A Guide to Maintaining Clinical Trial Integrity in Catholic Health Care

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Those who don't do clinical research in Catholic health care settings may hope a program can grow "despite" its faith-based setting. Those of us who do this work in faith-based organizations realize these settings can be truly beneficial and structured to allow ethical and significant research programs to grow and thrive. At the CHRISTUS Institute for Innovation and Advanced Clinical Care, we infuse Catholic identity, Church teaching and mission — along with federal regulations and clinical research operations — into all of the institute's operational processes. The impact of this integration goes far beyond regulatory compliance for those involved in CHRISTUS Health's nearly 700 active clinical studies and more than 10,000 participants.

This standardization and incorporation of mission and ethics into the program's operations fuels the growth of CHRISTUS Health's clinical research programs. The health care system has developed informational resources and makes subject matter experts available to sponsors and scientific investigators to ensure research protocols and practices are appropriate to a faith-based setting. In fact, the average time from a new study's submission to the research central office until its launch at CHRISTUS Health is less than 75 days, compared to the industry's average of 90 days. We believe that our approach would be useful to others in Catholic health care, and to mission- and values-driven secular health care. Our hope is that others find insights from this model and replicate its components for their clinical research programs. Throughout the COVID-19 pandemic, those working in health care so often saw how clinical research advances life-saving treatments.

ABOUT THE INSTITUTE

Driven by the mission to extend the healing ministry of Jesus throughout its work, CHRISTUS Health offers coordinated and organized advanced clinical care and research for patients through its Institute for Innovation and Advanced Clinical Care. The institute is an integrated, multidisciplinary enterprise that provides strategic planning, expert consultation and catalyst support services for clinical research growth across the health system. It includes a system office that delivers essential services to conduct and support research, such as an institutional review board, compliance, research education,

finance and reporting, and pre- and post-award services for clinical research studies.

The participating ministries of CHRISTUS Institute for Innovation and Advanced Clinical Care are organized across the United States into five geographic regions: 1) Louisiana, 2) Southeast Texas, 3) South Texas, 4) Northeast Texas and 5) New Mexico. Each of these five research hubs is led by a research leader — who reports to one system research executive. This forms a hub-and-spoke organizational chart, where one major location serves as a central point for coordinating clinical research initiatives to and from other locations. Some of the major clinical research focus areas at CHRISTUS Health include oncology, cardiology, electrophysiology, pediatrics, neurology, COVID-19 and wound care.

ENSURING ERD INTEGRATION INTO CLINICAL RESEARCH

To affirm integration of the *Ethical and Religious Directives for Catholic Health Care Services* (ERDs) into relevant clinical research matters, the institute created and deployed a multi-integrated operating model. (See graphic on page 21). To ensure its success, relevant stakeholders were involved during each step. Internally, we refer to these stages through the acronym "FIRE CONTROL."

1. Feasibility Review

The first step in the process is the feasibility review, which is an internal review that involves research leaders, local mission leaders, senior leadership team members and other department leaders who use a feasibility analysis tool to assess together if the clinical research project is an operational fit for the ministry. The tool captures and documents responses to a series of questions in six major categories: mission alignment; patient population and recruitment; study design; local operations and support; contract and research coverage analysis; and budget.

The review's mission alignment section allows each evaluator an early opportunity to assess whether the clinical research project abides by the ERDs by reviewing elements that may conflict with Catholic teaching. Examples include sterilization, some types of gene therapy or genetic modification of human tissue, or use and/or distribution of contraception. This section also checks if the project plans to exclude research participants with limited English proficiency, unless clinically justifiable. If any aspects of research are identified as not aligning with the ERDs or Catholic teaching, identity or mission during feasibility assessment, it is either immediately rejected or returned for appropriate revisions. For instance, a sponsor requested CHRISTUS Health participation in a clinical trial for a medicine used to treat infertility. The research protocol required sites to keep and distribute contraceptives. CHRISTUS' clinical research institute deemed the study 'not feasible' after failing to find an appropriate alternative.

2. Informed Consent Form Review

For some medium- to high-risk clinical research projects, a pregnancy prevention clause may be necessary within the research informed consent form for those initiatives that require disclosure per policies set forth by the Office for Human Research Protections and/or the Food and Drug Administration (FDA).[1, 2] A research informed consent form is typically a description of clinical investigation, risks, benefits, participation fees, confidentiality, compensation and/or medical treatment for injury, voluntary participation and more. CHRISTUS Health's institutional review board requires that the standard language for pregnancy prevention be used in all applicable research-informed consents, in addition to all parental permission and participant agreement forms for subjects aged 13-17 years.

