**Comments on Council of Europe's "Working document on research on biological materials of human origin" – DH-BIO/INF (2014)3**

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 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 at: http://pharmaprivacy.org/

The Industry Pharmacogenomics Working Group (I-PWG) is a voluntary and informal association of pharmaceutical companies engaged in research in the science of pharmacogenomics. The group was initially established in 2000 in response to regulatory requests for non-competitive information from industry about such research. I-PWG is committed to promoting a better public understanding of pharmacogenomic research. Topics include educational, informational, ethical, legal, and regulatory matters. Information concerning I-PWG membership and mission is described at: http://i-pwg.org/

IPPC and I-PWG member companies sponsor clinical research that is used to support applications to market new drugs. We appreciate this opportunity to jointly provide comments to Council of Europe Committee on Bioethics (DH-BIO) on its proposals to revise Recommendation (2006) 4 of the Committee of Ministers of the Council of Europe, on research on biological materials of human origin. Comments will focus primarily on the following issues including those as requested by the DH-BIO:

- Scope (Article 2)
- Identifiability of biological materials (Article 3)
- Prohibition of financial gain (Article 6)
- Removal of biological materials for storage for future research (Article 11)
- Storage for future research of residual biological materials (Article 13)
- Changes in use of biological materials or capacity to consent (Articles 12, 14, 17, and 20)
- Right to change the scope of, or to withdraw, consent or authorization (Article 16)
- Availability of results (Article 19)
- Governance (Articles 20-24)

**Scope (Article 2)**

We respectfully request that the DH-BIO consider biological samples that are no longer identifiable (anonymized or anonymous) to be out of scope of this recommendation. In circumstances where the biological samples have been anonymized or collected anonymously it may be impractical to ensure traceability of consent including the permissions granted by the persons concerned and the rights of a person to direct the future use and access to the sample.

If not deemed out of scope, then we recommend that the DH-BIO clarify how a researcher could reasonably maintain a link between the anonymised or anonymous sample and the original permissions within the informed consent while ensuring the privacy protections offered by anonymisation.

**Identifiability of biological materials (Article 3)**

We support the intent of this article yet recognize that there is opportunity for further clarification of categories by which biological samples may be identified in order to better align with existing frameworks including the ICH Harmonised Tripartite Guideline E15[1] which defines four general categories of coding: identified, coded, anonymised and anonymous. We believe such differentiation would support the justification of identifiability (Article 7) as well as support better understanding of the feasibility of additional tenants proposed by DH-BIO, for example related to re-contact of donors of identifiable biological material to seek additional consent (Article 17) or to provide relevant results.

If existing frameworks are not adopted, we ask that the definition of "identifiable biological materials" be clarified to make it clear that a biological sample is not considered identifiable unless other data capable of identifying the persons from whom such materials have been removed are linked to the sample. Re-identification of a sample of biological materials without access to either an identified reference sample or data set requires disproportionate effort. Furthermore, we propose that the definition of "non-identifiable biological materials" include samples where the link has been irreversibly broken, such as coded materials provided through controlled transfer to a researcher who has no influence over or access to the code. In such a case, it would take more than reasonable efforts to break the privacy protection provided by the third party.

**Prohibition of financial gain (Article 6)**

We suggest elaboration of this article to make its meaning explicit. For example, there are companies that collect biological materials under IRB/EC-approved protocols for the purpose of making them available through sale for research purposes. The article should clarify that the prohibition on financial gain does not extend to these activities which promote the efficient advancement of medical research and treatment and which do not have a negative or coercive effect on persons concerned. In addition, the article insufficiently distinguishes the question of financial gain derived from the knowledge obtained through the use of biological materials. To address this second scenario, we suggest further clarification to reflect that the use of biological materials by commercial entities would not be prohibited in circumstances where there may be commercial gain derived from the findings of research on biological materials, given the critical role this may play in the advancement of medicine. Furthermore, we recommend that DH-BIO distinguish other commonly accepted financial gain in the context of biological research, including where expenses are charged for minimal recovery of costs or payment for services, or where donors are provided fair compensation for time and effort.

**Removal of biological materials for storage for future research (Article 11)**

Article 11 explains that, prior to requesting consent, the donor should be presented with comprehensible information that is that is "as precise as possible" with regard to future research use, conditions applicable to storage and relevant conditions governing the use of the material. The requirement for this detail to be as "precise as possible" is of concern. We support permitting general or generic consent for future research on biological materials. It is often impossible at the time of the initial consent and collection to understand the range of analyses that researchers may wish to perform on such biological materials in the future. Nevertheless, we believe it possible to offer a comprehensible and acceptable level of detail to persons concerned utilizing a generic consent. In addition, this

standard is consistent with the recommendation given by the UK authority (HTA), which seeks to obtain generic consent in effort to maximise the utility of the sample for research:

> *UK HTA Code of Practice #1 – Consent:*
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> *40. Generic consent typically only applies to research. If conducting research on samples of tissue, it is good practice to request generic consent because this avoids the need to obtain further consent in the future.* [2]

Further, we recommend that within this article the DH-BIO consider scenarios in which approval by an authorised body (e.g. Ethics Committee) may waive the requirement for consent of the persons concerned and be permissible within the law.

