International Pharmaceutical
PRIVACY CONSORTIUM

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28 February 2011

Dr. Gulshan Rai
Director General, Indian Computer Emergency Response Team
Department of Information Technology
Ministry of Communications and Information Technology
India

Re: Information Technology (Reasonable security practices and procedures and sensitive personal information) Rules, 2011

Dear Dr. Rai:

The International Pharmaceutical Privacy Consortium (IPPC) is an organization formed in 2002 and comprised of chief privacy officers and other data privacy and security professionals from a number of research-based, global pharmaceutical companies. Most IPPC members have significant operations in India. The IPPC is committed to the promotion of sound policies for the protection of patient privacy and advancement of drug development and treatment. Information concerning IPPC membership and mission is described in Appendix A.[1]

We support the efforts of the Ministry of Communications and Information Technology to develop privacy and data protection rules for the protection of sensitive personal data. In furtherance of this objective, we wish to bring to your attention the unique needs of the biopharmaceutical industry with respect to collection, use and disclosure of personal data, and to highlight areas of the draft rules that we believe require further consideration in order to avoid unanticipated negative consequences. Specifically, we will address in these comments the following issues:

1) the territorial application of the rules;
2) the definition of "sensitive personal data";
3) pharmacovigilance;
4) biomedical research; and
5) commonly accepted practices for which consent should not be required.

As part of our work in addressing privacy issues in the biopharmaceutical industry, we have produced and are submitting for your further reference in Appendices B and C of this submission a copy of the IPPC's white papers on *Understanding the Clinical Research Process* and *Understanding Safety Surveillance*.

I. Territorial Application of Rules

As you are no doubt aware, India has become a center for data processing by many multinational companies. Many multinational pharmaceutical companies have established research centers in India or have partnered with domestic biomedical research organizations. It is important that the rules provide

[1] For further information concerning the IPPC, please visit our website at www.pharmaprivacy.org. All Appendices referenced in this comment, and additional documents adopted by the IPPC, are publicly available on this website.

clarity on the scope of their application to information collected outside of India that may be stored, accessed, or used within India. The IPPC further recommends that in order to avoid possible conflicts or inconsistencies with foreign laws, that rules relating to privacy (i.e., sections 4 to 6 of the draft rules) apply only to data collected within India while rules relating to security (i.e., section 7) could apply more broadly to data collected and processed on behalf of organizations in India.

II. Definition of "Sensitive Personal Data"

The draft rules would apply, inter alia, to information consisting of user registration details, financial information, and medical records and history. However, missing from this definition is the critical concept that the information must be individually identifiable. Application of privacy standards designed to provide transparency to people and to protect people from privacy-related harms has no relevance to data that is not individually identifiable. Accordingly, the IPPC urges the scope of the rules to be narrowed to data that reasonably can be used to identify an individual. Absent such a limitation, many beneficial uses of de-identified data, such as public health research using such data, would be prohibited or substantially impeded.

Moreover, where data can be identified principally only through access to a confidential key or some other reference dataset whose disclosure is limited by law or contract, the risk of re-identification is low. We believe the risk of data re-identification must be weighed against the beneficial uses of that data. Thus, for example, we believe that the public interest in advances in medical science warrants permitting pseudonymized (or partially de-identified) data to be used for biomedical research even though there may be some small risk that the data could be re-identified by a researcher.

III. Pharmacovigilance

Pharmacovigilance is the science of activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem (WHO). Adverse events include a range of negative or unexpected reactions to a drug – from relatively minor irritations to potentially life threatening conditions. As required by regulations around the world, in order to safeguard patient safety, pharmaceutical companies must apply internationally recognized Good Pharmacovigilance Practices (GPvP) during drug development and after obtaining marketing authorization. Good Pharmacovigilance Practices are followed in the collection, analysis, and communication of safety information to patients, healthcare practitioners, consumers, and regulators.