As a Catholic ministry, CHRISTUS Health provides standard clauses that avoid unethical actions within CHRISTUS Health (moral agency) or associated with CHRISTUS Health (moral cooperation) by emphasizing appropriate birth regulation means and not specifying certain pregnancy prevention means via inclusion of approved template language. In 2016, we developed a series of seven standard clauses — ordered from most preferred to least preferred — to allow flexibility for our clinical research sponsors and investigators. After review in 2021, our mission and ethics leaders developed two standard clauses in English and Spanish in lieu of the prior seven standard clauses to capture pregnancy precautions during and after study. If any adaptations of the standard clause result, they require reapproval by mission and ethics leaders before the clinical

research project can be submitted for ethical and board review.

3. Institutional Review Board/Ethics Review

Under FDA and Department of Health & Human Services regulations, all human subject research must be reviewed by an institutional review board prior to its start. Furthermore, the board should consist of reviewers with both scientific and non-scientific backgrounds, and not affiliated with the institution to ensure a balanced scientific and ethical review that protects participants' rights, integrity and welfare.[3,4]

CHRISTUS Health's institutional review board consists of additional reviewers, such as ethicists and mission leaders, to ensure alignment with Catholic teaching, the ERDs and protection of the most vulnerable populations (such as children, elderly, those who are poor and racial minorities). Additionally, to better serve our communities, CHRISTUS Health has established several academic partnerships — both Catholic and non-Catholic. By combining our strengths on research, these academic partnerships enable our communities more access to research participation without compromising our identity or integrity.

4. Contract Review

As part of launching a clinical research project, CHRISTUS Health enters into contractual agreements with all legal parties involved. These agreements allow for the legal exchange of clinical research funding, materials and data between the two parties, and memorializes the rights and obligations of each party. In each clinical research agreement at CHRISTUS Health, the parties are required to acknowledge that 1) CHRISTUS Health is a faith-based organization, 2) all operations at CHRISTUS Health are in accordance with the ERDs, as interpreted by a local bishop, and 3) CHRISTUS Health's operations — in accordance with the ERDs — and its principles and beliefs of the Roman Catholic Church are a matter of conscience. If CHRISTUS Health were to determine that any aspect of an arrangement would violate the ERDs, the options are to work together in good faith to resolve or terminate participation. Secondly, our health system ensures that each clinical research agreement is accompanied with a fair reimbursement and payment schedule for services rendered to remain

Research Review for Mission Alignment

A look at the stakeholders responsible for each aspect of CHRISTUS Health's "FIRE CONTROL" operating model.

FIRE CONTROL OPERATING MODEL COMPONENTS	• Stakeholders
FEASIBILITY REVIEW	• Regional Research Leaders • Research Executive • Ethics Executive • Mission Leaders
INFORMED CONSENT FORM REVIEW	• Regional Research Leaders • Research Coordinators and Nurses • Institutional Review Board • Ethics Executive • Research Sponsor
INSTITUTIONAL REVIEW BOARD/ ETHICS REVIEW	• Institutional Review Board
CONTRACT REVIEW	• Legal Counsel • Contracts Analyst • Research Sponsor
POLICIES AND STANDARD OPERATING PROCEDURES	• Research Executive • Institutional Review Board Staff
INITIAL AND ONGOING EDUCATION	• Research Executive • Institutional Review Board Staff
LANGUAGE ACCESS SERVICES	• Research Coordinators and Nurses • Language Access Service Vendors • Health Equity, Diversity and Inclusion Department

Source: CHRISTUS Health

responsible stewards of health care resources. Thirdly, we aim for favorable language in clinical research agreements for our patients (especially those in vulnerable situations) to ensure that there is a clear arrangement on how patients will be compensated in the rare event of a clinical research-related injury.

5. Policies and Standard Operating Procedures

Clearly written policies and standard operating procedures eliminate uncertainty, ambiguity and/or misinterpretation about how to apply the ERDs in clinical research. These allow CHRISTUS Institute for Innovation and Advanced Clinical Care to follow standardized processes and reduce errors. Some of the clinical research policies in effect cover topics such as research-informed consents, language access services and institutional review board, to name a few.

6. Initial and Ongoing Education

CHRISTUS' clinical research institute is committed to providing comprehensive initial and ongoing education opportunities to its clinical research workforce, medical residents and fellows, institutional review board members and physician investigators involved in its clinical research. As part of this effort, the institute rolls out an annual lecture series program on good clinical practices. Subject matter experts give bimonthly presentations on relevant and timely topics, including lectures specific to Catholic teaching, such as the "ERDs and Clinical Research" and "Ethical Research."

