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Two articles from the September 2020 issue of *Clinical Researcher* have been selected as the basis for a Home Study test that contains 20 questions. For your convenience, the selected articles and test questions are combined and posted in the form of this printable PDF at **https://www.acrpnet.org/professional-development/training/home-study/**, where the test may be purchased. *The test will be active until September 30, 2021.* This activity is anticipated to take two hours. **Answers must be submitted using the electronic answer form online (members $30; non-members $50).** Those who answer 80% or more of the questions correctly will receive an electronic statement of credit by e-mail within 24 hours. Those who do not pass can retake the test for no additional fee.

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CLINICAL RESEARCHER

SEPTEMBER 2020 HOME STUDY

Good Study Streamlining Practices

Article 1—**Clinical Study Reports 101: Tips and Tricks for the Novice**

LEARNING OBJECTIVE

After reading this article, the participant should be able to describe the purpose and structure of a clinical study report, and to follow the offered suggestions for using templates and efficient report development practices.

DISCLOSURE

Sheryl Stewart, MCR, CCRP: *Nothing to disclose*

1.   **What do "key messages" support in the context of a clinical study report?**
A.   Marketing language the study sponsor wishes principal investigators to highlight in their published findings.
B.   Study findings supportive of prespecified endpoints, clinical benefit, and any unique product features.
C.   Feedback from study participants regarding their relative satisfaction or dissatisfaction with the trial's results.
D.   Independent input from subject matter experts about the need for new products to address the health issue at hand.

2.   **Why is it important that a clinical study report follow a prespecified format?**
A.   So that participants can be properly credited for their experiences during a trial.
B.   So that principal investigators and study sites can be reimbursed by sponsors.
C.   So that any legal actions against product manufacturers can be researched.
D.   So that the study results are transparent and can support further scientific inquiry.

3.   **Which of the following sources offers a template for creating clinical study reports?**
A.   ICH GCP E6
B.   ClinicalTrials.gov
C.   CORE reference manual
D.   Transcelerate Biopharma

4.   Who would best be included as key stakeholders on the final review team for the clinical study report?

A.   Study volunteers, regulatory authority representatives, and sponsor's legal office.

B.   An independent IRB, doctors not involved in the study, and a sales representative.

C.   Relevant content experts, a biostatistician, and a data management team leader.

D.   An unbiased medical writer, the manufacturer of a similar product, and a CRC.

5.   How long on average did surveyed medical writers say it took to deliver the first draft of a clinical study report after receipt of the final tables, listings, and figures?

A.   Nearly 17 days.

B.   Nearly 26 days.

C.   Nearly 54 days.

D.   Nearly 83 days.

6.   The structure of headings or sections in a clinical study report is most similar to what other type of publication?

A.   A regulatory submissions document.

B.   A research manuscript.

C.   An IRB decision letter.

D.   A case report form.

7.   What aspect of "non-results" from a study is a matter of debate among medical writers where clinical study reports are concerned?

A.   Should results with very high levels of statistical significance be emphasized over those with very low ones?

B.   Should marketing plans and details of projected post-marketing surveillance by included in the report?

C.   Should many details from the study protocol be copied and pasted into the report or merely referred to?

D.   Should unverified observations from the study's principal investigator be included or documented separately?

8.   How can a biostatistician help the report's writer to better support its statements and conclusions?

A.   By creating or reformatting tables with relevant and clearly displayed data output.

B.   By rounding up the levels of significance for all findings the sponsor wants emphasized.

C.   By focusing on results from only the healthiest patients at the close of the clinical trial.

D.   By borrowing tables from successful studies of similar products now on the market.

9.   Which of the following is a resource for developing a patient safety narrative for a clinical study report?
A.   The Belmont Report
B.   The ICH E3 guideline
C.   The informed consent
D.   The ICH E6(R2) guideline

10.   Which of the following are suggested by the author to aid an efficient report review process?
1.   Encourage review team to backtrack to the non-results section for frequent revisions.
2.   Distribute review documents to reviewers one by one, making changes separately.
3.   Have reviewers review for content first rather than for formatting, grammar, and spelling.
4.   Task reviewer with working on the non-results section first and the results later.

A.   1 and 2 only
B.   1 and 4 only
C.   2 and 3 only
D.   3 and 4 only

Article 2—**Opinion: The Significance of Clinical Trial Transparency During the COVID-19 Pandemic**

LEARNING OBJECTIVE

After reading the article, the participant should be able to summarize historic issues surrounding the transparency of clinical trials results, and to relate these issues to current events associated with the responses of researchers and regulatory authorities to the COVID-19 pandemic.

