

INTERNATIONAL PHARMACEUTICAL PRIVACY CONSORTIUM

COMMENTS IN RESPONSE TO THE CONSULTATION PAPER ON THE USE AND SHARING OF PERSONAL INFORMATION IN THE PUBLIC AND PRIVATE SECTORS

I. INTRODUCTION

The International Pharmaceutical Privacy Consortium (IPPC) is an organization formed in 2002 and comprised of chief privacy officers and other privacy professionals from 15 research-based global pharmaceutical companies, all of which conduct business in the United Kingdom and other parts of the European Union.¹ Membership and mission of the IPPC is described in Attachment A.

The Data Sharing Review requested by the Prime Minister provides a welcome opportunity to assess the effectiveness of the Data Protection Act 1998 (the “Act”) in achieving a balance that protects individual privacy while still enabling the use and sharing of information to protect public health and advance medical science. With this in mind, it is appropriate to examine and compare application of the Act to application of data privacy laws in other EU member states. Although EU Directive 95/46/EC on the Protection of Individuals with Regard to the Processing of Personal Data and on the Free Movement of Such Data (the “Directive”) was intended to harmonise information practices across the EU, divergent interpretations of the Directive have resulted in disparities in its implementation.

Pharmaceutical companies use and share information for biomedical research and pharmacovigilance. Maintaining data confidentiality and subject privacy are essential to these activities. Privacy-protecting safeguards have been incorporated throughout the extensive regulatory systems under which pharmaceutical companies must operate and have been integrated into pharmaceutical processes. Data protection authorities and patients alike must have confidence that medical research and pharmacovigilance data are collected and processed in a way that respects the rights of data subjects. It is equally important to understand the way data is used during medical research and pharmacovigilance activities and to appreciate the real-world implications of greatly restricting or prohibiting certain data flows that are vital to live-saving research and safety reporting activities.

These comments are organised as follows: Section II provides background on the kinds of information pharmaceutical companies collect, hold and share; how this takes place; and the purposes for these processing activities (Consultation Questions 1 and 2). Section III responds to other specific questions posed in the Consultation Paper.

II. BACKGROUND

A. *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

¹ These IPPC comments were prepared in close consultation with IPPC member companies. However, the IPPC did not have sufficient time to obtain specific endorsement of these comments by every IPPC member company.

minor irritations to potentially life threatening conditions. As required by regulations in the EU and elsewhere, 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.

Access to identifiable information (*i.e.*, “personal 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 organisational 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 organisation 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 apart from the Data Protection Act. 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

² Available at: <http://eudravigilance.emea.europa.eu/human/docs/ICH%20E2D.pdf>.

undergo validation to ensure accuracy, reliability, and consistent intended performance. These controls are subject to inspection by health regulators.

B. Biomedical Research

i. Clinical Trials

Clinical trials are studies designed to evaluate the safety and efficacy of investigational medications by monitoring their effects on healthy volunteers or patients. Clinical trials are often randomized and controlled, meaning that the effects of an investigational medication are studied by comparing a group of patients receiving the treatment to a group not receiving the treatment (e.g., a placebo). The assignment of patients to each treatment group is random. This type of research necessarily involves direct interaction between the clinical trial investigator and research subjects. It also involves both the use of existing health-related data of research subjects (generally, to determine if the individual meets the inclusion/exclusion criteria for the study) and the creation and examination of new data. The IPPC has prepared the attached Clinical Research White Paper that provides detailed background on how clinical trials are conducted and the privacy controls that are incorporated into study procedures (see Attachment B).

The protection of patient privacy and data confidentiality in the conduct of clinical trials has long been a cornerstone of human subjects research. Pharmaceutical companies adhere to strict protections that have been incorporated into international standards for acceptable clinical research. For example, Good Clinical Practice guidelines adopted by the International Conference on Harmonisation³ specify that “[t]he confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s).”⁴ Moreover, “[f]reely given informed consent should be obtained from every subject prior to clinical trial participation,” and “[a] trial should be conducted in compliance with the protocol that has received prior institutional review board (IRB)/independent ethics committee (IEC) approval/favourable opinion.”⁵ Above all else, “foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual trial subject and society. A trial should be initiated and continued only if the anticipated benefits justify the risks.”⁶ These guidelines have also been reduced to law, both at the European Commission level through the Clinical Trials Directive (2001/20/EC)⁷ and in the UK through the Medicines for Human Use (Clinical Trials) Regulation 2004.⁸

A detailed explanation of the types of data that will be collected and transferred, the uses of those data, and the persons with whom the data will be shared and have access (including individuals acting on behalf of the sponsor) has been incorporated into the rigorous clinical study informed consent process (Consultation Question 16). Each Independent Ethics Committee overseeing a study is tasked with ensuring that researchers and the study sponsor have adequate mechanisms in place to protect subject privacy and data confidentiality.

