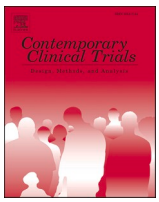
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Contemporary Clinical Trials 117 (2022) 106760

Contents lists available at ScienceDirect

Contemporary Clinical Trials

journal homepage: www.elsevier.com/locate/conclintrial



One committee to review it all: A single, multi-disciplinary COVID-19 research committee

Jocelyn Migliacci *, Ann Rodavitch, Gregory Riely, Paul Sabbatini, Collette Houston, Sara Hanley

Memorial Sloan Kettering Cancer Center, USA

ARTICLE INFO

Keywords:
COVID-19
Study start-up
Protocol activation
Protocol review committee
Cancer center support grant (CCSG)

ABSTRACT

On 1/20/2020 when the first case of a novel coronavirus (COVID-19) was confirmed in Washington state, its major impact was unknown. Memorial Sloan Kettering Cancer Center's (MSK) Hospital Incident Command System (HICS) was activated on 2/5, with our first COVID-19 case identified in early March. By 3/17, our Protocol Activation and Human Research Protection Program was fully remote and on 3/23, MSK leadership requested the creation of the COVID-19 Research Committee. Given the race to identify safe and effective treatments for COVID-19, modifications to workflows and review processes were needed. The goal was to provide quick access to COVID-19 treatments to our patients by creating a COVID-19 Committee as a "one-stop" committee, providing comprehensive review of clinical research related to COVID-19 including scientific review mandated by the Cancer Center Support Grant (CCSG) guidelines, prior to IRB review and protocol activation. Protocols that were reviewed by the COVID-19 Committee opened to accrual in an unprecedented 44 days from submission to the committee to open to accrual. Patients were accrued on most of the therapeutic protocols within 1 day of opening. These statistics have prompted our institution to explore how more protocols can benefit from this "one-stop" committee structure.

1. Introduction

Memorial Sloan Kettering Cancer Center (MSK) is one of the largest comprehensive cancer centers in the United States with 960 prospective clinical research protocols, 344 biospecimen research protocols (BRP) and 856 retrospective research protocols (RRP) open to accrual as of June 1,2021. In 2020, 373 prospective clinical research protocols were submitted for activation. Of these submitted in 2020, 51% (189 protocols) were industry sponsored, 35% (131 protocols) were institutionally sponsored (MSK and external institutions) and 14% (53 protocols) were either national group or externally peer-reviewed protocols based on the National Cancer Institute's (NCI) definitions of protocol category [1]. MSK's Protocol Activation and Human Research Protection Program (*the unit*) is a centralized unit responsible for the management of protocol activation, review, and regulatory monitoring throughout the lifecycle of the protocol (from the time of submission to the time a protocol is closed). The unit is housed within Clinical Research Administration (CRA) and comprises three sub-units: Protocol Activation Core (PAC), Protocol Review Core (PRC), and Human Research Protection Program (HRPP). PAC works with the study teams and Principal Investigators of protocols to prioritize protocols prior to submission and to guide a protocol through the review and activation process. Once a protocol is open to enroll participants, PAC's involvement with that protocol ends. PRC is responsible for ensuring protocols meet our predetermined minimal submission requirements before acceptance of the protocol from the study team/PI and manages 29 departmental and institutional committees, including the Protocol Review and Monitoring Committee (PRMC) which is mandated by the Cancer Center Support Grant (CCSG). These committees review new protocols, amendments, regulatory submissions, and conduct accrual and data and safety monitoring. HRPP manages all aspects of human research protection, including our Institutional Review Board (IRB).