DISCLOSURES

Dr. Kumari Priyanka, BDS, PGDCR; Tejas Thomas, MSc, PGDCR: *Nothing to disclose*

11.   The establishment of a database for clinical trials of experimental drugs was mandated by which FDA Act?
A.   The Federal Food, Drug, and Cosmetic Act of 1938
B.   The Food and Drug Administration Amendments Act of 2007
C.   The Food and Drug Administration Modernization Act of 1997
D.   The Food and Drug Administration Reauthorization Act of 2017

12.   How often are results and outcomes from clinical trials globally ever published?

A.   About 25% of the time.

B.   About 50% of the time.

C.   About 75% of the time.

D.   About 100% of the time.

13.   Key initiatives tied to the COVID-19 pandemic have been promoted by regulatory authorities on which of the following topics?

1.   Speeding clinical trials devoted to the disease.

2.   Disbanding redundant ethics committees.

3.   Encouraging sponsors on remote trial monitoring.

4.   Providing waivers for certain protocol deviations.

A.   1, 2, and 3 only

B.   1, 2, and 4 only

C.   1, 3, and 4 only

D.   2, 3, and 4 only

14.   What aspects of their virtual clinical trial capabilities do the authors mention as being improved upon by research teams during the pandemic?

A.   At-home care, remote monitoring, real-time data capture

B.   Budget forecasts, speed of billing, data-lock procedures

C.   Informed consent, randomization methods, patient follow-up

D.   Clinical study reports, peer review, publication of results

15.   How much time is commonly allowed between the completion of a clinical trial and posting of its results to public registries?

A.   Three months

B.   Six months

C.   Nine months

D.   Twelve months

16.   What do the authors say clinical data transparency can help study sponsors and researchers avoid?

A.   Legal challenges

B.   Duplication of effort

C.   Adverse events

D.   Intellectual property theft

17.   What do the authors say will build the general public's confidence in existing healthcare systems during the pandemic?

A.   An immediate lowering of healthcare costs.

B.   Study sponsors' pledges to deliver a vaccine quickly.

C.   Access to real-time study data.

D.   Personal testimonies from trial participants.

18.   What does 42 CFR Part 11 in the *Code of Federal Regulations* focus on?

A.   Registration and submission of trial results to ClinicalTrials.gov.

B.   Review of proposed clinical trials by institutional review boards.

C.   Use of electronic documentation in the conduct of clinical trials.

D.   Responsibility of the principal investigator for conduct of a trial.

19.   What do the authors cite as a possible drawback to the increased use of technology in clinical trials?

A.   Risk of data loss or contamination from power failures or security breaches.

B.   Rising costs of conducting trials must be passed on to the participants.

C.   Higher staff turnover rates and loss of time in training new staff on the technology.

D.   Inability to replace human interaction and personally deliver physical care.

20.   What do the authors cite as a difference between larger and smaller pharmaceutical companies in terms of meeting compliance obligations?

A.   Larger companies budget less for compliance-related activities.

B.   Smaller companies may need more external help with compliance.

C.   Larger companies can get away with disclosing less data from studies.

D.   Smaller companies are inspected far more often for compliance failures.

Clinical Study Reports 101: Tips and Tricks for the Novice

Sheryl Stewart, MCR, CCRP

The tenets of Good Clinical Practice (GCP), promulgated by the International Council for Harmonization (ICH), require that investigator-initiated trials (IITs), especially those involving an Investigational New Drug application to the U.S. Food and Drug Administration (FDA), have the principal investigator (PI), the institution, and the study team assume roles of both the sponsor (ICH GCP E6(R2), Section 5) and of the PI (ICH GCP E6(R2), Section 4).{1} If you are part of an IIT team, whether you are the investigator, a clinical research coordinator, or someone working in any of the many other important roles within the team, you may be tasked with authoring a clinical study report (CSR) at one time or another within the course of the study. At the very least, you may be asked to contribute to, or provide peer review of the document before it is submitted for its intended purpose.

The purpose of this review is to provide a framework for study team members, whether it's for a large team that includes regulatory and administrative support or for smaller teams with only one or two members, for writing and organizing the CSR.

Background

First, is important to understand the definition, requirements, and potential uses of a CSR. The report is a comprehensive look at all the data produced in a clinical study, presented in text, tables, and figure formats. It will often include discussions and conclusions that provide context to the findings regarding the drug, device, biological product, surgical method, counseling practice, or any other type of therapeutic product or practice under study and where it may contribute to an improvement on the state of the art for treating or preventing a particular health condition.

If a study has prespecified endpoints or parameters, the CSR will report the current outcomes and statistical parameters for these endpoints. Key messages will be referred to and highlighted throughout. Key messages are important study findings that support the prespecified endpoints, supply proof of the justification of clinical benefit, or differentiate the study product from others in the therapeutic space.

Most likely you already appreciate the ethical responsibility a clinical study team has to clinical study data transparency, which for that reason alone would make the production of some sort of CSR necessary. Indeed, the preparation and representation of study progress is prescribed in the aforementioned ICH GCP E6(R2) guideline,{1} which states that study sponsors should ensure that clinical trial reports are prepared and provided to regulatory agencies as they are required.

