## Original Research Article

# Tools and processes for tracking IRB approvals as a coordinating center for large multicenter clinical research networks

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**ABSTRACT**

**Background:** Data coordinating centers (DCCs) for multicenter research networks are often responsible for tracking clinical center (CC) IRB approvals. In networks with multiple studies the volume of documentation can be challenging to manage. DCC informatics specialists and coordinators developed simple electronic tools and processes to fulfill this responsibility.
**Methods:** Informatics specialists created a Microsoft Access database to track receipt of IRB approvals from CCs. The database monitors approval expiration dates for an unlimited number of studies and CCs and generates automated reports displaying information on all documented approvals. Coordinators formalized communication procedures for collecting approvals and disseminating information on file. The DCC established a central e-mail account to which CCs submit documentation. The DCC sends monthly e-mails notifying CCs that updated IRB reports have been posted. CCs determine what documentation must be sent to the DCC, and the DCC verifies that all submitted documentation is valid.
**Results:** The database increased DCC efficiencies with a semiautomated mechanism and standardized procedures. New communication processes strengthened compliance with regulatory guidance and client requirements to monitor data collection with appropriate human subjects protections in place. The IRB approval-related e-mail volume sent to CCs was reduced. Automated highlighting of approvals expiring soon reduced DCC coordinator efforts and minimized potential for noncompliance.
**Conclusions:** Although initial investment is needed, formalization of the database and processes result in resource savings throughout the organization's tenure as a DCC. The flexible nature of access databases makes them an efficient solution for tracking IRB approvals in networks with fluid center compositions.

**Keywords:** Data coordinating center, Multicenter research, IRB approvals, Electronic tools, Documentation tracking, Protection of human subjects

## INTRODUCTION

A data coordinating center (DCC) for a large multicenter research network takes on a variety of roles and responsibilities that contribute to the smooth and successful function of large clinical trials. Major responsibilities of a DCC can be categorized into four broad areas: trial operations, data management and analysis, quality control/quality assurance, and human subjects protection and regulatory affairs.[1] Findings from a Federal Demonstration Partnership survey of more than 6,000 faculty members who were lead investigators on

federally funded research grants suggested that investigators spend almost half of their time allotted for research projects on administration-related activities.[2] This echoes the administrative burden on both DCC staff and research network staff to ensure smooth network functioning. The survey also found that Institutional Review Board (IRB) approval processes constituted the highest administrative burden for research involving human subjects.[2]

By nature, research networks often conduct multiple complex trials concurrently and involve large numbers of staff across all participating sites. Networks that involve human subjects research have an additional responsibility to protect the rights, integrity, and confidentiality of clinical trial subjects and follow Good Clinical Practice guidelines.[3] Research coordinators at each clinical center are often assigned the responsibility of obtaining approval from their local IRBs to conduct each research trial in addition to attending to many other matters essential to trial operations. Thus, a DCC plays a key oversight role in ensuring that all participating centers have consistently met all requirements from their local review boards to be able to ethically conduct the research activities at their center. Tracking all active IRB approvals for all studies and across all participating clinical centers to ensure that all centers have obtained the necessary and appropriate permissions from their local IRBs to conduct each trial is a pivotal ethical obligation in clinical human subjects research.

RTI International serves as the DCC for multiple multicenter research networks and has thus prioritized this responsibility and developed innovative ways to reduce the burden associated with this important task. Historically, tracking of regulatory documentation had to be done on paper and involved complex filing systems for many of these research networks; however, the advent of recent technological developments and capabilities has expanded the platform and ability of DCCs such as RTI to develop advanced means of carrying out this responsibility.