MSK follows a two-stage review system, as mandated by CCSG guidelines. During the first stage, the disease- or discipline- stage, protocols are reviewed by the departmental committee of each investigator, depending on the investigators' roles. The Principal Investigator (PI) department (i.e., sponsoring department) and Co-principal investigator (Co-PI) departments (e.g. multimodality studies) listed on a protocol

* Corresponding author.
E-mail address: migliacj@mskcc.org (J. Migliacci).

https://doi.org/10.1016/j.cct.2022.106760
Received 4 February 2022; Received in revised form 31 March 2022; Accepted 11 April 2022
Available online 20 April 2022

generally review the protocol at a full committee meeting, while other participating departments often perform an expedited, feasibility review outside of a convened meeting (e.g., Radiology, Pathology, Laboratory Medicine, etc.). Protocols could potentially have 1 to 10 departmental reviews, but generally a protocol has less than 5. Protocols undergo review by institutional committees such as the Investigational New Drug (IND) Committee (INDC), Committee on Radiation (COR), Radioactive Drug Research Committee (RDRC), when applicable, as well as Research Council (RC), which is MSK's PRMC, the second stage of the review system, and finally the IRB.

The full activation review flow of a new, prospective protocol is determined by the study type, category, and sponsor. MSK has multiple established review flows, but the two most common review flows utilized are the MSK investigator-initiated trial (IIT) and external protocol review flows (Fig. 1). For external protocols, which includes all protocols where MSK is not the sponsor, the protocol is reviewed by all departmental committees simultaneously. Once the protocol is approved by the PI and Co-PI departmental committees, the protocol is submitted concurrently to RC, COR and the Institutional Biosafety committee, when needed, and once all reviews are complete, the protocol can be submitted to the IRB. For IITs, PI and Co-PI approval is required before submitting to any other participating committees for review. The IIT review flow is also illustrated in Fig. 1. All IITs with scientific endpoints also require approval from the Department of Biostatistics prior to RC and IRB review and review by the INDC committee if the study includes an investigational drug.

BRPs and RRPs have shortened review flows. Some departments require committee review by the sponsoring department, but other departments forego review. IRB is the only required review, as these protocols do not require oversight of our PRMS.

The institution strives to meet MSK's Time to IRB Approval (TTIA) and Time to Activation (TTA) goals. TTIA and TTA are defined as the time, in days, from the date a protocol is received by the primary department to the date of IRB approval or open to accrual (OTA), respectively. The goal TTA is 90 days for externally sponsored studies and 120 days for IITs, specifically with INDs requiring FDA approval. As illustrated by the review flows described above, most prospective protocols have multiple "stops" (i.e., committee reviews) as part of the activation process. Although the unit has refined the review processes over the years by creating expedited review flows for specific types of protocols (i.e., expanded access protocols (EAP), National Cancer Institute (NCI) Network), creating a more streamlined approach to reviewing and activating more trials within our prospective portfolio will help support our TTIA and TTA goals.

2. Methods

When COVID-19 arrived in New York City, MSK leadership recognized the need for modifications to workflows and review processes to accelerate activation of these important studies.

Fig. 2 illustrates the timeline of events leading up to and after the creation of the COVID-19 Committee. Our internally developed web-based Protocol Information Management System (PIMS), which is the central hub for all submissions, was leveraged to efficiently manage and track COVID-19 research. The COVID-19 Committee was created in PIMS within 7 days, which is a short timeline to roll-out major system changes involved in creating this new committee. As part of the enhancement, a COVID flag was added in PIMS, allowing our team to