Further, the guideline recommends study sponsors to rely on a subsequent guideline on Structure and Content of Clinical Study Reports (ICH E3).{2} Lastly, adhering to this ethical responsibility and following GCP have become mandated both in the U.S. and in Europe, where study data are expected to be recorded on ClinicalTrials.gov and the EudraCT database, respectively, for the sake of transparency and in support of further scientific inquiry, thus making the organization and preparation of study data in a prespecified format necessary.{3,4}

There are a few different uses for a CSR, though primarily it is utilized either to summarize the data and outcomes at the end of the study, or for marketing authorization. Those two purposes are specifically outlined in ICH E3 and ICH E6.{1,2} However, a CSR may also be written for

third-party payer reimbursement purposes, providing details in support of clinical benefit. Because in most cases CSRs will ultimately have a regulatory reviewer, authoring a report that is consistent in formatting and content with what is expected will hopefully not only enable a smooth review, but also will facilitate proper data cleaning, presentation, and timeliness that make the document fit for purpose.

Templates

ICH E3 offers a CSR template to guide you in terms of providing the proper data and content in a specified order and format. This guideline can be found either on the ICH website or the FDA website.{2,5}

It is important to note that there are no requirements to follow the template precisely. Not every section is appropriate for every study, and because the overarching purpose of a CSR is to provide proper representation of the study data and any key messages you want to report, flexibility is allowed and encouraged in order to meet those important goals. However, for anyone new to the process of crafting a CSR, this template is a helpful starting point.

Transcelerate Biopharma, a nonprofit organization involved in researching means to increase efficiency and innovation in the pharmaceutical research sciences, also has interpreted the ICH template and has produced a useful tool to improve this reporting.{6} If the instruction and guidance in the ICH or Transcelerate templates do not meet your needs, or you have further questions as to how to properly represent the study data, the CORE reference manual (Clarity and Openness in Reporting E3-based) is another resource. It was produced in 2016 in response to regulatory changes for public disclosure of clinical study data, and can provide direction and interpretation of the ICH E3 template.{7}

For the novice author of a CSR, however, the ICH E3 template, coupled with the Transcelerate template, should provide a strong starting point for the project planning of the report, as well as the document formatting.

Sidebar: Tips and Tricks for Getting Started

- **Review the template sections and start collecting the necessary documents you'll need to review and refer to in the document, such as the protocol, investigator brochure, monitoring plan, and the statistical analysis plan.**

- **Create a Microsoft™ (MS) Word document using template headings and list levels to help organize your thoughts about the project, draft the initial outline of the document, and to plan next steps in collecting information.**

    - **If MS Word is not a strong skillset for you, consider taking a MS Word course. There are many helpful online courses to assist with formatting, captions, redlining, pagination, headers/footers, etc.**

- **Save document with an additional backup on the computer and in a cloud-based, secure file with limited access.**

Determining Stakeholders

Once you've reviewed the template and created a draft outline of the project, determine the key stakeholders with whom you'll need to partner to complete this project. Likely you will need input from your clinical study management team, teammates responsible for data entering and cleaning, a biostatistician, any teammate or organization member able to perform literature reviews, those staff qualified to compose patient or adverse event narratives, and those team members who can help determine key messaging in this report. Lastly you will want to determine the group of key stakeholders who will be your final review team for the document—those who will help you finalize the document prior to submission.

Sidebar: Tips and Tricks for Stakeholder and Project Management

- **Identify the stakeholders for each section of the template per section (statistician, data management team, content experts).**

- **Collect and review resources, including any previous study publications, presentations, or reporting for any key messaging about the study drug, similar drugs, or the disease under study.**

- **Consider drafting a project charter or scope document to ensure commitment from all required teammates on scope, deliverables, and timelines.**

Determining Timelines

Once you have determined your key stakeholders, you will want to determine timelines to ensure steady progress continues to be made on the document. If you've chosen to utilize a scope document, you'll want to include these timelines in it, so the entire team is aware of the project process, the timing requirements, and each gating item (key gating items are summarized in Figure 1).

Figure 1: Preparing, Writing, and Review of the Clinical Study Report—Key Gating Items

Preparation of Data	Writing and Document Review
o Data cleaning and query resolution	o Write non-results sections
o Plan tables, listings, and figures (TLFs)	o Perform literature review
o TLF creation and revisions	o Write results sections
o TLF editing	o Cross team/stakeholder review
o Data-lock process	o Incorporation of revisions
o Final TLF preparation	o Finalize report for submission

Time management is paramount for clinical trial submissions to regulatory authorities. Attendees at medical writing conferences over the course of a five-year period (2008 to 2013, n=78) were surveyed to determine to how long each step of the CSR process can typically require.{8}

To complete a "moderately complex" CSR for a Phase III study with 200 to 400 participants, the surveyed medical writers responded with a mean answer of 16.9 days from the receipt of the final tables, listings, and figures (TLFs) to delivery of the first draft of the CSR. They estimated a mean of 25.7 days from the first draft to the final draft routed for review. The time from database lock to completion was reported to be on average 83 days.

