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Review Article

UNIQUE ELECTRONIC CASE REPORT FORM - IMPORTANCE TO CLINICAL TRIALS AND HUMAN HEALTH

SUPREET K GILL[1], AJAY F CHRISTOPHER[1], SANJIV KUMAR[2], VIKAS GUPTA[1], PARVEEN BANSAL[1]*

[1]Division of Clinical Research, University Centre of Excellence in Research, BFUHS, Faridkot, Punjab, India. [2]Department of AYUSH, National Medicinal Plant Board, New Delhi, India. Email: bansal66@yahoo.com

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ABSTRACT

Unique electronic case report form (eCRF) is a platform in which electronically maintained information about an individual's lifetime health status and health care records can be stored such that it can serve multiple legitimate users and along with serving as case report form of patients in clinical trials. Through unique eCRF individuals can access, manage and share their health information with others who are authorized, in a private, secure, and confidential environment. Unique eCRF has potential of integrating various domains of clinical trial like data capture, data cleaning, and data mining into one system and hence significantly contributes in clinical trial management. It also contributes in huge saving of a pharmaceutical company in terms of cost and time. eCRFs offer advantages such as improved data quality, online discrepancy management and faster database lock. The other potential advantages include integrated patient's health and financial data, audit trial capabilities, identifying eligible patients for clinical trials from patient's records, trial randomization, agile data transfer, follow patient outcomes, in creating patient registries, monitoring adverse drug reactions and pharmacovigilance reporting. Unique eCRF deserve a serious look because they are the most efficient way to connect patients to their medical data. They not only facilitate information sharing among doctors and guard against needless medical errors, but also offer a safety advantage in that health record would never again need to be stored. All eCRFs should be validated in compliance to 21 CFR part 11.

Keyword: Unique electronic case report form, Clinical trial, Integration of data, Saving cost, Auto alerts and correction.

INTRODUCTION

An electronic case report form (eCRF) is designed to collect the patient data in a clinical trial. The development of eCRF a significant part of the clinical trial and can affect study success [1,2]. Continuity of care depends on the availability of complete health care information on which current and future care can be planned and implemented. eCRF should be fully featured according to 21 CFR part 11 compliant giving both the investigators and monitors a powerful yet easy to use environment for data entry and monitoring. Patients have multiple records even within single institution often unknown to the individual care provider [3]. This could be overcome by the unique eCRF. For example aadhaar card was launched by Government of India as unique identification process by Unique Identification Authority of India, an Agency of Government of India to provide identification number to all persons residents of India [4]. This agency maintains a database of residents containing biometric and other data [5]. The card permanent retirement account number (PRAN) issued by central government under the new pension system that is required to maintain the subscriber's accounts and issue unique PRAN to each subscriber. Similarly each participant of trial will be provided with unique eCRF number in which all health and finance related information will be recorded. Health care informatics professional often have challenges to establish a means of identifying individual patients across care delivery systems. Unique eCRF can be designed to record all of the protocol required information to be reported to sponsor of each trial subject. Lacking an easy, uniform way to identify patients and link them to their health data, doctors, hospitals, pharmacies, insurance plans and others throughout health care have created a sea of unrelated patient-identity numbers that are bogging down our medical-records system. Transferring a single patient's medical data from one health provider to another is often a struggle, sometimes resulting in treatment delays and even needless medical errors. The vast majority of clinical research study protocol requires the collection of core research data that provides detailed information of the medical care and health information of individual participants in the clinical trials. Clinical trials require the collection of information about clinical trials participants from their medical history and healthcare experiences. A well-designed eCRF facilitates data collection and entry in a smart manner which directly benefits data management and statistical analysis [6]. It is the new way of conducting clinical trials-focusing on early integration to compress study timeline. Unlike traditional approaches which separate the collection and management of clinical trial data, eCRF combines data capturing, data cleaning, trial management and even data mining in one system. In addition eCRF would help reducing risk and improving efficiency throughout a study by eliminating the need for data reconciliation and the expenses of managing separate systems [7]. Thus, contributes in huge saving in cost and time of a pharmaceutical company.