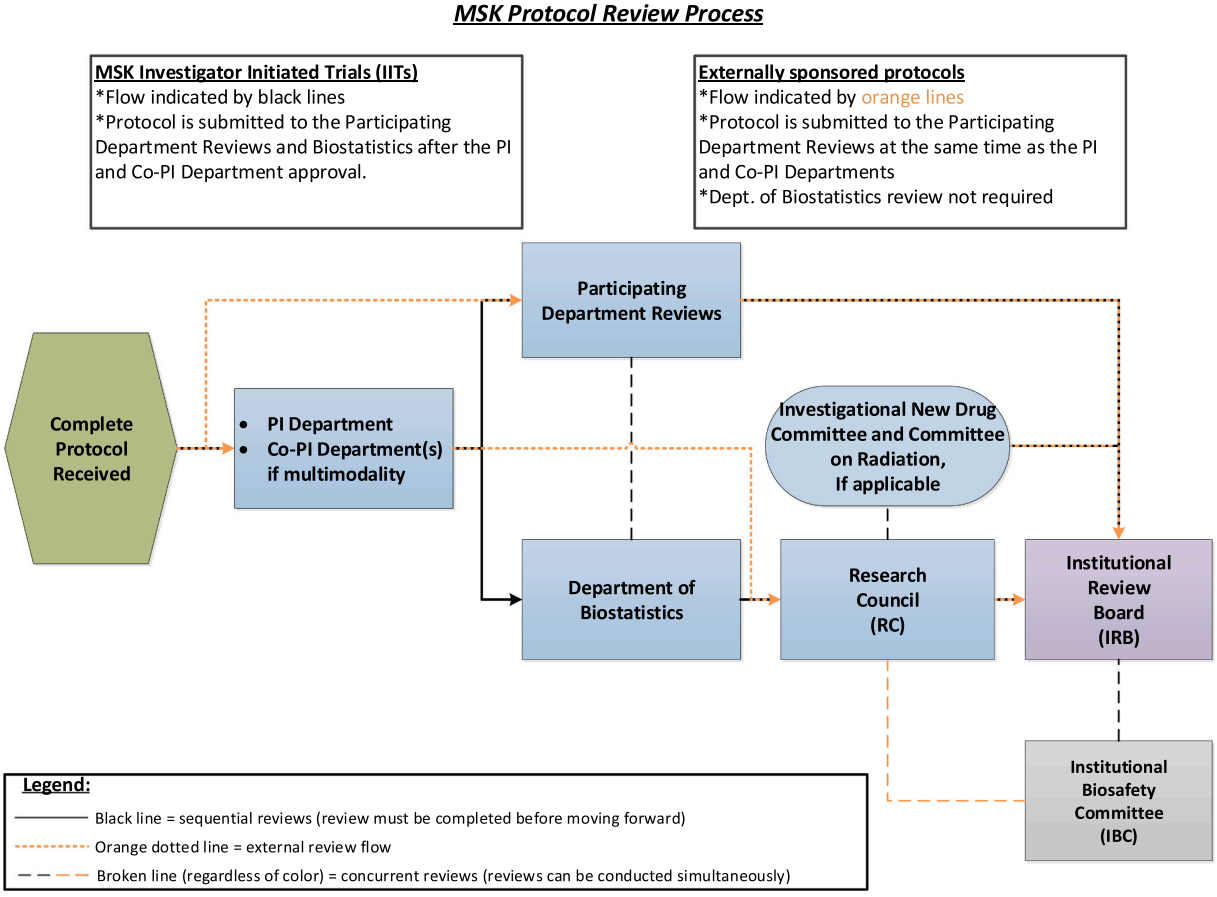


Fig. 1. The two most common review flows utilized by MSK are superimposed in this figure. The black lines indicate the investigator initiated trial review flow. The orange dotted lines indicate the externally sponsored trial review flow. The broken lines indicate concurrent reviews.

