17 June 2015

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. The vision of the IPPC is to be the leading voice in the global bio-pharmaceutical industry to advance innovative privacy solutions to protect patients, enhance healthcare, and support business enablement. Information concerning IPPC membership and mission is further described in Appendix A and at: www.pharmaprivacy.org.

The European Federation of Pharmaceutical Industries and Associations (EFPIA) represents the pharmaceutical industry operating in Europe. Through its direct membership of 33 national associations and 40 leading pharmaceutical companies, EFPIA is the voice on the EU scene of 1,900 companies committed to researching, developing and bringing to patients new medicines that will improve health and the quality of life around the world. Information concerning EFPIA membership and vision is further described in Appendix B and at: www.efpia.eu.

Similarly, the Association of Clinical Research Organizations (ACRO) represents the world's leading clinical research organizations (CROs) that provide a wide range of specialized services across the entire spectrum of drug development to research sponsors. ACRO and its members advocate on a global basis for safe, ethical, high-quality medical research so patients can benefit from the development of new treatments and therapies. Information concerning ACRO membership and mission is further described in Appendix C and at: www.acrohealth.org. As the drug development process is a shared enterprise, research sponsors and CROs have a similar interest in ensuring an appropriate ethical and regulatory framework governs the use of health databases and biobanks.

Comments on the draft WMA Declaration on Ethical Considerations Regarding Health Databases and Biobanks

IPPC, EFPIA and ACRO member companies sponsor research to improve the treatment and prevention of illness and disease and are committed to conducting research to the highest ethical, medical and scientific standards. This research may fall into one of the following categories:

(i) *In vitro studies that utilize human tissues or biological samples.* Such studies are typically conducted in pre-clinical development to identify drug candidates and assess their safety.

(ii) *Research conducted with human subjects or using data or biological materials from previous studies.* Such research may be conducted in the form of a clinical trial, which is used to support an application to market a new drug, or it may involve the analysis of data and biological samples collected in prior studies, often for purposes of better understanding the mechanisms of human disease in order to aid in the development of new drugs.

(iii) *Epidemiological research*. Such research involves the study of patterns and causes of diseases and conditions in defined populations. For example, one important sub-category of epidemiological research is pharmacovigilance, which involves monitoring the effects of drugs in order to identify and evaluate adverse reactions.

(iv) *Outcomes research*. Such research is used to measure the effectiveness of particular health care practices and interventions. It is used to understand how to most efficiently improve patient outcomes.

During this research, our member companies typically access information that has been key-coded, *i.e.,* directly identifying information such as name or indirect identifier such as date of birth have been removed and/or replaced with a code number. For example, in observational research using population-wide datasets or information derived from the provision of healthcare (*e.g.,* electronic health records), approved researchers are only provided with coded data. Similarly, when accessing human biological materials and information from biobanks, researchers are provided with data/samples that do not identify any particular participants, and they must execute data sharing agreements that prohibit any attempt to identify participants.

We support the efforts of the World Medical Association to develop a global policy regarding the use of health databases and biobanks. We agree with the WMA's statement, in the request for comments, noting that research is changing and that "[l]arge collections of data and human specimens allow for the development of new research strategies and models, as well as new predictive types of research and analysis." We also agree with the premise that despite these changes, informed consent or waiver of informed consent by an ethics committee remains an important instrument for protecting personal autonomy and human dignity.

Our comments on the draft Declaration on Ethical Considerations Regarding Health Databases and Biobanks focus on the following issues:

- Paragraph 8: Scope of Application — Meaning of "Anonymised" and "Non-Identifiable"
- Paragraphs 15 and 19: Opportunity for Individual Choice
- Paragraph 17: Withdrawal of Consent
- Paragraph 18: Consent for Future Use
- Paragraphs 19-21: Ethics Committees

Scope of Application — Meaning of "Anonymised" and "Non-Identifiable"