Unique eCRF - The wave of clinical trial future

Electronic data record of clinical trials helps to access patient's medical record. This significantly helps health care provider to obtain critical medical information about the patient [8,9]. Unique eCRF allow physician or investigator with proper authorization to access to relevant patient information for example medical history, drug exposure list and various allergies, irrespective where patient have previously treated. The importance of eCRF incuses greatly in treating unconscious patient who comes in emergency [10]. This would also help in treating patient who may not fully recall or understand details of medical history. Major benefits of the ability to access core dataset information for clinical research are to ensure the safety of research participants, improve data quality by reduction of transcription and re-entry of data, and decrease the burden of research for clinicians. eCRF data can be used to identify eligible patients for clinical trials, monitor adverse drug reactions (ADR), and follow patient outcomes. Unique eCRF would be specially designed to meet clinical practice needs, and would help clinical investigators in their research. The data are recorded through electronic data capture systems in clinical trials to collect, manage and report clinical and laboratory data [11]. This also provides an excellent tool for identifying and recruiting eligible patients to different types of clinical research studies. Include the following minimal dataset in eCRF to help researchers identify and screen potential study participants.

BENEFITS OF UNIQUE ECRF

Integration of health records

Unique eCRF would integrate electronic data collection, data storage and archival practices such as clinical trial management, data management and electronic data capture system with a single log in. All data are stored in one database, resulting in no complicated interfaces and no lag time with a wide breadth of functionalities to ensure data quality and real time information [12]. Unique eCRF would ensure that the integrity and quality of data being collected and transferred from study subjects to a clinical data management system are monitored and maintained, and quantified to ensure a reliable and effective base for not only new drug application submission and clinical science reports, but also corporate clinical planning, decision-making, process improvement, and operational optimization. Unique eCRF helps to integrate all the information useful for screening patient from clinical studies. These records include data on observations, laboratory tests, diagnostic imaging reports, treatments, therapies, drugs administered, patient identification information, legal permissions, and so on [13,14]. The integration of data collection, preprocessing, and machine-learning in a single software framework simplifies the whole process of clinical research. The ability to create an integrated record system depends on standardizing and integrating other aspects of the electronic record. The integration of health information record is necessary to support patient care. The eCRF platform creates the foundation for solutions that enable study management and bio banking. Using one platform to support multiple research functions across an organization minimizes redundancies and reduces cost. This solution supports integrated workflows for investigators, research coordinators, data managers and study participants [15]. The integration of health records would provide better connectivity to discrete health data. It would provide patient - centric data structure which accept information from multiple sources and will offer more improved quality of care coordination and patient safety [16]. This would help the investigator to assemble the actionable data needed to make more informed medical decisions more quickly. Integrated edit checks of data allows easier driving to clean data entry.

Real time data monitoring

The unique eCRF would allow real time data access, which will enable in efficient process monitoring of the complete clinical trial and hence more transparency to all of the parties involved. Increased data visibility not only allows faster query resolution, but also enables project managers to respond quickly to any trend in the trial (such as inaccurate completion of case report form pages), which, in the end, leads to a faster database lock. Unique eCRF would provide tools and services in better planning and conduct academic trials (investigator-initiated trials). This would facilitate comparative effectiveness in research [17]. eCRF would also help in clinical data management, which is a vital cross-functional vehicle in clinical trials to ensure high quality data are captured by sites staff and are available for early review. This will also contain check routines which reduce erroneous data entry. Another advantage is the continuous insight into the data and its data collection process and thus can maintaining a clear and clean clinical trial and allowing sponsor and even regulatory authority real-time asses of data and other trial related procedures [18,19]. This would optimize the monitoring through real-time data verification reducing the frequency of site visits and queries as most simple queries could resolved. The problem though, is the time required to acknowledge its existence, which in many cases takes months after the patient's visit. With this in mind, unique eCRF could be designed to facilitate remote notification and resolution. This results in cleaner database during the trial and quicker resolution of errors, maintaining consistency and auditability. It will also have auto-correction option, automatic alerts and queries will warn the users about inconsistent data being recorded. The gradually increasing use of electronic data-capturing technology to collect data in clinical trials has grown in recent years along with the use of eCRF has affected the activities of clinical research operations for industry sponsors, contract research organizations (CROs), and clinical sites [20,21]. If we comply this technology with applicable regulatory requirements it will offer more flexible, configurable, scalable, and auditable system features [22].

