO) still seems a distant dream, particularly to those working in clinical sites. What we can learn from the last 25 years is that expediting the uptake of AI will hinge at least partly on how effectively we prepare to adopt it.

AI – is it what you think

The speed of AI adoption across society over the past few years has been exceptional, and it is no surprise that the data-driven pharma industry is the target of much noise around its potential. The regulatory framework that clinical research is conducted under means the industry is unlikely to see clinical trials conducted in a radically different way for a while.

There is, however, the possibility to remove and reduce significant manual effort, resulting in a more efficient and cheaper process. The perception can be that AI is only for the largest companies, but while companies with deep pockets can certainly go all-in with recruiting experts and building bespoke systems, that is not the only mode of adoption.

The reality is that a lot of AI takes advantage of the increase in computing power that has driven previous waves of technological advancements. This computing power now allows the running of complex statistical algorithms and predictions based on exploring historical data. These approaches (ie, components of AI) are already present in the day-to-day lives of everyone in the pharma world, regardless of whether they work for small or large companies. Many of the more traditional eClinical solutions are now embedding, or will shortly embed, AI to improve functionality around areas such as anomaly detection in data, coding, extracting data out of unstructured systems, identifying adverse events, standardising and integrating data, and enabling all stakeholders to engage more efficiently with the data.

From an operational perspective, there is already AI-enhanced identification of patients and sites to optimise recruitment, the partial automation of document creation, the collation of documents for the trial master file and the delivery of training through bots. There is also the impact AI will have on the data available in the real world and healthcare, and therefore clinical research. For example, the ability to automate large parts of the imaging

> *The key to the successful integration of new AI use cases will be to adopt it in a controlled manner*

process has the potential to provide high-quality data much quicker and at a lower cost.

Adoption of AI

in short, those working in clinical research are likely already using AI. To get increasing benefits moving forward, a more proactive approach will be required, integrating new AI-driven use cases alongside the ongoing enhancement of existing technology.

The key to the successful integration of new AI use cases will be to adopt it in a controlled manner. For example, organisations may choose to focus initially on the clinical trial protocol. Creating a strong first draft of key study documents, such as the study protocol, is a good example of where generative AI is adding value. In due course, this could be paired with the current efforts to digitalise the protocol, which can generate significant downstream advantages as other documents and technology can pull from this digital footprint.

Another track could involve extracting more value from the data already being collected. The power of RBQM can be increased through AI, applying comprehensive study oversight with alerts and interventions, and more sophisticated analytics with suggested remedial actions. Clinical sites, if asked, may feel that a logical starting point is the adoption of comprehensive EHR to EDC technology that can pull across both structured and (using AI) unstructured data, reducing their efforts considerably.

In most of the above examples, the hurdles to adoption are likely to be similar to traditional technologies, rather than due to AI: does a named person have ownership of the new solutions as they are introduced into a company? Is there buy-in and understanding of the need for change from all levels? Is there a clear plan around change management? Is there a defined budget for implementation?

There is an obligation to make sure new tools are used appropriately and have the correct quality systems wrapped around them, but that has always been the case. These new functionalities, however, can be adopted in a measured manner providing an incremental, AI-driven advancement. This ensures that the operational impact of each step is manageable without the need to rip down all previous good practice and start again. Each organisation can have its own route forward, identifying easier wins for themselves and the pace they want to move at.

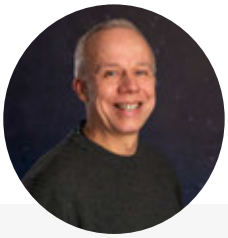
Conclusion

AI is becoming part of the technology landscape in clinical research, enhancing current solutions and enabling new ones. For most companies, what they will experience is an evolution, not a revolution, towards this new model. The use of standards is also expected to increase. This should help improve interoperability and, in turn, reduce change management challenges and costs, helping to accelerate the pace of adoption. The shift to a new model for clinical research – where broad swathes of activity are underpinned by a unified AI infrastructure – will remain out of reach for most. But, the gradual uptake of AI-infused solutions, combined with the use of 'data scientists', who have a hybrid understanding of technology, data and science, will see companies quickly generate improved value from their data ecosystems.

I wanted to finish with a disclaimer that no AI was used in the writing of this article. While that remains broadly true it occurs to me some of my fact-checking and grammar correction must these days have been powered by AI. I may not have trusted AI to write the article, but it has helped make the process more efficient – just like we are already seeing in clinical research.

Reference:

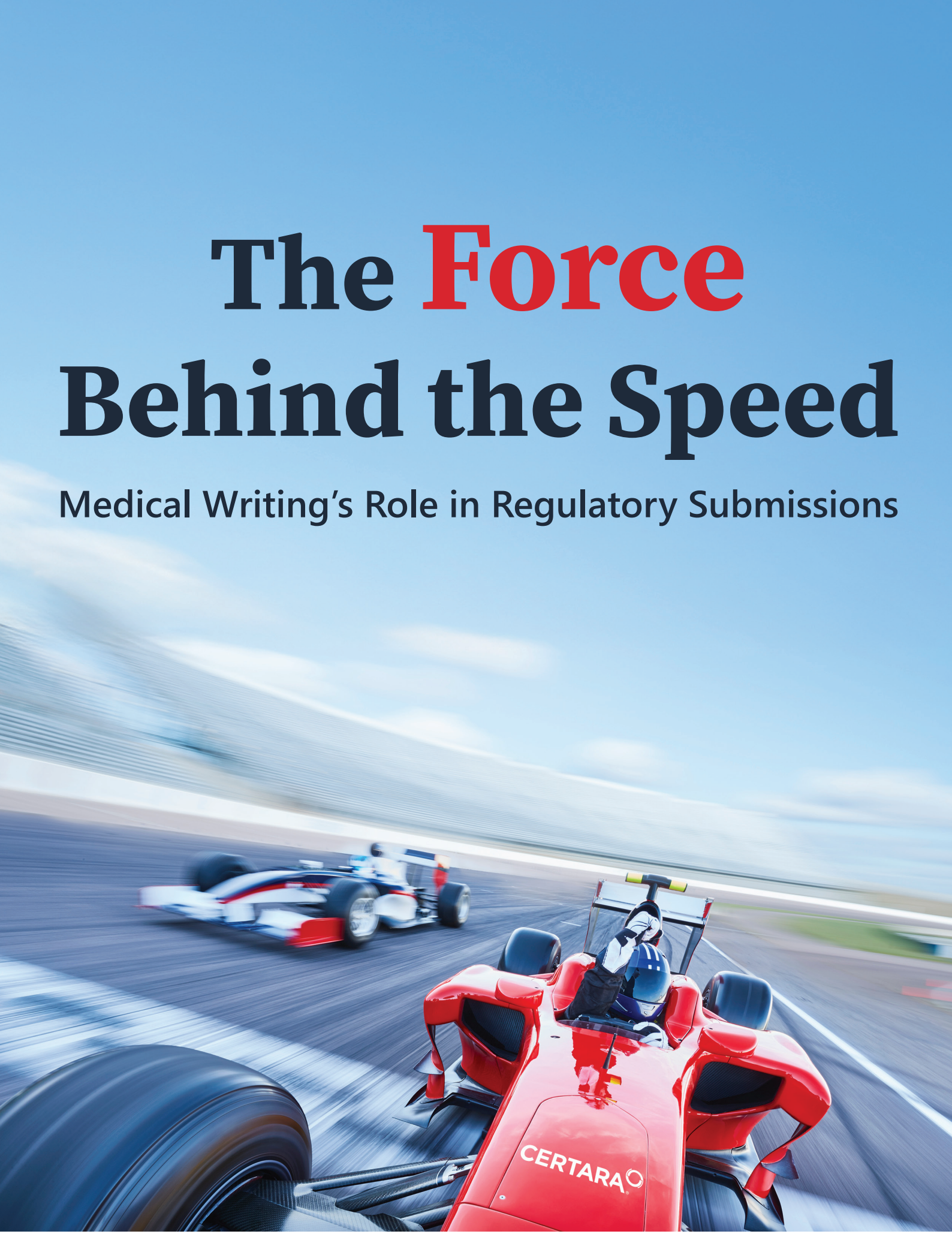
1. *Visit: g2.com/categories/electronic-data-capture-edc*



Rob Nichols, digital health consultant for **Coronado Research**, has extensive experience of delivering high quality strategic solutions to the pharmaceutical industry while working in first-in-class global clinical technology companies and contract research organisations (CRO), as well as seven years in the public health research departments of world-leading academic organisations. Subsequently, he has taken the knowledge gained while working for large established companies and applied it to start-up, scale-up and fast-growing ones in the eClinical space (including eDC, RBM and eCOA specialist companies). He now leads his own company, NB Solutions, and consults as a strategic advisor and board member for tech, CRO and investment companies.

The Force Behind the Speed

Medical Writing's Role in Regulatory Submissions



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The force behind drug development acceleration: medical writers

Foreword by Demetrius Carter, senior vice president of Regulatory Sciences & Medical Affairs at Certara, who looks at why long timelines and costs are standing in the way of drug development, and how medical writers can help to solve these issues

Certara is excited to partner with *ICT* to deliver a supplement focused on the impact of medical writing in facilitating new medicine approvals. Many of us entered the life sciences field eager to influence drug development, yet the process remains complex and burdened by bureaucracy, delays and inefficiencies. Tufts University's Center for the Study of Drug Development estimates that bringing a new drug to market costs $2.6bn, with cycle times often exceeding 10 years due to regulatory complexity, patient recruitment challenges and supply chain issues.[1]

The industry has embraced innovations like decentralised trials, electronic patient-reported outcomes and artificial intelligence (AI) to optimise clinical trials. Organisations like Certara further support acceleration through *in silico* modelling and model-informed drug development (MIDD). While these technologies focus on clinical trial execution, less attention has been given to optimising the regulatory dossier preparation process – critical for accelerating approvals.

This supplement explores key topics in regulatory writing. In *Fast Tracking the Writing of Master Protocols*, we provide best practices for streamlining protocol development. *Overcoming Challenges in Early Drug Development* examines how integrating first-in-human clinical study design with MIDD enhances decision-making and shortens timelines. *Advancing Paediatric Oncology Therapies* discusses innovative approaches to fast-tracking paediatric drug development. *Flight Path to Success* uncovers strategies for managing complex programs efficiently to reduce project delays.

In *Planning and Preparing Regulatory Submissions Using Top-Down Messaging*, we highlight Certara's expertise in regulatory submissions, demonstrating the value of early key message alignment. We also examine how technology is transforming medical writing. *Nightmares in Medical Writing* explores how AI-enabled document editing improves efficiency and reduces review cycles. *CoAuthor: Human in the Loop* showcases the power of generative AI (genAI) to enhance writer productivity, accuracy and consistency. *Strategic Authoring in Clinical Study Reports* highlights the value of applying redaction and anonymisation technologies to meet regulatory disclosure requirements.

By combining biosimulation, MIDD and technology-driven medical writing, we can accelerate drug development – reducing costs, improving patient safety and enabling faster regulatory decisions. At the forefront of these solutions, medical writers play a pivotal role: translating complex scientific data into clear narratives that facilitate regulatory review and approval.

Reference:

1. *Tufts Center for the Study of Drug Development (2014), 'The Cost to Develop an Approved New Drug Now Exceeds $2.5B', Applied Clinical Trials, 23(12)*

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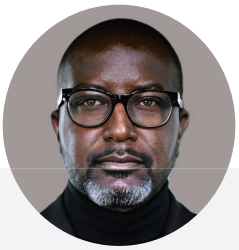

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Fast-tracking the writing of master protocol: driving efficiency in clinical trials

The changing regulatory landscape and increasing complexity, cost and time associated with traditional trial designs prompted the adoption of creative strategies to enable efficiency, accelerated development, flexibility and adaptability in study design – with improved patient-centricity – leading to alignment with regulatory and scientific goals. Moreover, the planned transition of clinical trials to the Clinical Trials Information System by 2025 presents additional regulatory, operational and financial challenges

Mirela Niculita at Certara

Transitioning clinical trials from the EU Drug Regulating Authorities Clinical Trials Database (EudraCT) to the Clinical Trials Information System (CTIS) under the EU Clinical Trials Regulation (EU-CTR) presents specific challenges with significant regulatory, operational and financial consequences, especially as the EU CTR becomes fully applicable from 30 January 2025.[1]

After 31 January 2025, all initial applications for clinical trials must be submitted exclusively through CTIS, with the EudraCT system no longer accepting submissions. Any ongoing trial approved under the previous Clinical Trials Directive (Directive 2001/20/EC) must have transitioned to CTIS by this date to remain compliant. A single Clinical Trial Application (CTA) is submitted via CTIS, covering both Part I and Part II. Part I is shared across all participating European Union/European Economic Area (EU/EEA) Member States (eg, trial design, investigational medicinal product information, risk-benefit assessment). Part II is specific to individual Member States (eg, patient information sheets, informed consent).

Once submitted, the sponsor must adhere to CTIS's standardised timelines:

1. ***Validation Phase:*** 10 days
2. ***Assessment Phase I:*** 45 days (Part I review)
3. ***Assessment Phase II:*** 45 days (Part II review).

Sponsor teams may face increased administrative burden due to the need to adhere strictly to new system requirements or face financial implications, such as increased costs for additional resources to ensure compliance and potential penalties for regulatory non-compliance. Writing a protocol for a clinical trial can be daunting when the need to maintain compliance and adherence to strict timelines by avoiding errors and rejections due to rushed submissions, all while meeting high clinical expectations associated with the design and execution of a clinical trial, is considered. As they explore innovative treatments that could improve patient outcomes, clinical trial designs are required to: maintain scientific rigour; be patient-centric; prioritise patient safety and minimise risk; enrol a diverse population representative of the target patient group; employ strategies to reduce trial complexity and optimise patient recruitment and retention; and leverage real-world data when applicable.

Regulators encourage the creation of master protocols to foster innovation and to address unmet medical needs more efficiently. The term master protocol is often used to describe the design of trials with various terms, such as umbrella, basket or platform.[2] A master protocol allows for the simultaneous evaluation of multiple interventions, populations or diseases under one overarching framework, thereby reducing the need for numerous separate protocols. Therefore, time and resources can be saved, while addressing the complexities of modern clinical research, especially in diseases with unmet needs like oncology and rare diseases.[3]

Building a master protocol within a single overarching structure can transform a complex, time-consuming endeavour into a streamlined process that facilitates rapid development and submission. Accelerating the writing of a clinical trial using a master protocol requires leveraging its standardised structure and pre-defined components to reduce redundancy, streamline processes and promote efficiency.

Master protocols can facilitate US Food and Drug Administration (FDA) approval of new drugs and deliver safe and effective medicines faster to patients.[4] Conducting multiple studies under a single protocol eliminates delays between sequential trial and duplicative infrastructure, leading to

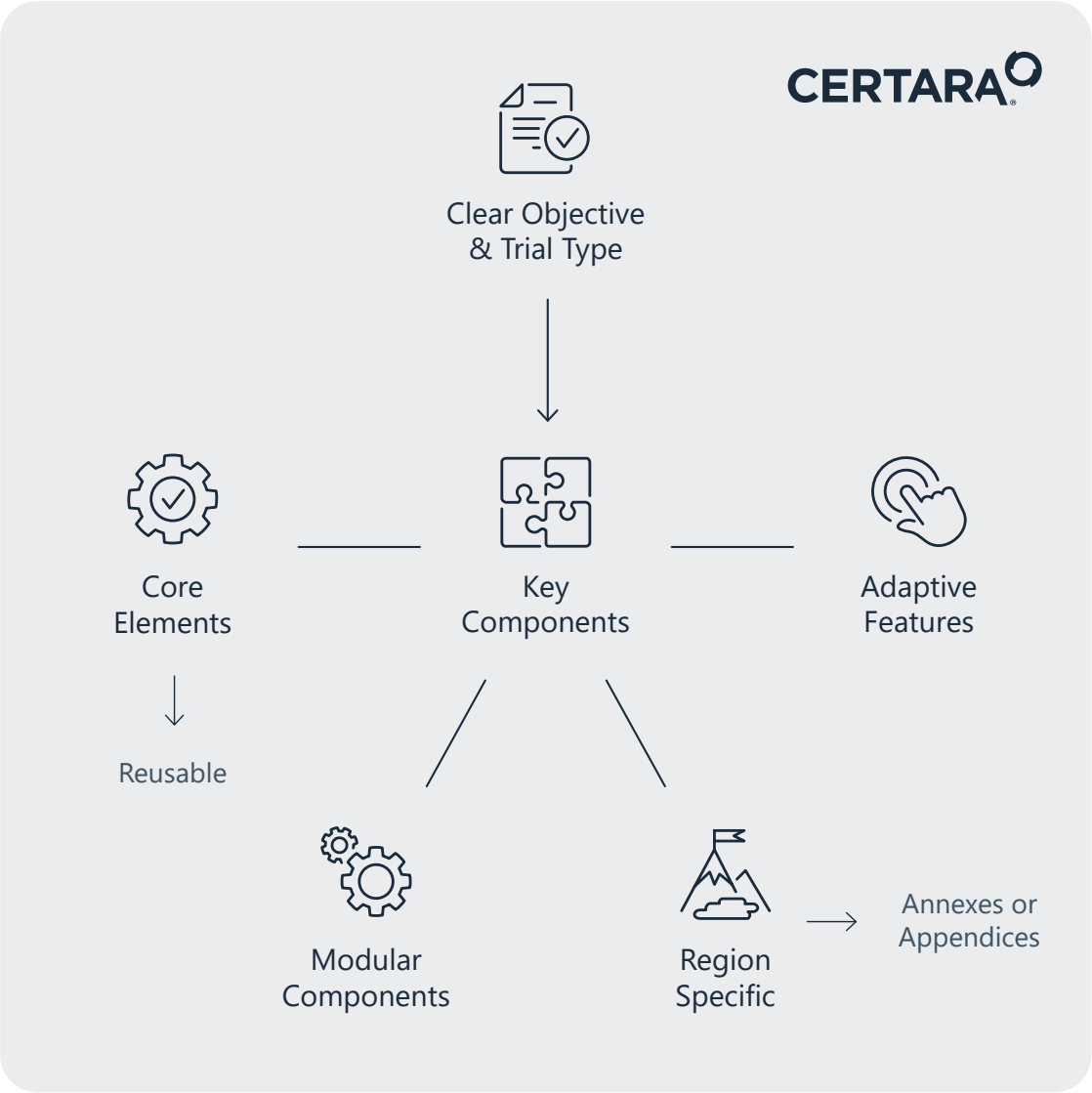

Figure 1: Key components and framework for developing a robust master protocol

faster results and earlier availability to comprehensive data that can be submitted as evidence for FDA review. Also, working under a master protocol enables early and ongoing engagement with the FDA, reducing surprises during the submission phase. However, a more stringent need for a master protocol addressing multiple regulatory requirements requires flexibility to accommodate divergent regulations, such as safety reporting or patient population inclusion criteria.[5] For example, the FDA may require more detailed adaptive design justification, while the European Medicines Agency (EMA) might focus on statistical considerations. The following targeted strategies are proven to be successful in fast-tracking master protocol writing from the onset or later during the document life cycle (**Figure 1**):

Define clear objectives and trial type
Establishing the scientific and clinical objectives early is critical in protocol development. Whether the aim is to evaluate multiple therapies for one disease (umbrella trial), test one therapy across different diseases (basket trial), or design an adaptive, ongoing platform trial, clarity on these goals shapes the document's scope and structure. Aligning with stakeholders on trial design early is critical to avoid rework later in the process.

Engage cross-functional teams early
Collaboration is the cornerstone of success and includes bringing together leading experts from multiple research fields, particularly for complex diseases and basket trials with multiple diseases. Engaging cross-functional teams from the start, including clinical, regulatory and biostatistics experts, ensures alignment on critical elements and minimises last-minute revisions.