Given the increasing magnitude of the workload at clinical centers that are managed by staff with diminishing resources is of utmost importance to maintain regulatory oversight of the centers participating in each trial. Of greatest significance to the DCC is ensuring that all clinical centers have the appropriate permissions to be able to transfer study participant-related data to the DCC. This is a critical responsibility that must be carried out to promote the safety and well-being of human subjects, ensure adherence to the ethical values and principles underlying research, and guarantee that only ethical and scientifically valid research is implemented. Thus, it is important to have adequate documentation that all IRB approvals were obtained to allay concerns from regulatory agencies and the general public about the responsible conduct of research.[4]

From a practical protocol implementation and conduct standpoint, it is also of critical importance for the DCC to ensure that site IRB approvals are valid throughout the entire life cycle of the protocol because failure to do so can also limit the scientific quality of the study. In general, all clinical center IRB-related activities are time consuming, and those activities often divert funds that were originally intended for scientific aspects of the protocols.[5] Thus, strategies and tools to reduce the burden of IRB-related tasks for clinical research center staff could result in cost savings for the entire multicenter research network. Having to conduct the review process at each local IRB in a multicenter research network also results in additional frustration associated with cumulative increases in time, cost, and IRB activity-related workload across all centers.[6] Federal regulations surrounding the expiration dates of IRB approval are not at all forgiving; thus, lapses in IRB approval are detrimental to the study as a whole because all research activity must be halted, and in some cases existing subjects must be discontinued from the study when IRB approval lapses.[7,8] Additionally, there is often significant variation in the date that each clinical center actually receives approval from its IRB[9]; this means that ensuring that the approval periods are valid for all research sites for a single protocol is always a moving target. The challenge of trying to manage those approval periods and prevent lapses across multiple centers is exponentiated when carrying out the same tasks for multiple protocols being conducted concurrently in a single research network. Automated tracking tools could also be especially helpful in practice-based research networks because clinicians in those research centers may be more unfamiliar with the regulatory requirements and procedures.[10]

There is relatively little knowledge regarding the overall compliance of centers in large multi-center research networks because there are few reports in the literature regarding IRB continuing reviews and lapses in approval.[7] However, Tsan et al. looked at the compliance rates for continuing review requirements for protocols at the Department of Veterans Affairs and found that the rate of lapse in IRB continuing reviews between 2010 and 2013 remained relatively high and constant (around 6%-7%).[7] Another practice-based research network with 19 IRBs had study enrollment interrupted at four sites for periods of time between 2 and 13 weeks because they did not receive renewed approved and stamped consent forms back from their IRB in time.[11]

Given the integral importance of this responsibility, it is surprising that there is limited information on both the extent of IRB compliance and documentation of strategies and techniques that other research networks and coordinating centers have implemented to carry out this responsibility. Collins et al. described the experience of a DCC for the DIG trial.[12] Abbott et al. have identified factors that have been associated with a reduced study cycle time and elaborated on collaborative efforts to

effectively maintain multicenter clinical trials.[13] In Table 1 we identify challenges with traditional DCC processes, which were generalized from the activities described by Collins et al in the DIG Trial and Abbot et al.[12,13]

**Table 1: Challenges associated with traditional DCC processes.**

| Traditional DCC process[12] | Challenges |
|---|---|
| **Study startup includes a long checklist to be completed[13]** | Costly delays between protocol development and first study participant enrollment. |
| **Acquire written confirmation directly from the IRB that the center had valid approval to conduct research on an annual basis and send reminders directly to each of the research centers' IRBs[12]** | Increases the number of individuals associated with the study. |
| **Seek copies of the minutes from the IRB meeting where approval was granted[12]** | Increases number of communications that must be documented, tracked, and updated over time. |
| **DCC enters dates for the initial review and scheduled continuing review into a database and created a program to generate a list of centers due to expire within 2 to 3 months. Manually send letters to the research staff reminding them that the continuing review was coming up.[12]** | Not feasible to implement in a large research network conducting numerous protocols at any given time with any significant resource constraints. |
| **Provide basic study progress information for each research site that can be used to provide updates to the local IRB.[12]** | Difficult to standardize the type of information the DCC would provide to the research sites.[11] |

Especially in a research network conducting multiple protocols at the same time, it is essential to look for techniques to increase efficiencies while still ensuring the same level of compliance.

Although the Office for Human Research Protections (OHRP) has indicated that it is ultimately the responsibility of the investigator at the clinical center to ensure that they remain in compliance with the regulatory requirement and approval periods, OHRP and others have also suggested that the IRBs themselves should develop administrative procedures such as a computerized tracking system to reduce local lapses and noncompliance.[7,8] Many IRBs are starting to use electronic systems to manage their own regulatory and approval activities. However, most of these systems do not currently address the issue of coordinating and conveying the approval information across multiple clinical centers and to DCCs if the clinical center is participating in a larger research network.