Pharmaceutical companies are responsible for the safety of their products, and have ethical, legal, and regulatory obligations to accurately collect, analyze, and report adverse events in a timely fashion both during clinical trials and after a drug is on the market. Internationally recognized pharmacovigilance practices are used to meet these obligations and comply with the requirements and expectations of health authorities. It is therefore critical that any rules governing the collection, use, and disclosure of personal data recognize the vital need for pharmaceutical companies to be able to continue to collect and analyze pharmacovigilance data. These important public health uses should be recognized as an exception to any more general requirements to obtain individual consent to the collection, use or disclosure of personal data. We urge sections 4, 5, and 6 of the draft rules to be modified accordingly.

Access to identifiable information may be required for GPvP purposes. Examples of uses of identifiable information during GPvP include:

1. To enable contact with patients or adverse event reporters (including healthcare professionals) to ensure appropriate treatment is given as promptly as possible. The pharmaceutical company may have access to information that may not be known to the patient/reporter/treating physician. It is critical that this information can be communicated quickly to help remediate any adverse events.

2. To obtain additional information necessary for analysis of possible safety issues. For example, further information might be necessary in order to determine the clinical/biological pattern of the adverse event and identify circumstances that could increase the risk of its occurrence. Such additional information is typically obtained through active contact (follow-up) with patients, healthcare professionals, or others. These follow-up attempts are required by regulation and are standard components of GPvP.

3. To meet the regulatory requirements of various health authorities around the world who require specific information in order to consider an adverse event report to be valid. ICH Guideline E2D requires one or more of the following: age (or age category, e.g., adolescent, adult, elderly), gender, initials, date of birth, name, or patient identification number.[2]

4. To compare newly received adverse event reports with previously received reports, for the purposes of identifying duplicate cases. Identifying duplicate cases is important to avoid overestimating the incidence of specific events either by company or regulatory safety experts.

A number of technical and organizational controls typically protect pharmacovigilance data from unauthorized access, use, alteration, loss, disclosure or other processing. It is standard practice for pharmaceutical companies to have separate groups within their organization that are responsible for pharmacovigilance as well as separate files and databases to support these activities. The employees of the company who are responsible for pharmacovigilance activities are bound by obligations of confidentiality covered by the company's employment contracts, policies or standard operating procedures. Even within a pharmacovigilance group, confidential information learned in the course of such activities is shared only as necessary to conduct activities such as statistical analyses and regulatory reporting. In all cases, these activities are subject to rigorous health regulatory controls. These regulatory controls require that (i) access to systems containing pharmacovigilance data be restricted to those who require it in order to perform job functions; (ii) audit trails be maintained that track all database changes; and (iii) systems undergo validation to ensure accuracy, reliability, and consistent intended performance. These controls are subject to inspection by health regulators.

IV. Biomedical Research

Personal health data is essential for, *inter alia*, conducting research involving genetics and biomarkers, seeking genetic patterns in the safety and effectiveness of drug therapies, determining the safety and effectiveness of new treatments, and locating appropriate participants for clinical research studies. The IPPC believes that the draft rules could have the unintended effect of stifling important biomedical research, and we urge that further consideration be given to how the rules should apply in this context.

Informed consent was originally conceived as a protection against physical harm to patients, permitting informed, competent patients to refuse unwanted medical interventions and to ensure patients were informed of the physical risks involved in medical research. However, informed consent has come to be used as protection against a broad range of nonphysical harms, such as breaches of privacy and confidentiality. The reliance on notice and choice as the basis for permitting analysis of patient information for pharmacoepidemiological research or using biospecimen samples for biomarker and genomics research is becoming increasingly unworkable. Despite the clear importance of the ethical principles of respect for persons and autonomy, which serve as the basis for informed consent requirements, these principles are not absolutes and must be balanced with other ethical principles, such as beneficence. Beneficence requires that members of society recognize the longer term benefits and risks that may result from the improvement of knowledge and from the development of novel treatments.