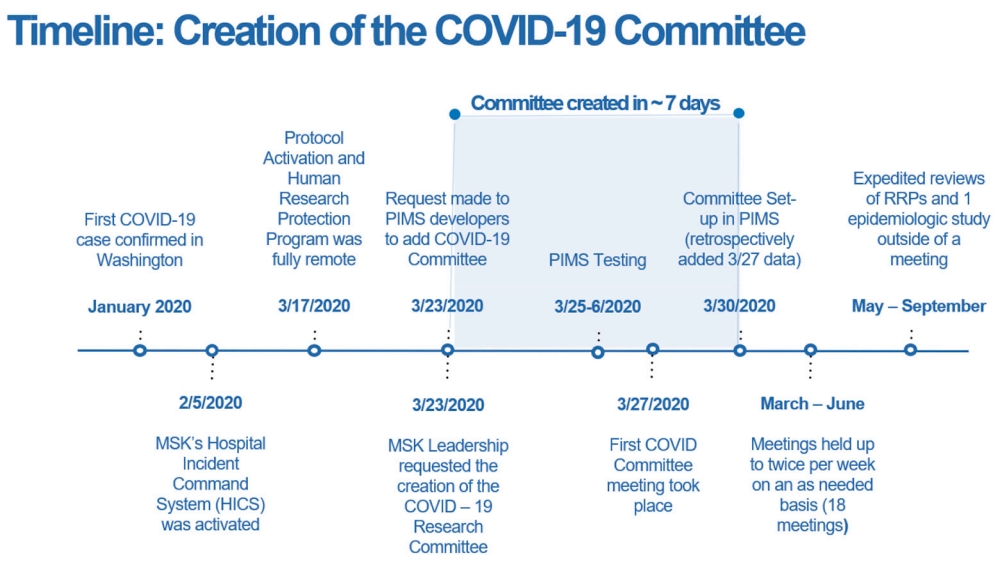


Fig. 2. This timeline illustrates the events surrounding the creation of the COVID-19 Research Committee. The Committee mobilized and began reviewing protocols in less than 1 week.

easily identify when a COVID study was submitted and override certain requirement from our routine workflow. The Committee members included faculty from multiple disciplines, disease management groups and departments, such as Medical Oncology, Pharmacy, Laboratory Medicine, Infectious Disease, General Council, IRB Leadership, Critical Care, Radiation Oncology, Biostatistics, Surgery, Nursing, Radiology, Health Informatics and Pediatrics. Assembling a committee representing all expertise and disciplines allowed for this committee to comprehensively review COVID-19 research which is a unique structure compared to other committees at the institution. Fig. 3 shows the condensed review flow for this new "one-stop" committee review, which takes place prior to required institutional committee reviews, including the IRB.

The charge of the new Committee was to: 1) prioritize and expedite all clinical research related to COVID-19 in support of the institutional effort to rapidly activate therapeutic and other COVID-19 related research, 2) to monitor the COVID-19 research portfolio to prevent overlap of efforts and 3) to list all studies on the Clinical Research internal Portal for transparency and awareness. Aside from creating a "one-stop" committee, the new COVID-19 workflow eliminated submission requirements such as: a research proposal submission form, service chief sign-off and our internal pre-review of the submission before accepting for committee review. When a submitted protocol was identified as COVID related, PAC, PRC and HRPP worked together to fast track the protocol.

3. Results

From March to June, the COVID-19 Committee held 18 meetings, often twice a week. These meetings were organized and completed virtually within 2–3 days of receiving a protocol. The Committee continued to review protocols through September 2020, outside of meetings. In total, reviewing 22 prospective (including 2 amendments to add COVID cohorts), 47 RRPs and 5 BRPs.