Some implementation tips are:

- ***Iterative reviews:*** Break the document process into manageable stages for faster sponsor approvals

- ***Early alignment:*** Conduct kick-off meetings to agree on overarching protocol goals and roles.

Leverage collaborative writing tools

Real-time collaboration can significantly reduce bottlenecks. The use of software tools may facilitate simultaneous drafting, reviewing and editing to foster a seamless workflow across teams, with direct benefit on the lag time between revisions, and the tracking of edits and comments.

Pre-plan key components and use a modular approach

A modular strategy allows for reusability and adaptability. By standardising core elements and pre-defining flexible modules, teams can rapidly adapt the protocol to address emerging requirements or add new sub-studies. Region-specific requirements can be detailed in annexes or appendices to a unified core protocol. These region-specific requirements can be tailored to align with local regulations, standards or practices, such as:

- Local pharmacovigilance reporting timelines, for example expedited safety reporting requirements differ between the FDA, EMA, and Japan's Pharmaceuticals and Medical Devices Agency (PMDA)
- Additional ethical approval requirements for specific regions, eg, General Data Protection Regulation (GDPR) compliance in the EU
- Demographic adjustments
- The inclusion of regionally approved concomitant medications or treatments
- Additional pharmacokinetic data collection (Japanese participants)
- Regional subgroup analyses
- Region-specific data privacy or transfer regulations, eg, EU GDPR vs US Health Insurance Portability and Accountability Act (HIPAA)
- Adaptation to regional standards for labelling.

In the context of CTIS requirements, content needs to be checked against the EU-CTR Annex I structure to ensure compliance and to streamline submission. Consideration should be given to employing standardised templates that are CTIS-specific. Some core elements to map are:

- Patient eligibility criteria
- Endpoints, data collection methods and analysis plans
- Global regulatory-compliant language templates.

Modular components:

- Arm-specific details, such as investigational treatments, biomarkers or population-specific data
- Modules designed for seamless integration with platform trial adaptations.

Incorporate adaptive features

Adaptive trial designs demand flexibility in master protocols. By incorporating pre-specified stopping rules, interim analyses and criteria for population expansion, teams can reduce the frequency and extent of future amendments. Modifications to trial arms can be performed without requiring a complete redesign or reapproval of the protocol, thus allowing fast adaptation to emerging data. Some examples include seamless transition between trial phases and interim analyses and decision rules for modifying treatment arms or adding new cohorts.

Focus on reusable content

Building comprehensive and reusable sections, such as background, study rationale and regulatory summary sections, can save considerable time and effort when updates are required or when documents are repurposed for regulatory submissions, such as investigational new drug/clinical trials application (IND/CTA) dossiers and investigator brochures. Thus, writing generalised background sections will require minimal updates later in the process. In addition,

Proactive planning, cross-functional collaboration and technological solutions are critical enablers of efficiency in this complex yet transformative approach to clinical research

the implementation of standardised terminology and formatting will ensure consistency across documents and facilitate the repurposing of content.

Leverage artificial intelligence (AI)-assisted writing tools

AI tools can streamline drafting, formatting and proofreading processes by handling repetitive or time-intensive tasks. These tools enhance accuracy and consistency while freeing time for higher-value activities, such as strategic decision-making.

Nonetheless, further activities can be pursued in parallel to ensure operational readiness or early regulatory and ethical engagement. These activities may require establishing central laboratories, imaging facilities and data management systems to support harmonised data collection; developing a centralised monitoring and quality assurance plan; and training clinical trial sites on the protocol complexity, if necessary.

Early consultations with regulatory bodies (eg, FDA, EMA, PMDA, etc) are critical for alignment on trial design, endpoints and statistical methods. Simultaneously, consultations with the FDA and EMA during the protocol development phase should be conducted through mechanisms like the FDA's IND process and the EMA's Scientific Advice procedure. Parallel submission pathways need to be leveraged to ensure alignment. In the context of CTIS requirements, sponsors need to consider additional efforts, such as transparency and disclosure information, and plain-language summary of the trial, as critical components of modern clinical research.

Conclusion

The development of master protocols can be approached creatively with strategies that could potentially significantly improve the process, while enabling teams to focus on delivering innovative trials that meet clinical and regulatory expectations.

Proactive planning, cross-functional collaboration and technological solutions are critical enablers of efficiency in this complex yet transformative approach to clinical research. By adopting these practices, organisations can accelerate protocol development, enhance adaptability and, ultimately, bring therapies to patients faster and more effectively.

References:

1. *Visit: ema.europa.eu/en/documents/other/member-states-guide-transition-trials-eudract-ctis-ctis-training-programme-module-23_en.pdf*
2. *Visit: www.fda.gov/regulatory-information/search-fda-guidance-documents/master-protocols-drug-and-biological-product-development*
3. *Visit: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/master-protocols-efficient-clinical-trial-design-strategies-expedite-development-oncology-drugs-andS*
4. *Redman M W et al (2015), 'The Master Protocol Concept', Semin Oncol, 42(5), pp724-730*
5. *Bitterman D S et al (2020), 'Master Protocol Trial Design for Efficient and Rational Evaluation of Novel Therapeutic Oncology Devices', J Natl Cancer Inst, 112(3), pp229-237. Published correction appears in J Natl Cancer Inst 2022, 114(2), p326*

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Flight path to success: how project and strategic relationship managers accelerate submissions

Getting a product to submission is no easy feat; one could liken a single submission to an airline flight. The pilot is the submission lead, but what people often overlook are the responsibilities of other crew members such as a navigator (project manager) and an air traffic controller (strategic relationship manager/account manager). How can these crew members help accelerate a flight, getting the submission to an agency faster and with more efficiency?

Renata Lavach-Savy and Kristen Brotzman at Certara

In comparing a pharmaceutical submission to an airline flight, one must first consider the many components needed for the flight, from fuel (ie, data from various studies) to in-flight snacks (ie, stylistic editing). Depending on the type of flight, what is needed is going to change; a transatlantic flight needs a lot more fuel than a flight from London to Paris. Similarly, what is needed to support a clinical trial application (CTA) is much less than for a new drug application (NDA). While the submission lead is the primary leader of the submission with the responsibility of ensuring its success, what people often overlook are the responsibilities of other crew members, such as a navigator (project manager) and air traffic control (strategic relationship manager [SRM]/account manager).[1]

The navigator's job is to support the pilot in tracking the course of the flight and the airplane's position, including consulting all navigational tools (radar, maps, etc). In a submission, a project manager is the navigator; they are developing timelines and monitoring the project health. Without a navigator, a pilot could likely have a successful flight, but, with a navigator, the odds of a successful and more efficient flight increase exponentially. Having a project manager can help accelerate your submission because their job is to bring organisation to the submission by maintaining a central source of truth that provides visibility into the health of a submission and helps identify and mitigate risks and pitfalls before they happen and potentially delay the submission.[2] This central source of truth typically encapsulates timelines, meeting minutes, action items, risk logs and any other tracking materials for the overall submission.

In order to create and maintain a central source of truth, a good project manager must organise the various components and steps in a submission application. This includes the following:

- The submission structure
- The agency or agencies being submitted to
- Whether the submission will stand alone or if there will be multiple global submissions
- The type of submission
- The documents to be included (considering the responsible party and effort required for each)
- The document activities, including pre-authoring steps of study completion as well as data collection, data generation and data analysis; authoring steps, which include writing, quality control reviews (QCs); stakeholder reviews, comment resolution meetings and approvals; and publishing, both document- and submission-level
- The potential external impacts, including pre-submission meetings with health authorities; feedback and questions from health authorities; and vacations and holidays.

By understanding all of the above, a project manager can dig into the granular components of tracking and developing a timeline for the project as well as make contingency plans for potential roadblocks. In addition, the project manager has the responsibility to develop regular communication methods, whether in regular meetings, electronic updates or other methods, to ensure the project is running smoothly. By creating these trackers and communications systems, it helps create transparency and accountability to ensure a project is moving forward as efficiently as possible.

Further, by creating this level of transparency and communication, a project manager has a live look at submission health and has the visibility to see potential pitfalls. For example, maintaining a central timeline allows the project manager, submission lead, SRM/account manager and the individual lead writers to ensure all documents and their owners are identified, the appropriate hierarchy of documents is established (eg, the completion of Module 2.7 documents

being contingent on a pivotal phase 3 study), enough time for each of the sub-steps is granted (eg, ensuring reviews are completed on time so QC does not need to be rushed), and all reviewers are confirmed to avoid last-minute potential changes from new team members. Identifying all of these key items helps streamline a submission, setting the flight up for success with the appropriate crew, the correct amount of fuel and the right map.

Of course, there may be unforeseen occurrences on any flight; there are things that are out of the pilot's control, like turbulence (in a submission, this would be agency feedback, review timelines not being met and unexpected data). As a navigator helps keep the plane on the appropriate path, a project manager drives a timeline continuously to ensure a smooth submission. Having that standardised and live-updated timeline is critical as are maintaining dashboards to understand the high-level view of the submission, having regular team and leadership communication to ensure alignment across the team – as well as to allow for the escalation of issues – and creating scenarios to account for both positive and negative agency feedback. In a submission, the trickle-down effect of one change or issue quickly snowballs into a larger problem (eg, one data issue in a clinical study can push out Modules 2.7, pushing out Module 2.5, pushing out the labelling), such that the project manager's ability to have visibility of the full submission as well as the granular detail of all the projects is critical to the acceleration and success of a submission.

But a sponsor is often working on more than one submission at a time. What happens when there are multiple planes in flight? This is where air traffic control, or an SRM/account manager in this analogy, comes in. An air traffic controller oversees all flights coming in and out of an airport (ie, a single sponsor); an SRM/account manager is overseeing all movement within a product programme and between multiple products, tasked with coordinating the logical flow of submissions and resources to avoid midair collisions.

The SRM/account manager oversees the entire sponsor engagement. They serve as the central point of contact between the organisations and provide strategic and tactical oversight as an account manager. Like air traffic control, an SRM/account manager keeps eyes on all flights, or submissions, that are incoming, outgoing and mid-air. Through overall sponsor management, an SRM/account manager ensures that adequate resources are available for each submission and that the team prioritises effectively, strategically deciding the lowest risk path that minimises the possibility of inter- and intra-submission collisions.

One way in which an SRM/account manager provides strategic consulting to optimise submission strategies is to review a multiple-country submission strategy and suggest the most efficient and realistic strategy to accelerate. A frequently overlooked issue is when the gap of time between submission in two countries is too long, meaning safety data cut-offs have elapsed and serious adverse event reporting must be re-performed. An SRM/account manager works along with the project manager to plan timelines that will avoid this risk, even after the unavoidable shuffles that occur during medical writing.[3] By being fluent in a sponsor's strategy and preferences, an SRM/account manager can drive discussions and ensure all team members are following sponsor procedures. An SRM/account manager typically onboards new team members and remains their source for sponsor preferences throughout the submission, alleviating that

burden from the sponsor. Like air traffic control, an SRM/account manager must be an exceptionally clear communicator, able to speak the language of all the various stakeholders. In order to verify that key messaging has been emphasised and that all regulatory guidelines were followed, an SRM/account manager may be tasked with reviewing module documents when a submission lead is not in place. Beyond tactical hard skills, the SRM/account manager also brings lessons learned from past engagements. For example:

- What feedback did the agency give the last time you went with this approach?
- How did you mitigate this risk previously?
- Which time-saving techniques worked well and which led to frustration?

Just like air traffic control, an SRM/account manager remains the 'calm in the storm,' ensuring that no matter what, the sponsor is successful. This may mean mentoring inexperienced team members or even sponsors at the beginning of their drug development journey. These efforts are often in conjunction with the submission lead. An SRM/account manager also ensures that all required regulatory documentation progresses on time, including those outside of submissions. Overall, when taking a flight, the goal is safe, on-time landing at the expected destination. If one had the option to safely arrive at our destination quicker, most would take that opportunity. The same logic applies to an agency submission. The goal is to get a complete and accurate submission to an agency that will be approved, but, if it can be done quicker and more efficiently, would we not all choose that option?

Engaging with project managers and SRMs/account managers on a submission will help accelerate that successful flight.

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References:

1. *Bose A et al (2024), 'Preventing Chaos: The Critical Role of the Submission Lead', AMWA Journal 39, pp20-24*
2. *Brotzman K (2023), 'Managing Various Components of the Authoring and Publishing Stages of an Application', American Medical Writers Association, webinar, 21 June*
3. *Visit: certara.com/brochure/writing-at-lightspeed-optimizing-submission-dossiers-in-todays-environment-through-better-planning/*

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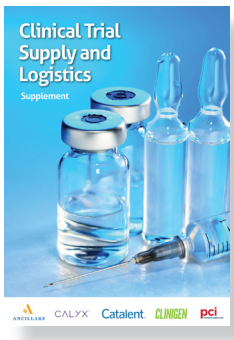

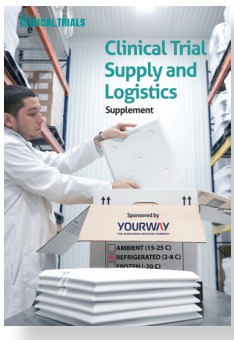

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The symbiotic role of AI and human intelligence in medical writing

Artificial intelligence is reshaping medical writing by streamlining the creation of clinical trial reports and regulatory submissions with unmatched efficiency and precision. Yet, its true power lies in a human-in-the-loop approach, where human expertise ensures scientific rigour, ethical integrity and compliance. Discover how AI complements, rather than replaces, human intelligence in driving progress in medical writing

Reema SelvaRaju at Certara

The use of artificial intelligence (AI) in regulatory writing has seen tremendous growth in recent years, and it will grow from $0.91bn in 2024 to $1.86bn in 2029 at a compound annual growth rate of 15.2% (Figure 1).[1] Many companies in this sector are focusing on advanced AI capabilities, such as AI-powered drafting, to improve both efficiency and accuracy in the creation and management of regulatory documents, including clinical trial reports, patient safety narratives and regulatory submissions. AI-powered drafting uses sophisticated algorithms to automatically generate initial drafts or outlines, harnessing the power of machine learning and natural language processing to aid content creation tasks.[1]

While AI is making significant strides, the key to its effective application lies in a human-in-the-loop (HITL) approach. The collaboration between human intelligence and AI offers immense potential to enhance and streamline the work of medical writers, with AI serving as a tool that empowers human expertise rather than replacing it.

The importance of human intelligence in medical writing

Regulatory writing involves the precise translation of complex scientific data into clear, accurate and contextually appropriate documents that play a crucial role in ensuring the safe and efficient development of medicines. Despite AI's powerful abilities to handle repetitive tasks and analyse large data sets, human intelligence remains indispensable in overseeing the final output. There is often a tendency to confuse data, information and knowledge: data

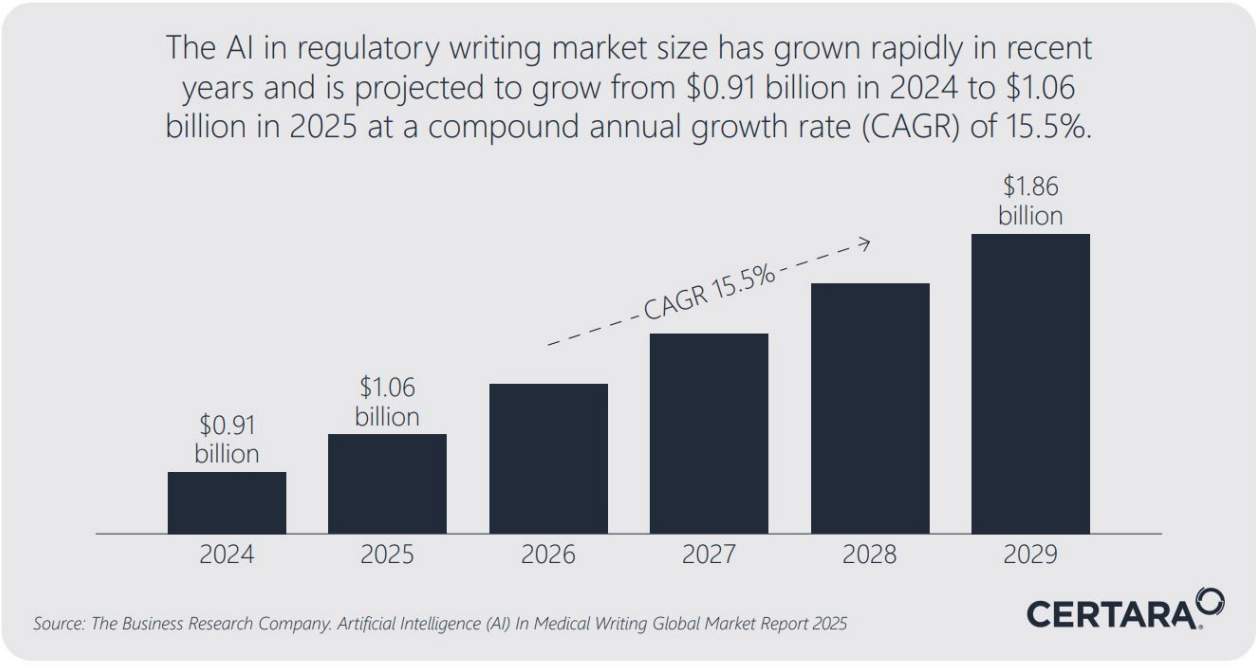

Figure 1: Growth of AI use in the regulatory writing market

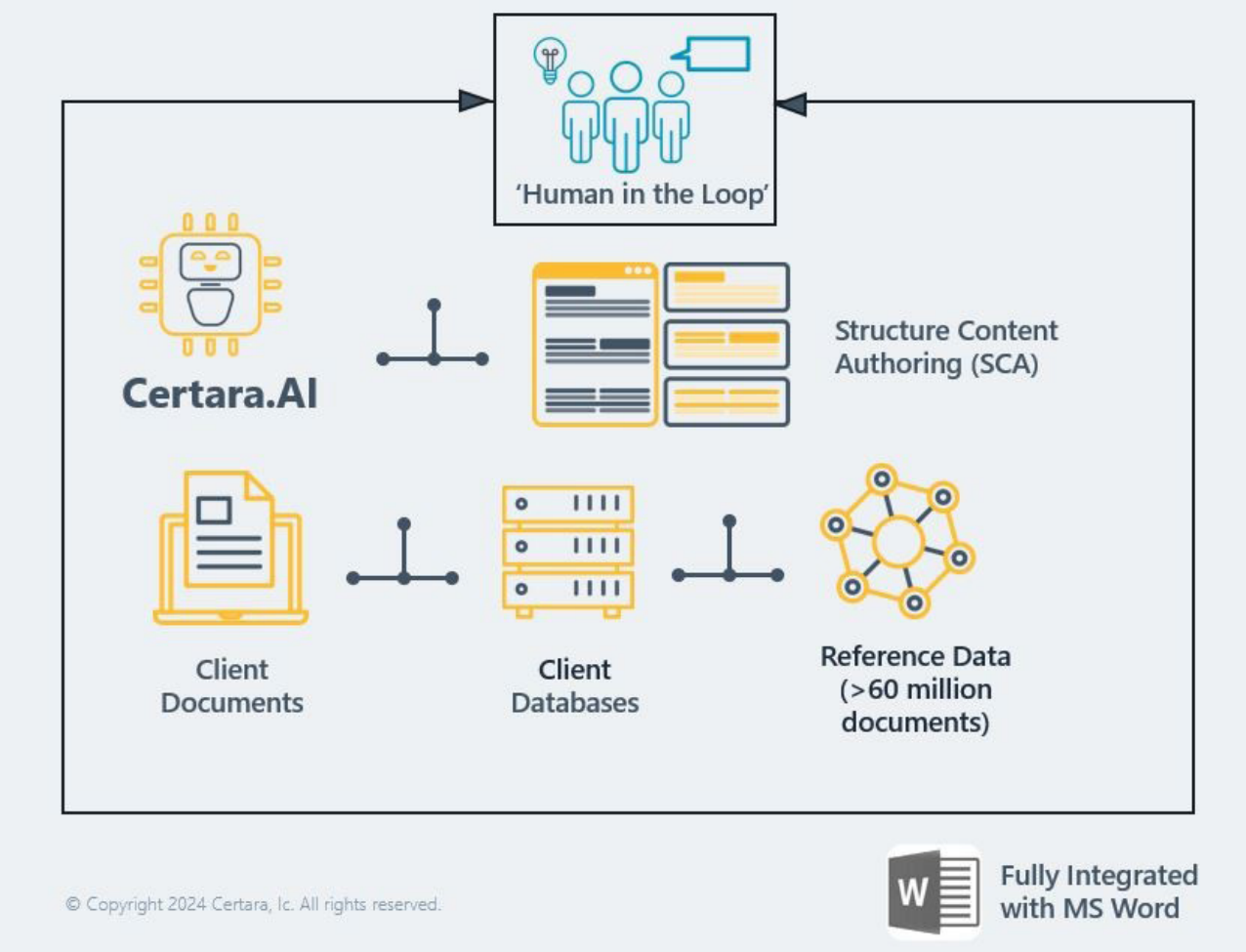

Figure 2: Empowering regulatory writers with AI technology

is unstructured facts; information consists of structured data; and knowledge is the ability to judge and use information to identify and solve problems.[2] AI lacks true creativity and understanding of the world, and is limited by the data it has been trained on. Knowledge, however, is intrinsic to human intelligence.