³ Available at <http://www.emea.europa.eu/pdfs/human/ich/013595en.pdf>.

⁴ Id. at 2.11.

⁵ Id. at 2.9 and 2.6.

⁶ Id. at 2.2.

⁷ Available at <http://www.eortc.be/Services/Doc/clinical-EU-directive-04-April-01.pdf>.

⁸ Available at <http://www.opsi.gov.uk/si/si2004/20041031.htm>.

Personal data is further protected by restricting the inclusion of identifiers in reporting study results to sponsors (Consultation Question 22). ICH GCP requires that unambiguous subject identification codes must be used in reporting data for each subject.⁹ A subject identification code is “a unique identifier assigned by the investigator to each trial subject to protect the subject’s identity and used in lieu of the subject’s name when the investigator reports adverse events and/or trial-related data.”¹⁰ Therefore, case report forms (CRFs), the mechanism by which investigators report results to pharmaceutical sponsors, contain subject identification codes instead of directly identifiable patient information such as name and address. The subject identification code list must be maintained “in a confidential manner” in the files of the investigator/institution.¹¹ The investigator also maintains on-site all source documents and records, such as pertinent hospital records, clinical and office charts, laboratory notes, etc.

Pharmaceutical company researchers who review and analyse CRFs generated in clinical trials do not have access to directly identifiable data about patients. This contrasts with external clinical investigators who actually undertake clinical trials sponsored by pharmaceutical companies. Investigators are neither employees nor agents of the sponsor. They are health care professionals independent of the sponsor who have contractually agreed to conduct a clinical trial at a trial site in accordance with a protocol that is approved by an independent ethics committee. Although often affiliated with academic medical centres, they may be solo practitioners or providers in an organised health care arrangement, and they usually conduct research on behalf of several sponsors.

The external clinical investigator is, of course, at all times aware of the patient’s identity. However, the investigator is bound by a health care provider’s duty of medical confidentiality to the patient, as well as the confidentiality provisions of the study protocol, not to reveal this information. What the investigator may not know, however, is whether a particular patient is in the experimental or control arm of the study. Namely, an investigator in a double-blinded study does not know whether a particular trial subject is receiving the investigational product, a comparator product, or a placebo. “Unblinding” may be necessary in the event of a medical emergency for a trial subject. Breaking the blind involves procedures specified in the study protocol that allow the investigator to find out which treatment or placebo the patient has received.

Pharmaceutical sponsors are by design unaware of the patient’s identity, with two limited exceptions. First, specific individuals employed by, or acting on behalf of, a pharmaceutical sponsor may have access to identified and/or identifiable information in the context of pharmacovigilance reporting and investigation. This issue has been discussed above; however, it is important to reiterate here that these activities are undertaken by individuals whose responsibilities are centred on pharmacovigilance requirements. Technical and organisational controls are used to protect the confidentiality of the information and to limit its broader dissemination within the organisation.

Second, a field monitor employed by the sponsor may be directed to review the source data at the study site. In accordance with ICH GCP, it is the monitor’s responsibility to “check[] the accuracy and completeness of the CRF entries, source data/documents, and other trial-

⁹ ICH Guidelines, supra note 3 at 5.5.5.

¹⁰ Id. at 1.58.

¹¹ Id. at 8.4.3.

related records against each other.”¹² In the course of this review with the clinical investigator, field monitors may have access to identified patient information at the study site. Monitors review this information on site, but they are not permitted to share this information within the sponsor organisation. Accordingly, such identified patient information that an individual monitor may see at the study site is accessible only for a limited duration for a specific purpose, and it is not transferred or included in any sponsor files or databases. Standard procedures prohibit broader dissemination because, among other things, such a disclosure could compromise good clinical practice.

ii. “Secondary Research”

As the term suggests, secondary 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 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.

The Association for British Pharmaceutical Industries (ABPI) has issued guidance on the secondary use of data for medical research purposes.¹³ The Guidance explains what type of medical data may be gathered and processed in accordance with the Act. The Guidance is effective in establishing a standard that safeguards privacy while enabling the pharmaceutical industry an appropriate opportunity to develop and deliver medicines which benefit society.

iii. Epidemiological Research

Epidemiological studies involve research on human populations in order to link human health effects to a cause. Certain types of epidemiological studies are conducted prospectively. For example, prospective cohort studies are one type of prospective epidemiological study which involves observation of a population over time to compare health impacts of one subset of individuals who were exposed to an intervention or other factor of interest to those who were not. Others types of epidemiological studies involve the retrospective review, collection and analysis of health-related information. One specific area of retrospective epidemiological research is health outcomes and cost-effectiveness research. Health outcomes and cost-effectiveness research evaluates and compares the costs and benefits of a particular pharmaceutical intervention in order to guide optimal allocation of healthcare resources.