Paragraph 8 of the Declaration (Preamble) states that "Health Databases and Biobanks that exclusively contain fully anonymised and non-identifiable data and biological material are not the subject of this declaration." However, there is no uniform, world-wide standard for

what qualifies as "anonymised" and "non-identifiable." Indeed, data protection authorities in some jurisdictions are of the view that if there is a risk, however small, that it may be possible to infer information about an individual, to "single out" an individual, or to link records relating to an individual, then the dataset cannot be regarded as fully anonymised.[1] This has led some legal scholars to argue that in the near future there will be no such thing as fully anonymised data.[2] Although this issue is hotly debated,[3] it points to the fact that there are different interpretations of what it means for data to be "non-identifiable." For example, in observational research using datasets containing disease surveillance data, information concerning individuals may be provided to researchers in a coded (*i.e.*, "pseudo-anonymised") form, often after the approval of an independent ethics committee. The researchers have no access to identified data, but the data provider — *e.g.*, the health service — retains the link back for purposes of providing data updates and having the ability to return information that may be medically or scientifically important. Is the disclosure of coded data to the researcher who has no access to the original identified data a disclosure of anonymised data, or is it a disclosure of identifiable data? Regulatory authorities in different jurisdictions have adopted different views. Yet, without agreement on this most basic concept, it is difficult to see how a meaningful global consensus can be reached on the appropriate ethical standards for use of "identifiable" data and biological samples. Indeed, without clarity on this point, there is the risk that the Declaration, in its current form, could be applied in radically different ways in different jurisdictions, which would defeat the goal of developing a common, global ethical standard.

Recommendation: The Declaration should recognize that the concept of "identifiability" generally falls along a continuum rather than being a binary distinction. Individual interests in informational self-determination — i.e,. the right to control how information about oneself is used and disclosed — are strongest where the data is most directly identifiable, weakest where the data can only be identified through the use of great effort and resources. Principles governing the use of data should reflect the level of identifiability.

Opportunity for Individual Choice

Paragraph 15 of the Declaration indicates that individuals must be given the opportunity to decide whether their identifiable information will or will not be included in a Health Database. It is unclear how this principle is intended to be applied to key-coded data, for example to data reported to sponsors of clinical trials or datasets derived from electronic health records and provided to researchers. In scenarios where researchers only need access to key-coded data, it is important to allow research that may advance medical science and benefit

[1] Cf, Article 29 Data Protection Working Party, 0829/14/EN WP216, Opinion 05/2014 on Anonymisation Techniques, Adopted on 10 April 2014.

[2] See, e.g., Paul Ohm, Broken Promises of Privacy: Responding to the Surprising Failure of Anonymization. UCLA Law Review, Vol. 57, p. 1701, 2010.

[3] Compare Paul Ohm, supra note 2, to Ann Cavoukian & Khaled El Emam, Dispelling the Myths Surrounding De-identification: Anonymization Remains a Strong Tool for Protecting Privacy. Information and Privacy Commissioner, Ontario, Canada, June 2011.

patients. For example, data derived from a person's medical history (diseases and conditions, treatment, etc.) may be needed for public health research to understand the cause of disease or evaluate the effective use of treatments. While it is not necessary (or desirable) to link the information back to a named individual, this coded information may nevertheless be considered "identifiable" under the laws of some jurisdictions. It is to the benefit of future and current patients that researchers be allowed to access such key-coded data, subject to appropriate controls.

An exception to the requirement for consent is provided for in Paragraph 19, which provides that "In the event of a clearly identified and immediate threat where anonymous data will not suffice, the requirements for consent may be waived to protect public health. An independent, dedicated ethics committee should confirm that each exceptional case is justifiable." The use of an independent ethics committee as an alternative to consent should be given greater emphasis throughout the principles. Particularly in the context of human biological samples, it may not be possible or practical to seek re-consent for further research. Samples are regularly collected with donor informed consent and/or ethics committee approval. The ability to use ethics committee approval as an alternative to informed consent avoids unnecessary re-identification of individuals from coded data and allows the re-use of old samples where re-consent may not be practical.

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Recommendation: We support the inclusion of a waiver of the consent requirement where appropriate for protection of public health. The decision to grant such a waiver should be able to be made either on a case-by-case basis by an independent ethics committee, after careful consideration of the risks and benefits, or to be established by policy makers as a matter of law or public policy.