AI as a tool that enhances efficiency and accuracy

The integration of AI in regulatory writing is accelerating, particularly with the use of machine learning (ML) and natural language processing (NLP). These AI technologies help process and interpret vast amounts of data, enabling medical writers to focus on higher-level decision-making. For example, AI can assist in generating initial drafts, checking for consistency and even analysing data for potential trends, all of which can significantly expedite the writing process. Structured content authoring, an approach that organises content into reusable, modular components, is particularly powerful in medical writing. As described in **Figure 2**, when combined with AI's processing power, this methodology can efficiently analyse vast amounts of data, enabling the rapid identification of key insights and trends, which streamlines the creation of complex regulatory documents. AI's ability to quickly automate the drafting of documents integrated with the HITL approach empowers writers to dedicate more time to refining the content, ensuring it adheres to regulatory standards and making informed decisions based on their expertise.[1]

While AI excels in automating routine tasks, it is ultimately human intelligence that ensures documents are scientifically accurate, ethically sound and aligned with the latest regulatory requirements. The collaboration between human judgment and AI's technical capabilities is where true innovation and efficiency arise.

The risks of over-reliance on AI: why human oversight is crucial

AI's growing role in regulatory writing presents significant advantages, but it also comes with risks.

> *Human expertise is essential for addressing ambiguity, making nuanced decisions and mitigating potential biases in AI outputs*

AI models, by design, are inherently probabilistic, meaning they make decisions based on patterns in historical data rather than fixed rules.[3] This can lead to errors when AI encounters complex or unfamiliar data that does not fit past patterns. In situations like predicting the safety and efficacy of a drug, AI may be confident in its output but still produce inaccurate or misleading results.

Moreover, AI models are often based on 'black box' algorithms where its decision-making process is not entirely transparent. This opacity presents a challenge in ensuring accountability, especially when the decisions made by AI are critical in contexts like regulatory submissions and drug development.[4] Without human oversight, errors in AI-generated content may go undetected, potentially leading to regulatory non-compliance or compromising patient safety. The lack of contextual understanding and the risk of perpetuating biases further highlight human intervention's importance.

HITL: Combining AI's power with human expertise

The most effective way to integrate AI in medical writing is by adopting a HITL approach. In this model, human writers actively guide and refine AI-generated content, leveraging AI's ability to handle large-scale data and automate repetitive tasks while ensuring that the final product is accurate, contextually appropriate and compliant with regulatory standards. Human expertise is essential for addressing ambiguity, making nuanced decisions and mitigating potential biases in AI outputs. By involving humans in the decision-making process, medical writers can ensure that AI's capabilities are fully leveraged while maintaining control over the ethical and regulatory aspects of the work. This collaboration allows AI and human intelligence to work in tandem, with each complementing the strengths of the other to produce superior outcomes.

Ethical and accountability considerations in AI adoption

As AI becomes more integrated into medical writing, questions of accountability and ethical responsibility will only grow. One of the significant challenges in AI adoption is the explainability of the algorithms used.[4] AI-guided systems function independently of their developers and may evolve in ways that the developers may not foresee. This creates a gap in responsibility, and is especially concerning in high-stakes areas like drug development, where the wrong decision can have severe consequences.[5] AI usage must be guided by ethical considerations, with humans ensuring that the output adheres to both regulatory requirements and broader societal norms. Over-reliance on AI risks overlooking critical human judgment, leading to decisions that may be statistically accurate but lack the broader contextual understanding required in regulatory writing.

A future of collaboration between AI and human intelligence

AI has the potential to drastically improve the efficiency and accuracy of medical writing, particularly in regulatory contexts. However, the true value of AI lies not in replacing human expertise but in augmenting it. As AI continues to evolve, the collaboration between AI and human intelligence will become increasingly essential. The HITL approach will drive innovation and ensure that medical writing remains accurate, ethical and aligned with regulatory standards, benefiting both the industry and patients alike.

References:

1. *Visit: thebusinessresearchcompany.com/report/artificial-intelligence-ai-in-medical-writing-global-market-report*
2. *Lambooy J (2004), 'The transmission of knowledge, emerging networks, and the role of universities: An evolutionary approach', European Planning Studies, 12(5), pp643-657*
3. *Visit: unu.edu/article/ai-not-high-precision-technology-and-has-profound-implications-world-work*
4. *Visit: who.int/publications/i/item/9789240029200*
5. *Visit: who.int/publications/i/item/9789240088108*

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Advancing paediatric oncology therapies: challenges, innovations and best practices

Paediatric oncology presents a unique set of challenges due to the complex and life-threatening nature of these diseases.[1] This article explores the existing regulatory frameworks, scientific innovations and novel strategic approaches that sponsors can employ to accelerate the development of innovative treatments and improve outcomes in paediatric cancer

Ananth Kadambi, SY Amy Cheung, Justin Hay, Roman Casciano, Jacquelyn Binns, and Suzanne Minton at Certara

Rapid development of effective therapies for paediatric cancers is critical for at least three major reasons. First, despite available approved therapies, cancer remains one of the leading causes of death among children worldwide.[2] Second, paediatric cancers present a unique therapeutic challenge as they often differ biologically from adult cancers. Thus, they can require tailored approaches for effective treatment.[2] Unlike adult cancers, which often result from lifestyle factors, paediatric cancers are frequently linked to developmental and genetic factors. Furthermore, they are highly heterogeneous, with numerous subtypes and genetic mutations. Many of these subtypes are not fully characterised, leading to complications in treatment selection. Third, paediatric cancer incurs an emotional and psychological toll on patients and their families, which amplifies the urgency of delivering effective therapies. Paediatric patients with cancer undergoing treatment face challenges, such as long-term side effects and disrupted development.[3]

While the pharmaceutical industry has made significant advancements in developing safe and effective oncology therapies for children in the past 20 years, there remains an unmet need for innovative approaches to optimise dosage for paediatric patients, accelerate time to approval, and ensure timely market and patient access.

Furthermore, there are numerous challenges associated with paediatric drug development that need to be confronted. Model-informed drug development (MIDD), real-world data (RWD) and real-world evidence (RWE) focused on paediatric subgroups can play a crucial role in supporting efforts to address them.

Regulatory landscape and challenges

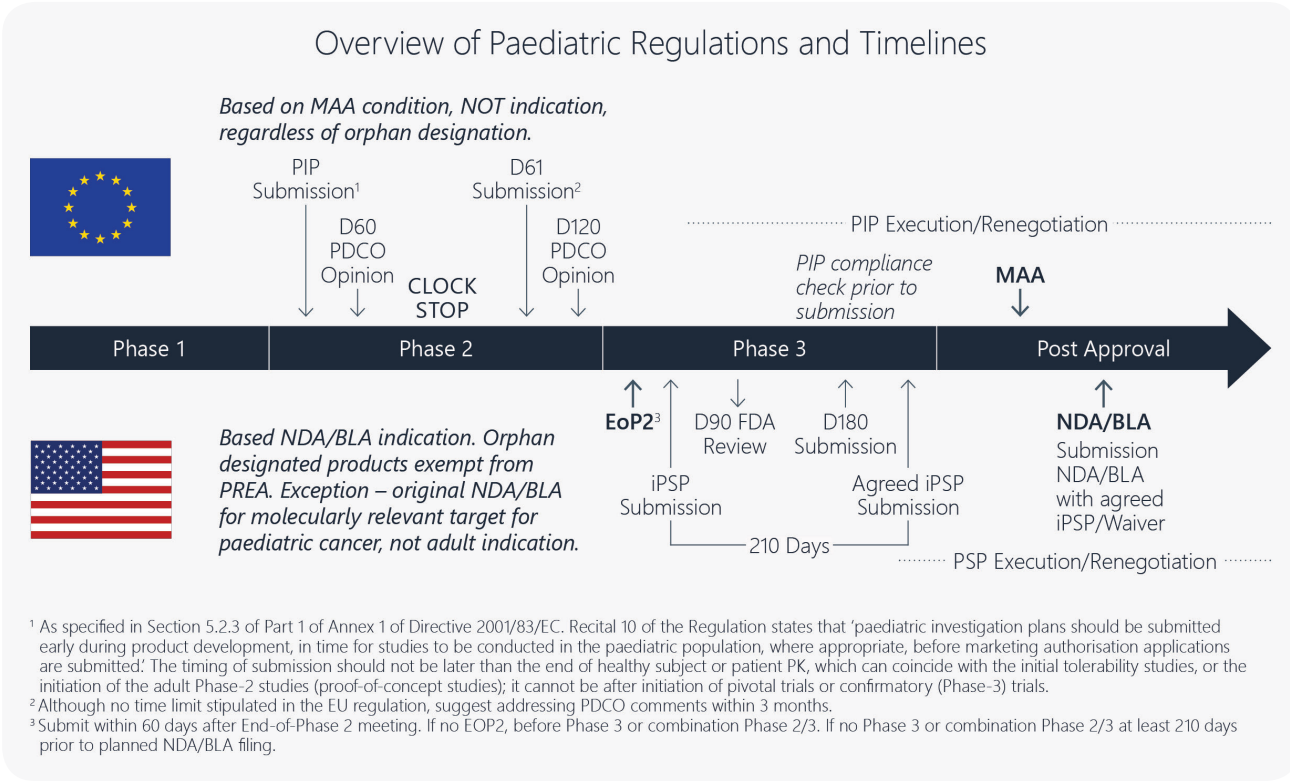
Legislation supporting paediatric drug development

Several regulatory initiatives aim to facilitate the development of paediatric drugs. The US Food and Drug Administration's (FDA's) Research to Accelerate Cures and Equity (RACE) for Children Act, and Pediatric Research Equity Act (PREA), along with the EU's Paediatric Regulation – Regulation (EC) No 1901/2006 and 1902/2006 – mandate that sponsors consider paediatric studies early in their drug development plan (**Figure 1**).[4] These frameworks aim to accelerate approvals and address unmet needs for paediatric treatment options, in particular for paediatric oncology, and help bridge the gap between adult and paediatric oncology drug development. The RACE Act, for example, focuses on requiring paediatric investigations for drugs developed for adult indications that are relevant to paediatric populations. However, regulatory agencies developed these regulations independently. This has often led to hurdles for sponsors in meeting the diverse requirements of regulatory agencies across regions, leading to delays in regulatory approval and increased costs.

Risks in paediatric drug development

The development of paediatric therapies involves unique challenges, as younger children are not the equivalent of small adults; rather, their developing organs and physiology require precise dosing strategies to avoid adverse effects while maximising therapeutic benefits. As a consequence, basing paediatric doses on established safe and effective doses from adult studies may not be appropriate. Nonetheless, in certain cases, the inclusion of adolescent patients (defined as ages 12 to 17 years) in relevant adult oncology clinical studies should be facilitated.[5]

Additionally, R&D and regulatory hurdles can delay children's access to potentially life-saving treatments. These include the likelihood of regulatory agencies requiring that sponsors conduct additional paediatric-focused studies to extend the label of approved medications to children. Identifying and enrolling paediatric oncology subjects in clinical studies to satisfy these requirements can be challenging and costly, highlighting the need for viable solutions to reduce the risk associated with paediatric oncology development programmes.[6] Commercial risks also play a significant role. The paediatric market is often



[1] As specified in Section 5.2.3 of Part 1 of Annex 1 of Directive 2001/83/EC. Recital 10 of the Regulation states that 'paediatric investigation plans should be submitted early during product development, in time for studies to be conducted in the paediatric population, where appropriate, before marketing authorisation applications are submitted.' The timing of submission should not be later than the end of healthy subject or patient PK, which can coincide with the initial tolerability studies, or the initiation of the adult Phase-2 studies (proof-of-concept studies); it cannot be after initiation of pivotal trials or confirmatory (Phase-3) trials.
[2] Although no time limit stipulated in the EU regulation, suggest addressing PDCO comments within 3 months.
[3] Submit within 60 days after End-of-Phase 2 meeting. If no EOP2, before Phase 3 or combination Phase 2/3. If no Phase 3 or combination Phase 2/3 at least 210 days prior to planned NDA/BLA filing.

Figure 1: Proactive strategic planning for paediatric drug development should occur early in the clinical development process. Sponsors are required to follow regulatory guidance and timelines concerning the planning and conduct of paediatric clinical studies to remain compliant with the regulatory procedures, and to ensure that key milestones are achieved and not delayed

perceived as less profitable due to its smaller patient population and the extensive resources required for drug development. This perception can limit financial incentives for developing paediatric therapies.[7] Sponsors may therefore hesitate to invest in paediatric programmes, despite the potential for significant societal benefits. Overcoming these barriers requires innovative financial and policy incentives to encourage investment in paediatric oncology research.

Emerging trends and future directions

Early planning and collaboration

Successful paediatric oncology drug development requires early and strategic planning. Sponsors should integrate paediatric considerations from the outset, aligning clinical study designs with both regulatory and payer requirements. Clinical studies should account for the unique needs of paediatric patients using patient-centric approaches. Developing age-appropriate formulations and proposing scientifically sound yet efficient paediatric development programmes, typically via a Paediatric Investigation Plan (EU) and/or a Pediatric Study Plan (US), can streamline regulatory approval, ensuring receipt of cohesive feedback and reduced delays.

Furthermore, RWD and RWE are invaluable for understanding disease dynamics and patient variability. Integrating patient and caregiver perspectives will further ensure that study designs address meaningful outcomes. Patient-centric approaches also emphasise the importance of minimising the burden of participation for paediatric patients and their families. Streamlined study protocols, innovative data collection methods and flexible study designs can reduce disruptions to daily life while maintaining robust scientific rigour. Engaging patients and families as stakeholders can foster their trust and collaboration, helping to increase study enrolment and decrease dropouts.

Increased role of modelling and simulation

Regulatory authorities are promoting the use of MIDD to address data gaps and optimise study designs. Quantitative MIDD tools enable researchers to simulate clinical scenarios, predict outcomes and refine therapeutic strategies (**Figure 2**).[8]

For example, physiologically based pharmacokinetic (PBPK) modelling and quantitative systems pharmacology (QSP), offer comprehensive insights into drug behaviour and disease mechanisms.[9,10] Likewise, model-based meta-analysis (MBMA) allows for quantitative evaluation of alternative therapies from past randomised clinical trials (RCTs) to inform future treatment approaches for both novel compounds and alternate patient populations, including paediatric

subjects.[11] These and other MIDD tools enable researchers to explore various paediatric dosing regimens, assess the impact of paediatric-specific patient variables, optimise dosing and evaluate the efficacy of novel treatments.

By integrating available adult data and employing MIDD tools, sponsors can extrapolate short- and long-term adult efficacy and safety outcomes data to children before initiating lengthy and costly paediatric trials. An additional unrealised benefit to-date is that MIDD approaches can integrate RWD to support personalised medicine approaches, enabling more focused paediatric study design and increasing the likelihood of success.[12]

Advancements in therapeutic modalities

The past decade has seen exciting advancements in therapeutic modalities for paediatric cancer. Moving beyond traditional chemotherapy, radiation and surgery, the therapeutic arsenal now includes targeted therapies, monoclonal antibodies (mAbs) and immune-based treatments. Emerging therapies, such as chimeric antigen receptor T-cell (CAR T-cell) therapy, show promise for treating advanced paediatric oncology conditions. CAR T-cell therapy has demonstrated remarkable efficacy in treating refractory paediatric acute lymphoblastic leukaemia, offering hope for patients with otherwise limited options.[13]

mAbs and multi-specific antibodies are also transforming the treatment landscape. These therapies target specific cancer cell markers, reducing damage to healthy tissues and minimising side effects compared to conventional treatments. Additionally, antibody-drug conjugates (ADC) combine the precision of mAbs with the potency of cytotoxic agents. This design enhances their effectiveness against drug-resistant paediatric cancer types while minimising damage to healthy tissues.[14]

Targeted radioligands, also known as radioligand therapy (RLT) or targeted radionuclide therapy (TRT), are another class of emerging treatment that utilise a radioactive isotope attached to a cell-targeting molecule to deliver radiation directly to cancer cells. RLT/TRT can be a standalone treatment or part of a combination strategy, and offers potential advantages over traditional therapies, including increased efficacy and reduced toxicity.