Reduces cost and time

The ultimate goal for all clinical trials is to evaluate the safety and efficacy of the investigational product and to prepare for its registration afterwards. This process has always been subject to business pressure that is trying to move the product to market faster, while at the same time spending less money [23-25]. It is therefore very important to take advantage of all business benefits that are provided by electronic data capture vendors [26]. Unique eCRF would also improve speed and quality of the patient recruitment process and will also the study status by accurate understanding of real patient populations involvement in trial. This would also provide support to conduct observational and outcomes research studies in real-world settings. Technology-driven strategies and initiatives have potential to alleviate the significant pressure to market a medicine as early in patient life as possible both to increase the total revenue and to shorten time to market sales. The competitive pressure in today's marketplace is forcing the biopharmaceutical industry to seek better ways of reducing drug development times and increasing productivity. The market acceptance of eCRF technology has fueled new demands for improvement, configurability, and intelligent features [27,28]. It is recognized that clinical data are key corporate assets in today's biopharmaceutical industry, and that turning data into meaningful information is a critical core function for sponsor firms to make faster and more flexible assessments of compounds in development to design better clinical protocol for target population with specific indications and enable innovative study initiatives and new programs [29]. Figure 1 shows the advantages provided by unique eCRF.

Selection of patient

Unique eCRF significantly helps in screening patient who meets the inclusion criteria. Clinical researchers gets idea that the patient indicated fulfill all the trial related criteria or not. Careful conducted clinical trials are the fastest and safest way to find treatment that work to improve health. Clinical trials can be divided into interventional and observational trials. Interventional trials determine whether experimental treatment or new ways of using known therapies are safe and effective under controlled environmental condition. Observational trials address health issues in large group of people or population in natural setting. One of the crucial components of a successful trial is the selection of an appropriate study population. Using inclusion/exclusion criteria is an important principal of medical research that helps to produce reliable results [30]. Inclusion criteria are characteristics that the prospective subjects must have if they are to be included in the study, while exclusion criteria are those characteristics that disqualify prospective subjects from inclusion in the study. Inclusion and exclusion criteria may include factors such as age, sex, ethnicity, type and stage of

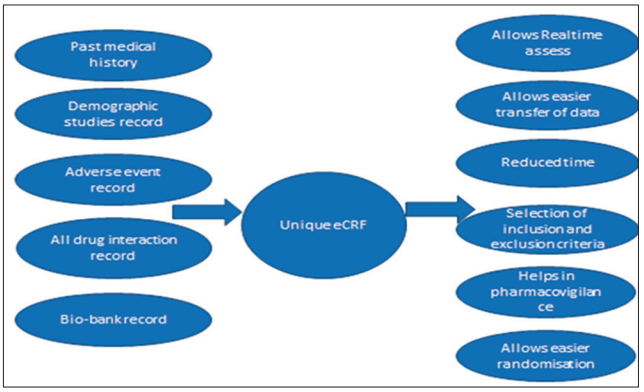

Fig. 1: Data entered into unique electronic case report form and

disease and the subject's previous treatment history, and the presence or absence (as in the case of the "healthy" or "control "subject) of other medical, psychosocial, or emotional condition [31]. This could make the matching process for patients to studies more accurate. This also develops a standardized process for requesting patients' authorization to be contacted about participating in clinical research. Investigator should ensure that all patients understand that their entry into a given health care system constitutes consent to allow their de-identified data to be used for observational studies in a way that protects their confidentiality while advancing new medical discovery. The unique eCRF has the potential to cater all these needs at a single platform. Thereby making it a smart and a necessary choice to the investigator.

Demographic patient record

Unique eCRF will also categories patient according to their age, gender, race, etc., the participants of clinical trial study if classified according to age will help investigator sponsor to evaluate the effectiveness of drug by age, gender and racial subgroup and hence dosage modification can be done according to specific subgroup. The demographic categories include such as:

- Age: According to age trial participants can be classified as - neonates, infants, adults and geriatrics
- Gender: Male and female
- Ethnicity: White, Black, Asian etc., [32].

Some diseases are age related, some occur in specific gender only this functionality will help the investigator to evaluate the prevalence of disease in specific population. For example in geriatric patient chronic obstructive lung disorder and Hodgkin lymphoma is mostly seen and in infants pneumonia, jaundice mostly occurs after birth [33]. Similarly in male's prostate cancer has high prevalence whereas in females systemic lupus erythematous is mostly seen. Apparent differences among demographic groups that can affect health-related behaviors and health outcomes can be influenced by two broad categories of factors that often interact and overlap: (1) Extrinsic factors (e.g. socioeconomic and cultural influences, diet, environment); and (2) intrinsic biological factors (e.g. genetics, hormones, metabolism, organ function, body weight). For a drug expected to be used in children, evaluation should be made in the appropriate age group. When clinical development is to include studies in children, it is usually appropriate to begin with older children before extending the trial to younger children and then infants [34].