With regard to the requirement that "*The persons concerned should be offered the possibility to exercise choices with regard to the type of research use of their biological materials*", we would like to emphasise that this is logistically difficult to implement and may increase the risk that research conducted is not aligned with the expectations of persons concerned. As long as providing biological materials is a voluntary activity and the scope of use of the materials is defined, it should not be required to give persons additional choices. Individuals may always choose not to give biological materials if they are opposed to the stated research uses. Subsequent provision of choices could divide the research cohort, potentially introducing an element of bias in future analyses because the samples utilized are no longer representative of the cohort. This may be of particular concern in future research use of clinical trial specimens to address hypothesis related to safety or efficacy of a drug or class of drugs that arise later in development or post-approval.

**Storage for future research of residual biological materials (Article 13)**

We concur that consent for storage and future research use of samples should be sought prospectively where practical. In circumstances where prospective consent has not been obtained and where it is not feasible or practical to seek additional consent, we recommend that DH-BIO provide for approval by an authorised body (e.g. Ethics Committee), thereby waiving the requirement for consent of the persons concerned as permissible within the law. This approach is described with approval in Declaration of Helsinki:

> [3] *32. For medical research using identifiable human material or data, such as research on material or data contained in biobanks or similar repositories, physicians must seek informed consent for its collection, storage and/or reuse. There may be exceptional situations where consent would be impossible or impracticable to obtain for such research. In such situations the research may be done only after consideration and approval of a research ethics committee.*

**Changes in use of biological materials or capacity to consent (Articles 12, 14, 17, and Article 20)**

Articles 12, 14, 17 and 20 describe an expectation to re-contact persons concerned and obtain additional consent under circumstances, for example:

- *Articles 12 and 14*: Where capacity to consent is attained (e.g. a minor reaching age of majority) the consent of that person for continued storage and use of biological materials should be sought.
- *Article 17*: If the proposed use of identifiable biological materials in a research project is not within the scope of prior consent or authorisation, if any, given by the person concerned, consent or authorisation to the proposed use should be sought and, to this end, sufficient efforts should be made to contact the person concerned.
- *Article 20.3*: Any change of purpose of a collection should be subject to independent examination and, where necessary, may require that appropriate consent or authorisation of the persons concerned be requested.
- *Article 20.7*: Information about the management and use of the collection should be made available to the persons concerned and should be regularly updated.

It may be impractical or unduly burdensome to re-contact persons concerned in order to carry out any of the above requirements. Significant time may have elapsed and/or there may no longer be a direct or even indirect link between the holder of the biological material and the donor of the biological material. Further, if the persons concerned did not initially indicate willingness or desire to be re-contacted then the act of re-contacting to seek additional permission or notify of changes could result in undue stress or burden on the person concerned. We ask the DH-BIO to qualify these statements to reflect that seeking to re-contact should be undertaken as feasible and under advisement of an appropriate ethical body. In addition, where re-contact is deemed not feasible by the researching entity, we ask that alternate options provide a waiver of consent requirements, including approval by an authorised body (e.g. Ethics Committee). We note that this requested qualification would harmonise Article 17.2 with Article 20.3, where it is stated that an independent review should occur first and then, if necessary, efforts be made to contact the subject for consent. We would also support greater weight being given to the role of ethics committees in the review and approval of research proposals and the appropriateness of re-contact.

**Right to change the scope of, or to withdraw, consent or authorization (Article 16)**

We agree with the right to withdraw consent or authorization for storage and use of biological materials and maintain that this right exists only as long as the biological materials remain identifiable. However, we recommend against providing the person concerned with the right to change the scope of authorization as such changes are difficult to manage. The logistical issues are similar to those presented above in the comments on Article 11 relating to choice on the use of biological materials. Namely, individuals may protect their right to choice and autonomy by withdrawing their consent outright. Additional choice as to the scope of authorization will compromise the value of the collection on the whole as the samples later utilized may not be representative of the original cohort (see comments in response to Article 11 for more detail).

We suggest clarifying that the right to withdraw consent or authorization for storage and use of biological materials is feasible only when samples remain identifiable in Article 16.2.

**Availability of results (Article 19)**

We agree that results of research should be transparent and disclosed in a timely manner as consistent with the rights, obligations, and legitimate research needs of the entity conducting the research. However, we suggest that this article be amended to acknowledge the need to protect proprietary or confidential information. Such protections are vital to the advancement of medicine.

**Governance (Articles 20-24)**

We generally concur with the governance articles as described and note the following exception:

Article 20.9 describes the expectation to publish an annual report describing past and planned activities as well as access by third parties. This may be difficult to implement in a meaningful way specifically with regard to the pharmaceutical biobank and collections obtained for clinical trial research due to the number of trials conducted and the global nature of the studies. Please note, IPPC and I-PWG member companies make a practice of publishing human subject research in peer reviewed journals and thereby achieve publicity of valuable research while protecting the proprietary value of each company's research results and scientific processes.

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

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[1] International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, *Definitions for Genomic Biomarkers, Pharmacogenomics, Pharmacogenetics, Genomic Data and Sample Coding Categories*, 1 November 2007.

[2] Human Tissue Authority, *Code of Practice #1 – Consent, available at* http://www.hta.gov.uk/legislationpoliciesandcodesofpractice/codesofpractice/code1consent.cfm.

[3] Declaration of Helsinki, *Ethical Principles for Medical Research Involving Human Subjects*.