The role of emerging technology in paediatric cancer research

Additional technological innovations, such as advanced biomarker assays, artificial intelligence (AI) and machine learning (ML), are revolutionising data collection and analysis in paediatric oncology.[15] AI and ML algorithms can analyse complex data sets, identify patterns and predict treatment outcomes, accelerating the discovery of new therapeutic targets.[16] Wearable devices and digital health tools are also gaining traction as a means of providing real-time monitoring of patients' health status and informing patient-reported outcome (PRO) measures. These technologies enhance data accuracy, reduce the need for invasive procedures,

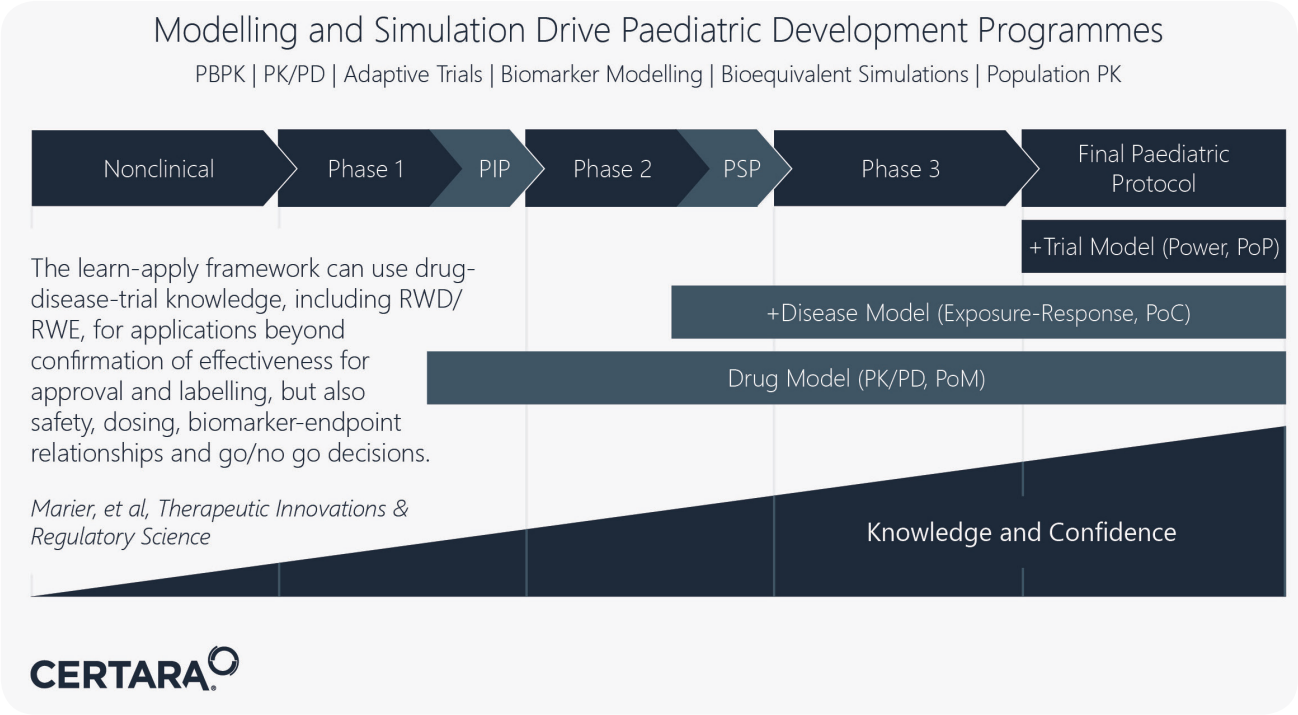


Figure 2: The drug development industry is increasingly applying MIDD strategies beginning early in clinical development to generate strategic insights into paediatric efficacy, safety, dosing strategies and other elements relevant to the design and approval of rigorous paediatric trials. MIDD can also take advantage of RWD/RWE to fill paediatric evidentiary gaps in RCTs, generating insights that can strengthen protocol design

> *Paediatric oncology drug development demands a multifaceted approach, combining scientific innovation, regulatory foresight and paediatric patient-centred design*

and empower patients and families to actively participate in their care. The continued evolution of digital health solutions holds the potential to transform paediatric oncology research and clinical practice.

Removing barriers to global regulatory and research harmonisation

Harmonising regulatory frameworks globally can reduce duplication and streamline paediatric drug approvals. Researchers are increasingly using extrapolation strategies, such as matching exposure-response data between adult and paediatric populations, to accelerate drug development. The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) E11A guideline, for instance, provides a structured approach to extrapolating existing data for paediatric applications, addressing knowledge gaps and optimising trial designs – a framework that has been adopted by major regulatory agencies.[17]

Additional benefits could be derived if key stakeholders, including regulatory bodies, were more proactive in removing obstacles to collaborative efforts. For example, incentivised data-sharing initiatives could help surmount challenges in global paediatric oncology research. By pooling resources and expertise, as well as being more open to innovative practices, industry stakeholders can overcome limitations due to small paediatric patient populations and achieve more robust and generalisable results. Such innovative approaches would also promote equity in access to innovative therapies, ensuring that children worldwide benefit from scientific advancements, and removing barriers to important research that has failed to progress efficiently to date due to cross-border data-sharing restrictions.[18]

Conclusion

Paediatric oncology drug development demands a multifaceted approach, combining scientific innovation, regulatory foresight and paediatric patient-centred design. By embracing technologies like MIDD, further recognising the value of RWD/RWE-based evidence to supplement RCTs and inform MIDD approaches, and fostering global collaboration, stakeholders can overcome existing challenges and deliver life-saving therapies to children more efficiently. As the field continues to evolve, sustained investment in research, infrastructure and policy development is essential. By prioritising the unique needs of paediatric patients, and fostering a culture of innovation and collaboration, the pharmaceutical industry can transform the paediatric oncology R&D landscape, leading to improved outcomes for countless children and their families.

References:

1. *Cheung SYA et al (2024), 'Paediatric oncology drug development and dosage optimization', Front Oncol, 29(13), pp1-15*
2. *Visit: cancer.org/cancer/types/cancer-in-children/differences-adults-children.html*
3. *Cadet T et al (2016), 'A Holistic Model of Care to Support Those Living with and beyond Cancer', Healthcare, 4(4), p88*
4. *Liu ITT et al (2024), 'The RACE Act and Paediatric Trials of Adult Cancer Drugs', Paediatrics, 54(4), p.e2024066920*
5. *Visit: fda.gov/regulatory-information/search-fda-guidance-documents/considerations-inclusion-adolescent-patients-adult-oncology-clinical-trials*
6. *Zimmerman KO et al (2019), 'Duration of Paediatric Clinical Trials Submitted to the US Food and Drug Administration', JAMA Pediatr, 173(1), pp60-67*
7. *Speer EM et al (2023), 'The state and future of paediatric research-an introductory overview: The state and future of paediatric research series', Pediatr Res, 24, pp1-5*
8. *Mitra A et al (2022), 'Applications of Model Informed Drug Development (MIDD) in Drug Development Lifecycle and Regulatory Review', Pharm Res, 39, pp1663-1667*
9. *Verscheijden LFM et al (2020), 'Physiologically-based pharmacokinetic models for children: Starting to reach maturation?' Pharmacol Ther, 211(107541), pp1-14*
10. *Azer K et al (2022), 'Quantitative system pharmacology as a legitimate approach to examine extrapolation strategies used to support paediatric drug development', CPT Pharmacometrics Syst Pharmacol, 11(7), pp797-804*
11. *Barrett et al (2020), 'Paediatric Extrapolation in Type 2 Diabetes: Future Implications of a Workshop', Clin Pharmacol Ther, 108(1), pp29-39*
12. *Madabushi R et al (2022), 'Review: Role of Model-Informed Drug Development Approaches in the Lifecycle of Drug Development and Regulatory Decision-Making', Pharm Res, 39(8), pp1669-1680*
13. *Boettcher M et al (2022), 'Development of CAR T Cell Therapy in Children-A Comprehensive Overview', J Clin Med, 11(8), p2158*
14. *Stokke JL et al (2021), 'Antibody-Drug Conjugates for the Treatment of Acute Paediatric Leukemia', J Clin Med, 10(16), pp3556*
15. *Yang Y et al (2023), 'Artificial intelligence applications in paediatric oncology diagnosis', Explor Target Antitumor Ther, 4(1), pp157-169*
16. *Ramesh S et al (2021), 'Applications of Artificial Intelligence in Paediatric Oncology: A Systematic Review', JCO Clin Cancer Inform, 5(12), pp1208-1219*
17. *Visit: ich.org/page/efficacy-guidelines*
18. *Lalova-Spinks T et al (2024), 'EU-US data transfers: an enduring challenge for health research collaborations', npj Digit Med, 7, p215*

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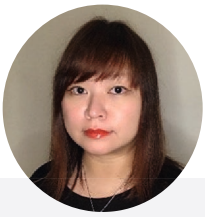

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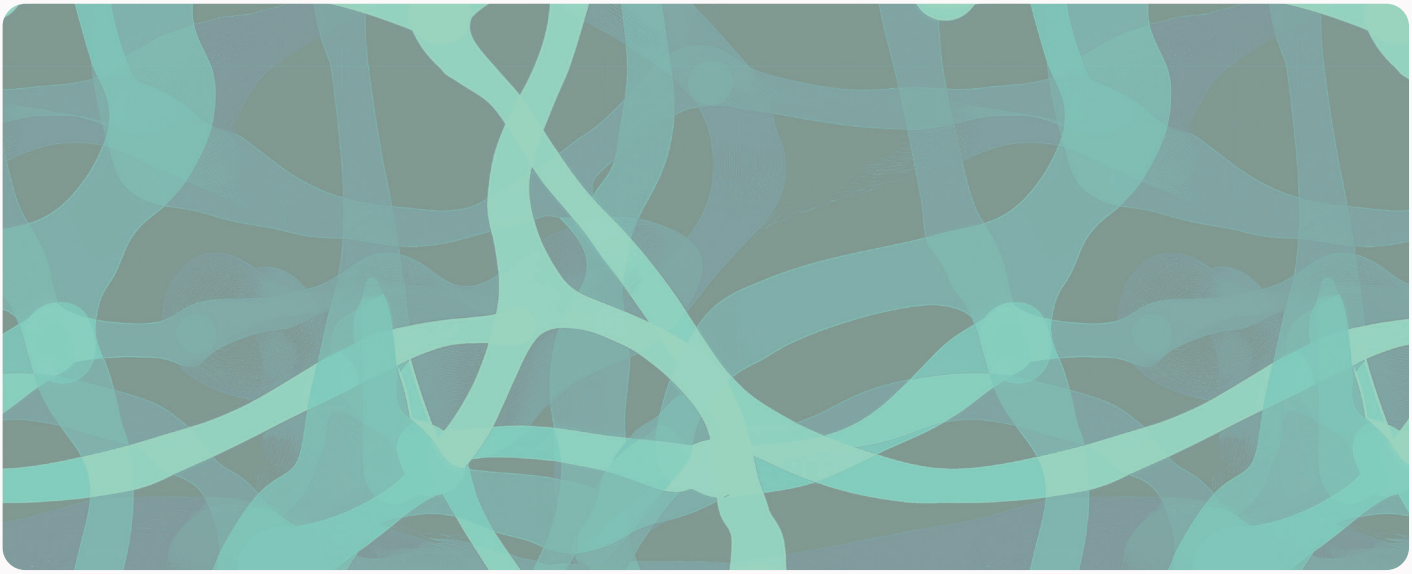

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Strategic authoring in clinical study reports: balancing data privacy and disclosure

With the increasing emphasis on public disclosure of clinical trials, sponsors are challenged to protect personal and commercial data within lengthy clinical reports. As public disclosure is now mandatory, timely data protection is critical. The Strategic Medical Authoring for Regulatory Transparency (SMART) approach helps by utilising regulatory guidance to establish best practices in medical writing for future disclosures, while also optimising documents for AI tools – improving the safeguarding of sensitive information throughout the clinical trial process

Anaya Rehman and Honz Slipka at Certara

The push towards greater transparency in clinical trials started back in the early 2000s, with the establishment of clinical trial registry bodies such as ClinicalTrials.gov by the US National Institutes of Health.[1] This initiative received further re-affirmation with the introduction of European Medicines Agency (EMA) Policy 0070 in 2014, which mandates proactive clinical trial data disclosure for marketing authorisation applications in the EU.[2] Following on, Health Canada launched its Public Release of Clinical Information (PRCI) initiative in 2019, reinforcing the global push for transparency.[3]

In today's fast-paced regulatory landscape, regulatory compliance can only be achieved through public disclosure of clinical information. Increased transparency fosters scientific innovation and is essential for advancement of medical research as it allows for transparent exchange of knowledge for secondary analysis.[4,5] Public access to clinical information increases public trust and enables patients to make informed health decisions.[6] However, to ensure this transparency of clinical trial data, sponsors face the challenge of adequately protecting sensitive information.

The protection of confidential information, be it personal or business, comes with a unique set of challenges, ranging from accurate data capture to tight regulatory timelines. A key path to success is to design and author documents with public disclosure as the ultimate goal. This necessitates a proactive collaboration amongst the medical writers and the transparency and disclosure experts.

Here, we outline an innovative approach for authoring clinical documents in a way that enhances efficiency in regulatory clinical trial document anonymisation – Strategic Medical Authoring for Regulatory Transparency (SMART). The SMART approach emphasises data protection from the inception of the drug development process, significantly improving the accuracy, consistency and speed at which clinical trial documents are anonymised. The SMART approach to authoring can make this public disclosure process faster and less resource-intensive – a critical advantage in today's regulatory environment. It is not necessarily a novel concept but rather a blend of regulatory insights and experience in medical writing and document disclosure, all brought together.

Data privacy in clinical study reports

A typical clinical study report is a comprehensive document that contains detailed information for a clinical trial, including the methodology, statistical analysis and results. It may also contain personal data. Regulations such as the Health Insurance Portability and Accountability Act (HIPAA) in the US, or the General Data Protection Regulation (GDPR) in the EU, have strict data privacy measures to ensure protection of personal data. Under GDPR, 'personal data' is described as any information connected to a person or a data subject, that can be distinguished – directly or indirectly – through identifiers such as a name, identification number, location data or online identifier, or various factors related to their physical, physiological, genetic, mental, economic, cultural or social identity.[7] Similarly, under HIPAA, there are 18 personal identifiers that are considered protected health information. These include: personnel names; geographic information smaller than a state; all elements of dates related to an individual (except the year); telephone numbers; fax numbers; email addresses; social security numbers; medical record numbers; health plan beneficiary numbers; account numbers; certificate/licence numbers; vehicle identifiers and serial numbers; device identifiers and serial numbers; web URLs; IP addresses; biometric identifiers (like fingerprints); full-face photographs; and any other unique identifying characteristic or code. Such regulations mandate strict data privacy measures, the non-compliance of which may result in legal penalties.[8]

As a result, these identifiers must be adequately anonymised to ensure de-identification of data before public

disclosure. Achieving this necessitates the implementation of robust anonymisation techniques, such as pseudonymisation, generalisation, suppression and randomisation, to adequately protect the sensitive information contained within the documents.[9,10,11] The SMART approach is closely aligned with the need to anonymise these identifiers. By focusing on the inclusion of only necessary content, and structuring documents in a way that isolates personal data, the SMART approach streamlines the anonymisation process. The result is a fast, efficient and more consistent compliance with regulatory standards, without compromising the data utility of clinical documents. The goal is to facilitate the public disclosure of clinical data while ensuring protection of personal privacy.

Strategic Medical Authoring for Regulatory Transparency

Standardising the authoring of clinical study reports promotes consistency in data presentation, making the review process more efficient by reducing errors and discrepancies.[12] According to the American Medical Writers Association (AMWA), the most common issue regulators encounter in documents is the excessive length, verbosity and repetition, and it is agreed that adherence to standards adds value to regulatory documents.[13] Hence, a templated approach helps streamline authoring, enabling more automation and reducing manual effort. This standardisation not only simplifies compliance with regulatory requirements but also accelerates the overall approval process, eventually shortening the time required to achieve marketing authorisation. The SMART approach focuses on this streamlined standardisation in document authoring. This is achieved through a strategy of Omit, Limit and Commit.

Omit

Remove unnecessary information in the clinical reports, such as excessive confidential business information or non-essential social details in narratives. This ensures that the information contained is essential for the scientific understanding of the content and does not over-complicate documents, making them more concise and easier to interpret.

Limit

Cut down on variations in personal data presentation through consistent formatting, and only document sensitive or personal information in a single location within a clinical study report (CSR). This enhances clarity and uniformity across documents.

Commit

Use terminology harmonisation and predefined structure templates to leverage artificial intelligence (AI) tools for automating the identification and protection of sensitive information. This allows for compartmentalisation of information and makes it easy to locate for anonymisation.

Such strategic authoring reduces excessive and unnecessary information and makes documents disclosure-ready. This allows efficient regulatory compliance while ensuring personal privacy is always maintained.

Best practices for SMART approach

To elaborate on the concept further, it is essential to understand how it relates to

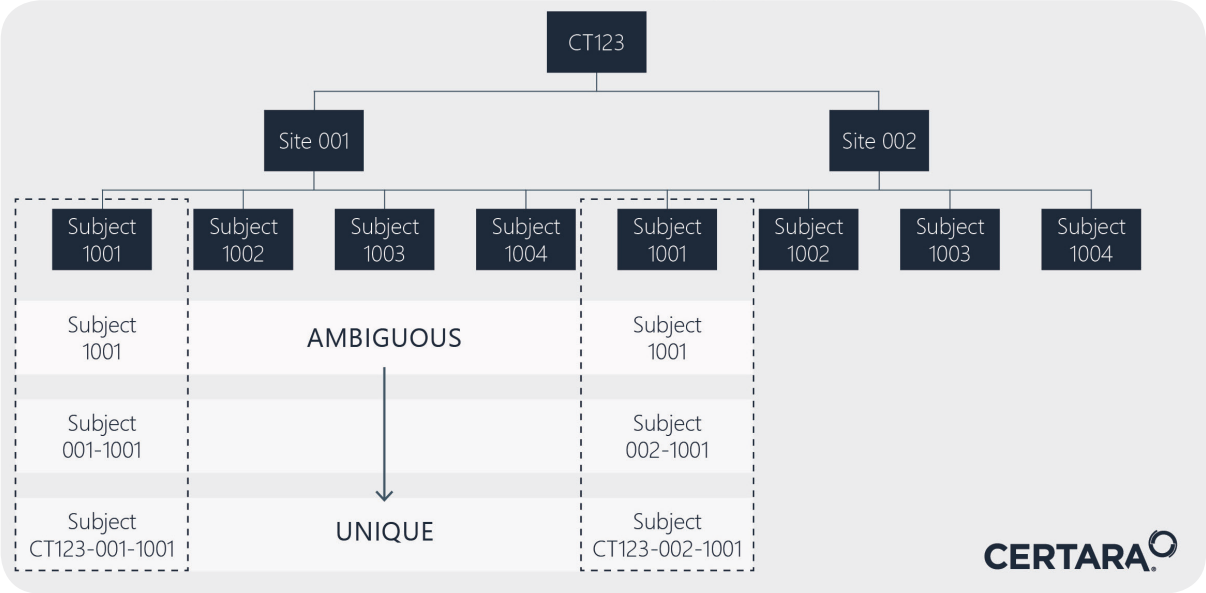

Figure 1: Example of USUBJID use to resolve ambiguity in multicentre trials. Clinical trial CT123 has two sites (001 and 002), with participants ranging from 1001 to 1005 at each site. The USUBJID for two participants from two sites will be CT123-001-1001 and CT123-002-1001. However, if the participants are referred to as 1001, it lacks uniqueness in the identification. By limiting variations of subject IDs and the consistent use of a USUBJID across documents ensures the correct linking of individuals to the correct sites

Table 1: Benefits of SMART Approach for Direct and Indirect Identifier Anonymisation

Benefits	Direct Identifiers	Indirect Identifiers
Consistent Anonymisation	The SMART approach proposes minimising the occurrence and repetition of data. Listing the study personnel on a dedicated page, and then referring to those individuals by their study role, minimises the need to reference which names should be redacted and which need to be retained, resulting in consistent data treatment.	Participant in a study can have over 20 dates associated with their narrative. The SMART approach guarantees consistent date formatting, and when using methods such as date-shifting, it ensures chronological lineage and consistent data utility.
Accurate Identification	Subject IDs can often look like study ids or other coded information. By using a consistent harmonisation of terminology suggested in SMART, false negatives and false positives of Subject IDs are less common.	There are over 30 different ways to identify someone as a smoker. Having consistent terminology (for example, using MeDRA terms) can help an automated programme quickly and correctly identify this information.
Decreased Resources	Signatures and handwritten texts are often not machine-readable. Using SMART and only adding personnel signatures in predetermined and cross-study-consistent locations decreases the resources necessary to find, identify and redact these items.	Decreasing verbatim text in narratives limits the effort required to identify sensitive or identifying information in those statements. SMART approach recommends minimising unnecessary information.

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Table 1: Benefits of SMART approach for direct and indirect identifier anonymisation

the identifiers and how medical writers can employ best practices. Personal identifiers can be broadly divided into two types: direct and indirect. Direct identifiers are used to uniquely identify a clinical trial participant in a study, whereas indirect – or quasi-identifiers – indirectly identify individuals.