Of the 20 new prospective, 5 were removed from the activation

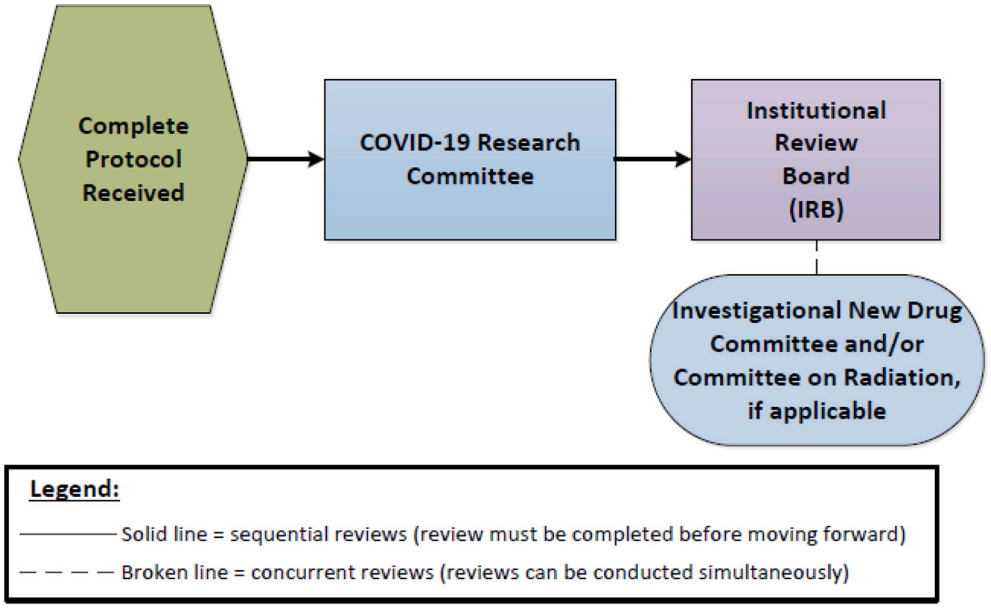


Fig. 3. Condensed protocol review process for COVID-19 research.

pipeline for various reasons (2 withdrawn from activation, 1 rejected by the Committee, 1 transferred to the standard review flow and 1 closed prior to opening to accrual). The remaining 15 protocols (100%) opened to accrual (OTA) as of June 1, 2021, with a median TTIA and TTA of 27 (range: 4–267 days) and 44 days (range: 9–376 days), respectively. There were two outliers that took longer than 200 days to open due to a major sponsor protocol amendment and contract negotiation delays.

In comparison, the Medicine Committee, which reviewed all non-COVID protocols with a PI from the Department of Medicine, received 132 protocol between March and September 2020 for review. As of June 1, 2021, 108 (~83%) were OTA with a median TTIA and TTA of 119 and 194 days, respectively. The 24 remaining studies which are not yet open have been in the activation pipeline for a median of 323 days (range:246–418 days).

This unique single committee structure enabled protocols to be activated and enroll patients in a shortened timeframe. Since the COVID-19 Committee included multiple disciplines within one committee meeting where varied scientific expertise were represented, the scientific rigor and quality of the review was not impacted, and no disadvantages were noted by the speed of the review process. While IRB review was not modified, when needed, the IRB held ad hoc meetings to ensure the research studies were available to MSK patients as quickly as possible. Notably, 5 of the 8 therapeutic protocols have enrolled 146 participants (in total), with first patients enrolled in $\leq$1 day of each study opening to accrual.

3.1. Challenges

As study teams were identifying studies and developing research protocols, it was important that we received the protocols into the unit as quickly as possible and identified them as COVID research. Once a submission was received, PRC and PAC collaborated in preparing the protocol for the COVID Committee. We were faced with the challenge of mobilizing a group of experts from various departments and roles within the institution to complete reviews and schedule meetings within 1–2 days. The Committee pushed forward without a standardized process or known regulations for reviewing COVID-19 research in the first months of the pandemic.

In addition to protocol approvals, key operational tasks, including budgets, contracts, order sets, etc., were handled outside the unit and needed to be considered and completed while a protocol was moving through the review process. The unit communicated bi-weekly progress reports with the finance, legal and study teams who we depended on to complete crucial tasks allowing the study to open and enroll patients.

4. Discussion

The remarkable accomplishments we have made at MSK by quickly and efficiently operationalizing this specialized committee during unpredictable and unprecedented times demonstrates that significant and innovative changes can be successfully implemented in a very short period of time, when needed. The unit is exploring how to generalize this new “one stop” COVID-19 protocol review process for a larger group of protocols at MSK after successfully fast tracking the review and activation of COVID-19 protocols. Important considerations include the volume of the portfolio and how best to reorganize our processes. The time commitment and emphasis on quick turn-around from a single, multidisciplinary committee with the appropriate expertise for all diseases or disciplines, responsible for the initial scientific review of concepts and protocols for all 300+ protocols in our activation pipeline each year also needs to be considered. Multidisciplinary committees organized by disease management teams (DMT) may be a feasible option in reducing the time to activation for a portion of new research protocols. At MSK there are roughly 20 DMTs that can be leveraged for protocol review, however, not all are formally structured, with varying levels of functionality. Consolidating all disease- or discipline- specific reviews into a single review committee would reduce the amount of time committee members spend meeting and reviewing protocols as well as the amount of time administrative staff spend on processing, organizing, and facilitating reviews. Every committee meeting takes roughly 3–5 h to secure reviewers, organize, facilitate, follow-up, write letters and respond to comments for a single meeting or up to an hour to process an expedited review. If a protocol has different PI and Co-PI departments, and 3 ancillary departmental reviews (e.g., Radiology, Pathology and Biostatistics), reducing from 5 separate reviews to one convened committee meeting could save 8–12 h of work per protocol. With 300+ protocols a year, this could save 2400–3600 h of work per year.