¹² ICH GCP, *supra* note 2, at 5.18.4(m).

¹³ Available at http://www.abpi.org.uk/%2Fpublications%2Fpdfs%2FGuidelines_SecondaryUseData.pdf.

In some types of epidemiological research, aggregated data that cannot be identified back to an individual may be sufficient for researchers' needs. In still other research, such as longitudinal studies, data individuation may be necessary in order to monitor individual health outcomes over time. Data individuation involves the attribution of codes to separate clinical cases, in order to ensure coherence and to avoid confusion with information on different patients.

Informational elements that could, in the absence of controls, be considered "indirect identifiers" are sometimes needed for epidemiological research. For example, dates related to an individual's treatment are often necessary to assess the sequence and timing of drug exposures and health-related impacts. Similarly, broad geographic identifiers are often needed (e.g., to compare the overall incidence of some condition in a population to those taking a preventive medication).

III. RESPONSE TO QUESTIONS

A. Question 9

The Data Protection Act achieves a pragmatic balance between protecting individual privacy and facilitating data access for public health and medical research purposes. This is seen in the definition of "personal data" in Section 1 of the Act ("personal data" means data which relate to a living individual who can be identified (a) from those data, or (b) from those data and other information which is in the possession of, or is likely to come into the possession of, the data controller). Recent guidance issued by the ICO further expands upon this point: "[T]he fact that there is a very slight hypothetical possibility that someone might be able to reconstruct the data in such a way that the data subject is identified is not sufficient to make the individual identifiable."¹⁴ In contrast, certain other EU jurisdictions are concerned about the theoretical risks of a data subject's identification from information that relates to that individual but is not directly identifiable (for example, a birth date in combination with a medical condition; or coded health research data, where the code is held by a third party under an obligation of confidentiality). The IPPC supports the Act's focus on whether the data controller "is likely" to come into possession of information enabling identification of the data subject.

This is not meant to suggest that certain measures to protect data for which there is only a remote risk of identification are not warranted. However, it is impractical and an impediment to research to apply the full 'bundle of protections' specified in the EU Directive to data that is highly unlikely ever to be identified. For example, pharmaceutical researchers should not be required to obtain a subject's consent before using encoded data for research when the key-code necessary to identify data subjects is held by a third party under an obligation of confidentiality. Protections required should be commensurate with the sensitivity of the data and its level of identifiability. Accordingly, we suggest that the concept of 'identifiable' should be seen along a spectrum, not as an is/is not proposition.

The pragmatism of the Act is also seen in its acceptance of the processing of sensitive personal information for medical research in Schedule 3 (i.e., "the processing is necessary for medical purposes and is undertaken by a health professional or a person who in the

¹⁴ "Data Protection Technical Guidance: Determining what is personal data", at p. 7, *available at*: http://www.ico.gov.uk/upload/documents/library/data_protection/detailed_specialist_guides/personal_data_flowchart_v1_with_preface001.pdf.

circumstances owes a duty of confidentiality which is equivalent to that which would arise if that person were a health professional. . . . '[m]edical purposes' includes the purposes of preventative medicine, medical diagnosis, medical research, the provision of care and treatment and the management of healthcare services"). The explicit recognition of medical research as a legitimate basis for processing represents a determination that the public interest is advanced by promoting medical science. Additional guidance from the Information Commissioner's Office (ICO) on what it means for processing to be "fair" and for "specified and lawful purposes" in the context of medical research would provide further clarity for researchers struggling to understand their data protection obligations.

B. Questions 9, 13 & 25

Both the Data Protection Act and the EU Directive pose some challenges for multinational companies who need to share information between affiliates across international borders. Pharmaceutical companies need to transfer data outside of the EEA for a variety of purposes. These include the transfer of:

- pharmacovigilance data to foreign health authorities, as required by applicable national regulations;
- data concerning research subjects for purposes of analysis and submission of applications for marketing authorisation;
- information on clinical investigators conducting research sponsored by the company, for required reporting purposes.

Mechanisms exist to enable the transfer of data to countries outside of the EEA that have not received an adequacy determination; however, each of these mechanisms has disadvantages or limitations. For example, the safe harbour negotiated with the United States applies only to transfers to the US. The Model Clauses require a web of contracts. Binding Corporate Rules is an attractive concept in theory; however, the process for BCR approval across EU member states is lengthy and burdensome.

Modifications to the BCR approval process announced in 2007 hold promise. These modifications would allow a company to negotiate a pan-European BCR with a lead data protection authority (DPA) and have that DPA shepherd the BCR through reviews in other member states. However, while the UK Information Commissioner's Office has embraced the BCR process, other member states appear unwilling or unable to fast track BCR approval based on another DPA's review. The pharmaceutical industry has a great deal of experience in the use of the mutual recognition procedure for approval of product marketing authorisations and we support the creation of a similar process for approval of pan-European BCRs.