ADR record

Unique eCRF will record all the medical histories of patient which includes the history of previous treatment, details of prior hospitalization and treatment received, details of on-going treatment of patients, medicines, if any taken daily by patient and history of all the allergic reactions, which had occurred in past to the patient [35,36]. All the previous laboratory test report data will also be recorded [37,38]. ADR means a noxious and unintended response to a drug, which occurs at doses normally used or tested for the diagnosis, treatment or prevention of a disease or the modification of an organic function [39]. All details of adverse reaction are recorded as:

- Full description of reaction (s), including body site and severity
- The seriousness of the ADR that is, life-threatening condition, hospitalization, significant disability etc.,
- Description of the reported signs and symptoms
- Specific diagnosis for the reaction
- Onset date and time of reaction
- Stop date and time or duration of reaction
- Relevant diagnostic test results and laboratory data
- Setting (e.g. hospital, out-patient clinic, home, nursing home)
- Outcome (recovery and any sequel)
- For a fatal outcome, stated cause of death
- Relevant autopsy or post-mortem findings
- Relatedness of product to reaction (s)/event (s).

In clinical trials the records of all the ADR, which are associated with the investigational product will be recorded in unique eCRF by investigator from the trial site. ADR of particular investigational product has to be reported to the Institutional Review Board/Institutional Ethic Committee, sponsor and regulatory authority. It should also include every detail of reaction along with details of reporter that is profession and specialty of include the concomitant treatment given to patient in the report. Unique eCRF will record all the information about adverse reaction and will help in easier reporting to regulatory authority, sponsor, Institutional Ethic Committee/Institutional Review Board at the same time because eCRF will directly update the information to all regulatory authorities that are involved in the trials.

Prevention of duplication of subject

Unique eCRF could be the safest and most efficient way to manage health-care data as it would guard against misidentification and make it much easier to pull together a patient's records from disparate providers [3]. Every patient would have single record and the information can be reused again and same patient's enrollment again can be prevented. Repetition of lab investigation can also be prevented saving the time and cost. Prevention of duplication is also necessary because if same subject is enrolled double time, this will result in false data collection and analysis and therefore resulting in altered trial results. The unique eCRF forms could be created in the library with edit checks. These edit checks are available in the new trial as soon as the eCRF form has been added. This functionality reduces the current development time for edit checks programming significantly.

Patient disease registry

Unique eCRF software can be configured to build a registry database for a specific disease or diagnosis data collection and analysis. Disease registries often play a big role in post marketing surveillance. Electronic data entry would facilitate a quicker and easier data collection of the large volume of data. The data can be recorded in registry pages designed as for the registry scope, purpose and protocols [40]. Most of the research case report form cannot be easily populated with data collected. The data information collected for most of the field must be filled in for registries. A registry is a list of patients presenting with the same characteristics. These characteristics can be of disease (disease registry) or of specific exposure (drug registry). Registries will allow the confidential disclosure of agreements that could provide architecture for the structured preference and consent forms needed for clinical research. Injecting these agreements into the hospital system could reduce risks to institutions [41]. Registries will help the end-users to easily avoid data entry errors and non-conformities, in order to guarantee a high quality of clinical data.

Drug interactions records

The interaction of different drugs could also be recorded in unique eCRF. This would help clinician to known the effects of drugs given in combination to the individual and can also record the side-effects of drugs given together. For drugs that are frequently co-administered it is usually important that drug-drug interaction studies be performed in non-clinical and, if appropriate in human studies [42]. This is particularly true for drugs that are known to alter the absorption or metabolism of other drugs or whose metabolism or excretion can be altered by effects by other drugs. Interactions between investigational new drug and other drugs should be defined during drug development. The objective of drug-drug interaction studies is to determine whether potential interactions between the investigational drug and other drugs exist and, if so, whether the potential for such interactions indicates the need for dosage adjustments, additional therapeutic monitoring, and a contraindication to concomitant use, or other measures to mitigate risk [43]. All drug interactions of patient's from past history will help investigator to plan for future dosage of drugs when given in combination during clinical trial.