Direct identifiers

The most commonly occurring direct identifier is the subject ID. It is used to track and manage participant data. Before applying SMART to subject ID, one must understand the components of a universal subject ID or USUBJID. A typical USUBJID consists of a study ID, site ID and the subject ID in the following format:

[STUDY ID]-[SITE ID]-[SUBECT ID]

Consistent use of a USUBJID across documents allows uniqueness in the identification of individuals and ensures correct linking to their respective sites (see **Figure 1**). By 'committing' to a harmonised format, 'limiting' USUBJIDs to the narratives section and 'omitting' their use elsewhere, SMART streamlines USUBJID use. From a disclosure-readiness perspective, this consistency allows locating these direct identifiers within the documents more efficiently, thus requiring less time. Much like predefined structure templates, this consistency facilitates leveraging the use of AI tools to automate identification and protection of information.

Indirect identifiers

Indirect identifiers cannot independently identify participants or personnel within the study, but can be used in combination with other data in the study to uniquely identify individuals. It is that much more important that these types of identifiers are anonymised consistently and not missed within the clinical trial documentation. The SMART approach may be adapted for indirect identifiers in a similar fashion, by ensuring that the identifiers are systematically structured, thus enhancing traceability. For example, 'committing' to a harmonised formatting for ages (eg, values in digits versus in words) and 'omitting' non-standard units (ie, using metric instead of Imperial units) produces a high-quality disclosure-ready document. Similarly, 'omitting' the use of atypical formats, such as in the case of dates and using a standardised format (eg, ddMMyyyy) not only expedites writing but also detection during the latter disclosure-related anonymisation processes. It is crucial to point out that the aim here is not to prescribe a single specific format for these indirect identifiers, but rather understand the importance of consistency in whatever format is used. SMART may not only be employed in how data is presented but also its location within the clinical documents. Restricting or 'limiting' the occurrences of participant level identifiers to narratives reduces the overall effort required to sift through lengthy documents to identify personal information down the lane.

Future trends in data transparency

The process of de-identification can be laborious, often involving sifting through thousands of pages of clinical documents with dense medical jargon to identify personal information. The process of manual de-identification requires countless man-hours that cost drug developers time and money. To make this process more efficient, AI plays an increasingly larger and more important role. In the broader regulatory affairs landscape, the integration of AI-enabled technology is revolutionising clinical data protection. This shift towards technology-enhanced practices is not just a trend but a necessary evolution to keep pace with increasing regulatory demands.

In terms of data transparency, AI enhances efficiency and the speed required to de-identify information accurately and consistently every time while ensuring regulatory compliance. In short, it has the capability of enhanced data protection through innovation and plays a crucial role in addressing the global drive for transparent clinical data sharing. Furthermore, AI allows the processing of large data sets, and this relies heavily on its capacity to identify repeating patterns and trends within data presentation. If the data is largely inconsistent or noisy, it yields poor quality outputs, however, having a structured and consistent medical authoring process across the entire regulatory document development cycle through strategies, such as the SMART approach, allows pharmaceutical companies to leverage generative AI technologies more effectively, enhancing their overall efficiency. Through standard guides for authoring, SMART enables increased automation by creating consistent inputs for the AI-enabled software, ensuring overall document disclosure readiness. By focusing on AI-driven accuracy and consistency, regulatory professionals can ensure that their anonymisation processes are not only compliant, but also efficient.

Conclusion

As the focus on transparency and public disclosure increases, drug developers are challenged with regulatory disclosure of lengthy clinical documents. Personal data protection must be done in a timely fashion, that may be achieved through improved authoring practices. The SMART approach intends to structure and design clinical documents in the most disclosure-friendly way possible, allowing transparency specialists to leverage AI-enabled tools to their fullest capability. Overall, it effectively safeguards personal data while minimising human error and any potential misses in the de-identification of personal information, ultimately speeding up the entire process.

Disclaimer:
The views expressed by the authors are their own and do not reflect the official position or policies of Certara. The information shared is based on expertise and experience in the field and is intended solely for informational purposes.

References:

1. *Visit: https://clinicaltrials.gov*
2. *Visit: ema.europa.eu/en/clinical-data-publication/support-industry-clinical-data-publication/external-guidance-implementation-european-medicines-agency-policy-publication-clinical-data-medicinal-products-human-use*
3. *Visit: canada.ca/en/health-canada/services/drug-health-product-review-approval/profile-public-release-clinical-information-guidance/document.html*
4. *Visit: https://www.canada.ca/en/health-canada/programs/public-release-clinical-information-drug-submissions-medical-device-applications.html*
5. *Visit: medrxiv.org/content/10.1101/2024.08.11.24311808v1*
6. *Hägglund M et al (2022), 'Patient empowerment through online access to health records', BMJ, p378*
7. *Visit: gdpr.eu/eu-gdpr-personal-data/*
8. *Benitez K et al (2010), 'Evaluating re-identification risks with respect to the HIPAA privacy rule', Journal of the American Medical Informatics Association, 17(2), pp169-177*
9. *Visit: pubmed.ncbi.nlm.nih.gov/35271377/*
10. *Onesimu J A et al (2022), 'Privacy preserving attribute-focused anonymization scheme for healthcare data publishing', IEEE Access, 10, pp86979-86997*
11. *Marques J F et al (2020), 'Analysis of Data Anonymization Techniques', In KEOD, pp235-241*
12. *Ahluwalia K et al (2022), 'The future of CMC regulatory submissions: streamlining activities using structured content and data management', Journal of Pharmaceutical Sciences, 111(5), pp1232-1244*
13. *Cooper J et al (2021), 'Value of Medical Writing: The Regulator's Perspective' AMWA, 36(4)*

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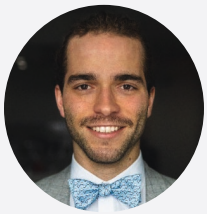


Honz Slipka MSc is a senior transparency specialist at **Certara**. With a background in neuroscience, and experience working with health information technology, Honz possesses a thorough understanding of health data management, global regulatory standards and best practices in the field of clinical data privacy. He leads and manages a portfolio of global pharmaceutical companies, and strives for innovation by leading the field of science, healthcare and research into the modern age of technological efficiency, clinical transparency and data utility.

Overcoming challenges in early drug development: start with the end in mind

Bringing a drug from concept to commercialisation is no small feat. With high attrition rates, lengthy timelines and exorbitant costs, the drug development process often feels like navigating uncharted territory. For R&D leaders, early strategic planning isn't just a box to tick – it's the foundation for success.

By 'starting with the end in mind', teams can align efforts on a path that not only reduces risks but accelerates progress, cutting through complexity with clarity and innovation.

Understanding the landscape

The development landscape is shifting, and so are the challenges within it. Regulations are ever-evolving but often lag behind scientific innovation, which can be hard to reconcile. Simultaneously, burgeoning competition across therapeutic areas demands differentiation and speed.

Key challenges in early development

Early-stage drug development comes with challenges on multiple fronts:

- ***Resource constraints:*** Emerging companies may lack funding, manpower or the expertise to craft comprehensive plans
- ***Complex regulations:*** Navigating diverse regulatory standards across global markets adds layers of complexity
- ***Preclinical mysteries:*** Selecting the right animal models or predicting human outcomes via preclinical data can be daunting
- ***Stakeholder alignment:*** Reliance on multiple independent consultants and siloed decision-making often leads to inefficiencies.

These barriers underscore the need for deliberate planning, seamless collaboration and dynamic adaptation.

Strategies for success

Evaluate the competitive landscape
Assess market unmet needs and the differentiators that make a therapy stand out, such as reduced side effects or advancements in delivery mechanisms.

Account for modality-specific nuances early
Different drug modalities – small molecules, biologics, cell therapies, oligonucleotides and more – each bring unique challenges that must be addressed proactively.

Foster cross-disciplinary collaboration
Break down silos early to align functions such as toxicology, drug metabolism and pharmacokinetics (DMPK), clinical pharmacology, and chemistry, manufacturing and controls (CMC) for unified progress.

Leverage model-informed drug development (MIDD) to support decision-making
Modelling is a key tool to predict outcomes, refine dosing strategies and help tailor therapies for specific populations.

Unlock the power of medical writing for a seamless journey to first-in-human (FIH)
Streamline early drug development by aligning critical regulatory documents with evolving data. By fostering collaboration across non-clinical, clinical and regulatory teams, you can ensure consistency, address safety considerations, and accelerate progress towards FIH studies with confidence and precision.

Why MIDD is crucial

Modelling transforms development by reducing reliance on trial-and-error methods. It enables predictive simulations, optimising dose selection, trial design and candidate prioritisation. Benefits include better decision-making, cost and time savings, and improved portfolio management.

Building a path forward

Early challenges are inevitable but not insurmountable. A strategic, forward-thinking approach can turn obstacles into opportunities. By addressing bottlenecks and leveraging the right tools, companies can boost success and reduce time-to-market. Whether navigating regulations or determining dosage: start with the end in mind.

Why partner with Certara?

To see how innovative thinking can reshape your drug development strategy and to leverage the best expertise at the right time, turn to leaders in model-informed approaches like Certara. Its science-first expertise, integrated technological tools and proven record for advancing therapeutics make it an invaluable partner. Start designing with the future in focus – a transformative collaboration awaits.

CERTARA

Early Development Model

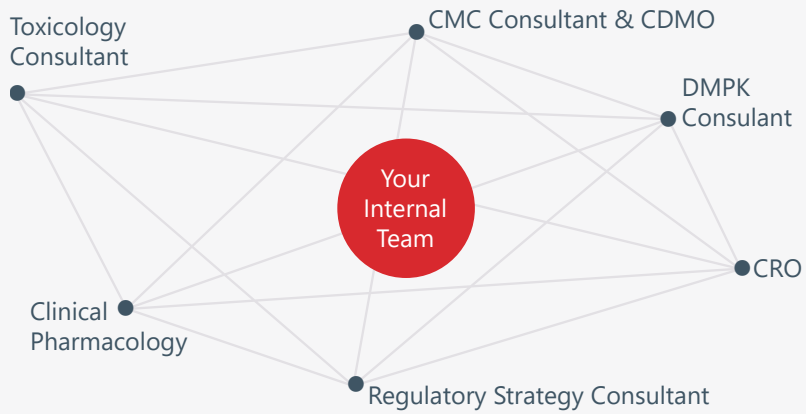
Derisk & streamline your early development framework

Certara's flexible early development model, built on experience from hundreds of projects, streamlines operations, reduces risk, and accelerates early development. Leveraging Model-informed Drug Development (MIDD), we optimise programmes with advanced modelling, clinical trial simulations, and real-world data insights.

Typical start-up early development model

Current model challenges

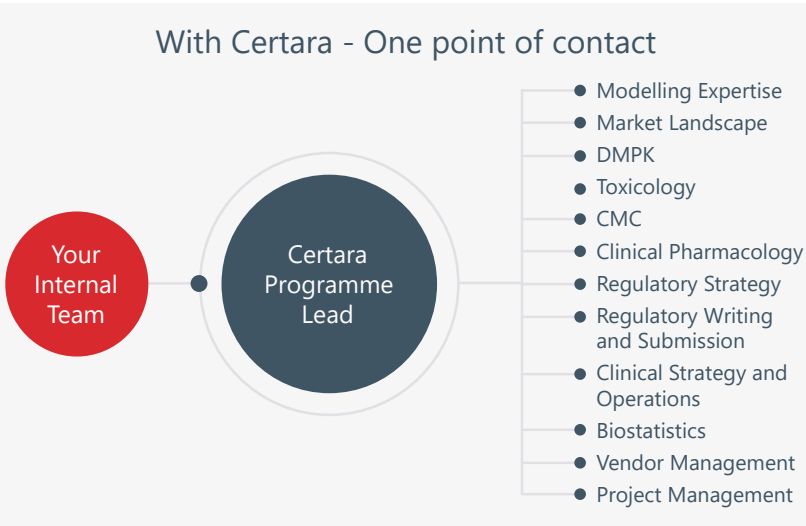
- Lack of full control and visibility into project timelines
- Multiple points of failure
- Complex communication management, information flow
- Lower productivity



A new paradigm with Certara early development model

Benefits of working with Certara

- Flexible and scalable model
- Leverage Model-informed Drug Development to build the right body of evidence needed for approval
- Expert resources with thousands of years of combined experience in end-to-end drug development that work as a team



Questions?

Learn how Certara can help your early development programme today

About Certara

Certara accelerates medicines using proprietary biosimulation software, technology and services to transform traditional drug discovery and development. Its clients include more than 2,400 biopharmaceutical companies, academic institutions and regulatory agencies across 66 countries.

Nightmares in medical writing: maintaining quality on compressed timelines

How did a partnership with PerfectIt help Certara medical writers to maintain the quality of their work while ensuring tight deadlines are met?

Rose Pabelonia at Certara

Medical writing is not for the faint-hearted. Tight deadlines, high stakes and unrelenting pressure to maintain precision can make every day feel like an overwhelming challenge. Ever wake up from a stressful dream where everything feels out of control? For medical writers, that's not just a dream – it's a reality. These challenges aren't just professional obstacles, they're the stuff of literal nightmares.

When researchers analysed thousands of recorded dreams, they identified the most common themes of nightmares: helplessness; being chased; accidents; and apprehension. Each of these aligns uncannily with the reality of medical writing:

- ***Helplessness:*** A submission deadline approaches, and the impossible decision looms – rush an incomplete document, or push the timeline back?
- ***Being Chased:*** Whether it's the regulatory agency's requirements, feedback from stakeholders or endless notifications from collaborators, you're always running against the clock
- ***Accidents:*** A misplaced figure, an overlooked inconsistency or a formatting glitch at the last minute means the writer works overtime to fix the issues
- ***Apprehension:*** That gnawing sense of dread; what critical error

might still be lurking, waiting to be discovered at the eleventh hour? What medical writer can hear the words 'corrupted table' without flinching?

These aren't just abstract fears. They are vivid, lived experiences for medical writers who must deliver high-quality work under unyielding time constraints. They underscore a fundamental truth: this kind of work requires extraordinary precision and focus.

The twin nightmares: deadlines and quality

At the heart of every medical writer's nightmare are two relentless forces:

- ***Deadlines you can't control:*** Timelines are often set by external factors like regulatory requirements or business needs. Writers have no say in these dates but are expected to meet them, no matter how tight they are
- ***The demand for uncompromising quality:*** Regulatory documents must be scientifically accurate, consistent and clear. Any error, however small, invites questions, delays approvals and can even put lives at risk.

It's a no-win situation. Compressing timelines means quality must be maintained at speed – an inherently contradictory demand.

Why quality keeps Certara awake

In medical writing, quality isn't a 'nice to have'; it's the foundation of trust with regulatory bodies, clients and colleagues. Poor quality documents lead to delays when regulatory agencies question inconsistencies, holding up approvals; the erosion of confidence where errors damage reputations, both for the writer and their organisation; and increased stress, where the burden of fixing preventable mistakes only compounds the pressure. When you're racing to meet a deadline, even small errors can snowball into significant setbacks.

The repetitive nightmare of quality control

Much of what haunts medical writers comes down to the repetitive, manual nature of quality control. These are the tasks that sap time and energy:

- Cross-checking against client style preferences
- Manually scanning for inconsistent abbreviations
- Fixing formatting errors, like date formats or spacing issues
- Catching typos or minor inconsistencies that distract from the content.

Each task is tedious but essential.

Certara has faced these nightmares first-hand. Before embracing automation, Certara's quality control (QC) process was manual, repetitive and prone to bottlenecks. Every step demanded meticulous attention:

Cross-checking
Writers manually reviewed documents against style guides and regulatory requirements. This involved endless toggling between references and documents.

Formatting
Dates, spacing, capitalisation – these seemingly minor details often became time sinks. Microsoft Word's basic tools for finding and replacing inconsistencies were slow and unreliable, especially with track changes enabled.

Abbreviation checks
Ensuring abbreviations were defined and used consistently was a tedious, error-prone task, particularly in lengthy documents.

These processes required significant time and mental energy, leaving less space for strategic thinking or addressing the document's scientific content. While this approach ensured quality, it came at a cost: it was slow, inconsistent and prone to human error, especially when deadlines were tight. The tipping point came when Certara realised that manual QC, while thorough, was holding the team back. The demands on medical writers and editors had grown too complex and too fast-paced for purely manual processes to keep up. Certara needed a solution that could handle repetitive, mechanical tasks efficiently, free writers and editors to focus on higher-value work – like data accuracy and message clarity – and standardise processes to reduce variability and errors across projects.

PerfectIt: a case study in streamlined QC

PerfectIt became a cornerstone of Certara's QC process, particularly in automating the following tasks:

- ***Style guide consistency:*** PerfectIt flagged inconsistencies in abbreviations, capitalisation and preferred terminology, ensuring adherence to client-specific style guides
- ***Formatting:*** The tool automated checks for common formatting errors, saving hours of manual work
- ***Abbreviation usage:*** PerfectIt identified undefined abbreviations and ensured their consistent use throughout documents.

By integrating PerfectIt, Certara saw immediate improvements:

- ***Consistency without compromise:*** Every document adhered to the same standards, reducing variability between writers and editors
- ***Time savings:*** Automating repetitive tasks gave our team more time to focus on content accuracy and clarity
- ***Reduced fatigue:*** Writers and editors no longer had to toggle endlessly between documents and references, making the work less draining.

Lessons learned

Certara's journey to automation wasn't an overnight transformation; it was a process of trial, adjustment

and learning. Some key takeaways from Certara's experience include the following:

Understand the bottlenecks
Before automating, map out your workflows and identify the steps that consume the most time or lead to the most errors.

Invest in training
Tools like PerfectIt are only as effective as the people using them. At Certara, we focused on training our team to ensure they could use the tool to its fullest potential.

Customise for your needs
PerfectIt's custom style sheets allowed us to tailor the tool to fit specific client or project requirements, ensuring that automation complemented, rather than replaced, our existing processes.

Results

After using PerfectIt for a year, Certara conducted a survey of 200 medical writers and editors to evaluate the impact of PerfectIt, with 71 responding. Of those respondents, 83% rated PerfectIt as beneficial for improving document quality, and 77% reported that it enhanced efficiency.[1]

The feedback revealed two major benefits:

- ***Fewer distractions:*** Writers and editors could focus on the document's accuracy and message instead of hunting for errors
- ***Smoother QC processes:*** By catching stylistic issues early, PerfectIt streamlined the quality control process, reducing stress and last-minute corrections.

PerfectIt didn't just save Certara time, it helped teams achieve deep focus – the kind of concentration where you can tackle complex problems and deliver top-tier work.

So, do we sleep better now?

Even with automation, medical writing will always come with its fair share of challenges. Deadlines will still loom, and the stakes will remain high. However, by integrating tools like PerfectIt into its workflows, Certara has significantly reduced distractions, allowing its teams to achieve deeper focus and greater efficiency.

While automation hasn't entirely eliminated the issues, it has enabled Certara's medical writers and editors to address them more effectively. For medical writers, the goal isn't just to meet deadlines, it's to deliver documents that are accurate, consistent and clear, even under pressure. And to sleep peacefully at night. That's a dream worth pursuing.

Reference:
1. *Certara (2025), PerfectIt Survey for Writers*

Rose Pabelonia, senior technical editor at **Certara**, has been at Certara for five years, where she serves within the Document Quality team. She has extensive experience as a technical editor, company trainer and project leader. She is resident expert and lead for implementing and training medical writers and technical editors on PerfectIt at Certara.

PerfectIt

Harness technology to accelerate medical writing excellence

Medical writing is more than a process - it's a craft, a commitment, and a critical bridge between scientific discovery and patient care. We recognize that every document you create carries immense responsibility: ensuring clarity, safeguarding accuracy, and upholding regulatory standards.

The pressure to deliver flawless, compliant content on tight deadlines is relentless, yet your expertise transforms complex data into life-saving information. At PerfectIt, we understand the vital role you play in advancing science and protecting patients, and we're here to support you with tools that accelerate quality checks without compromising the precision your work demands.