Withdrawal of Consent

Paragraph 17 of the Declaration states that "Individuals must have the right, at any time and without reprisal, to withdraw their consent for their identifiable information to remain in a Health Database. . . ." It is important that the Declaration distinguish between withdrawal of consent for data and samples to be used in new research projects and attempts to withdraw consent to the use of data already collected as part of an ongoing or completed research study. The scientific validity of research studies could be compromised if subjects were allowed to withdraw consent with retroactive effect.

Indeed, there are some circumstances where data need to be retained to meet legal or regulatory requirements. For example, health authorities in many countries require that data collected in a clinical trial in reliance on consent continue to be included in the study database and in the analysis of results even following a data subject's withdrawal from a study and revocation of consent. For example, the US Food and Drug Administration has issued guidance indicating that data must be retained for participants who decide to discontinue participation in a clinical study of an investigational product, who are withdrawn by their legally authorized representative, or who are discontinued from participation by the clinical investigator. The

guidance indicates that if data are removed from the study database, the scientific validity of the study may be compromised. The guidance states clearly that clinical trial participants are not permitted to control the use (inclusion or exclusion) of data about them: "The agency needs all data in order to be able to determine the safety and effectiveness of the drug or device. The fact of having been in an investigation cannot be taken back. Also, if a subject were able to control the use (inclusion or exclusion) of his or her data, and particularly if the clinical investigation were not blinded, the bias potential would be immense."[4] Similarly, recital 76 of the EU Clinical Trials Regulation states: "With a view to respecting [personal data protection rights], while safeguarding the robustness and reliability of data from clinical trials used for scientific purposes and the safety of subjects participating in clinical trials, it is appropriate to provide that, without prejudice to Directive 95/46/EC [concerning the protection of personal data], the withdrawal of informed consent should not affect the results of activities already carried out, such as the storage and use of data obtained on the basis of informed consent before withdrawal."

Recommendation: The Declaration should distinguish between withdrawal of consent for data and samples to be used in new research projects and attempts to withdraw consent to the use of data already collected as part of an ongoing or completed research study. The scientific validity of research studies could be compromised if subjects were allowed to withdraw consent with retroactive effect.

Consent for Future Use

For clinical trials, where patients take part in studies of potential new medicines, specific informed consent is sought for each trial and remains a fundamental part of a pharmaceutical sponsor's responsibility to patients. For other research where pharmaceutical researchers access data from electronic health records and disease registries to monitor safety signals and develop products of value to patients and healthcare providers, it is not possible to describe all potential uses at the point of data collection, and the current ability to re-use data collected under broad consent and accessed under strict privacy controls is vital.

Paragraph 18 of the Declaration provides that if certain conditions are satisfied, then "conditional broad consent" for future use of health data or biological materials may be acceptable. In contrast, "blanket or open consent for future use . . . not envisaged at the time of collection is not ethically acceptable." This paragraph appears to recognize that it is often not possible to describe with specificity all future research uses of data and biological samples at the time of collection. Research inquiries evolve as new data and observations confirm or disprove old hypotheses.

Individuals may vary in their willingness to provide consent to future uses depending upon the specificity with which such uses are described. Informational self-determination is

[4] United States Food and Drug Administration, "Guidance for Sponsors, Clinical Investigators, and IRBs: Data Retention When Subjects Withdraw from FDA-Regulated Clinical Trials" (September 2010) at fn. 4.

protected when individuals are given sufficient information concerning future uses such that those who consent will not later be surprised by how their data and samples have been used.

Recommendation: We recommend that the current ability to get broad consent for re-use of data for future medical or health research should be retained. Researchers should describe future use and data access in terms that are reasonable at the point of data collection and ensure that data are not used in any manner incompatible with that purpose or purposes.

The ability to obtain independent ethics committee approval in situations where it is unclear whether secondary research is compatible with the original purpose is an important alternative to re-consent and enables secondary research that may not have been possible to predict at the time of data collection but which would benefit society and patients. An independent ethics committee should also be consulted to determine whether a new consent is necessary. This, in turn, should require an assessment by the ethics committee of the level of identifiability of the data, the scope of the prior consent and likely expectations of research participants, and the risks and benefits of the research.