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[2] *See* http://www.fda.gov/RegulatoryInformation/Guidances/ucm129457.htm

Example: Secondary Research Using Key-Coded Data

One example of how the draft rules could impede biomedical research involves the analysis of key-coded data collected in prior clinical or other research studies for additional research purposes. These additional purposes could, for example, involve further examination of the disease or condition in question, or examination of some unanticipated, secondary benefit of an investigational drug. Because secondary research purposes have not been, nor can they be, specifically determined at the time of the primary research, they can only be described in broad strokes or general terms in the initial clinical research informed consent process.

Researchers working for the sponsor to conduct secondary research analyses have no need, intent or reasonably available means to identify patients. Indeed, the purposes of secondary research typically are similar to retrospective epidemiological analyses and include, among other things, further analyses of factors involved in disease and treatment of disease. In both primary and secondary research using key-coded data, researchers within the sponsor organisation do not have access to the confidential key that would reveal data subjects' identities. Access to identified or identifiable information by field monitors and pharmacovigilance staff should not be imputed to sponsor researchers who use key-coded data for primary and secondary research purposes but do not have access to the confidential key.

To require sponsors to obtain specific detailed consent for secondary research uses would necessitate recontacting subjects. Since subject contact information is held by external investigators involved in the original study, it is presumably these investigators who would need to contact patients, even though these investigators may not otherwise be involved in the secondary research project. The inability to recontact subjects (e.g., because of relocation of the data subjects or lack of cooperation by original study investigators who are not involved in the secondary analyses) will reduce population sample size, thereby increasing statistical uncertainty in secondary research conclusions and in many cases completely prevent the research from proceeding. Moreover, in many cases the inability to recontact subjects to obtain consent may not be random and may vary in ways that bias study results.[3] These risks and burdens are unnecessary given the protections already in place that prevent secondary researchers from identifying data subjects.

V. Commonly Accepted Practices

The IPPC believes that certain commonly accepted practices should be excluded from requirements to provide choice before collecting and using individuals' personal data. This is consistent with the approach to privacy protection being considered by the United States Federal Trade Commission[4] and with exceptions to consent that are embedded in the European Data Protection Directive 95/46/EC. Such commonly accepted practices might include:

- Product and service fulfillment;
- Organizational restructuring;
- Fraud prevention; and
- Legal compliance.

In the case of product and service fulfillment, we believe that consent can be inferred from the context of the transaction. In the other cases, we believe that public policy reasons dictate that consent should not be required. For example, consent should not be required to disclose personal information to

[3] *cf.* S. J. Jacobsen et al., "Potential effect of authorization bias on medical record research", 74 Mayo Clin. Proc. 330-38 (1999).
[4] *See* US Federal Trade Commission, "Protecting Consumer Privacy in an Era of Rapid Change: A proposed Framework for Businesses and Policymakers" (December 2010).

successors-in-interest of a product or service (through merger or acquisition) and for subsequent uses and disclosures of the personal information by such successors-in-interest, to the extent these uses and disclosures would have been permitted by the prior entity.

We thank you for your consideration of our comments and would welcome the opportunity to discuss these issues with you. Please do not hesitate to contact us with any questions.

Sincerely,

Peter Blenkinsop
Secretariat and Legal Counsel

APPENDIX A: INTERNATIONAL PHARMACEUTICAL PRIVACY CONSORTIUM

MEMBERS

The IPPC is an association of companies that face worldwide responsibility for the protection of personal health information and other types of personal data. Members of the IPPC include:

- Abbott Laboratories
- AstraZeneca
- Baxter International
- Bristol-Myers Squibb
- Elan Pharmaceuticals, Inc.
- Eli Lilly and Company
- GlaxoSmithKline
- Merck & Co., Inc.
- Novartis
- Pfizer Inc.
- Genentech (Roche)
- Sanofi-aventis
- Takeda Pharmaceuticals

MISSION

The IPPC was formed in 2002 to promote responsible privacy and data protection practices by the research-based, global pharmaceutical industry. Maintaining data confidentiality and subject privacy are essential to clinical research, pharmacovigilance, and other activities of the pharmaceutical industry. The IPPC seeks to increase awareness of privacy and data protection issues and to engage government in a dialogue about the need for data to support cutting edge biomedical research and other public health activities. The IPPC pursues opportunities to collaborate with government and other stakeholders to develop data protection practices that enhance data subject privacy.