**METHODS**

In close collaboration and consultation with the DCC study coordinators, RTI informatics specialists developed an in-house Microsoft Access database[14] that can be used to track receipt of IRB approvals from multiple clinical centers. The database is not only capable of tracking whether a current and valid IRB approval for the clinical center is on file at the DCC, but it has also been designed to track the actual approval start and expiration dates within the system. The customizable and easy-to-use system has been set up to receive input for an unlimited number of centers and so that the multiple individual participating hospitals within the center that are governed by separate IRBs can be tracked separately.

The database has the capacity to generate automatic reports showing all IRB approvals the DCC has received and entered into the system, but it also has the functionality to produce separate reports organized by individual protocol or clinical center.

The Access database tracking system is also able to highlight any IRB approvals that will expire within a user-defined time period (e.g., within 6 weeks) and any individual IRB approvals that may have already expired on the automated reports. In these cases where the clinical center may be delinquent in submitting its IRB documentation to the DCC, the DCC has oversight to disengage access to privately managed data entry systems until active documentation of IRB approval is submitted.

The database has been constructed in a way that enables user-friendly data entry and navigation to generate reports for the DCC coordinators who may have limited experience with programming or maneuvering through large databases. The user menu is straightforward and simple, requiring only minimal training for new users who wish to use the database.

Upon the opening of the database, users are directed to the menu that displays the basic functions that can be performed. Users can add or change the master lists of protocols and clinical centers whenever a new protocol becomes active or a new clinical center joins the research network. There is a form to enter DCC IRB approval information if needed so that all IRB information for the entire research network can be stored in a single location. The most commonly used functions in the database are the "Site IRB Information" and "Reports" options. These are the areas in which users can enter updated information or generate printouts of the information that has been entered to date.

The database has been structured in such a way that the first screen the user sees after opening the database file is

a report of all expired or soon to expire IRB approvals by clinical center. Any expired IRB approvals are highlighted in yellow so DCC coordinators are easily reminded of clinical centers that they need to follow up with to obtain updated IRB documentation (Figure 1).
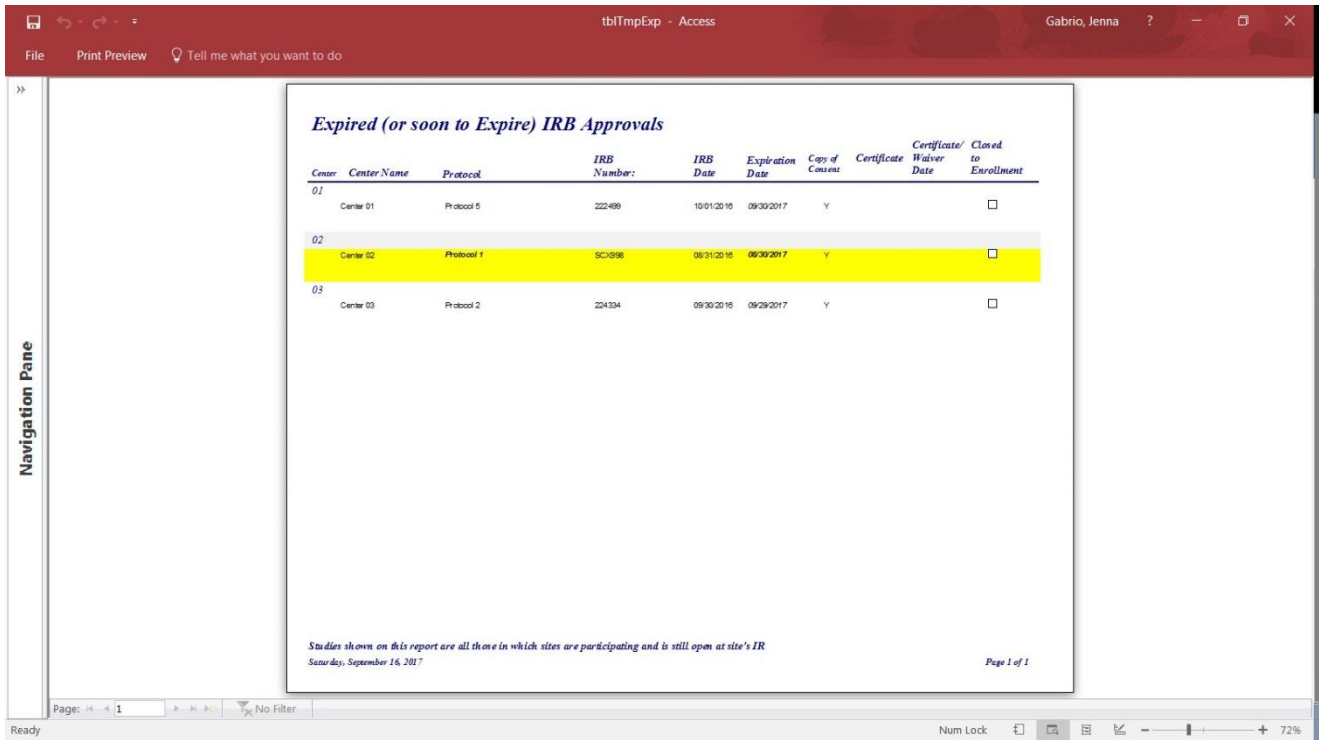