Ethics Committees

As previously stated, the ability to get independent ethics committee approval is an important alternative to consent when it is not possible to obtain informed consent or appropriate to use fully anonymised data. To reduce the burden on ethics committees and avoid unnecessary delays to research, it is important to consider how approval mechanisms can be optimized.

For example, in the UK, organisations responsible for the management of research tissue banks may apply for ethical review of their arrangements for collection, storage, use and distribution of tissue. For approved research tissue banks, this then facilitates programmes of research without the need for individual, project-based ethical approval. This process has an option for the applicant to seek generic ethical approval prospectively for a range of research to be carried out by the establishment responsible for the bank and/or by other researchers to whom tissue is released by the bank within the conditions of the ethical approval. Such approval may be given for a period of up to five years and is renewable.

Recommendation: Further consideration should be given to the development of mechanisms that provide appropriate ethical review and approval of access to samples and data, in a manner that is proportionate and facilitates further research.

Thank you for the opportunity to comment upon the draft Declaration. Please do not hesitate to let us know if you have any questions concerning our submission.

APPENDIX A: INTERNATIONAL PHARMACEUTICAL PRIVACY CONSORTIUM

MEMBERS	Members of the IPPC include: • AbbVie • Amgen • Astellas Pharma • AstraZeneca • Baxter International • Bristol-Myers Squibb • Celgene • Eli Lilly and Company • GlaxoSmithKline • Johnson & Johnson • Merck & Co., Inc. • Novartis • Novo Nordisk • Otsuka • Pfizer Inc. • Roche • Sanofi • Shire • Takeda Pharmaceuticals
VISION	The vision of the International Pharmaceutical Privacy Consortium is to be the leading voice in the global bio-pharmaceutical industry to advance innovative privacy solutions to protect patients, enhance healthcare, and support business enablement.
MISSION	As an organization of pharmaceutical companies, the IPPC advances the protection of individual privacy, anticipates and responds to new challenges affecting the protection of health information, augments member companies' data protection capabilities through the development and sharing of industry best practices, educates internal and external stakeholders on data protection in the pharmaceutical industry and the importance of data to pharmaceutical innovation, and provides a forum to ensure that the global pharmaceutical industry speaks with one, coherent voice on data privacy issues.

APPENDIX B: EUROPEAN FEDERATION OF PHARMACEUTICAL INDUSTRIES AND ASSOCIATIONS

VISION	EFPIA supports a vision of modern, sustainable healthcare systems in Europe. We want systems that provide patients with equal and early access to the best and safest medicines; that support innovation while realistically balancing benefit and risk; that empower citizens to make informed decisions about their health and ensure the highest security of the medicines supply chain. Such a vision will also assist policymakers in sustaining Europe's economic growth and competitiveness, by balancing healthcare budgets and helping to provide for a healthy and productive workforce. It also offers the most effective approach to deliver the innovative medicines needed to tackle current and potential health threats.
COMMITMENT	Reducing inequalities in health, accelerating patients' access to innovative medicines and improving patient safety – these are our primary commitments. By working in partnership with all relevant healthcare stakeholders, we seek to develop practical solutions to make these goals a reality. We believe that Europe's citizens support these commitments, creating a mutual agenda. We therefore call upon stakeholders to collaborate in implementing policies that recognise the pharmaceutical industry's role in improving European public health, economic wealth, and in enhancing Europe's industrial and science base. Together, we will help create a healthcare sector fit for the 21st century.

APPENDIX C: ASSOCIATION OF CLINICAL RESEARCH ORGANIZATIONS

MEMBERS	*Regular Members:* ◆ BioClinica ◆ Covance ◆ ICON ◆ INC Research ◆ inVentiv Health Clinical ◆ PAREXEL International ◆ PPD ◆ Quintiles	*Associate Members:* ◆ PRA ◆ Theorem Clinical Research
ABOUT	ACRO represents companies that provide a variety of specialized services that support the development of new pharmaceuticals, biologics, and medical devices. The Association provides an active voice for the CRO industry globally. Through its member companies, ACRO helps improve the quality, efficiency and safety of biomedical research. ACRO member companies employ more than 110,000 professionals worldwide, conduct research in 142 countries and contribute to the development of approximately 95% percent of all new drugs and biologics approved globally.	

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