GOALS

The IPPC goals are to:

- Engage government and stakeholders in the biomedical research and healthcare communities in a constructive dialogue on significant issues of privacy and data protection.
- Serve as a resource for sound analyses of privacy and data protection requirements and compliance tools tailored to the pharmaceutical industry.
- Serve as a forum for industry dialogue and promote responsible privacy and data protection practices.
- Promote consistent privacy and data protection standards that can be achieved on a worldwide basis.
- Remain on the leading edge of privacy and data protection.

SCOPE OF ACTIVITIES

The IPPC advances understanding of existing and emerging data protection and security rules in Europe, the US, and other key countries. The Consortium engages regulators and policymakers in the following areas:

- Biomedical research
- Pharmacovigilance
- Sales and marketing
- Market research
- Human resources programs
- Other corporate programs

APPENDIX B: PHARMACOVIGILANCE WHITE PAPER

Understanding Safety Surveillance

Pharmaceutical companies have ethical and regulatory responsibilities to collect, analyze, and communicate information about the safety of their medicines. These responsibilities begin in a drug's research and development and continue throughout the drug's lifespan.

Safety in Clinical Studies

Pre-approval clinical studies are conducted to evaluate the safety and efficacy of a new medicine. Phase I studies are structured to test the safety of an investigational compound in small numbers of subjects. The outcomes of these studies are used to help design and determine dosing in later studies. All of the information that is known about a drug's safety profile is included in the Investigator Brochure that is provided to clinical investigators. Any events that occur that are not included in the Investigator Brochure are classified as "unexpected." Any events that are fatal, life-threatening, require inpatient hospitalization, result in significant or persistent disability or incapacity, or result in congenital anomalies are considered serious adverse events (SAEs). If a sponsor believes that an unexpected, serious adverse event is causally related to the study medicine, the sponsor is required to report the "Suspected Unexpected Serious Adverse Reaction" (SUSAR) to regulatory authorities on an expedited basis. Within 7 days of becoming aware of any fatal or life-threatening event, a sponsor must report the event to regulatory authorities. Additional follow-up information on the patient's status must be provided in 15 days.

Whenever a potential new serious risk is discovered, the study sponsor is required to notify investigators. Either the sponsor or the investigators will inform the independent ethics committees overseeing the study, who in turn will determine how this information is to be communicated to patients. Patients may be asked to renew their informed consent to participation in the study following receipt of this new information.

Postmarketing Surveillance

While the most commonly occurring side effects can be identified during pre-approval clinical studies, rare adverse events, as well as those with long latency periods, may not be detected until after a medicine is approved for widespread distribution. Unsolicited, "spontaneous" reports may be received from healthcare providers or other caregivers, patients, lawyers, the media, or regulatory authorities, among other sources. Any events that are not listed in the medicine's label (*i.e.* the Prescribing Information or Summary of Product Characteristics) are classified as unexpected. All spontaneously reported serious adverse events must be reported to regulatory authorities within 15 days, regardless of believed causation. The 15 day reporting timeframe begins whenever any person in the company, or a person working on behalf of the company, becomes aware of the event. The manufacturer is subsequently expected to report any significant follow-up information it learns about the case. At periodic intervals, the manufacturer is required to submit aggregate reports of all safety data collected on the medicine.

In most pharmaceutical companies, as soon as a report of a possible adverse event is received, the information is entered into a safety database. Physicians, scientists, and other professionals in the company's medical safety department review each case and determine whether expedited or regular, periodic reporting is required. Additional information may be requested to better understand the circumstances surrounding a particular case. The medical safety department professionals also determine whether, as a result of the new information, changes to the medicine's label are necessary.

Whereas only a few years ago, most safety data was reported to regulatory authorities using paper forms, today most reporting is conducted electronically. Electronic reporting has the advantage of allowing simultaneous transmission of safety data to multiple regulatory agencies around the world.