Currently, MSK’s internal review process exceeds the required level of scrutiny by CCSG guidelines. The guidelines indicate that “disease- or discipline- (e.g., Phase 1, molecular pathways, cancer immunotherapy, etc.) focused groups (for brevity’s sake, hereafter referred to as disease groups), consisting of scientists, clinicians, nurses, pharmacists, etc., with expertise in a disease or discipline are responsible for the initial scientific review of concepts and protocols. Biostatistical input is not essential during the first stage of review, although Centers may want to incorporate biostatistical review of investigator-initiated trials.” [2] Our proposed “one-stop” committee review would fulfill the requirement of at least one review at the disease-specific level. MSK’s current additional review requirements (i.e., departmental reviews from all involved departments) are not necessary per CCSG guidelines, but are important for assessing feasibility, investigator and departmental participation and logistics for safely completing protocol activities.

4.1. Anticipated challenges to overcome

As discussed in the introduction, our institution currently bases a protocol’s required review flow on the sponsor type. Perhaps the first step in implementing a new condensed review flow is to focus on externally sponsored studies. Typically, external studies have been vetted by the FDA, external IRBs and other review bodies. The protocol enters the activation and review space in a final or near final format and may be active at other centers. The review committee has a clear and defined review scope that focuses on feasibility, disease specific prioritization and scientific integrity. Alternatively, MSK sponsored IITs are designed and written by MSK investigators. The committee reviews are more involved and additional required reviews are incorporated into the review flow, such as the Biostatics Design Workshop. This workshop often results in significant improvements to the study design. If the institution were to forego this workshop style review, significant training would be needed to transfer the value of these reviews into the one-stop committee review. Similarly, the PI’s departmental committees review scope is much broader when written by MSK investigators. Protocols are in the development stage and crucial feedback from the primary department or other committees are made, which often results in improving the quality of clinical research at the center.

Condensing departmental reviews into a single comprehensive DMT review is a significant cultural shift and may be applicable to certain protocol types only. Some departments believe that it is a conflict of interest to have the DMT that is responsible for the study review their own research and prefer that an outside service review the research. Other DMTs may have competing priorities among the different departments within their DMT and will need to negotiate and navigate through this process collaboratively. The standardization of our DMTs will need to be considered as well. Identifying the line between implementing too much structure versus inadequate or inefficient reviews will be important to navigate. Lessons from the unified committee structure for COVID related protocols will provide guidance in developing a nimbler system with faster throughput while maintaining the integrity of the review process including meeting the CCSG requirements.

Funding acknowledgement

This study was funded in part through the NIH/NCI Cancer Center Support Grant P30 CA008748.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] National Cancer Institute, P30 Cancer Center Support Grant: Data Table Guide v3.1.1. https://cancercenters.cancer.gov/GrantsFunding/DataGuide#dt4, 2022.
[2] National Cancer Institute, Cancer Center Support Grants (CCSGs) for NCI-designated Cancer Centers Application Guidelines: PHS 398 Research Plan (Protocol Review and Monitoring System). https://grants.nih.gov/grants/guide/pa-files/PAR-21-321.html?utm_source=dlvr.it&utm_medium=twitter, 2022.