**Figure 1: First screen encountered after opening the IRB tracking database displaying all expired or soon to expire IRB approvals in the research network.[15]**
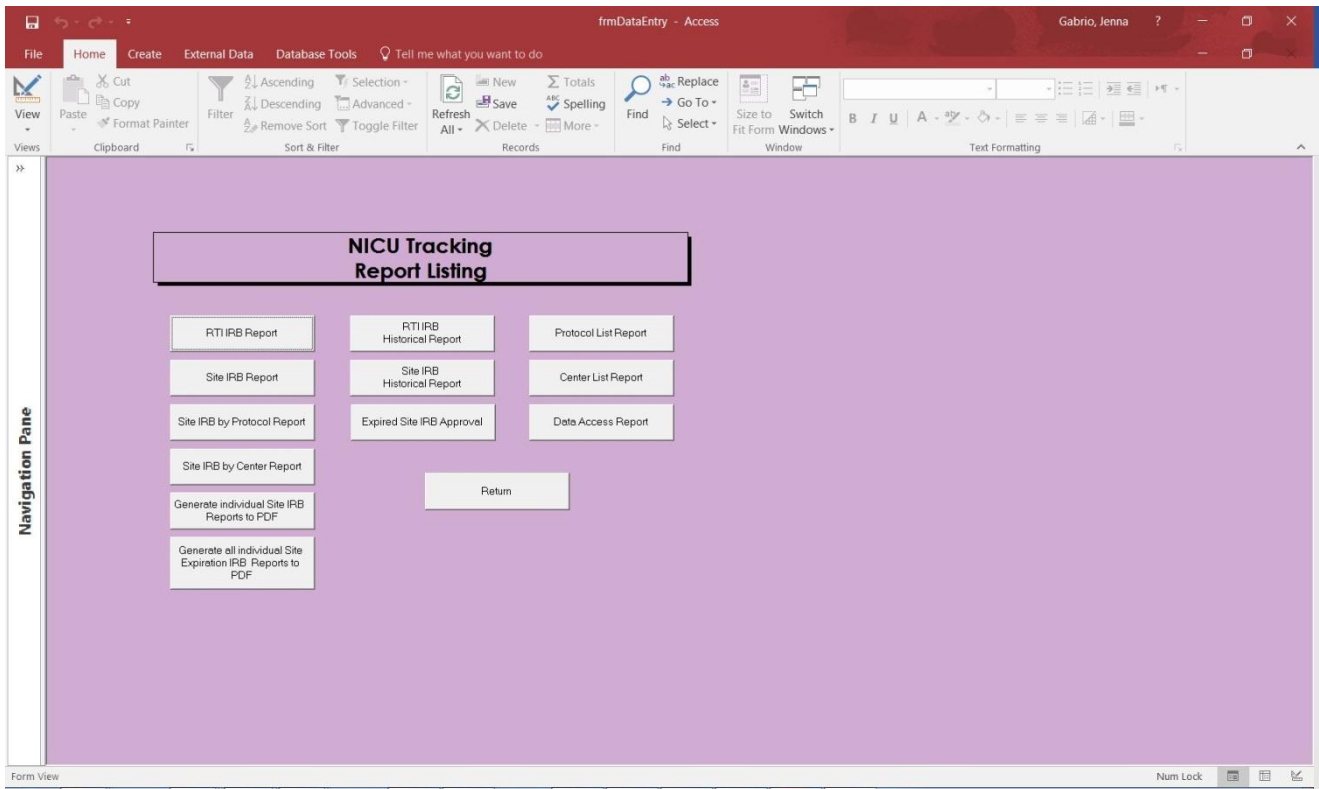