Why use PerfectIt?

Boost productivity	Quickly identify inconsistency issues like hyphenation, capitalization, and acronyms - freeing your team to focus on high-value tasks.
Ensure compliance	Customize PerfectIt for your house style, lexicon and other preferred terminology, ensuring compliance with individual submission requirements.
Integrate with workflows	PerfectIt works directly in Word and PowerPoint, and you choose when to run checks. It fits smoothly into your existing workflow without disruption.
Rock-solid security	PerfectIt operates entirely offline, keeping your sensitive data secure.

"I want to give myself as much time as possible to enhance clarity and check accuracy. That's why I use PerfectIt on every submission.

"Every submission has multiple rounds of review, and PerfectIt saves me time on each of them.

"The result is a clearer, better submission."

— Kate McKiernan, Medical Editor

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Planning and preparing regulatory submissions using top-down messaging

Developing and agreeing to key messages for marketing applications is a critical step in preparing successful submissions. Based on experience across dozens of major marketing applications, building key messages by drafting the US Annotated Label (Prescribing Information) has proven to be the most effective and efficient method

Mark Bowlby, Brenda Taylor and Steve Sibley at Certara

Key messages, which serve as guideposts for all content development, are important for the submission documents and labelling. There are many ways to approach this. Many sponsors use storyboards, key messaging documents, target product profiles (TPPs), or the Draft or Annotated Label (US prescribing information [PI]) as tools for building and capturing key messaging. A significant pitfall with many of these approaches is that the messages are often aspirational and disconnected from data. In addition, the storyboard, key messaging documents and TPPs are internal documents that require time, effort and prioritisation from key team members, and distract the team from preparation of the actual submission documents – especially during the critical period after phase 3 clinical data becomes available.

The conventional sequential bottom-up approach to authoring submission documents starts with reports at the base of the electronic common technical document (eCTD) pyramid. This allows the respective reports to progress to a 'near final' stage, so results can then progress into summaries and the Label (**Figure 1**). An alternative workflow is to start with a Label outline or TPP, ideally long before submission preparation. Shells of Module 2 summaries can then be drafted and aligned with the Label or TPP, in parallel with study report shell preparation.

The Label and TPP can also be used to:

- Seek guidance from regulatory agencies throughout clinical development
- Apply adjustments to the development plan as needed (eg, additional studies or changes in study design and/or endpoints)

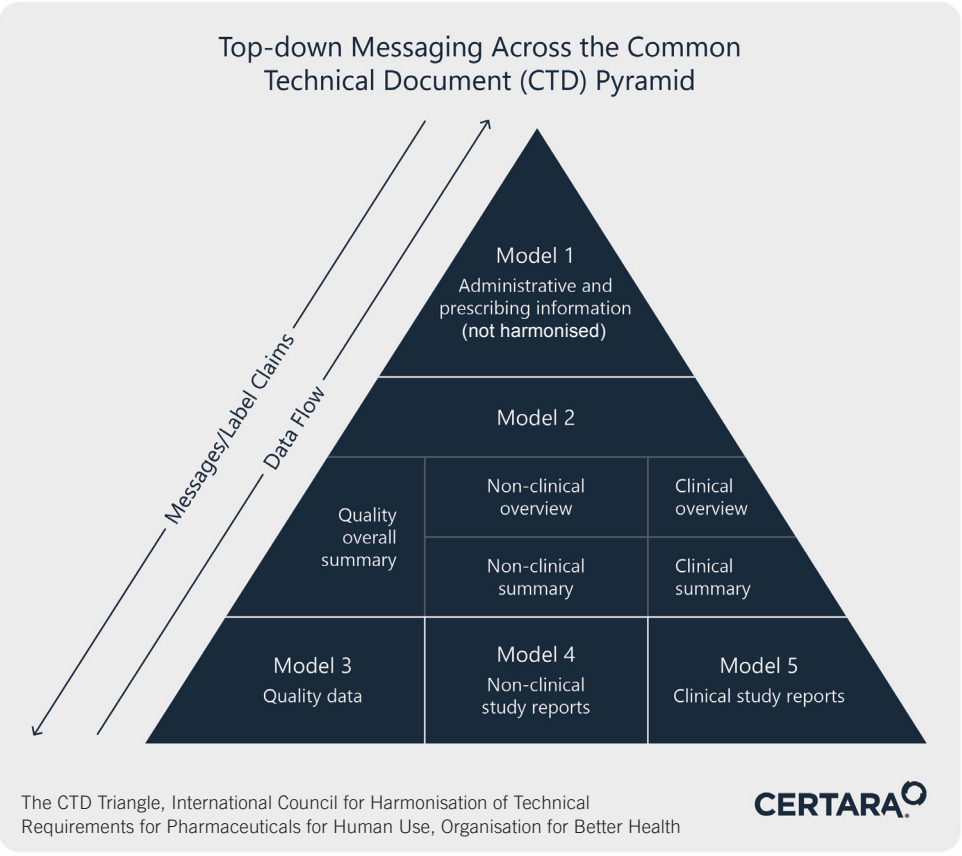

Figure 1: Top-down messaging across the common technical document pyramid

- Effectively account for the interdependencies across the Modules
- Update the Label on an ongoing basis to keep the programme on track.

The main goals of using a top-down approach include driving earlier creation of shell/prototype summary documents using expected label claims and messaging, and ensuring development of all the data needed to support the desired Label claims (ie, avoid gaps). The four widely used tools that can enable this approach are listed below in **Table 1**. A top-down approach enables earlier writing (ie, prior to the last study report/data becoming available), a roadmap for writing lower-level documents and a faster, less hierarchical approach to writing. However, few team members are familiar with the top-down approach, as writing is based on unknown pivotal clinical results, and the documents will require rework if those final study results differ significantly from expectations. In this model, work starts a minimum of nine months to several years before final phase 3 top-line results.

Connections among documents

One of the most important aspects of message development in a marketing application is that the message must be consistent throughout the application. While the exact wording may vary, it certainly must not be contradictory. Top-down messaging makes it easier to achieve this consistency throughout an application because the messaging is developed earlier, points to the specific supporting source data, and the submission team can trace and incorporate that message in all documents from the Label to the source report.

The TPP provides a strong foundation for the development programme and should be started early in drug development, ideally

Parameter	Target Product Profile (TPP)	Prescribing Information (Label)	Storyboard	Key Messages
Start Time	Start pre-IND	Typically started during phase 3	Typically started during phase 3	Typically started during phase 3
Period of Use	Continuous throughout product's life cycle	Continuous throughout product's life cycle	Abandoned once phase 3 data is released	Abandoned once phase 3 data is released
Complexity	Can be very complex and comprehensive	Most complex and comprehensive	Simple to complex, not comprehensive (typically includes messaging for only what is considered most critical)	Simple to complex, not comprehensive (typically includes messaging for only what is considered most critical)
Breadth	Includes CMC, non-clinical, clinical	Includes CMC, non-clinical, clinical	Typically includes only non-clinical and clinical	Typically includes only non-clinical and clinical
Commercial Role	Influenced by commerical needs	Influenced by commercial needs	Typically less commerical input than for TPP and label	Typically less commerical input than for TPP and label
Primary Usefulness	Guides development programme	Serves as official prescribing information to physicians and patients	Messaging in Module 2 shells and early drafts	Messaging in Module 2 shells and early drafts
Internal or External Document	Internal	External	Internal	Internal

Table 1: The four tools of a top-down approach

The TPP provides a strong foundation for the development programme and should be started early in drug development, ideally before the pre-investigational new drug (IND) meeting

before the pre-investigational new drug (IND) meeting. The TPP is updated frequently as new results are generated and as the competitive market changes. The benefit of starting a TPP early is that it can guide drug development and be used to obtain guidance from health authorities. Conversely, storyboards, key messaging and labelling typically start late in development during phase 3.

Updating the TPP is an iterative process. Early in development, chemistry, manufacturing and controls (CMC), non-clinical, and clinical base case and best case information are added, along with any regulatory requirements in these areas. As studies are completed and data is generated, TPP updates need to be balanced with submission document authoring. **Figure 2** shows some of the messaging flow across the Label and Modules 2 and 3.

In top-down authoring, any of the four key messaging tools can be used to inform Module 2 shell development. The Clinical Overview (Module 2.5) includes much of the information typically messaged in these documents, but with additional detail and source references. The Module 2.5 shell can be derived from desired messaging content and existing study results. For example, the safety section of Module 2.5 must address the Contraindications, Warnings and Precautions, and any Black Box warnings in the Label, by using clinical study and development terminology. In turn, the messages

PI Section	Clinical Summaries	Non-clinical & CMC
1. Indications & Usage	2.5 Clinical Overview	
2. Dosage & Administration	2.7.2 Summary of Clinical Pharmacology & 2.7.3 Summary of Clinical Efficacy	2.6.2 Pharmacology & 2.6.6 Toxicology
3. Dosage Forms & Strengths	2.7.1 Summary of Biopharmaceutics	3.2.P.1 Description & Composition of Drug Product
5. Warnings & Precautions	2.7.4 Summary of Clinical Safety	2.6.6 Toxicology
7. Drug Interactions	2.7.2 Summary of Clinical Pharmacology	2.6.4 Pharmacokinetics
8. Use in Specific Populations	2.7.3 Summary of Clinical Efficacy & 2.7.4 Summary of Clinical Safety & 2.7.2 Summary of Clinical Pharmacology	2.6.6 Toxicology
9. Drug Abuse & Dependence	2.7.4 Summary of Clinical Safety	2.6.2 Pharmacology
10. Overdose	2.7.4 Summary of Clinical Safety	2.6.6 Toxicology & 3.2.S.1, 3.2.S.3, 3.2.P.1 (DS & DP information)
12. Clinical Pharmacology	2.7.2 Summary of Clinical Pharmacology	2.6.2 Pharmacology & 2.6.4 Pharmacokinetics
13. Non-clinical Toxicology		2.6.6 Toxicology
14. Clinical Studies	2.7.3 Summary of Clinical Efficacy	
16. How Supplied/Storage & Handling		3.2.P.1, 3.2.P.8 (DP Description & Stability)

CERTARA

Figure 2: Mapping of messages to-and-from the US PI Label

Most importantly, because the storyboard/key messaging document is not a submission document, focus shifts off this document to authoring the actual submission documents once phase 3 data is available

in the draft Label and Module 2.5 get incorporated into the clinical summaries (Modules 2.7.1 to 2.7.4). Examples include: incorporating key messages for drug-drug interactions into the Summary of Clinical Pharmacology (Module 2.7.2); results for the primary endpoint into the Summary of Clinical Efficacy (Module 2.7.3); and adverse events and laboratory results into the Summary of Clinical Safety (Module 2.7.4). It is important to note that all of these messages will be cross-referenced to the clinical study reports (CSRs) or other data that serves to support those messages. The top-down approach can also be used for the non-clinical sections of the submission to design what non-clinical studies are needed; those expectations can be shelled into the non-clinical Module 2 summaries. However, with non-clinical, more data is flowing bottom-up from reports to summaries and the Label than is desirable for clinical results.

Real-world experience

If a TPP was not generated early in development, a messaging document (eg, storyboard, key messaging, or annotated label) needs to be created starting from nine to 18 months prior to submission. Across dozens of major marketing applications with storyboards, key messaging documents or annotated labels, there's a clear winner among these options: the Annotated Label.

Storyboard/key message document

The storyboard and key messaging documents can be grouped together as they are often different in name only. Typically, a storyboard or key messaging document in Word or PowerPoint begins with two columns (eg, Topic/Message and Sources), but can be made incredibly complex. Key topics, such as indication, unmet need, patient population, primary efficacy, dosing, adverse events and precautions are identified and serve as the main rows in the table. The storyboard/key messaging documents adopt and adapt existing marketing 'aspirational' wording, as well as wording already used in TPPs, protocols and briefing documents. Sponsors typically develop 'desired' wording for each item and the studies or sources that would support that wording. The assigned team then reviews and refines the wording over several months up to availability of phase 3 data.

What are the pros and cons with this approach? The initial drafting helps the team establish expectations for the data and messaging. However, the wording that was great in the storyboard/key messaging document often does not work within actual submission documents. In addition, the wording is usually only connected to a general, rather than specific, source. Most importantly, because the storyboard/key messaging document is not a submission document, focus shifts off this document to authoring the actual submission documents once phase 3 data is available.

Annotated Label (US PI)

In this approach, sponsors work from required labelling language and approved labels for similar products to draft the content. A lead writer typically drafts one section of the label at a time, then issues it to the team and schedules a one-hour meeting to review that section. This is repeated each week for months until all sections have been reviewed and agreed. A key aspect of this approach is that the team identifies and inserts EXACT annotations for every sentence and number (eg, Module 5.3.5.1, Study 304 CSR, Table 11.4.3.1.2).

What are the pros and cons with this approach? Because the agreed messaging is the actual annotated label wording, reusing that wording in other documents in the submission ensures consistency top-to-bottom (ie, Modules 1 through 5 in the submission). In our experience, Annotated PI wording can be used almost verbatim in the Module 2 summary documents. Most importantly, because the Annotated PI is part of the submission, it is necessary to continue development after phase 3 data is available.

Based on these experiences, our best practice recommendation for developing messaging for a new marketing application is to use

Developing messaging long before phase 3 data enables smoother and faster submission after final data becomes available

the US Annotated Label for this purpose. However, if you do not have direct access to the label, or your submission is not for the US, we recommend using the Clinical Overview (and Non-clinical Overview for non-clinical) for this messaging purpose, following the same approach of building a section at a time and identifying the specific cross-references to source.

Conclusion

Consistency of messaging across Modules 1 through 5 in a marketing application is critical but can be difficult to achieve. A top-down approach to messaging has multiple benefits compared to a bottom-up approach as follows:

- Top-down messaging can drive drafting of summaries prior to final data availability
- The TPP can help guide the development programme and support meetings with health authorities.

Developing messaging long before phase 3 data enables smoother and faster submission after final data becomes available.

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Mark Bowlby PhD, senior director of Global Submissions at **Certara**, has over 28 years of experience in the clinical research and drug development fields, working at large pharmaceutical companies prior to Certara. He's been a submission lead for numerous small molecule and biologics marketing applications to the US Food and Drug Administration and European agencies. With broad experience as a regulatory medical writer, he's led the authoring of investigator brochures (IBs), clinical study reports, clinical summaries and overviews, briefing packages, and many other regulatory documents. Earlier in his career, he planned and wrote numerous biomedical manuscripts, posters and slide decks regarding his scientific research and postdoctoral work. Therapeutic areas of expertise include ophthalmology, neurology, psychiatry, chronic pain, oncology, renal disorders and cardiac disorders.

Brenda Taylor MS, is director of Global Submissions at **Certara**. Brenda has over 24 years of experience in the biotechnology and pharmaceutical industry, spanning small molecule drugs and biologics. She has been a submission lead for numerous investigational new drug and marketing applications to FDA and Japanese agencies. A prolific author of IBs, both non-clinical and clinical summaries and overviews, briefing packages, and other regulatory documents, in addition to white papers and manuscripts related to submission leadership and improving the submission process. Therapeutic areas of expertise include oncology, allergic reactions, cardiovascular and anti-infective agents.

Steve Sibley MS is vice president of Global Submissions and Submission Leadership at **Certara**. With a career spanning more than 30 years in the pharmaceutical industry, Mr Sibley provides regulatory writing consulting services and leads the Global Submissions Service Line within Certara Drug Development Solutions (CDDS). He has led global submission teams and authored critical documentation on more than 45 marketing applications and more than 30 investigational drug applications. Mr Sibley's work has covered the full range of therapeutic areas, with a particularly strong background in oncology, cardiology and rare diseases. Mr Sibley draws on his substantial industry knowledge and leadership skills to mentor and train other submission leads.

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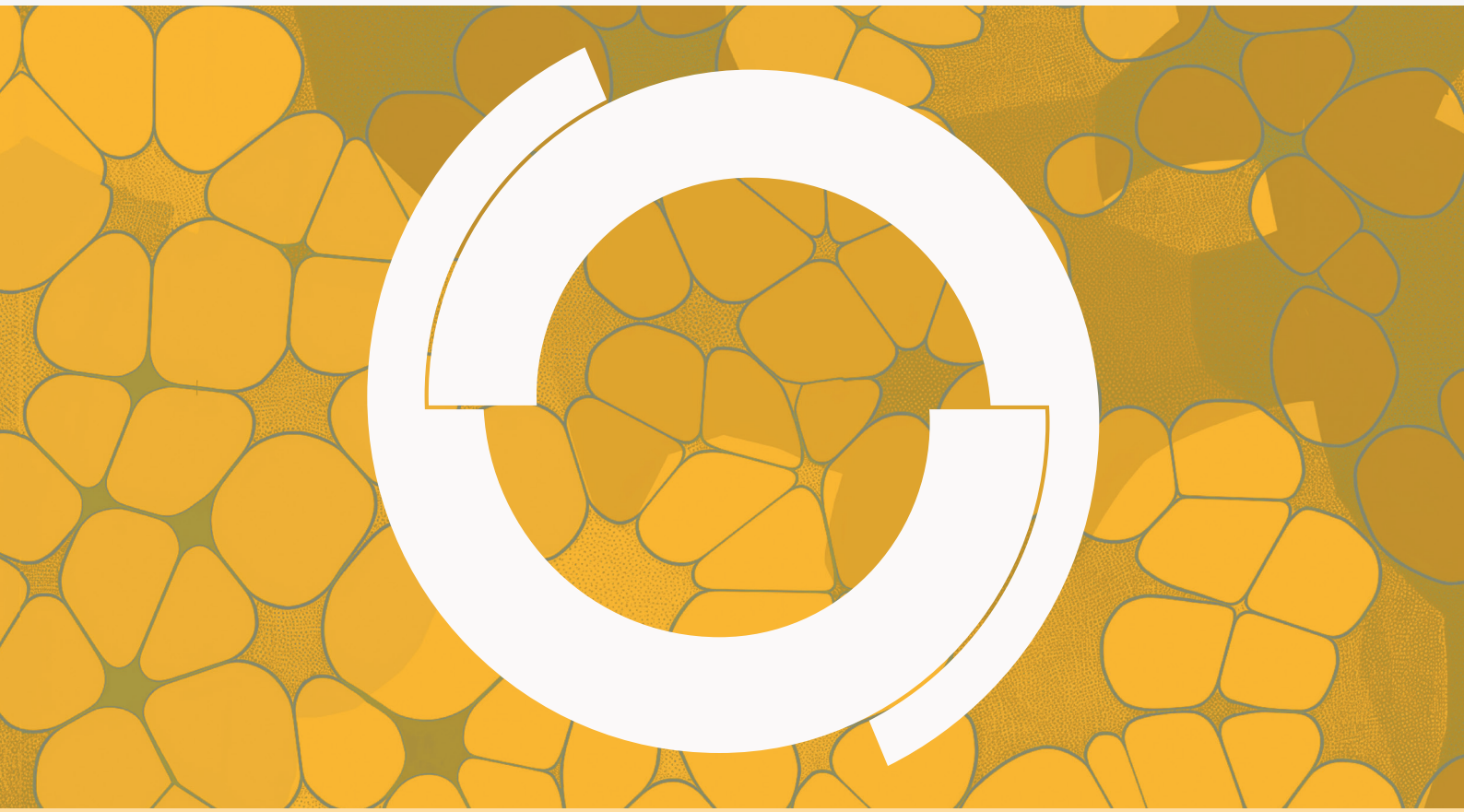

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PBC's Clinical Outsourcing Group events

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COG UK: London, UK – 4-5 March 2025 – thepbcgroup.com/cog-uk

COG Nordics: Malmö, Sweden – 1-2 April 2025 – thepbcgroup.com/cog-nordics

COG: New England – Burlington, MA, US – 29-30 April 2025 – thepbcgroup.com/cog-new-england

COG: DMV Area – Bethesda, MD, US – 13-14 May 2025 – thepbcgroup.com/cog-dmv

COG: CRO Summit Europe – Amsterdam, the Netherlands – 16-17 September 2025 – thepbcgroup.com/cog-cro-summit-europe

COG: Bay Area – Burlingame, CA, US – 21-22 October 2025 – thepbcgroup.com/cog-bay-area

COG: Europe – Amsterdam, the Netherlands – 18-19 November 2025 – thepbcgroup.com/cog-europe

COG: CRO Summit – Raleigh, NC, US – 2-3 December 2025 – thepbcgroup.com/crosummit

COG Europe 2024 review: Advancing patient-centric clinical research

The Clinical Outsourcing Group (COG) Europe 2024 meeting marked a significant milestone in exploring and advancing clinical research practices across the European region.