Allows easier randomization process

A randomized controlled trials are scientific experiment, where people are randomly allocated one or other of different treatment under

study [44]. eCRF can integrate with randomization system to deliver seamless, integrated and easy to use system. Randomization is the process of randomly allocating patients to treatment groups, which is a crucial step in a clinical trial to minimize bias. Sponsor would be able to randomly select the number and will divide them into different groups under study. Randomized controlled trials are often used to test the efficacy or effectiveness of various types of medical intervention and may provide information about adverse effects, such as drug reactions. Random assignment of intervention is done after subjects have been assessed for eligibility and recruited, but before the intervention to be studied begins. Random allocation in real trials is complex, but conceptually, the process is like tossing a coin. After randomization, the two (or more) groups of subjects are followed in exactly the same way, and the only differences between the care they receive, for example, in terms of procedures, tests, outpatient visits, and follow-up calls, should be those intrinsic to the treatments being compared. The most important advantage of proper randomization is that it minimizes allocation bias, balancing both known and unknown prognostic factors, in the assignment of treatments [45].

Spontaneous pharmacovigilance reporting

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse reactions and other medicine-related problems [46]. For providing post marketing safety information on drugs it is essential to have spontaneous reporting about drugs. A spontaneous report is an unsolicited communication by healthcare professional or consumers to a company, regulatory authority or other organization (e.g. WHO) that describes one or more ADR in a patient who was given one or more medicinal product [47]. Unique eCRF will also help in pharmacovigilance reporting because every adverse event of the investigational product will be recorded. Pharmacovigilance researchers have been seeking a real time, continuous and prospective approach. Towards this goal, we propose a high throughput system that demonstrates the relevance and significance of using the eCRF for pharmacovigilance [48,49]. A big advantage for using the eCRF for pharmacovigilance is the potential to perform active and real time surveillance, and the probable reduction of errors caused by biased reporting [50].

Clinical trial management

Unique eCRF would be a real time planner of each site and patient's status of advancement in the enrollment, data entry and confirmation of data and follow-up visits. It would also provide detailed overview of the status of data entry and completion of each enrolled patient's record. It would have the visible and user friendly alerts related to the project's milestones and deadline requirements, associated queries and data clarification forms along with the tools and views on completed patients and failures. Unique eCRF will allow real-time data management because it would be easier to enter and analyze data, receive alerts and follow the trial's success and team's updates through standard reports. Unique eCRF would allow more efficient management of public health issues [51,52]. This would also facilitate the reuse of data and the closer co-ordination between care providers and patients, resulting in safer and more evidence-based diagnosis and treatment. Health care services has presented extreme challenges for the biopharmaceutical industry, suggesting the need for sponsor companies to invest significantly in technological solutions and add an additional emphasis on business process re-engineering and improvement to long-term clinical efficiencies and cost benefits. The need to improve clinical efficiencies and accelerate study times continues to grow, driving industry sponsors to seek and promotes flexible eCRF trial design, build, and speedy deployment, robust data management, real-time data visibility, reporting and analysis, and global trial management and study scalability [53]. Hence, the unique eCRF would help by shortening the clinical trial lifecycle by collecting quality data more quickly and accelerating the availability of data, which are the solutions to a critical path bottleneck that the industry has been working on for many year [54].

Agile transfer or exchange of data

Unique eCRF encompasses the substandard-based exchange of health information from facilities of clinical trials during all phases of project: Experimental designing, institutional review and oversight, enrollment, data collection, analysis and interpretation. eCRF allows doctors, nurses, pharmacist, other health care providers and patients to appropriately access and securely share a patient's vital medical information electronically-improving the speed, quality, safety and cost of patient care [55]. The exchange of information from investigator to CRO or sponsor is easier and transfer could be done at regular interval [56,57]. Information that is needed to be exchanged between the clinical study and Institutional Review Boards, Ethics Committees, regulators or government funding agencies to ensure the safety of subjects in the study becomes easier. Real-time access to the data also allows monitoring of event rate, compliance and adherence to study protocol, which may trigger the conduct of safety review of the study as specified in protocol.