While there was a wide range for the timelines reported, these data provide the novice CSR author a basic reference point for how long the individual processes can expect to take with experienced medical writers. Fortunately, while TLFs are being crafted, multiple other "Writing and Document Review" tasks from Table 1 can be performed simultaneously.

At Last…the Writing!

Typically, the flow of your CSR will progress under six primary headings or sections, not unlike those used in a research manuscript. On the front end, even before the background and introduction, the document will include a title page, synopsis, table of contents, list of abbreviations, ethics statements, and details on the study's administrative structure. The primary sections to come after that are highlighted in Figure 2 and summarized in turn below.

Figure 2: Primary Sections

Background, Introduction	Non-Results Section	Results Section	Discussion	Conclusion	Executive Summary

Background and Introduction

When available, utilize any state-of-the-art analysis of the product/therapy from the protocol for your CSR introduction. If not available, you can briefly summarize the study design, objectives, and population and then you'll need to craft a novel but brief state-of-the-art analysis based on literature review.

Be sure to align with the key messaging of your study and the indications of your study drug, device, or other type of therapeutic product or method. Utilize good literature review practices, such as choosing peer-reviewed publications, editorials from key opinion leaders in the therapeutic area, and studies with large or randomized cohorts, for support. This section will likely be no longer than one page.

Non-Results Section

Whether to cut and paste the procedures and assessments, primary and secondary endpoints, parameters or hypotheses, planned statistical analyses, monitoring plans, adverse event definitions, and assessment rules directly from the protocol or to simply refer to the protocol and the other study documents in an appendix is a topic of debate amongst medical writers of CSRs. Keep in mind that the CSR should be able to stand alone as a document, and thus while it is important to keep the document concise, it must be comprehensive enough for the reader to understand the study design, objectives, endpoints, processes, and intended analyses without having to refer constantly to the protocol. Regardless, in any summary of the study design, processes, and endpoints, be sure to align with any previously utilized language for consistency across study documents.

Results Section

Using the template and your tables as your structure, summarize the data and pull out any signals and trends, aligning with key messaging where possible. Start with patient disposition and demographics as per the template. Note any protocol deviations that may or may not have impacted patient safety or the evaluation of the outcomes.

Assess and evaluate the study outcome results against primary endpoints and secondary endpoints before discussing any additional secondary outcomes. You should not simply restate the data in the tables; however, refer to specifics in the tables when summarizing.

If you find that you cannot make a statement or conclusion given the TLFs you have, or you are consistently having to perform your own math to support your statements, consider asking your biostatistician to create the tables that will represent the data in a way that will better support your statement. For instance, it is acceptable to state that "most" of the patients responded to the study drug if more than 50% did so; however, if you are having to consistently add up percentages in a table to be able to state, for example, that 77% of the patients responded in a certain way and 33% responded in another, then you should have the biostatistician reformat the data output so it represents the percentages you want to report.

Patient narratives are an important source of context for the reader of the CSR. Depending on your study, you may need to collaborate with either your teammates responsible for assessment of adverse events or the study database administrator to help generate patient and/or event narratives for the CSR. If tasked with compiling or editing patient narratives yourself, the ICH E3 guideline prescribes the necessary components of a comprehensive patient safety narrative (Section 12).{2}

Narrative writing advice has also been previously published and would be a helpful source of direction for the novice narrative writer.{9,10} Narratives are suggested for every patient who experienced a safety endpoint event or death during the course of the study. Tie in patient narratives where appropriate when discussing safety events or refer to the patient narrative section when highlighting a particular patient's data.

Discussions and Conclusions

Discussion and conclusion sections can either be placed after each section or placed at the end of the document. They should not simply restate the previous table summaries, but provide context and align the results with key messaging. Use an evidence-based approach, including literature references to provide more context as to the nature of the study outcomes with respect to the state of the art for the product/therapy, outcomes from alternate approaches, or further justification of clinical benefit with regard to potential disease progression. The conclusion section at the end of the document is often in bulleted format—not only for ease of the reader, but also to clearly highlight the key messaging and important outcomes you wish to impart.

Executive Summary

The executive summary, while placed at the front of the document prior to the introduction, is often easiest to construct last, as an overall summary of the entire document. The key elements of this summary should briefly recap the study design and objectives. Most likely only the primary and secondary endpoints should be included, unless additional outcomes proved compelling and important within the course of the study. Refer to any important literature comparisons as they relate to any conclusions made about the success or outcomes of the trials. Conclude the executive summary in a similar fashion to the overall study conclusion.

