International Pharmaceutical
PRIVACY CONSORTIUM

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3 August 2011

VIA EMAIL TO COFEMER@COFEMER.GOB.MX

Lic. Alfonso Carballo Pérez
Director General
Comisión Federal de Mejora Regulatoria

Re: 03/1877/060711 (Reglamento de la Ley Federal de Protección de Datos Personales en Posesión de los Particulares)

Dear Mr. Carballo Pérez:

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 member companies have significant operations in Mexico, with substantial economic investment in scientific research, human health, animal health, and related IT systems and customer operations. Our companies also partner with local governments and non-governmental organizations to ensure Mexican citizens have access to medicines and important vaccines. 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]

Because information is critical to scientific research and improvements in human health, members of the IPPC support the efforts of the Ministry of Economy to develop data privacy and security rules for the protection of personal data. In furtherance of this objective and in order to avoid unanticipated, negative consequences, we wish to bring to your attention some unique impacts of the proposed regulations on the biopharmaceutical industry. Specifically, we will address in these comments the following issues:

1) the use of key-coded data in scientific research;
2) sensitivities related to the exercise of ARCO rights during ongoing clinical studies;
3) support for exempting from notice and consent requirements the processing of personal data for public health activities;
4) support for Coordination at the administrative level for the joint issuance of secondary or interpretative regulations between departments impacting our member companies such as those issued by the Comisión Federal para la Protección contra Riesgos Sanitarios (COFEPRIS); and
5) the importance of aligning Mexican privacy rules with international standards that govern privacy in the global health care and biopharmaceutical industries.

[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.

I. Application of the Regulation to Key-Coded Scientific Research Data

IPPC Recommendation

Article 35 of the final regulation should explicitly state that key-coded scientific research data is not identifiable, as defined in Article 5, § VII, by persons without access to the key.

The Ley Federal de Protección de Datos Personales en Posesión de los Particulares (LFPDPPP or "the Act") defines "personal data" as "any information concerning an identified or identifiable individual." (LFPDPPP Art. 3, § V.) The draft regulation, in turn, defines an identifiable individual as one who can be identified, directly or indirectly, by reference to any information concerning his physical, physiological, mental, economic, cultural or social characteristics. (Art. 5, § VII.) The regulation further states that a person shall not be considered identifiable if identification requires disproportionate time or effort.

The IPPC agrees with the proposed definition of what constitutes an identifiable individual but encourage the issuance of further guidance on its application to key-coded research data in order to avoid future interpretive uncertainty. "Key-coded data" is data which has had information that identifies a particular data subject – i.e., name, address, national health number, etc. – replaced with an identification code that is not derived from information related to the data subject. In clinical trials, keys are maintained securely at the trial sites, and only key-coded data is reported to the pharmaceutical sponsor. Pharmaceutical researchers do not have access to the keys, and, therefore, the time and effort required to re-identify the key-coded data by such researchers would be disproportionate.

The IPPC asks that Article 35 of the final regulation explicitly state that the use of key-coded research data is not identifiable and therefore not subject to "personal data" requirements when used by researchers to conduct analyses and to develop, test, and confirm research hypotheses. In contrast, we note that key-coded data would be considered "personal data" subject to the requirements of the regulation when in the hands of persons with access to the key. For example, pharmaceutical companies are required under health regulations to employ field monitors to verify that patient data reported by clinical investigators is accurate. Such monitoring and auditing is designed to prevent fraud and ensure scientific integrity. Field monitors have access to the keys and, therefore, would be subject to the requirements of the regulation.

To implement our recommendation, we suggest the addition of the following language to Article 35 of the regulation:

> The key-coding of statistical, historical, or scientific information for further use by scientific researchers shall be considered an acceptable dissociation procedure under Art. 3 § VIII of the Act. The use of key-coded data shall therefore be exempt from the requirements of the Act and this regulation by researchers without access to the key, provided the data controller implements reasonable and appropriate controls to prevent the use or disclosure of the data for purposes other than historical, scientific, or statistical research.

II. Restriction on Exercise of ARCO Rights During Ongoing Clinical Studies

IPPC Recommendation

The final regulation should permit the restriction of ARCO rights as necessary to maintain the integrity of historical, scientific or statistical data. Similarly, researchers should be permitted to continue to process personal data created or collected in a clinical study prior to the revocation of consent by a research subject.

Information integrity is critical to scientific research. For this reason, during ongoing clinical studies, it is often necessary to limit research subjects' access to study records because it may prejudice the outcome of the trial. This may be necessary because, for example, the research subjects may be participating in a blinded study where they are not supposed to know what treatment they are taking (or, indeed, whether they are taking a placebo) or what the clinical investigator has observed. Temporary restrictions on access are necessary in order to preserve the scientific integrity of the study. Research subjects are able to access records about them when the study concludes or after their withdrawal from further participation. Therefore, the final regulation should permit the restriction of ARCO rights during ongoing clinical studies. To implement this recommendation, we suggest the addition of "ongoing clinical research studies" to the list of reasons in Article 75 for which ARCO rights can be restricted.