**Figure 2: IRB tracking database user menu.[15]**

**Figure 3: "Snapshot view" form in IRB tracking database.[15]**



**Figure 4: Overview of process to ensure IRB approvals for all participating clinical centers are valid.[15]**

Informatics specialists also designed several features where the individual Site IRB Reports and Site Expiration IRB Reports can be created and saved in PDF format for posting on the private website with the click of a single button. This built-in feature results in efficiency for the coordinators because they do not have to repeat the report-generation process for each individual clinical center.

Other reports that are available for printing within the system are copies of all active protocols, all active centers, IRB Approval status for all clinical centers by protocol, IRB Approval status for all protocols by clinical centers, and cumulative listings of all site IRB approvals organized by clinical center or protocol (Figure 2).

Additionally, there are multiple formats in which DCC coordinators can view and enter data. RTI informatics specialists created a "Snapshot View" form where all IRB approval date information records can be seen for all centers and all protocols at the same time/in the same screen. This facilitates the data entry process for the DCC coordinator, especially when a single clinical center has submitted multiple updated IRB approval documents and information for multiple studies should be entered at the same time (Figure 3).



**Figure 5: Sample IRB information report for an individual clinical center.[15]**

Alternatively, there are separate features and forms for a more controlled data entry environment and specific pieces of information (e.g., dates for a specific protocol for a specific clinical center) can be entered in a paper form-like page. This is advantageous because it helps to ensure that data are being entered in the correct location for the correct clinical center and protocol and that other records are not being altered by mistake.

Once the database and automated reporting structure was set up, the DCC study coordinators established more formal procedures and processes for both collecting updated IRB approvals from clinical centers and informing the clinical centers of the status of the IRB approvals that the DCC currently has on file (Figure 4).

Given that there are typically a number of DCC coordinators working in the same research network, RTI established a central e-mail account to which research staff at the clinical centers should submit all updated IRB approval documentation. Upon receipt of the updated documentation, a primary DCC coordinator was designated the responsibility of acknowledging receipt of the updated documentation, filing the updated documentation onto the project share drives, and entering the updated information into the tracking database on an ongoing basis. Then, once per month this primary DCC coordinator generates the individual automated center reports of all IRB approvals and posts them to the research network private website. The clinical centers are able to access the report for their center through the website and can then see pages showing studies with IRB approvals that are delinquent and those that are active but nearing their expiration date. Based on these reports research staff at the clinical centers can determine what documentation must be sent back to the CC to keep all of their records up to date (Figure 5).

**RESULTS**

The development and implementation of the IRB tracking database has increased efficiencies for both the participating clinical centers and the coordinators at the DCC tasked with the responsibility of ensuring that all clinical centers have sent in valid IRB approvals for all studies in which they are participating and transmitting data. The database and process of posting the automated IRB reports to the private website has drastically reduced the volume of e-mail regarding IRB approvals sent to the clinical centers for DCCs managed by RTI. The DCC coordinator no longer has to send individual e-mails to the clinical centers notifying or reminding them that an IRB approval is about to expire. Instead, they send a single monthly e-mail to all clinical centers at the same

time notifying them that the site IRB reports have been updated and research staff should review them to see if any additional action is required from their center. This benefits the staff at the clinical centers as well because they no longer have to monitor their e-mail for reminders about specific IRB approvals that are about to expire and can instead visit the central report listing on the private website and check periodically for updates needed for their center at that single location.