Sidebar: Tips and Tricks for the CSR Writing Process

- **Create all headings and/or multilevel lists before you start writing.**
- **Request a "soft" database extract and a pre-run of the TLFs.**
  - **Often this first quick look at the TLFs will reveal any discrepancies in data entry or queries that can then be resolved before the TLFs undergo the larger review process.**
- **Begin a rough draft of the results sections from these early tables. Though some changes in the data will likely occur, most data will stay the same and key messages will remain valid, thus you can get a head start on the document while waiting for final tables.**
- **Insert TLFs without captions until you are sure you will not be updating or switching out tables.**
- **Wait until the end of the review process to:**
  - **Create any hyperlinks**
  - **Finalize your table of contents and table of figures**
  - **Insert your bibliography**
  - **Insert your listings and appendices**

Review Process

The review process can either facilitate a better document or it can slow down the entire process. The purpose of a cross functional review of a CSR is to confirm accurate key study messaging and data; allow medical review of the patient narratives, outcomes, and conclusionary statements; review the logical flow of ideas; and ensure that the CSR language is consistent across any other study document (i.e., the protocol, statistical analysis plan, etc.).

Sidebar: Tips and Tricks for an Efficient Review Process

- **Request reviewers to initially review for content, as errors in formatting, grammar, and spelling are fine to notate, but are much less important (and likely will be caught later) than providing content review.**
- **Start the review team working on the non-results section first and finalize it before sending them the results section.**
- **Discourage the review team from backtracking to the non-results section, as it should be considered finalized unless something major changes.**
- **Maintain the documents for review in a secured, shared, cloud-based content management application, such as Box.com, so reviewers can review and provide revisions in real time with each other and avoid version confusion.**

Conclusion

CSRs are required by regulatory authorities to report and summarize the outcomes of a clinical study. Pre-project stakeholder determination and timeline planning can help with project management. Templates contained with the ICH E3 guideline can help organize the project as well as help create and finalize a document that is fit for purpose and meets the content expectations of the regulatory reviewer.

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Sheryl Stewart, MCR, CCRP, (ssstewart70@aol.com) is a Medical Writer working in the medical device industry in southern California.

Opinion: The Significance of Clinical Trial Transparency During the COVID-19 Pandemic

Dr. Kumari Priyanka, BDS, PGDCR; Tejas Thomas, MSc, PGDCR

Clinical trials lay the foundation for biomedical research to generate robust evidence on the safety and effectiveness of proposed treatments and/or preventive interventions for eventual use in routine clinical care. Clinical trials directly engage volunteer participants who trust the investigators to conduct their studies based on the best available scientific knowledge and ethical practices.

In this paper, we consider how data sharing and transparency are important practices of research for the drug and device development industry to follow in order to maintain the trust and confidence of the public. We also relate the history of how these practices have been developed in the U.S. to their current importance in the midst of the COVID-19 pandemic.

Background

Issues surrounding clinical trial data transparency came to light with the first requirements for trial registration from the U.S. Food and Drug Administration (FDA) Modernization Act of 1997. This act mandated the establishment of a database for clinical trials of experimental drugs being used to treat life-threatening conditions.

In 2000, ClinicalTrials.gov went live to allow public access to clinical trial data. Over the last decade, several other milestones were implemented worldwide for maintaining clinical trial

transparency and compliance.{1,2} The World Health Organization (WHO) and the Declaration of Helsinki have also stressed the importance of clinical trial transparency.{3,4}

Transparency in clinical trials begins with registering a trial on a public database and continues with access to patient-level data for subsequent analyses and publication of the trial results, irrespective of the outcome.{5} Several large pharmaceutical companies have initiated transparency methods to ensure their research practices are compliant with a variety of laws, regulations, and guidelines.{6,7} Many of them have also collaborated with external medical and scientific researchers to advance their clinical research and thereby enhance public health.

Despite widespread efforts by regulators and sponsors to ensure compliance and clinical data transparency for all clinical trials conducted globally, results and outcomes from only about half of all trials are ever published.{8} Overall, lack of transparency leads to serious implications for patients, healthcare professionals, and health systems.

The New Challenge

On January 30, 2020, the WHO declared the novel acute respiratory infection caused by the SARS-CoV-2 virus, termed Coronavirus Disease-2019 (COVID-19), as a Public Health Emergency of International Concern.{9} As of July 20, 2020, more than 14 million people worldwide are confirmed to be infected, leading to increasing fatality rates.{10}

Numerous pharmaceutical companies and research institutions are conducting clinical trials to develop new or repurposed medicines and other therapies to combat COVID-19. More articles are published each day on potential treatments or diagnostics for this pandemic, but evidence on the efficacy and safety parameters of interventions seems to have been overpassed along the way. Thereby, regulatory authorities and medical professionals are facing difficulty in decision-making on the best treatment options.

In the past, regulators and sponsors have had differences of opinions in publishing their confidential and proprietary information and certain patient-level data. This may be the time to pause and re-analyze whether clinical trial transparency would help the world overcome this pandemic with the best treatment option available.