Analyzing Safety Data

Information that has been entered into a company's safety database undergoes both qualitative and quantitative analyses by medical safety department professionals to identify possible safety signals. Qualitative analysis involves an examination of the circumstances leading to an adverse event to identify a possible causal link. Quantitative analysis involves using statistics to determine whether certain adverse events are occurring with a greater frequency than previously expected. Both qualitative and quantitative analyses are necessary to identify and evaluate possible safety signals. Often, however, it is not possible to fully evaluate a possible safety signal using spontaneous report data alone. Further investigation of possible safety signals may involve re-examination of previously collected clinical study data to determine whether such signals were present during clinical trials, undertaking new clinical studies designed to produce information concerning the possible signal, or conducting observational/pharmacoepidemiologic studies.

Confidentiality of Safety Data

A number of technical and organizational controls typically protect pharmacovigilance data from unauthorized access, use, alteration, loss, disclosure or other processing. It is standard practice for pharmaceutical companies to have separate groups within their organization that are responsible for pharmacovigilance, as well as separate files and databases to support these activities. The employees of the company who are responsible for pharmacovigilance activities are bound by obligations of confidentiality covered by the company's employment contracts, policies, or standard operating procedures. Even within a pharmacovigilance group, confidential information learned in the course of such activities is shared only as necessary to conduct activities such as statistical analyses and regulatory reporting. In all cases, these activities are subject to rigorous controls and inspection by health regulators. These regulatory controls require that (i) access to systems containing pharmacovigilance data be restricted to those who require it in order to perform job functions; (ii) audit trails be maintained that track all database changes; and (iii) systems undergo validation to ensure accuracy, reliability, and consistent intended performance.

APPENDIX C: CLINICAL RESEARCH WHITE PAPER

Understanding the Clinical Research Process

The evolution from scientific hypothesis to approved and marketed medicine is a lengthy and arduous process that typically spans many years of research and development. To understand clinical research and data flows, one must understand what medicines are, how they are created, how they are tested and monitored, and how they are approved.

Preclinical Studies

Described in its most basic form, a drug is a chemical compound or biologic product designed to affect a process in the body. Before a drug is tested in humans, it goes through several types of preclinical research in a laboratory. Preclinical research could include research in (i) test tubes to analyze the biochemical interactions of the drug with other molecules, (ii) non-animal systems such as cell and tissue cultures, (iii) computer models, and (iv) animal research to evaluate physiological responses.

Once a compound shows, via such non-human research, promise of safety and effectiveness in potentially addressing a particular need in humans, it may then be considered for human evaluation, or clinical development. Prior to initiating research in humans, the pharmaceutical sponsor must make appropriate regulatory filings and obtain the appropriate government's agency permission and independent ethics committee approval to initiate clinical studies, *i.e.,* studies involving humans.

Clinical Studies

There are traditionally four phases to clinical drug research. The objective of Phase 1 studies is to understand how the investigational compound is handled / metabolized by the body and to assess whether the compound is generally *safe* and tolerable for use in humans. Researchers typically conduct studies in a small number of healthy volunteers to answer this question. These volunteers are typically paid for their participation and often the studies are conducted in specialized clinical units to allow close monitoring. For certain types of investigational compounds, such as anticancer agents, Phase 1 studies may be conducted using participants who have the type of disease the compound is intended to treat. Phase 1 studies indicate whether the investigational compound is well tolerated, and researchers gain a better understanding of the safe dosage range for the potential new medicine and possible side effects.

The objective of Phase 2 studies is to evaluate whether the investigational compound has the desired effect in the target patient population in the identified safe dosage range. In contrast to Phase 1, Phase 2 studies typically are conducted with volunteer participants who have the disease or condition under consideration. It is common in clinical studies to randomly assign some of the volunteers to receive the compound being evaluated (the "treated group") and to give the other volunteers (the "control group") either a placebo or an active control that is formulated to resemble the compound. A placebo lacks any active ingredient(s), while an active control is an existing treatment to which the proposed drug will be compared in effectiveness and safety. In the majority of Phase 2 studies, neither the volunteer nor the investigator know the treatment that the volunteer participant is receiving during the conduct of the study, i.e. the study is conducted in a double-blind fashion. To ensure a fair and meaningful comparison, the participants in the treatment and control groups are closely matched in age, gender, race, health condition, life-style habits and other characteristics that

may impact the outcome of the study. Comparing the study results from the group who received the compound with results from the control group assists researchers, drug developers, and later the regulator reviewers, in assessing whether the compound is having the desired effect.

