CLINICAL AND MEDICAL CONTROLLED DOCUMENT (CMCD) POLICY			
Identifier	**Version**	**Title**	**Effective Date**
CT29-POL	2.0	USE OF HUMAN BIOLOGICAL SPECIMENS	01-Jul-2016

TABLE OF CONTENTS

1. PURPOSE & SCOPE

The purpose of this clinical and medical controlled document (CMCD) policy is to describe the requirements for Pfizer's practices regarding the collection, acquisition, storage, use, and disbursement of Human Biological Specimens (i.e., biospecimens). The term policy will be used throughout the remainder of this CMCD policy.

In addition, this policy describes the overall process for obtaining, banking, and coding human biological specimens and data derived from such specimens, specifically specimens collected via clinical trials (CTs) that will be used in broad exploratory research and that will be stored in the Pfizer BioBank or Tissue Bank.

Pfizer adheres to high ethical principles and complies with all applicable laws, rules and regulations. Pfizer requires ethical review and, in most cases, a prior informed consent (and assent, where appropriate) of the donor before the collection, acquisition or use of human biological specimens. Exceptions where biospecimens may be used without individual donor consent are addressed in Section 3.4 *Use of Human Biological Specimens*.

In many cases applicable laws, rules and regulations do not provide clear or comprehensive guidance on the use of human biological specimens; accordingly, this policy sets a minimum global standard. This policy is in addition to any other applicable Pfizer policies and procedures.

This policy applies to:

- All new and ongoing activities defined in this Policy occurring on or after its effective date that involve the collection, acquisition, storage, use, and disbursement of human biological specimens globally.

- Pfizer colleagues who are involved in activities related to the policy, as well as to those parties with whom Pfizer contracts (e.g., contract research organizations, vendors or consultants) to perform such activities, unless Pfizer has agreed that such parties may follow their own processes with respect to these activities.

- Research and business units as well as the functional lines responsible for clinical and medical activities including research, development, regulatory, pharmacovigilance, and product quality.

- Under this policy human biological specimens shall include, but are not limited to, the following:
    - Fluid samples such as blood, blood derivatives (e.g., serum, plasma), urine, cerebro-spinal fluid, and saliva
    - Tissue biospecimens such as excised tumors, biopsy materials, fetal tissue, and autopsy biospecimens
    - Materials processed from human biological specimens such as cell lines, microsomes, DNA, RNA, and stem cells, except, and to the extent that laws, rules, or regulations applicable to such research and research samples (e.g., Human Tissue Act 2009 in the UK) specify that any such processed materials do not qualify as human tissue. Human cell lines available from the American Type Culture Collection or a similar repository where the cells and all of the information known about the cell lines (perhaps, including the donor) are publicly available are not in scope. Please consult with Pfizer Legal to confirm the position on this issue.
    - Human organs, including, without limitation, the brain

2. TERMS, ACRONYMS, AND REFERENCES

Terms used in this policy that require further clarification are defined in the CMCD Global Glossary. Global acronyms can be found in the CMCD Global Acronyms List. Applicable global regulations and global CMCDs are listed in the CMCD Global References List.

3. POLICY STATEMENTS

A designated member of the Pfizer team that proposes to collect, acquire, store, use, or disburse human biological specimens is responsible for ensuring the criteria contained in this policy are met.

Exceptions to this policy require documented approval of senior management, including the Chief Medical Officer and Pfizer Legal.

3.1. Collection of Human Biological Specimens

Pfizer will not collect human biological specimens without the documented informed consent (and assent, where appropriate) of the donor or the donor's legal representative. The informed consent document (ICD) must:

1. Be reviewed and approved by a qualified institutional review board/independent ethics committee (IRB/IEC) in accordance with recognized international standards for the protection of human research subject(s)

2. Be signed by the donor or the donor's legal representative

3. Identify both the material to be collected and its anticipated future use

A donor's participation in a clinical study shall not be conditioned on his or her informed consent (and assent, where appropriate) for the use of biospecimens that is not related to a clinical endpoint, the drug(s) being investigated in the trial, or the inclusion/exclusion criteria for the study.

A CT subject/parent/legally authorized representative may request to destroy biological specimens collected during a CT. Biological specimens may be destroyed in order to fulfill ethical requirements, including the terms of the ICD and protocol, and any applicable laws, rules, and regulations.

3.2. Acquisition of Human Biological Specimens

Pfizer will not acquire human biological specimens from others (e.g., a biospecimen banking service) without their contractual assurance that the biospecimens were collected in accordance with the informed consent (and assent, where appropriate) requirements outlined in Section 3.1 and are in accordance with all applicable laws, rules and regulations.

The purposes for which Pfizer can use the specimens, as well as any obligations upon Pfizer regarding the handling and use of the specimens and any associated data, must be clearly stated in the contract. In addition, the contract must indicate there are no legal, ethical, or other restrictions against transferring the materials to Pfizer, nor against Pfizer's use of them. It is not necessary for Pfizer to perform first-hand review of the ICD(s) under which the biospecimens were collected. However, if Pfizer does review these materials, due diligence must be applied

such that the specimens are procured for use consistent with the terms outlined in the ICD. If assistance is needed, consult Pfizer Legal.