Audit trial services

A systematic and independent examination of trial-related activities and documents to determine whether the evaluated trial - related activities were conducted, and the data were recorded, analyzed, and accurately reported according to the protocol, sponsor's standard operating procedures (SOPs), good clinical practice (GCP), and the applicable regulatory requirement (s). Every action on the unique eCRF portal is tracked and logged in the database, in conformity with regulatory standards and guidelines, since maintaining an audit trail is a 21 CFR Part 11 compliance requirement. eCRF Audit trail logs all changes on data and actions, including username, timestamp and user IP address: Changes made on electronic CRF records, every parameter change of status, systems logins and attempts, users creation, de-activation and grant assignments. The audit trail data can be downloaded and formatted for authorized end-users and readily accessible for internal checks and risk analysis periodic reviews or available for regulatory audits and FDA inspections. Each and every detail of trial would be recorded according to the protocol because software of eCRF will be in compliance to the GCP [58]. It would keep records of the sponsor's audit plan and procedures for a trial audit which should be guided by the importance of the trial to submissions to regulatory authorities, the number of subjects in the trial, the type and complexity of the trial, the level of risks to the trial subjects, and any identified problem. The observations and findings of the auditor would be documented. Coordinators can receive instant feedback when entries are incomplete, inconsistent with previously recorded data, or do not match the required form of the database. In these cases, instant feedback reduces the number of review - query - resolution loops and eliminates the need for data entry technicians to double-enter all collected research data. eCRFs could easily be searched, reviewed, and audited [59]. Therefore unique eCRF allows clear audit trail through individual log-ins.

Financial aid/compensation details

The details about payment of patients or individual involved in trials can also be recorded in detail in unique eCRF. Payment should be given according to the protocol and through eCRF the sponsor, and regulatory authority will also get real time information about how and how much payment is given to individual. Both the amount and method of payment should be recorded and managed to assure that there is no undue influence on the trial subjects. Payment should be properly proportionated and scheduled and should be set forth in written informed consent form. The information about compensation to person involved in trial should also be recorded in patient history. If, any event because of which trial has been stopped in between, unique eCRF will even store all the information of trial, subject involved, compensation given and even why the trial has been stopped. This will not only keep record of patient who are involved in trial but will also keep record of individuals who have left the trial and even reason why he/she have left the trial and also the compensation if any received by the person. The sponsor's policies and procedures should address the costs of treatment of trial subjects in the event of trial-related injuries in accordance with

the applicable regulatory requirement. When trial subjects receive compensation, the method and manner of compensation should comply with applicable regulatory requirement.

DRAWBACK OF ECRF

Patient's privacy breaches

Unique eCRF would improve the doctors' or investigator's ability to share information and make it easier for hospital to differentiate one person from another. However, it would empower government and cooperation to exploit the heath care technology. Patient cannot control that who sees, uses and sells their sensitive health data. It would make it easier to use nation's health information for their own gain without patients even knowing it. Without privacy patient won't trust doctors. Both patients and analysts have expressed concern that eCRF systems will threaten patient privacy and be vulnerable to security breaches [60]. With a fully interoperable eCRF could be accessed from anywhere in the country and transmitted illicitly across the world quickly, cheaply, and with little risk of detection [61]. The security of health information is, in fact, compromised with alarming frequency as a result of computer theft, sale of used computers without removal of data from hard drives, hacking, inadvertent disclosures, and deliberate misuse of information by those with access to it [62]. Table 1 shows comparison between advantages and disadvantages of unique eCRF.

High initial cost

Despite of benefits there are disadvantages associated with it such as financial issues, including adoption and implementation cost, ongoing maintenance cost. Adoption and implementation cost purchasing and installing hardware and software and training end users [63,64]. The credibility of the numerical results of the analysis depends on the quality and validity of the methods and software (both internally and externally written) used both for data management (data entry, storage, verification, correction, and retrieval) and for processing the data statistically. The computer software used for data management and statistical analysis should be reliable, and documentation of appropriate. This therefore also increases the cost. Moreover, more than one software is needed to increase the efficiency e.g. like firewall software for protection this therefore increases the cost.

Susceptibility of software to viruses

Technology is not perfect. Electronic system can develop problem that leads to crashes and viruses. This problem can occur on software, hardware and on any network. Errors which result from computer crashes or from maintenance shutdowns may lead to lost orders. They may also result from system inflexibilities that significantly impede providers' ability to enter non-standard specifications or to order non-formulary medications [65]. Usability problems, such as display and navigation deficiencies, can also cause errors [66]. The anonymous and transient nature of the internet, it can be difficult for trial coordinators to assess the suitability of internet resources that are not directly associated with well-known academic institutions. The transient and anonymous nature of the internet is illustrated by the practice of citing the date of access for electronic resources and by the fact that many documents on the internet do not have a documented author. If a trial relies on a third-party internet resource, there is always the possibility that the third-party website ceases to exist prior to the completion of the study, leaving the coordinators to find an alternative resource to complete the trial.