The two-day summit brought together trial sponsors, healthcare and innovating vendors to address key developments in clinical trials.

Leadership and innovation

COG Europe distinguished itself with exceptional C-suite participation, featuring influential leaders from prominent organisations including Biophytis, Node Pharma, Pleco Therapeutics, Alloksys Life Sciences and Biozen.

This high-level engagement demonstrated the industry's commitment to driving meaningful change in clinical research.

Patient-centric approaches

The meeting established patient-centricity as a cornerstone of future clinical trials, with industry leaders **Rob van Maanen** (chief medical officer at Biophytis) and **Helen Blanco** (chief operating officer at Node Pharma) championing practical strategies for enhanced patient engagement. Their insights provided actionable frameworks for implementing patient-focused trial designs.

Supply chain excellence

Supply chain optimisation was addressed, with **Benedict Hirth**'s pioneering work on simulation technology leading the way. The vendor management panel, featuring experts **Vanessa Dekou** and **Astrid Pañeda Rodríguez**, offered valuable insights into managing increasingly complex trial logistics.

Technological innovation

The integration of artificial intelligence (AI) in clinical operations saw meaningful progress through practical applications, particularly in: medical writing advancement, led by **Robin Brohl**; operational efficiency improvements, demonstrated in **Sam Vakili**'s workshop; and real-world implementation strategies that moved beyond theoretical discussions.

Regional impact and growth

The Netherlands emerged as a leading hub for clinical research, with the conference highlighting successful cross-border collaboration initiatives. The strong representation from the Benelux region demonstrated the area's growing influence in clinical research innovation.

Audience engagement

The event's success was underscored by its impressive attendance profile, drawing C-Suite executives and senior leaders from across Europe's biopharma sector. This high-level participation facilitated meaningful discussions and connections that will drive future industry developments

COG: CRO Summit 2024 review: A landmark event in clinical research

The inaugural COG: CRO Summit in Raleigh, North Carolina, US, established itself as a groundbreaking industry event, uniquely created by clinical research organisations (CROs) for CROs. This pioneering conference successfully brought together an impressive array of CRO organisations, from global leaders to specialised regional players.

The summit demonstrated exceptional engagement from industry leaders, featuring an unprecedented assembly of CRO executives and decision-makers. The stellar line-up included representatives from: Worldwide Clinical Trials, Vial, Vantage Biotrials, PharPoint Research, Veristat, Everest Clinical Research, Spaulding Clinical, Lexitas, Altasciences, Excelya, Biorasi and Clinilabs.

Strategic partnerships and collaboration

Steve Chriscoe from Worldwide Clinical Trials led compelling discussions on enhancing sponsor-CRO partnerships, setting a collaborative tone for the entire summit. The focus on practical relationship-building strategies provided attendees with actionable insights for improving industry partnerships.

Digital transformation

Sarah Ruiz of Vial delivered a comprehensive exploration of digital trial implementation, highlighting concrete steps for modernising clinical research operations. The presentation offered practical solutions for integrating digital technologies into existing trial frameworks.

Operational excellence

The summit made significant progress in addressing operational challenges faced by CROs, through focused sessions on: vendor alliance optimisation and audit preparedness, led by **Vatche Bartekian**; financial management and transparency insights from **Paul Johnson**; as well as innovative approaches to trial management and execution.

Leadership insights

The Navigating the Future panel, skillfully moderated by **Sybil Wilson**, brought together an impressive array of industry leaders who shared strategic perspectives on: current biopharma landscape evolution; practical AI implementation strategies; industry consolidation opportunities; and future growth trajectories.

Innovation and global perspectives

Showcasing innovative approaches to clinical research, including: practical AI implementation strategies from **Kirk Wroblewski** and **Shae Wilkins**; Asian market patient engagement insights from **Hiroki Matsushima**; data-driven diversity approaches presented by **Ryan Brown**; and novel site selection methodologies from **Krystyna Kowalczyk**.

Audience engagement

The summit achieved remarkable attendance metrics: over 70% C-Suite executives and senior directors/VPs; strong representation from US, Canada and Europe; significant participation from North Carolina's local market; and a carefully managed 2:1 ratio of CRO to vendor attendees.

Future impact

This inaugural summit has established itself as a crucial platform for CRO collaboration and knowledge-sharing. The event's success demonstrates the industry's need for focused, CRO-specific forums that address

unique challenges and opportunities in clinical research.

COG UK 2025 preview: Back for its third edition!

The COG UK conference, taking place on 4-5 March 2025 at the Copthorne Tara Hotel London Kensington, London, UK, promises to be a landmark gathering for the UK's clinical research sector. This meeting, now in its third annual edition, brings together senior executives, innovative biotech leaders and key decision-makers from across the British clinical-stage life sciences landscape.

Key conference themes

- ***Patient-centric trial innovation:*** Strategies for meaningful patient engagement beyond tokenistic approaches; enhancing diversity and stakeholder collaboration within the NHS framework; and novel approaches to patient recruitment and retention in the UK market
- ***Strategic outsourcing and partnerships:*** Evolution of functional service provider (FSP) models and pricing transparency; vendor oversight in the context of ICH E6 (R3); and academic-industry partnerships leveraging the UK's research infrastructure
- ***UK clinical trial landscape navigation:*** Optimising trial execution within the NHS ecosystem; implementing the National Clinical Value Review (NCVR) initiative; and strategic site selection and R&D incentive optimisation
- ***Funding and investment:*** Post-Brexit funding strategies for clinical-stage companies; creative funding models and equity structures; and leveraging the UK's position in global biotech development.

Year-on-year, COG UK attracts the region's active, clinical-stage biopharma community, with the audience made up of C-suite executives and senior directors, heads of clinical operations and development, senior outsourcing and procurement professionals, as well as a hand-picked selection of CROs and functional service provision (FSP) vendors.

COG Nordics 2025: Innovation in Nordic clinical research

The COG: Nordics conference is scheduled for 1-2 April 2025 at the Scandic Triangeln in Malmö, Sweden, showcasing the region's leadership in clinical research innovation. This meeting, now in its second year, brings together senior executives from across the Nordic life sciences sector.

Key conference themes

- ***Nordic healthcare excellence:*** Leveraging the region's advanced healthcare infrastructure; utilising comprehensive national quality registries; and maximising the potential of digitalised healthcare systems
- ***Digital innovation and decentralised trials (DCTs):*** Implementation of DCTs; digital biomarker validation and endpoint selection; and technology integration in clinical research
- ***Strategic outsourcing:*** Evolution of FSP models in the Nordic context; vendor selection and partnership optimisation; and cost-effective trial management strategies

- ***Patient-centric research:*** Innovative approaches to patient engagement; cross-stakeholder collaboration within Nordic healthcare systems; and patient recruitment and retention strategies.

COG Nordics attracts the region's active clinical-stage biopharma community, with the audience made up of C-suite executives and senior directors, heads of clinical operations and development, and senior outsourcing and procurement professionals, as well as a hand-picked selection of CROs and FSP vendors.

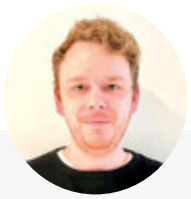
COG New England 2025: Returning to the world's largest biopharma hub

The COG: New England conference takes place on 29-30 April 2025 at the Boston Marriott Burlington, Massachusetts, US. This edition promises to be our largest yet, a landmark gathering for the region's thriving biotech ecosystem.

Key conference themes

- ***Patient-centric trial innovation:*** Advanced strategies for rare disease patient recruitment and retention; implementation of patient-focused protocol design; integration of patient voices in clinical development; and novel approaches to diversity and inclusion in clinical trials
- ***Strategic outsourcing excellence:*** FSP vs full-service outsourcing models for emerging biotech; vendor selection and oversight optimisation; CRO partnership management for small to mid-sized companies; and budget optimisation and resource allocation
- ***Technology and data innovation:*** AI implementation strategies for smaller organisations; data-driven approaches to site selection and patient recruitment; digital measurement technologies in DCTs; and real-world data utilisation in clinical research
- ***Clinical development strategy:*** Early-phase trial design and execution; cell and gene therapy trial management; oncology trial optimisation; and risk-based monitoring approaches.

COG New England attracts the North Eastern US' active, clinical-stage biopharma community, with the audience made up of C-suite executives and senior directors, heads of clinical operations and development, and senior outsourcing and procurement professionals, as well as a hand-picked selection of CROs and FSP vendors.



David Jones is head of content at **PBC Group**, leading content research, creation, strategy and speaker engagement across the **Clinical Outsourcing Group** series. David has over a decade's experience in business-to-business media with a deep understanding of conference organisation, as well as digital media. In his role, David works closely with all stakeholders throughout the clinical research ecosystem to create impactful conference programmes that address key challenges and regulatory concerns faced by those carrying out research within a commercial, non-profit or academic setting. Reach out to David directly at **djo@thepbcgroup.com** to learn more about the COG meeting series.

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RISKY REPORTS

What are the potential practical applications of generative AI in pharma safety reporting?

SMALL BUT MIGHTY

Ensuring drug safety can be a challenge for smaller pharma and biotech companies. How can this be overcome?

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Using AI to identify clinical trial safety reporting requirements

Artificial intelligence (AI) has the potential to assist in gathering regulatory intelligence and defining safety reporting rules. However, despite AI's promise to streamline regulatory affairs, the current literature often falls short in documenting actual applications, focusing instead on theoretical possibilities. What are some current possibilities and challenges in the use of generative AI for identifying local reporting requirements for drug safety in practice, and what potential does this approach have in replacing the traditional use of regulatory experts, manual information gathering and human analysis?

Martti Ahtola at Tepsivo

We use generative artificial intelligence (genAI) to answer questions about everything from bicycle repairs to drug discovery. The potential uses of AI in clinical trials include, for example, identification of signals of adverse events and toxicities, data analysis, identification of clinical trial cohorts, support in decision-making, and process streamlining.

There is naturally a lot of interest in using AI for expert tasks such as gathering regulatory intelligence and determining the safety reporting rules for clinical trials, and with the current pace of development, it seems like it is no longer a question of 'when'. AI is already being used to help experts in the pharma industry enhance their abilities and perform skills-heavy or time-consuming tasks.

Traditional process

For non-experts in the field of pharmacovigilance (PV), drug safety in clinical trials often means reporting adverse events and handling safety data forms. Pharmacovigilance experts, however, approach PV from a broader perspective, considering international standards, national laws and local guidelines. They understand how to analyse safety data, differentiate between immediate and periodic reporting, and would usually have follow-up questions related to the study set-up: Where is the trial conducted? What is the product? Are there relevant past studies?

If the country, product and regulations are familiar, PV or regulatory experts can often predict the requirements. But unfamiliar scenarios or complex global studies demand deeper analysis to determine processes and reporting parameters. A unified, accurate global regulatory intelligence database remains an aspiration for most organisations. Regulatory intelligence databases may have accurate details for some regions but lack completeness or up-to-date information for others. The maintenance of a regulatory intelligence database requires ongoing review and updates, and it is never complete.

Traditionally, regulatory intelligence experts gather data by scouring regulatory websites, using news services or subscribing to regulatory intelligence databases. They then update internal systems, implement monitoring rules or draft new procedures based on these insights.

Current use of AI for this purpose

Much of the literature on AI in drug development focuses on its potential, which might suggest to an AI model that practical applications do not exist. However, the AI revolution is already underway. The rapid development and implementation of AI across all industries likely means there are already hundreds of practical applications in the area of pharmaceutical regulatory affairs alone.

GenAI excels at tasks with well-defined rules or patterns, like summarising text or creating content from clear prompts. For topics well represented in training data, it provides accurate, detailed and consistent information at scale. However, while AI shows great promise, can it replace a regulatory specialist today? Specifically, can it identify local PV reporting rules for clinical trials, or support the set up of a centralised, AI-driven safety monitoring system for global trials?

Regulatory challenges

AI is a powerful tool for transforming the drug development landscape, but ethical and operational challenges remain significant. Organisations often prohibit uploading confidential or personal

information to AI models, while AI-based systems in clinical trials require validation to ensure safety and compliance. Overall, there's still uncertainty surrounding the applicable regulatory requirements.

A key obstacle to AI implementation in drug development is uncertainty around its regulation. For instance, while genAI might assist with identifying and interpreting regulatory requirements, the decision-making role of AI in safety assessments raises concerns. Regulators expect applicants to understand and follow available requirements and guidelines, but these can be hard to locate or interpret, or don't fully address specific trial questions.

Though contacting regulatory authorities is an option, language barriers, understaffing or delays can hinder timely responses. Traditionally, regulatory affairs specialists bridge these gaps, providing trusted expertise. Could AI replace such specialists by interpreting requirements and tailoring solutions for specific situations?

How up to date is the information?

A key challenge for genAI is that its performance depends on the quality and recency of its training data. It struggles with poorly represented topics, recent changes or niche subjects like specific safety reporting requirements during clinical trials. Models trained on outdated data may generate plausible but incorrect information, especially for emerging or specific issues. While some genAI chat services access online resources or allow integration with vector databases for supplementary files like regulations, maintaining up-to-date information remains challenging. Regulatory requirements can change unpredictably, requiring manual effort to gather and ensure the latest documents are included. However, in most cases, evolution of the regulatory requirements is slow and the legislation can remain the same for decades with only minor amendments.

AI tools are evolving rapidly, with frequent updates introducing features like internet access and seamless integration with reference databases. This progress may soon render concerns about outdated training data irrelevant, making it easier to use genAI to maintain current and accurate regulatory information, such as safety reporting rules for clinical trials.

Reliability

Another challenge is the reliability of genAI models. For well-represented topics, they provide accurate and relevant information, but for niche or poorly represented subjects, they may generate incorrect or fabricated answers, even with prompt engineering to acknowledge gaps in knowledge. Detecting inaccuracies is difficult without prior knowledge or thorough fact-checking, especially since the responses are generally convincing and easily accessible.

The quality of AI-generated answers about regulatory requirements often depends on the country. For example, Sweden's well-structured, bilingual

regulatory website allows clearer answers compared to the UK, with post-Brexit regulatory uncertainty, or China, where evolving rules and language barriers limit accuracy. In countries with less developed PV systems or inaccessible legislation, AI is prone to 'hallucinate' or suggest contacting authorities for clarification.

Would using genAI for regulatory intelligence mean replacing one set of challenges – manual work of monitoring the regulatory news, contacting authorities for clarification and maintaining regulatory intelligence database – with another set of difficulties such as fact-checking and prompt engineering?

Situation in practice

Using AI for regulatory tasks is simple, with several free genAI tools offering commercial options for business use. When asked a high-level question like, 'What is the applicable legislation for reporting drug adverse events during clinical trials in Australia?' the tools provide similar answers, but each has unique characteristics. Often the situation is that one tool gives straightforward responses, another offers detailed answers with extra context and a third option is somewhere in the middle, but still not necessarily providing the 'perfect answer'. For example, one tool referenced the Therapeutic Goods Administration (TGA) Act 1997, related regulations, and guidelines from the National Health and Medical Research Council (NHMRC). It also included a disclaimer to check the latest updates. Another tool cited the same Act but dated it 1989, while a third referred to 1989 and the Therapeutic Goods Regulations 1990.

These discrepancies highlight the need to use multiple tools for accuracy in the current situation and if a reference database is not used. The second tool provides additional context, such as Clinical Trial Notification (CTN) and Clinical Trial Approval (CTA) schemes and ICH-GCP guidelines, which are not directly related to the question but useful for broader understanding.

While detailed responses can clarify unfamiliar requirements, they may confuse users seeking concise answers. Ultimately, legal requirements are only one part of understanding PV needs for clinical trials, and users should choose the tool that gives the more comprehensive responses, unless the goal is to get strict 'yes or no' answers, or to get the exact number of days for reporting suspected unexpected serious adverse reaction (SUSARs).

Time-saving

The legislative answers from the AI tools can vary significantly, but all the tools deliver responses within seconds, saving considerable time compared to traditional methods. Typically, the first step would be to check the organisation's regulatory intelligence database, which might have the information. If the data is assessed to be reliable and up-to-date, getting the answer could take just minutes. However, outdated or missing data often leads to further searches, possibly involving lengthy legislative documents requiring keyword searches or AI assistance. This can already take hours, even days in the most extreme cases.

If the regulatory database lacks information entirely, the next step is often search engines, however search results can vary based on multiple factors and may not directly answer the question. For instance, searching for Australia's drug adverse event reporting legislation might lead to TGA pages for sponsors

> *The legislative answers from the AI tools can vary significantly, but all the tools deliver responses within seconds, saving considerable time compared to traditional methods*

or unrelated guidelines. A more specific search like 'Australia Clinical Trials Legislation' might list the Therapeutic Goods Act 1989 and related regulations but still require additional validation to confirm relevance. This highlights the traditional search process' time demands and challenges in identifying accurate, trustworthy information compared to the efficiency of genAI.

Fact-checking

Fact-checking genAI responses takes time, similar to searching through regulatory databases or using search engines. Using multiple models can help gauge reliability, especially if responses are similar or contain identical parts, suggesting accuracy or shared data sources. However, identical errors could also indicate shared flawed training data. There is already a large amount of comparison information available between different tools and models, so it is easy to get information and pick up on differences with a few comparison questions by a subject matter expert who has information about the topic. Fact-checking just one question is time-consuming, especially when using multiple models with differing answers or responses packed with alleged facts.

What kind of errors can be expected?

The difference in the years of the Act and regulations are easy discrepancies to look at. For example, apparently the year 1997 in the Australian Therapeutic Goods Administration (TGA) Act 1997 might refer to an amendment to the Act from 1997. Based on a quick review, those 1997 amendments have nothing to do with adverse event reporting in clinical trials. The error could stem from the restructuring of the Australian regulatory organisation in 1997 and the history of the therapeutic goods regulation, and the document written about the history.[1]

A similar issue can be found with the Therapeutic Goods (Clinical Trials) Regulations 2018. Search engines do not reveal any legislative documents about clinical trials from the year 2018, however: the Australian clinical trial handbook had major updates in 2018; safety monitoring and reporting in clinical trials involving therapeutic goods had a major 2016 update that came into effect after 2018; and Good Clinical Practice guidelines and the NHMRC guideline for Risk-based Management and Monitoring of Clinical Trials Involving Therapeutic Goods were published in 2018.[2,3,4,5]

The examples highlight the difficulty in the ability to quickly confirm whether there is some truth in a response, even with a regulatory intelligence database and search engines to hand.

Is AI ready for regulatory intelligence?