7. Language Access Services

Access to language services is not only about potential research participants, but also for all those impacted by the study's clinical research results and validity. Excluding groups with limited English proficiency from studies leads to biased and exclusionary results, not only with medications and treatments, but clinical protocols and algorithms.[5] As noted by specific directives in the ERDs, duties to the community and vulnerable persons compel Catholic health care to minimize any communication barriers to prevent further exclusion (beyond those of the study) and the growth of any existing vulnerabilities.[6]

Secular rules are in unison with faith-based commitments. Since 1964, the United States has passed a series of acts, laws, executive orders and regulations to enhance language access services to all in health care. Provisions in federal government and FDA regulations require investigators to obtain informed consents in a language that is understandable to the clinical research participant or their legally authorized representative.[7,8]

The CHRISTUS Institute for Innovation and Advanced Clinical Care ensures fair and equitable selection of volunteer research subjects for its clinical trials and research projects and therefore promotes health equity, diversity and inclusion. This commitment encourages potential clinical research subjects who altruistically volunteer despite any English-speaking barriers, including non- or limited-English proficiency, deafness and hearing difficulties.

We have set the tone for reliable and consistent language access services at the system level for all our patients by establishing a system policy, adopting standardized processes and retaining credible vendors. We provide our clinicians and other team members with the tools necessary to deliver language access services through: 1) live/onsite professional interpretation, 2) qualified bilingual staff, 3) document translation, 4) video remote interpretation and 5) over-the-phone interpretation.

In addition to these day-to-day steps related to clinical care, CHRISTUS Health requires the full-length informed-consent document to be translated into the subject's language. We also use a CHRISTUS-approved bilingual witness for clinical research studies with linguistic distribution of more than 1,000 study subjects, or more than 5% of the study's subject population (whichever is greater). In addition, we use a translated short-form consent with a CHRISTUS-approved bilingual witness for clinical research studies with linguistic distribution of less than 1,000 study subjects or lower than 5% of the study subject's population (whichever is smaller). These services are available at no cost to clinical research subjects and their legally authorized representatives. Per our policy, we do not allow minors or family members of patients to serve as interpreters during the informed-consent process.

As a result of the use of professional interpreters and translators in clinical research, many benefits emerge, including the assurance of clinical research participants' understanding,

upholding the quality and efficiency of interpretation services, and reducing or eliminating clinical research participant safety risks to study participants due to misinterpretation.

MODEL'S IMPACT ON CLINICAL RESEARCH

Having mission- and ethics-based standards that go beyond federal regulations and expanding clinical research programs are not mutually exclusive. Faith-based or not, it is imperative that all clinical research institutions follow applicable federal regulations. Sometimes these regulations may conflict with the Church's teachings. Examples include pregnancy prevention methods, gene therapy research and selection of subjects. However, our FIRE CONTROL operating model helps to maintain the delicate balance between the ERDs, federal regulations and clinical research operations.

CHRISTUS Health's clinical research institute has expanded significantly while hardwiring mission, identity and teachings rooted in sources such as the ERDs. Since the application of our innovative operating model, the total number of active clinical research studies has more than doubled in the last five years, including a growth of 28% in fiscal year 2021 (compared to the previous fiscal year) — despite the period's height of COVID-19 cases — and a continued growth of 12% in FY2022, so that the system is involved in almost 700 studies a fiscal year. Furthermore, the number of our research participants per fiscal year has consistently been between 10,000 and 15,000 since FY2017, and we continue to recruit from diverse populations.

CONCLUSION

By sharing our FIRE CONTROL operating model, we hope others may draw from it to find new ways to advance the care provided through clinical research. By using clinical research that is innovative, ethical and financially responsible, not only can we improve the experience of research participants and the potential study outcomes, we can help to ensure the human dignity of every patient.

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NOTES

1. "2018 Requirements (2018 Common Rule): 45CFR46.116," U.S. Department of Health & Human Services, January 2019, https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/revised-common-rule-regulatory-text/index.html.
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6. United States Conference of Catholic Bishops, "Directive 3" and "Directive 8" in *The Ethical and Religious Directives for Catholic Health Care Services: Sixth Edition* (Washington, DC: United States Conference of Catholic Bishops, 2018).
7. "Title 45," Electronic Code of Federal Regulations.
8. "Title 21," U.S. Food & Drug Administration.

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