There are many controversies and diverse questions related to the importance of transparency that are yet to be answered. It is always debatable whether the industry is following the right track by disclosing or withholding certain clinical trial data.

The Impact of COVID-19 on the Clinical Research Industry

The outbreak of COVID-19 has created a global health crisis and has deeply impacted almost everyone's daily lives. Although COVID-19 has harmed the global economy, with many major businesses experiencing huge losses and countless small ones being forced to close, everyone is looking toward the clinical research industry as offering a ray of hope against a worst-case scenario for this outbreak.

Despite the many trials being conducted on COVID-19, due to a perceived lack of high-quality published trial data, some regulatory authorities and healthcare systems are expressing indecisiveness about the status quo of this worldwide effort. This could lead to a delay in availability of effective treatments, impacting public health and the global economy.

Across the industry, regulatory authorities, trial sponsors, healthcare professionals, and patients are facing serious challenges in fighting this pandemic (see Figure 1 for a summary). In the following sections of this paper, we will take a closer look at each of these sectors.

Figure 1: Challenges Across Multiple Sectors from COVID-19
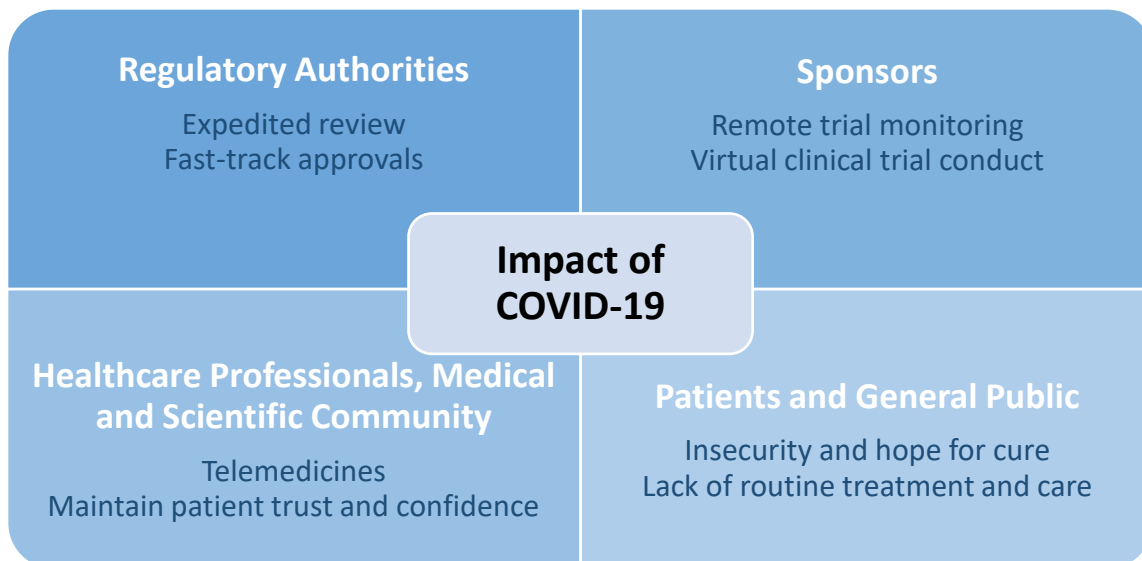
Regulatory Authorities

A number of regulatory authorities (the FDA, European Medicines Agency, Medicines and Healthcare products Regulatory Agency, Health Products Regulatory Authority, and others) have released several guidance documents and dedicated the work of various ethics committees to expediting regulatory and ethical review processes to maintain high standards during this pandemic.{11–15} Most of the regulators have also implemented a fast-track approval system considering human safety as priority.

For instance, the European Commission published Recommendation (European Union) 2020/403, considering the shortage of necessities during the outbreak to supply non-CE marked devices in the interest of protection of health, as long as they comply with necessary specifications. However, documentation is the key that would be required for any future inspection purposes.{16}

Some of the key initiatives from regulators deal with such concerns as those listed below{[17]–20}:

- Prioritize, expedite review, and provide fast-track approval for clinical trials devoted to COVID-19
- Engage ethics committees to ensure patient safety concerns
- Support sponsors to amend any existing trial protocols or suspend trials, if possible
- Encourage sponsors on matters related to remote trial monitoring and providing investigational medicinal products to trial participants
- Report serious adverse events and submit annual safety reports and end-of-trial notifications
- Provide waivers as necessary in case of protocol deviations and serious breaches

Regulatory bodies are working closely with innovators/sponsors to foster the development of safe and effective medical countermeasures against the COVID-19 pandemic. They are under extreme pressure to ensure that the best treatment options are available at the earliest to protect public health and safeguard the public from the use of fraudulent products claiming to prevent, treat, or diagnose COVID-19.

Despite several initiatives from regulatory authorities, many ongoing clinical trials are unregistered, and their data continue to be unavailable to both the general public and the scientific community. In addition, some trial data are not even being shared with regulators appropriately, leaving them handicapped in terms of enforcing standard drug approval processes and, in turn, in protecting the public.