The objective of Phase 3 studies is to firmly establish the safety and efficacy of the investigational compound through randomized, controlled, double-blind trials conducted in larger groups of volunteer participants. Where appropriate, further studies may evaluate the compound in special populations, or assess the effects of its prolonged use. At the conclusion of successful Phase 3 studies which show that the compound is effective and well tolerated at the suggested doses, the sponsor of the research will submit an application to the appropriate regulatory body seeking approval to market the product.

Once the drug is marketed, it may be further studied in post marketing research, or Phase 4 studies. The objective of these studies may be to learn more about the safety and efficacy profile of the drug by studying it in broader populations, assess real world experiences with the drug, study the medicine in different healthcare settings, or to satisfy any applicable post-marketing requirements for final approval of the drug.

Study Preparation

Clinical studies are designed to specifically address and meet the objectives of each Phase of research. Designing studies to meet these objectives is a complex endeavor, and planning is essential to successfully navigate the clinical research process. Filing the appropriate applications with regulatory bodies and independent ethics committees is a prerequisite to conducting research in humans with an investigational compound. As part of the approval process, sponsors of research compile a clinical development plan, preliminary protocol, preclinical data, chemical composition and information on the manufacturing process.

Central to all studies is the sponsor's and researcher's focus on protecting the rights, safety, and well-being of research participants. Many factors go into the preparation for a study, ranging from protocol development, to investigator and site identification, to appropriate monitoring of participants' responses to treatment. Many of these processes involve an assessment of appropriate research participant populations and their ability to meet the rigorously established inclusion criteria, which determine whether a potential participant qualifies to participate. Inclusion and exclusion criteria are carefully developed for each compound individually by the sponsor company in consultation with the appropriate regulatory agency. The selection of participation criteria is driven by the need to document with scientific rigor the drug's effect on humans, and depends on the investigational compound's proposed indication for use, intended patient population, incidence of the pertinent medical condition, and other factors.

The sponsor of drug research, either independently or in conjunction with the independent researchers who will ultimately conduct the clinical studies, works to finalize the clinical development plan to address the types and design of studies to be undertaken and the precise questions to be addressed. The sponsor may also seek outside researchers' input to finalize the protocol, which is a written plan describing in detail the planned conduct of the study. The protocol is prepared in accordance with the internationally accepted guidelines, the International Conference on Harmonisation / Good Clinical Practices Guidelines (ICH/GCP).

The protocol serves as the roadmap by which investigators will conduct the research. It includes details such as the method of assignment to treatment groups, dosage and duration of

treatment, number of sites contemplated, and the number of participants sought. It also delineates inclusion and exclusion criteria. The protocol also provides the measurement parameters for safety and efficacy, general procedures such as the types and frequency of patient evaluations and visits, and appropriate processes to address participant withdrawal from the study.

Partnerships in Clinical Research

Drug developers serve as sponsors of clinical research, and as such, perform critical evaluations to identify appropriate sites and independent investigators to conduct the research. Interacting with site personnel and potential investigators is critical for sponsors. Sponsors must locate healthcare professionals who will have access to populations meeting enrollment criteria and who are appropriately trained to conduct studies, including knowledge of the many applicable regulatory requirements and privacy laws. Sponsors will then engage those sites and investigators to conduct the studies in accordance with the developed protocol.

To assist in the clinical research process, sponsors of research sometimes also engage contract research organizations (CROs) and/or field monitors, known as clinical research associates (CRAs) to undertake on the sponsor's behalf many of the research oversight functions.