Using AI tools will save both experts and non-experts time and resources. AI can already be used to map out the basic safety reporting requirements globally, identify the most relevant documents and resources to look at, and the correct authorities to contact. It is possible to use a vector database – a game changer if there's a collection of regulatory documents available, or it is possible to download and gather the relevant documents. With a suitable vector database, genAI can be used for those parts of the process it is most suited for: to sort through large amounts of complex information and guide users through the safety reporting process set-up. The answers are not perfect, but there are no perfect solutions. Using AI will reduce the reporting set-up time and the need for resources in one way or another, no matter what the situation is, with existing information and resources. By the time this text gets published the tools are already one step ahead, and perhaps this is even clearer.

References:

1. *McEwen J (2007), 'A History of Therapeutic Goods Regulation in Australia'*
2. *Visit: tga.gov.au/sites/default/files/australian-clinical-trial-handbook.pdf*
3. *Visit: nhmrc.gov.au/about-us/publications/safety-monitoring-and-reporting-clinical-trials-involving-therapeutic-goods*
4. *Visit: tga.gov.au/resources/publication/publications/ich-guideline-good-clinical-practice*
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Martti Ahtola is chief operating officer of **Tepsivo**, a pharmacist from Finland and a graduate of the University of Helsinki, Finland. Martti has extensive experience spanning the international pharmaceutical industry, as well as within pharmacist roles in one of Finland's largest community pharmacies and a major hospital pharmacy.

Navigating drug safety challenges in small pharma and biotech: practical solutions

Small pharmaceutical and biotech companies play a vital role in drug innovation and patient care. However, they face unique challenges in managing drug safety commitments due to limited resources and relatively low case volumes. What are these challenges, and their practical solutions?

Preeti Verma at Qinecsa

Small pharmaceutical and biotech companies have been identified as leading stakeholders in the development of new therapies, driving innovation and growth.[1] Emerging biopharma companies originated 67% of all new drugs in 2022, and they are also launching these drugs more often.[2] Small and emerging companies can bring an agile approach to development, particularly in rare disease and emerging therapy areas.[3] However, these companies also face unique challenges in managing drug safety commitments due to limited resources and relatively low case volumes.[4]

So, what are the key challenges facing small pharma and biotech companies, and what practical steps can they take to optimise pharmacovigilance (PV) operations in line with global requirements?

Challenge 1: Dealing with regulatory requirements

As biotech companies drive launches of new products, they are also expanding internationally.[5] This means they are having to navigate the complexities of both global and local regulatory environments. While this is a challenge for drug developers of any size, small pharma and biotech companies face specific hurdles – limited infrastructure and processes hinder their ability to proactively address varying regulatory requirements across different regions. An up-to-date pharmacovigilance system master file (PSMF) is essential for inspections but poses challenges without dedicated resources.

While emerging players often have exceptional scientific expertise, they can lack the regulatory experience needed to navigate the ambiguity of certain regulations, making it challenging to adopt consistent approaches across territories. Emerging companies rely heavily on external contract research organisations (CROs) and consultants to support global and local regulatory intelligence, however, there are concerns over the possibility for conflicting interpretations. Small biopharma companies also report lower CRO satisfaction across the board than large pharma companies.[1]

Challenge 2: Developing a PV framework

Establishing a PV framework is critical for small companies, but it often evolves from an inherited set of loosely defined processes as the need for consistency increases. It is helpful when there is a corporate culture of quality through leadership alignment and cross-functional collaboration, but gaining senior attention for PV can be challenging.[6]

The right framework depends on factors such as development phase, company strategy, expertise and resources. However, limited time means teams tend to be reactive rather than proactive. There is no standard of minimum requirements for standard operating procedures (SOPs), so determining the right level of governance through SOPs and work instructions (WIs) remains unclear, and the number and scope of SOPs varies widely among PV departments. Outsourced or in-house models are viable, but expertise is crucial. Vendor accountability – defined through quality agreements with measurable metrics and key performance indicators (KPIs) – is essential for oversight.

Challenge 3: Sourcing considerations

Resource models vary based on factors like company portfolio, development

stage, case volumes, budget and strategy. Small companies often opt for hybrid models, combining in-house staff, contractors, outsourcing partners and PV consultants.

Proactive resource management helps ease resource burdens during PV peaks and dips, and companies must find pragmatic solutions to remain compliant. Some specialty responsibilities, like case processing and aggregate reporting, have traditionally been outsourced, while the appetite for outsourcing of medical roles is growing.[7]

Specialty PV providers are preferred for their personalised attention, and some companies are exploring 'one-stop shop' options to reduce the time taken to train the vendor staff and potentially reduce overall cost. Regardless of the resourcing model, clear role definitions, governance and metrics are crucial.

Challenge 4: Fit-for-purpose database and technology needs

Technology usage among small pharma and biotech companies varies based on company history and portfolio. For some companies, Microsoft Excel spreadsheets are sufficient, while more established companies with a long-term strategy and larger portfolios often opt for dedicated safety database systems or use a provider for these services. This can become complicated when managing multiple CROs – each with different database systems – across different studies, and the inconsistencies created can place an unnecessary burden on teams.

Budget constraints also pose a significant challenge, making advanced database systems unattainable for many small companies. To address this, a simplified, cost-effective database solution is crucial. It should be accessible and scalable, allowing for efficient data collection, storage and analysis without extensive IT infrastructure.

Overall, technology solutions should streamline data integration from various CROs, standardising data collection, centralising processes and minimising manual efforts. Automation features can reduce costs per case processed, making it a strategic imperative for small companies to ensure drug safety while optimising budgets in their mission to bring innovative therapies to patients.

The solution: A PV departmental plan

Given the challenges described above, there are several practical steps companies can take to optimise PV operations in line with global regulatory requirements. Creating a roadmap for PV organisational development and management is crucial to overcome the challenges of limited time and resources, and a potential lack of processes and experience of the regulatory landscape.

A PV departmental plan should align PV needs with the overall corporate strategy, identify unnecessary activities and reduce costs. Regular reviews should ensure alignment with short- and long-term strategic goals and KPIs.

Practical approaches to optimise PV operations

Below are some of the practical steps small pharma and biotech companies can take to optimise PV operations (**Figure 1**):

Augment resources and regulatory expertise

Small pharma and biotech companies should leverage internal and external

Priority	Challenge	Requirement
Create a PV departmental plan	Insufficient time and resources Lack of process/experience	Strategic guidance for short- and long-term organisational needs
Understand regulatory requirements	Limited infrastructure Inexperienced staff	Global and local expertise to address regulatory requirements
Optimise sourcing	Managing vendor oversight	Combination of in- and outsourcing, with defined responsibilities, governance and metrics
Identify opportunities for technology	Multiple vendors Small volumes, limited budgets	Affordable technology to improve consistency and increase efficiencies
Develop a PV framework	Inherited framework Time contraints lead to reactivity, not proactivity	Appropriate governance through SOPs and guidance documents

Figure 1: Actionable steps to optimise PV in small pharma and biotech

resources to fill gaps in PV teams. Specialist PV providers can offer in-depth knowledge and reduce management burden. They can help respond to audit findings, plan product launches or acquisitions, aid expansion into new regions and develop strategic plans. PV specialists can offer both global and local regulatory expertise, ensuring regulatory requirements are met.

For example, websites collecting patient data and advertising products in different regions will be in the local language to promote reporting. However, local processes often include different quality assurance steps for translation and the review of translated materials – these must be met alongside existing global requirements. A PV specialist can help small pharma and biotech companies understand these complexities and consider how to standardise both local and global processes.

Optimise processes and sourcing

Managing vendor oversight can be a key challenge for emerging companies. Implementing an end-to-end PV management process, with defined responsibilities, governance and metrics, can help to overcome this challenge. A specialist provider can help to consolidate processes across studies, products and regions. This streamlining of processes improves vendor oversight, strengthens PV management and ensures high-quality outputs.

This is also an area where technology can be harnessed to reduce the complexity of multiple processes and sources. For example, a unified adverse event platform can use digital tools to collect data from multiple global sources and offer automatic translation, streamlining how data is processed, removing the need for complex process, and creating unified data outputs and workflows no matter the source.

Leverage technology

Multiple vendors, small case volumes and limited budgets can all be challenges when small pharma and biotech companies are trying to identify opportunities to use technology in their PV activities. However, there are cost-effective technology solutions that can improve consistency and increase efficiencies. Streamlining operations and partnering with specialist service providers can help integrate simple, fit-for-purpose technologies into PV processes. These may include integrated databases and global regulatory intelligence tools. For example, advanced regulatory intelligence tools, powered by artificial intelligence, can assess vast amounts of data, identify relevant regulations and provide real-time updates. This facilitates informed decision-making, ensures compliance and positions the organisation to capitalise on opportunities that may arise from regulatory changes.

Develop a PV framework

Inherited frameworks can lead to a lack of appropriate governance, while time restraints can lead to reactivity, not proactivity. A robust PV framework should include appropriate governance through SOPs and guidance documents. If small pharma and biotech companies are looking to purchase PV frameworks as a service, there are some key things they should consider. These include that engagements are led by PV experts who understand the requirements of regulators, client challenges and the evolving landscape.

Frameworks should also offer service flexibility and scale, and be cost-effective. It can also help to join insight networks where PV leaders in small pharma and biotech companies share their experiences, and discuss the specific challenges of delivering drug safety strategies and developing a robust PV framework in smaller organisations.

Conclusion

Although the specific needs of small pharma and biotech organisations may differ, there are many similarities in the overarching challenges they face. Specialist PV providers can assist in identifying and implementing a pragmatic and actionable departmental plan. This plan helps emerging companies navigate the complex regulatory landscape, establish robust PV frameworks, optimise resource allocation and streamline processes through appropriate technologies. By implementing these approaches, small pharma and biotech companies can continue to drive innovation while maintaining compliance and patient safety.

References:

1. *Visit: mckinsey.com/industries/life-sciences/our-insights/cros-and-biotech-companies-fine-tuning-the-partnership*
2. *Visit: iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/global-trends-in-r-and-d-2023*
3. *Visit: iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/emerging-biopharma-contribution-to-innovation*
4. *Visit: nejm.org/doi/full/10.1056/NEJMra1510070*
5. *Visit: mckinsey.com/industries/life-sciences/our-insights/building-a-global-biotech-taking-a-first-time-launch-into-international-markets*
6. *Visit: appliedclinicaltrialsonline.com/view/pharmacovigilance-company-wide-challenge*
7. *Visit: biopharmatrend.com/post/30-pharma-rd-outsourcing-is-on-the-rise/*

Dr **Preeti Verma**, senior director, solution architect leader at **Qinecsa**, is a qualified MD with over 15 years' experience in clinical practice and the pharmacovigilance industry. She is a highly experienced client partner and consensus builder, enabling her to develop strategic solutions that address client needs.

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Optimising clinical data management: the role of standardisation, AI and outsourcing

Ram Yeleswarapu at Indegene talks to *EPC* about the growing significance of the study data tabulation model (SDTM) in clinical data management (CDM) and its expanding role in the clinical trials landscape, highlighting the need to accelerate SDTM adoption and harness artificial intelligence, machine learning and automation to enhance data integrity, streamline regulatory submissions and drive greater efficiency across CDM operations

***EPC*: What are standard data tabulation models (SDTMs) and how are these being used in clinical data management (CDM)?**

Ram Yeleswarapu (RY): The SDTM is a standardised format developed by the Clinical Data Interchange Standards Consortium (CDISC). It is the accepted format for tabulation data submissions to the US Food and Drug Administration (FDA). The adoption of SDTM in clinical trials continues to grow as organisations increasingly recognise the benefits of standardised data formats in streamlining clinical trial processes. SDTM is a cornerstone of CDM as it enhances data review and validation, optimises regulatory submissions, accelerates approvals, and improves overall process efficiency in clinical trials, ultimately speeding up drug development. Some key benefits of SDTM in CDM include:

Data quality and integrity

SDTM provides a common language, structured framework, and clear guidelines for organising and formatting clinical trial data. By reducing errors and inconsistencies, it streamlines data management and simplifies data exchange and collaboration. As a result, researchers can focus on critical aspects of the trial while easily comparing and analysing data across studies. This enables more effective data analysis, leading to deeper insights, informed decision-making and accelerated drug development.

Regulatory compliance

Regulatory authorities like the FDA and Japan's Pharmaceutical and Medical Devices Agency (PMDA) require clinical trial data to be submitted in SDTM format as it enables them to quickly assess data safety and efficacy while minimising back-and-forth queries. Since SDTM-compliant data sets are accepted by global regulatory agencies, life sciences organisations can efficiently scale their submissions worldwide. Additionally, SDTM allows seamless integration with eCTD (electronic common technical document), which is essential for global regulatory submissions. Moreover, SDTM maintains a clear audit trail from raw data to submission-ready data sets, enhancing data integrity and traceability by making it easier to identify and resolve discrepancies.

Supports adoption of advanced analytics and artificial intelligence and machine learning (AI/ML)

The standardised format for creating and maintaining clinical trial data in SDTM makes it easier for AI/ML models to efficiently process and analyse large data sets. This enables AI-powered risk-based monitoring, anomaly detection and predictive modelling to leverage high-quality, structured data, leading to more accurate and reliable insights. Additionally, since SDTM provides a consistent data format across trials, AI models can seamlessly perform meta-analyses, cross-study comparisons and historical trend analyses, enhancing the ability to identify patterns, optimise trial designs and drive data-driven decision-making.

***EPC*: In what ways can streamlined CDM improve clinical trial processes?**

RY: Enhancements in SDTM and analysis data model (ADaM) creation, coupled with the automation of tables, listings and figures (TLF) generation, have significantly improved the efficiency and quality of clinical trial data management. From being key strategic focus areas to

prime candidates for outsourcing and generative AI (genAI) adoption, SDTM, ADaM and TLF automation have drawn the highest interest across the industry. Their pivotal role in optimising clinical trial operations underscores their impact on reducing time-to-market for life-saving treatments. Some key areas that significantly benefit from streamlining CDM include:

Data integrity

Streamlined systems utilise standardised electronic case report forms (eCRFs) and data dictionaries to minimise ambiguity and inconsistencies in data collection. Additionally, real-time data validation and edit checks help detect and correct errors early in the process, ensuring greater accuracy, completeness and reliability of clinical trial data.

Effective collaboration

A centralised system enables seamless data sharing and collaboration among researchers, sponsors and stakeholders. With real-time data access, researchers and monitors can make faster decisions and proactively address issues as they arise. Additionally, integrated communication tools and workflows streamline information exchange, ensuring quick and efficient collaboration among trial participants.

Regulatory submissions

High-quality, well-organised data accelerates regulatory submissions, enabling faster regulatory reviews and approvals for new drugs. Automated processes enhance data consistency, reducing errors and the need for rework. Additionally, streamlined workflows and efficient data management help shorten trial timelines, leading to faster study completion. Optimised processes further minimise delays, ensuring trials stay on schedule and within budget.

***EPC*: Is outsourcing a good option for companies looking to improve cost-effectiveness and efficiency?**

RY: Outsourcing clinical data management eliminates the need for large infrastructure investments, improves access to specialised expertise, strengthens data accuracy and quality, and increases scalability to handle fluctuating data volumes, which all result in faster study completion times. Companies are increasingly delegating tasks such as SDTM mapping, complex report generation and database setup to specialised providers, but one area that remains largely in-house is protocol development – this serves as the blueprint for the entire trial, defining its objectives, study design and overall strategy.

However, outsourcing is not a one-size-fits-all solution, and organisations must carefully assess their external collaborations. Companies must thoroughly vet potential partners, ensuring that data security, regulatory compliance and quality standards are rigorously maintained. Additionally, clear communication and oversight are essential to balancing external expertise with internal control, ensuring that critical trial functions remain aligned with corporate objectives and regulatory expectations.

***EPC*: How can genAI be integrated into current human-led processes?**

RY: The potential impact genAI on clinical trials is transformational when integrated efficiently with human-led processes. One of the key advantages

of genAI is the ability to build and utilise digital libraries. Clinical trial documents are highly structured and standardised, making them ideal candidates for automation. By leveraging natural language processing (NLP), users can create a digital library that provides an overview of each protocol section based on selected criteria. These libraries can also sort protocols by factors such as trial phase, design and other relevant factors, greatly improving the efficiency of protocol management.

Another benefit of genAI lies in the automation of eCRF creation. Users can automate the reading and understanding of protocols, generating forms based on existing digital libraries, thus improving the efficiency of creating electronic case report forms (eCRFs). GenAI also supports versioning capabilities and maintains audit trails of edits, which facilitates the amendment process. Additionally, eCRFs can be generated in table format, mirroring how they appear on electronic data capture (EDC) platforms, enhancing readability and analysis.

Screening and extracting relevant information from the protocol is a crucial task in clinical data management. With genAI, users can automate the creation of an entire study, including adaptable eCRFs for various EDC systems, by extracting relevant information from the protocol. By improving data extraction from historical protocols, digital libraries simplify protocol design by facilitating search and analysis. The ability to download data from these libraries provides quick access to sorted and analysed information, helping users identify and match protocol concepts to existing libraries, which ensures efficient document creation.

For data management, users can further streamline the documentation process by creating data management plan documents, swiftly editing check validation specifications, and generating test cases for documents that were automatically created, all while leveraging existing standards and libraries.

***EPC*: Will the next five years see a significant change in CDM?**

RY: Enhancing data quality, accelerating technology adoption, streamlining data management for global trials, optimising regulatory submissions and driving patient-centricity will remain the core priorities for life sciences companies over the next five years. These pillars will shape both short- and long-term investments, ensuring greater efficiency, compliance and innovation in clinical research. To maximise impact and accelerate adoption, several key trends are expected to emerge, transforming the way trials are conducted and data is managed:

AI, automation and real-world data (RWD)

AI-powered data cleaning, validation and standardisation will reduce manual effort and errors, while genAI will accelerate study setup through automated protocol authoring, eCRF design and SDTM transformations. AI-driven anomaly detection will proactively identify risks, minimising costly interventions. RWD integration from electronic health records (EHRs), wearables and patient-reported outcomes will provide a more holistic view of patient health, supported by improved interoperability for seamless data exchange. These advancements will fuel decentralised clinical trials (DCTs) and synthetic control arms, making trials more efficient, ethical and patient-centric.

Evolution of clinical data management roles

The evolving CDM landscape will demand new skills as AI, automation and RWD reshape clinical research. CDM roles will shift from manual processing to strategic data governance, quality assurance and compliance. AI-driven automation will streamline tasks, enabling focus on risk mitigation and regulatory adherence. Expertise in AI/ML for data validation, anomaly detection and predictive analytics will be essential, along with proficiency in genAI for protocol authoring and SDTM transformations. Managing RWD from EHRs, wearables and DCTs will require strong data integrity and regulatory expertise. Collaboration with data scientists, IT professionals and AI engineers will be key, leveraging low-code/no-code tools and agile methodologies to adapt to new technologies and trial designs.

Data integrity and compliance

AI-powered automation will ensure cleaner, standardised data, accelerating submission readiness and compliance with evolving global standards like SDTM and ADaM. Seamless RWD integration, facilitated by improved interoperability standards – such as CDISC and Health Level 7 Fast Healthcare Interoperability Resources (HL7 FHIR) – will further enrich submissions. Regulatory agencies may adopt AI for faster reviews, and predictive analytics will help sponsors proactively address queries. Ultimately, these advancements will accelerate approvals and deliver new treatments to patients faster.

Ram Yeleswarapu, senior vice president of Enterprise Clinical Solutions at **Indegene**, has more than 25 years of life sciences industry experience and expertise spanning clinical development and post-market support. He is responsible for establishing and growing the Indegene clinical business with a focus on clinical digital transformation initiatives across large pharma and emerging biotech. As an entrepreneur, he co-founded and led a full-service CRO's global growth. At Indegene, he leverages insights from real-world data, cutting-edge digital technologies, deep domain expertise and global delivery to orchestrate digital first propositions across data, content and core clinical development operations. Ram is an alumnus of Indian Institute of Technology, Madras, India.

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