Another difficulty that multinational corporations face concerns compliance with foreign laws and litigation procedures. Articles 7(c) and 26(d) of the Directive permit the processing and transfer of personal data for purposes of compliance with legal obligations. However, some EU jurisdictions interpret these clauses narrowly, in effect limiting their application to compliance with local legal requirements. While the UK has been more flexible than some other EU countries in its approach, further consideration should be given as to how the UK can weigh into the Article 29 Working Party on this important issue. This also highlights a problem with the Directive as a whole – its inconsistent interpretation and implementation has led to a situation in which companies either must adopt universally processes designed to comply with the most stringent national laws or must maintain separate compliance processes for each country.

C. Question 20

The development of electronic health record (EHR) systems has the potential to improve the quality of health care delivery by providing authorised health care professionals with ready access to medical information about the patient. EHR systems also have the potential to improve public health by enabling better post-marketing drug surveillance and facilitating the locating of potential subjects for clinical trials and other health care research. However, before these advances can be achieved, cultural and legal resistance based on data privacy fears must be addressed.

The direction of drug R&D is to develop medicines that are optimal for smaller and smaller populations. The basic idea behind this is that rather than conclude that Drug A is better than Drug B for the general population as a whole, scientific investigation may prove that Drug A is better for a certain subsection of the population while Drug B is better for another subsection. However, as inclusion and exclusion criteria for clinical trials narrow, it becomes increasingly difficult to find eligible clinical trial subjects. EHRs provide a mechanism by which eligible patients can be readily located.

EHRs also enable improved detection and investigation of drug safety signals. Uncommon and serious drug reactions can often be difficult to detect during clinical development. The occurrence of unexpected adverse events post-marketing requires fast detection and investigation to ensure that appropriate warnings can be provided to at-risk populations without denying access to those patients who can use the medicine safely.

The public's support for the development and implementation of EHR systems will likely depend on the public's confidence that EHRs have been adequately secured. Robust data security is essential to protect EHRs from unauthorised access, which could lead to embarrassment, stigmatization, or discrimination. At the same time, authorities should recognize the substantial public interest in permitting the use of EHRs for medical research, provided appropriate safeguards are put in place. Such safeguards might include, for example, providing researchers with access only to coded/pseudonymised data. The research value of medical data is not usually dependent upon the ability to directly identify the research participants, *i.e.*, the data does not have to be identifiable to the researcher or "personal" as defined under the Act. This understanding is critical to public support for medical research and should be emphasised by the ICO in public discourse.

D. Question 22

As previously discussed, investigators in clinical studies encode the data before reporting results to study sponsors. The key code is maintained by the investigator. Researchers employed by a pharmaceutical sponsor are not able to identify study subjects except by reference to the subject's code. While the data is not truly "anonymised" since a link to subject identities still exists, provided the key code is maintained securely, the data is *effectively* anonymised with respect to the pharmaceutical company researchers.

Similarly, in longitudinal studies, individual health outcomes need to be monitored over a period of many years. It is necessary to be able to correlate medical events and conditions that relate to the same individual. Controlled and secure methods of key coding or

'pseudonymisation' provide a means by which individual patient outcomes can be tracked over time while patient privacy is safeguarded.

Nevertheless, some DPAs regard pseudonymised data as "personal data" subject to the full requirements of the EU Directive. The IPPC believes that whether data is identifiable depends on whether the person who has control of the data has access to the means to identify the subject of the information, not on whether some third party under an obligation of confidentiality has such means. The IPPC therefore supports the view that coded (pseudonymised) data are not "personal data" triggering application of the Directive.

III. CONCLUSION

The IPPC is grateful for this opportunity to provide comments on the Consultation Paper, and we welcome further dialogue about these critical issues.



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:

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|---|-------------------------------|
| § Abbott Laboratories | § Novartis |
| § AstraZeneca Pharmaceuticals | § Pfizer Inc. |
| § Bristol-Myers Squibb | § Roche |
| § Elan Pharmaceuticals, Inc. | § sanofi-aventis |
| § Eli Lilly and Company | § Schering-Plough Corporation |
| § GlaxoSmithKline | § Takeda Pharmaceuticals |
| § Johnson & Johnson | § Wyeth |
| § Merck & Co., Inc. (<i>operating as Merck Sharp & Dohme in most countries outside USA</i>) | |

MISSION

The IPPC works 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:

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

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



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 endeavour, 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 favourable 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.

This paper was prepared by the members of the International Pharmaceutical Privacy Consortium to provide basic background to privacy officials about the clinical research enterprise.