The automated reports that highlight approvals that are about to expire have also reduced the burden on the DCC coordinator to manually check the expiration dates of numerous studies. The automated process reduces the likelihood of oversight of the dates that have already passed or are rapidly approaching because the records that are affected are automatically highlighted by the Access database system. Previously, spot checking the dates by hand was associated with an increased chance for oversights simply because by nature the document contained a large number of dates.

Implementation of the database and report generation processes also facilitated preparation of annual IRB

renewal submission to the DCC IRB. For this annual submission to the DCC IRB the DCC must submit renewal dates for each of the clinical centers and for all of the open protocols; thus, the automated reports that can be generated by specific protocol greatly facilitated this process. In the past DCC coordinators have had to manually look up and supply this information to the DCC IRB. However, the DCC IRB has since allowed the reports generated from this system to suffice as records of the dates each center received IRB approval for each protocol.

Having a central IRB database as a DCC also makes management of the regulatory processes easier for DCC staff internally. If a question arises about an IRB approval for a specific clinical center, all DCC staff can go directly to the database to look up the specific information needed. Instead of looking through multiple folders and sifting through old e-mails for documentation and records of IRB approval that were sent in, DCC staff can run a customized report to look up the information in question, or they can navigate within the database to drill down to the specific information they may need for a particular study and particular center.
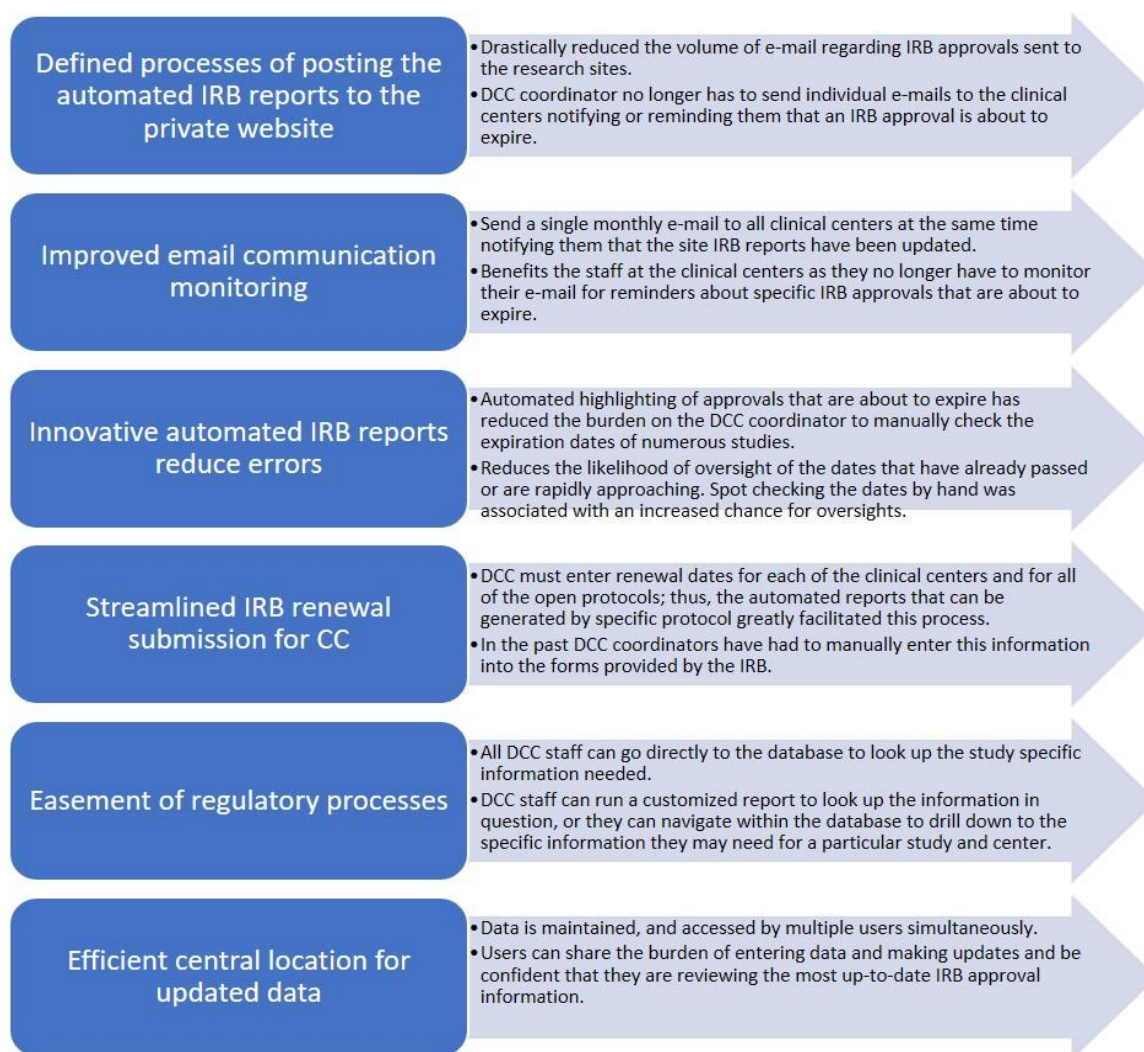