Corporate Sponsors and Other Researchers

Currently, there are no FDA-approved medical products for the prevention or treatment of COVID-19, and pharmaceutical company, academic, and government researchers are striving to find a potential drug candidate in record time. Globally, more than a hundred potential drug and vaccine candidates have been proposed to the WHO, but only a few are in the clinical evaluation stage.{21,22}

Certainly, technology and digital information could be the key to such rapid changes in the industry. Although there is room for flexibility, pragmatism, and speed, it is also important for sponsors and other researchers to adhere to well-established standards for quality, efficacy, and safety to promote the wellbeing of the public.

A whole new era of conducting virtual clinical trials is under way, and a great deal of responsibility rests on the shoulders of research teams to maintain patient safety and data integrity. Companies and institutions are evolving their capabilities and improving their methods for real-time data capture; moreover, many have deployed methods such as at-home care and remote monitoring to minimize the impact of pandemic conditions on ongoing clinical trials.{23–26}

FDA guidance issued in the context of COVID-19 also states that it is important to report any changes implemented during trials in the wake of the pandemic.{27} Henceforth, it is crucial for sponsors and other researchers to stay abreast of the concerns and guidelines of their local or regional regulatory agencies, and to document every action taken in their trials. Meanwhile, they should engage with sites, healthcare professionals, and patients to disclose study data appropriately.

Healthcare Professionals and the Medical and Scientific Community

During this COVID-19 outbreak, healthcare professionals and research scientists are in urgent search of a remedy to provide quality treatment to their patients and improve their quality of life. At the same time, they must ensure that preventive medicine options are in place to protect the general public's safety.

There are several challenges that these professionals and the principal investigators of studies are currently encountering in terms of maintaining patients' trust while prioritizing safety:

- Out-of-home travel restrictions due to government-enforced lockdowns in several countries
- Steps being taken to implement telemedicine and telehealth systems
- The need for frequent communication with patients{28–30}

It is therefore important to maintain transparency at all stages of research, as this helps healthcare professionals to choose the right medicine and provide high-quality care and treatment to their patients.

Patients and the General Public

The COVID-19 outbreak has left the general public clueless about many factors affecting its health and safety in pandemic conditions. Incomplete information about clinical trials and available treatment options are causing anxiety and confusion.

For example, many patients with chronic diseases who are trial subjects for non-COVID-19 conditions (and their caretakers) face dilemmas about their future care and treatment, as many ongoing clinical trials are being suspended or halted for safety concerns.{31,32} Patients may be required to self-isolate, causing more difficulties for trial investigators seeking to maintain medical oversight.

Meanwhile, we are seeing heightened urgency concerning who will have access and when to the results of COVID-19 trials as many companies and other research institutions race to cure this pandemic, which we will look at more closely in the next section. Any lack of clinical data

transparency can cause patients to lose trust in their physicians and become extremely demotivated and insecure, leading to psychological and behavioral changes.

Importance of Clinical Trial Transparency During the COVID-19 Pandemic

In the midst of these difficult pandemic conditions, research scientists and pharmaceutical companies are prompted to dive deep to find a solution to the novel viral infection and patients are demanding clinical trial information. Most regulatory guidelines allow 12 months to elapse between study completion and posting of the trial results to public registries. Although some regulations do not mandate clinical trial disclosure for early-phase trials, it would be worthwhile publishing important trial observations in the public domain sooner rather than later, especially in situations such as the pandemic.{33}

Currently, WHO data present several potential COVID-19 drugs and vaccines that are being tested in various ongoing clinical trials.{34,35} Several sponsors have claimed their potential drug or vaccine candidates to be in advanced stages of clinical trials, but have revealed only incomplete data and preliminary trial observations, leaving the community in a dilemma about the safety and efficacy of the medicine.{36–38} In the urgency of the situation, it is of utmost importance for sponsors to comply with regulations while also considering patient safety in disclosing essential critical trial data.

In light of the ongoing health crisis, let's consider the stakeholders and a few best practices each should follow that could benefit the clinical research industry and ultimately the whole world:

- **Regulatory authorities:** Availability and disclosure of full clinical trial data in a timely manner will help everyone to make the right decisions during the drug approval process. This will ensure that the best treatment option will be available as early as possible to overcome this global health crisis.
- **Corporate sponsors and other researchers:** Clinical data transparency could avoid duplication of research efforts and unnecessary financial losses while encouraging improvement in the design, conduct, and oversight of clinical trials, thereby providing appropriate diagnosis, treatment, and prevention of COVID-19.