Table 1: Pros and cons of unique eCRF number

S. no.	Benefits	Drawbacks
1	Integrated health record	Patient's privacy breaches
2	Real time data monitoring	Initial high cost
3	Reduces cost and time	Susceptibility of software to viruses
4	Clinical trial management	Hardware crashes
5	Demographic study record	Prone to mistakes
6	Adverse event reporting	Undesirable synchronization of records
7	Inclusion and exclusion criteria selection	Internet connectivity problems
8	Agile transfer of data	
9	Prevention of duplication of data	
10	Records of drug interactions	
11	Easier randomization process	
12	Spontaneous pharmacovigilance reporting	
13	Financial aid/compensation details	
14	Audit trial services	

eCRF: Electronic case report form

Prone to mistakes

People make mistakes. Doctors, nurses, billing specialist who are imputing information are prone to make mistakes. Security of data is a factor. Medical records should never be altered, however the possibility of changing files may occur either intentionally or unintentionally [67]. Sources of such errors include: Fragmentation of data; failure to integrate all hospital systems; and human - computer interface difficulties rooted in the machine rules' failure to reflect work organization or expected provider behavior [68,69]. Hence therefore there is a need of specialist staff like IT/programmer. Information technology skills required at investigator sites.

Undesirable synchronization of records

Medical record synchronization is another drawback. Different facilities could have their information updated at same time, which could lead health care provider not having updated information when they become available [70]. It is important to identify potential sources of bias as completely as possible and hence that attempts to limit such bias may be made. The presence of bias may seriously compromise the ability to draw valid conclusions from clinical trials. Some sources of bias arise from the design of the trial, for example an assignment of treatments such that subjects at lower risk are systematically assigned to one treatment. Other sources of bias arise during the conduct and analysis of a clinical trial.

Internet connectivity problems

Other disadvantage of an online system includes system performance, lack of live support personnel, and the setup cost. The speed of the online system can be slowed significantly during peak internet traffic and this can prolong every step of a study, from registration to data entry [71]. The lack of a 24 hrs call-in center can lead to the loss of some patients because some study centers may not be able to use online help to solve their difficulties with the study protocol or the registration and randomization steps. To set up and maintain an online clinical trial system requires experienced computer professionals. This might be too expensive for smaller trials where the administration budget is modest.

CONCLUSION

Unique eCRF is a new technology which will be of great importance to clinical trials and to healthcare system. It would be electronic record of each person involved in the clinical trials. Unique eCRF would be designed using the good clinical guidelines ensuring that computer systems are 21 CFR part 11 compliant and that all the SOPs related to data management are in place and adhered to. Unique eCRF will provide a number to every individual in the trial. According to 21 CFR part 11 compliance requires that all persons accessing the clinical data management system must have electronic signatures of their own. All the personnel who access the unique eCRF number must have their unique electronic signature/user IDs. The information of the person involved can only assed through that number like PRAN card, Aadhaar card and permanent account number card. Unique eCRF number will be confidential to patient. It will contain all the information of patient involving all past and present medical history (including vaccination and immunization details), current medical status of person, all the drug allergies to the patient, all the laboratory tests reports will be

stored. Unique eCRF would maintain the confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with applicable regulatory requirement. The world is looking toward development of new drug molecules every minute. Due to increased drug demand and new disease entities like severe acute respiratory syndrome, Ebola virus, there is a great need of development of new drugs. For every new drug a very regulated and controlled clinical trial is the first tool for any drug manufacturing and drug research enterprise. Multicentric clinical trials are the back bone of drug development at international scenario. It is quite likely that same patient may enter in the same clinical trial at different drug trial center. Hence, there is a great need of development of a unique eCRF that could serve as a guide to physician, researcher or any regulatory bodies for avoiding duplicating/manipulations in clinical research. This manuscript is intended to compile and design a unique eCRF to serve above purpose. It will also highlight other potential uses of eCRF as well as drug to draw out some drawbacks related to this new design of unique eCRF. A streamlined unique eCRF end-to-end implementation guarantees the highest quality in the shortest time for the full life cycle of the trial.

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