**Figure 6: Summary of advantages afforded by the use of an IRB tracking database.**[15]

The database is advantageous because it creates a central location that can be updated, maintained, and accessed by multiple users simultaneously. If needed users can share the burden of entering and updating data. Users can also be more confident that they are reviewing the most up-to-date IRB approval information because the process has been set up in such a way that allows efficient accrual, processing, and entry of new information (Figure 6).

## DISCUSSION

Although an initial investment is needed to design a database system to track IRB approvals, the development and formalization of the process to use the database will result in significant time and cost savings throughout the tenure of the DCC. The very nature of an Access database allows for flexibility in the number of studies being tracked, the number of clinical centers involved in the research network, and the changes in composition of the research network over time. These inherent capabilities make the database a low-cost resource over time that can be used to provide both a current and historical picture of the IRB landscape across clinical centers. Ultimately, both the database and processes that have been developed at RTI to track all IRB approvals from clinical centers as a DCC are assets for helping all clinical centers avoid gaps in IRB approvals for numerous studies and a means of ensuring adherence to the ethical standards and requirements for participation in human subject research.

On January 25, 2018, the National Institutes of Health (NIH) issued a policy indicating that all of its agencies' research networks should move toward the single IRB model to lessen the burden of seeking approval from local IRBs and to enable the research to "proceed as quickly as possible without compromising ethical principles and protections for human research participants."[16] Although NIH has laid out this goal of moving toward this new streamlined review process for the future, it will likely still take time for all research networks to effectively implement the single IRB model in practice. As research networks begin to make this transition toward the single IRB model, they may do so in stages or in pilot studies. Such stages may involve a subset of consenting clinical centers to test out approval for a newly implemented research study using a rotating Lead IRB for each study. Rather than having one single IRB to approve all new studies, the Lead IRB responsibility rotates between centers to distribute the burden of review across all participating centers. Tools such as the database will still be relevant in this environment because research networks will still need to track which site IRB is serving as the Lead IRB, and the approval and expiration dates, for each study. In the pilot stages when only a subset of centers might be participating in the single IRB process the database can also be used to keep track of that information to show which clinical centers are participating in the single IRB process and which are still operating under the regulations of their own local institutions. Furthermore, multicenter studies that are not necessarily conducted in an NIH-funded research network or a formal research network with another sponsor might not necessarily be able to move to the single IRB approach yet either.

Even in light of the recent policy shifts, IRB tools and tracking processes such as those developed by RTI are still relevant and useful in the current research environment, especially considering the number of ongoing multicenter studies that were not set up under the single IRB approach model and where local IRB compliance needs to be monitored through completion. NIH has also recently collaborated with other agencies to develop a single IRB platform for multisite clinical studies: the NCATS Streamlined, Multi-site, Accelerated Resources for Trials (SMART) IRB platform. Both the RTI IRB Tracking Access database and SMART IRB platforms were developed with the same primary objective: "to provide flexible resources that investigators nationwide can use to harmonize and streamline IRB review for their own multi-site studies."[17] If the single IRB approach is successfully adopted by all multicenter studies and research networks, the digital tools and processes for IRB tracking will still be used in that environment to carry out similar monitoring functions with the major difference being that there may just be fewer clinical centers to monitor.

## ACKNOWLEDGEMENTS

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