- **Healthcare professionals and others in the medical community:** Appropriate disclosure of clinical trial data will help the medical community to make the right decisions in a timely manner by choosing the most effective therapies for the treatment and prevention of COVID-19. It could further help in explaining available experimental drugs or vaccines to COVID-19 patients. This will further enhance patients' confidence and trust in the entire healthcare system.
- **General public, including patients:** Access to real-time data for members of the general public will build confidence in existing healthcare systems and in the security of their own health. This could motivate more people to take more effective steps toward "flattening the curve" of this outbreak and others to come.

Guidance for Transparency: Trial Registration, Data Disclosure, and Reporting Practices

As per the U.S. Final Rule (effective from January 18, 2017) for Clinical Trials Registration and Results Information Submission (42 CFR Part 11 in the *Code of Federal Regulations*) and Section 801 of the FDA Amendments Act (FDAAA 801) implemented in 2007, it is important for sponsors to register clinical trials on drugs, biological, and device products and submit their results to the ClinicalTrials.gov registry.{39,40} Similarly, the Clinical Trial Regulation (EU) No 536/2014 in the European Union implemented a portal to register EU-based trials on a database to ensure transparency in their conduct.{41}

According to the WHO best practices, results from every clinical trial should be uploaded in the respective local trial registry no later than 12 months after primary or study completion date.{3} The regulations are enforced for the benefit of the sponsors, regulatory authorities, healthcare professionals, and patients. This could further enhance public confidence in the clinical trial process, new medicines, and regulatory systems. It could also help healthcare professionals in deciding on treatment options.

These measures are fostered to accelerate further research by accumulating knowledge and technical ability. Therefore, duplication of trials, safety or efficacy failures, redundant data, and workforce investment in research may be avoided, and this could stimulate growth and

development of commercial and academic research centers, medical facilities, and research expertise.

Meanwhile, FDA guidance first released in March 2020 and revised in July 2020 provides insights to sponsors and investigators on maintaining compliance with the tenets of Good Clinical Practice and minimizing risks to trial integrity in these pandemic conditions.{20}

Navigating a New Regulatory Landscape

The clinical research industry is adapting to rapid, pandemic-driven changes that have affected activities at all levels, starting from the regulatory authorities, sponsors, contract research organizations, and trial sites and reaching all the way to trial participants. There is more room for new technologies and start-up innovators to address the increasing demands of managing clinical trial data sources and remotely connecting with patients, to name just a few challenges.

Clinical trials are mostly patient-centered, and before long, the industry will be highly efficient in conducting clinical trials virtually with connected devices, medications delivered at home, and timely long-distance communication, therefore achieving accurate data capture and transparency and, at the same time, gaining and improving patient trust. Overall, the potential downside of increasing dependence on technology would be that it cannot replace human interaction and deliver the physical care provided by doctors in person.

Conclusion

COVID-19 is a severe and ongoing novel pandemic that has caused immense social and economic regression across the globe. Pharmaceutical companies worldwide are under public and competitive pressure to explore innovations in drug development and revamp their reputation.

During this time of increasing need for self-care and prevention, humankind is becoming even more dependent on technology and sponsors are implementing decentralized and stay-at-home clinical trials. Thereby, use of remote trial technologies could further overcome ethical and regulatory barriers to enhance patient safety and trial data integrity compared to traditional trial

designs. However, lack of human connection in such conditions may have drawbacks that should be taken into consideration.

Pandemic situations definitely demand transparency in clinical trials. Lack of full, conclusive scientific evidence from the various ongoing COVID-19 trials could lead to ignorance of an effective treatment to curb the spread of the disease. Although there are various regulations and policies in place, sponsors and companies are still striving to understand the public scope of in-depth disclosure of trial plans and outcomes.

It is important for sponsor companies and others conducting studies to maintain high standards in research and to meet all regulatory and local requirements. Generally, bigger pharmaceutical companies are able to meet their compliance obligations with a dedicated team and all the requisite tools at hand, while smaller companies may fall short in disclosing data and/or meeting other expectations appropriately without significant external assistance. Nevertheless, smaller companies are gradually paving their way to gaining the necessary skills and resources.

Compliance also adds value to the credibility and reputation of these companies and researchers. Therefore, it is critical to report any observations and publish trial results appropriately to avoid any gaps in knowledge and deliver effective treatments for this global disaster. The future of clinical trials could be overwhelmingly positive if we consolidate the advances being made now and proceed toward greater data transparency.

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Dr. Kumari Priyanka, BDS, PGDCR, (kumari.priyanka@indegene.com) is Manager in Regulatory Solutions department at Indegene Pvt Ltd in Bangalore, India and lead author of this article. She leads Regulatory practice in Indegene with extensive experience in Regulatory Intelligence, Strategic Consultation, Regulatory Submission and Clinical Trial Disclosure services across geographies and product lines.

Tejas Thomas, MSc, PGDCR, (tejas.thomas@indegene.com) is a Senior Regulatory Associate with Indegene Pvt Ltd, Bangalore, India. She is proficient in disclosure planning, tracking workflow related to trial transparency, and ensuring timely and accurate disclosure of clinical data as required by international law/guidance policy.