Once investigators and sites are selected and approvals to conduct the study in humans have been obtained from the government agency and the relevant independent ethics committees, the study can begin. The success of a study ultimately hinges on the collection of accurate data, which the sponsor oversees through the use of study monitors, whose responsibilities include authenticating source data.

Data Collection, Processing and Transfer

As collection of medical information is instrumental to the conduct of clinical research, procedures to address data integrity and confidentiality are routinely implemented. Before each research volunteer is enrolled in a study, the researchers seek his or her informed consent to participate. The informed consent process, in addition to the other details of a proposed study protocol, are reviewed and approved by appropriately constituted independent ethics committees.

The independent ethics committees, typically constituted of medical professionals and non-medical members, are responsible to ensure the protection of the rights, safety and well-being of research participants involved in a trial and to provide public assurance of that protection, by, among other things, reviewing and approving/providing favorable opinion on, the trial protocol, the suitability of the investigator(s) facilities, and the methods and material to be used in obtaining and documenting informed consent of the trial subjects. Once the independent ethics committee approves the study and documentation to be shared with potential research participants, the investigator is permitted to proceed.

During the informed consent process, the investigator and clinical study staff explain to the participants the purpose of the study, the expected procedures, the types and frequency of evaluations, the potential health and informational risks and benefits of the study, and the voluntary nature of their participation, including the participant's right to withdraw from the study after it has begun. The informed consent process also includes a description of the individuals and entities who will have access to study data, and the likelihood that such data will be shared with affiliates and regulators. Sponsors require potential participants to document their understanding of the information provided to them and encourage potential participants to ask any questions they may have. This deliberate

process of explaining all key elements of the study and seeking a participant's permission to enroll is critical to assuring voluntary and informed participation.

The success of a clinical research project depends on the sponsor's ability to collect accurate and complete data for analysis. The critical mechanism by which clinical investigators communicate study results back to the drug sponsor is the case report form (CRF), which can be either a hard copy document or an electronic data record. The CRF is the primary data capture tool in clinical research studies. By completing the CRF, investigators are able to provide the sponsor with the necessary data that the sponsor will analyze. Use of the CRFs ensures consistency in reporting of data across multiple studies. The length and complexity of a CRF may vary from study to study. However, regardless of a study's design or level of complexity, a sponsor, through the CRF, seeks to capture essential data, attempts to minimize data redundancy, and seeks to ensure data compatibility for analysis across multiple studies for an investigational compound. CRFs generally do not contain directly identifiable patient information, such as name and address, however, they may include patient initials as a mechanism to ensure the accuracy and integrity of the information gathered. Rather, CRFs are typically coded to protect the identity of participants, yet retain an ability to assimilate health and chronological data from the same participant for a meaningful analysis of the study results.

Data is collected from research participants at many different times throughout a study. Research participants' data and samples may be collected directly from them based on investigator interviews or physical examinations. Also, data may be sent to laboratories engaged to perform specific tests necessary for the study. These laboratories may be at the investigator site or at another location. A "central" laboratory, possibly located in another state or country, may be used to ensure consistency in tests or analysis of clinical measurements to permit more accurate comparison of results across several study sites.

Data collected at the study site and transmitted to the sponsor is typically entered into databases. It is then reviewed for accuracy and any anomalies. If, as a result of this data integrity review, certain data is questioned, the sponsor may direct one of its agents, such as a CRA, to review the source data and work with the investigator to correct the CRF if a transcription error is identified. Once the sponsor is satisfied that the data set is complete and accurate, it then begins the process of analyzing the data and assessing the results of the study. Upon conclusion of this analysis, the sponsor will take steps to prepare a study report, which may be included in submissions to various regulatory authorities.

Role of Government Regulatory Agency

The permission to market a drug is granted to drug sponsors by a government regulatory agency. The drug developer applying for marketing authorization must provide the agency with a comprehensive review of conducted clinical and non-clinical studies. If the presented results satisfy the requirements established by the government agency's scientists and policy-makers, the drug application may be approved. Otherwise, additional studies and supporting information may be required for approval.