Scientific integrity also requires that researchers be permitted to continue to process personal data created or collected in a clinical study prior to the revocation of consent by a research subject. As a practical matter, a patient's decision to revoke consent amounts to a decision to withdraw from the research study. Standard practices and regulatory guidelines in Mexico and abroad provide that the data collected on a patient prior to withdrawal from a clinical trial must be available for further review, analysis, and disclosure for purposes of the clinical trial.[2]

This practice is supported by international standards and guidelines. Indeed, guidelines issued by the *International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use* (ICH) state that "ignoring the patients who dropped out of the study and drawing conclusions based only on patients who completed the study can be misleading."[3] Similarly, guidance issued by the United States' Food and Drug Administration states as follows:

> [D]ata collected on study subjects up to the time of withdrawal must remain in the trial database in order for the study to be scientifically valid. If a subject withdraws from a study, removal of already collected data would undermine the scientific, and therefore the ethical, integrity of the research. Such removal of data could also put enrolled subjects, future subjects, and eventual users of marketed products at an unreasonable risk. [4]

In order to ensure that data collected on study subjects up to the time of revocation of consent can continue to be processed, we recommend that Articles 18 and 90 of the regulation refer back to

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[2] For example, *see* International Conference on Harmonisation efficacy guideline E3, *Structure and Content of Clinical Study Reports*, for a discussion of information that should be included in clinical study reports for patients who are discontinued from a study after enrollment.

[3] ICH efficacy guideline E3, *Structure* and *Content of Clinical Study Reports,* at § 11.4.2.2.

[4] US FDA, "Guidance for Sponsors, Clinical Investigators, and IRBs: Data Retention When Subjects Withdraw from FDA-Regulated Clinical Trials," *available at* http://www.fda.gov/downloads/regulatoryinforamtion/guidances/ucm126489.pdf.

Article 26 § V of the Act and affirmatively state that such processing is in the "public interest." We believe that this is consistent with Article 8 of the Act which states that revocation of consent shall not have "retroactive effects."

III. Exemption from Notice and Consent Requirements for Pharmacovigilance

IPPC Recommendation

The final regulation should exempt activities in furtherance of safeguarding public health, such as the processing of personal data for purposes of reporting and analyzing drug adverse events, from the requirements to provide a privacy notice and obtain the data owner's consent.

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 in Mexico and 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 that Article 12 of the draft Regulation 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.[5]

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.

To ensure that the processing of personal data for pharmacovigilance purposes remains unhindered, we suggest the addition of a new article to the regulation, which would provide as follows:

> Art. [X]. The processing and transfer of personal data for purposes of public health activities shall not be subject to the requirements of Articles 12, 20, and 61 of this regulation

IV. Need for Coordination Between IFAI and COFEPRIS

IPPC Recommendation

The final regulation will have unique impacts on the pharmaceutical industry. Close coordination is needed between the IFAI and Comisión Federal para la Protección contra Riesgos Sanitarios to ensure data protection requirements are harmonized with health authority requirements.

Article 64 of the draft regulation requires the IFAI to coordinate with other governmental agencies and departments on an as needed basis. The IPPC supports active coordination between the IFAI and COFEPRIS to ensure that the regulation does not have unintended impacts on the pharmaceutical industry. We look forward to working with both authorities to ensure that personal data of patients and medical research subjects continues to enjoy robust protection without unnecessarily impeding medical research and pharmacovigilance activities.

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

V. Need for International Coordination on Privacy Standards

IPPC Recommendation

International cooperation and coordination is needed to ensure consistency in privacy guidelines and requirements. The regulations should recognize that compliance with existing international standards such as EU-US Safe Harbor, EU Binding Corporate Rules, and the Asia-Pacific Economic Cooperation (APEC) privacy principles may also be a way to demonstrate compliance with the Act and regulations.

Article 39 § VII of the Act requires the IFAI to cooperate with other international bodies and supervisory authorities, in order to assist in the area of data protection. Similarly, §§ V and IX respectively call for the dissemination of international best practices and standards for information security and the participation of the IFAI in international data protection forums. The IPPC supports the goal of harmonizing data protection requirements in Mexico with requirements in other parts of the world.

Articles 66 to 70 of the draft regulation address binding self-regulatory arrangements as a means of demonstrating compliance with the Act and regulation. The IPPC believes such self-regulation can play an important role in demonstrating compliance both for processing of personal data within Mexico and for transfers of personal data from Mexico to other countries:

- Because of the compliance difficulties that are created for multinational companies when multiple jurisdictions apply their laws to the same processing of personal data, the IPPC encourages Mexico to grant recognition to EU-approved binding corporate rules as a binding self-regulatory arrangement that demonstrates compliance with the Act and regulation. Similarly, BCRs should be recognized as satisfying the conditions under Articles 60 to 63 for transfers of personal data, provided that the BCR covers data flows from Mexico.
- The IPPC supports recognition of a company's certification to the Safe Harbor Agreement between the European Union and United States as also demonstrating compliance with Articles 60 to 63 of the draft regulations, provided a company extends its certification to personal data flows from Mexico to the United States.

We thank you for your consideration of our comments and would welcome the opportunity to discuss these issues with you. 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*.

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
- Eli Lilly and Company
- GlaxoSmithKline
- Merck Sharp & Dohme
- 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.

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.