3.3. Banking of Human Biological Specimens

As part of its research program, Pfizer collects, stores (i.e., "banks"), and uses biological specimens from human subjects for exploratory research through the Pfizer BioBank and Tissue Bank.

Fundamental Pfizer principles governing human biological specimen banking include the following:

- **Full disclosure** - Pfizer banks biological specimens for use in exploratory research only in ways consistent with the informed consent (and assent, where appropriate) under which the specimens were obtained, and as approved by an ethical review board independent of Pfizer after full disclosure of how the specimens were obtained and the type(s) of testing or use that will be performed.

- **Confidentiality** - Pfizer is committed to the protection of the privacy of the individuals from whom the specimens were/are obtained for exploratory research, and to ensuring that neither the specimens nor any information associated with such specimens or data generated during research involving such specimens are inappropriately disclosed to any third party. In the case of banked biological specimens collected via Pfizer CTs, specimens for exploratory research are coded to protect the confidentiality of the individuals from whom they were obtained.

- **Compliance with applicable regulations and recognized ethical guidelines** - Pfizer is committed to ensuring that its banking activities (whether performed by Pfizer or its contractual partners) are conducted in accordance with applicable laws, rules and regulations and established ethical principles.

Pfizer has designated a "BioBank Custodian," who has stewardship responsibility for the banked human biospecimens for exploratory research that are stored at its BioBank and Tissue Bank facilities. Pfizer's Legal Group and Data Privacy Office will provide guidance to ensure consistency in adherence to all applicable laws, rules, regulations, ethical standards, and Pfizer policies. In recognition that human research is a dynamic field, Pfizer reviews its practices on a

regular basis and continues to monitor international public discourse on this subject. External ethical experts have been, and will continue to be, engaged by Pfizer as necessary.

3.4. Use of Human Biological Specimens

The ICD should describe the planned and potential future uses of the collected biological specimens, and Pfizer is bound by that description, unless further ethical approval is obtained. For biospecimens obtained from Pfizer CTs, it may be necessary to consult the protocol and/or other study documents to fully understand the use(s) of the biospecimens which the IRB/IEC approved.

If a proposed Pfizer use is not encompassed within this description, or if the scope of use in the consent document is unclear, additional ethical review and, in appropriate cases, donor consent (and assent, where appropriate) is obtained before the biospecimen is used. See Appendix 1 *IRB/IEC Requirements for New Uses of Biospecimens* for further guidance.

In the case of human biological specimens collection in a clinical study prior to April 1, 2005 (the first issuance of Policy CT29), at a minimum, elements (a) through (c) of Section 3.1 *Collection of Human Biological Specimens* must be followed in order to use such specimens.

For specimens procured from external sources (see Section 3.2 *Acquisition of Human Biological Specimens*), Pfizer will only use the specimens for the purposes described in the contract under which the specimens were procured. Use of human biological specimens for other purposes requires a new or amended contract with the provider that states the additional use(s) which may be made of the specimens and warrants that these use(s) are in accordance with the terms of the informed consent (and assent, where appropriate), as well as all applicable laws, rules, and regulations.

3.5. Disbursement of Human Biological Specimens

When disbursing specimens to external parties (e.g., vendors, academic collaborators) Pfizer will notify the third party of the allowable usage(s) of the specimens, as described in the ICD and/or ethical approvals (for specimens procured through Pfizer-sponsored studies) or in the contract under which Pfizer procured the specimens (for specimens acquired externally which Pfizer is permitted to provide to third parties). The receiving party must agree in writing to use the specimens specifically for those purpose(s). If Pfizer is requested to provide human samples

procured through Pfizer-sponsored studies in order to conduct investigator-initiated research, please refer to CT25-GSOP *Pfizer Non-Sponsored Research*.

Shipment of human biological specimens must adhere to all applicable laws, rules, and regulations.

3.6. Special Population: Pfizer Employee

- Pfizer recognizes that employees are a special population and their donation of biological specimens for Pfizer activities requires additional safeguards to avoid any appearance of coercion. Pfizer employees are not precluded from donating specimens based solely on their status as Pfizer employees.

4. APPENDIX 1 – INSTITUTIONAL REVIEW BOARD / INDEPENDENT ETHICS COMMITTEE REQUIREMENTS FOR NEW USES OF HUMAN BIOLOGICAL SPECIMENS

If required, additional ethical review is obtained by an appropriate IRB/IEC, that is, the IRB/IEC with jurisdiction over the original biospecimen collection, unless:

- A regional IRB/IEC provides a decision covering all local sites under its jurisdiction, rendering it unnecessary to approach the individual IRB/IECs;
- The IRB/IEC with jurisdiction over the original collection delegates review to a different IRB/IEC in writing; or
- The IRB/IEC with jurisdiction over the original collection is unavailable, in which case an appropriate substitute may be identified in consultation with Pfizer Legal.

The IRB/IEC may require that informed consent (and assent, where appropriate) for the new use be obtained from the original donor or his/her legal representative, provided the donor's identity can be determined. If such contact is impossible or impractical, Pfizer will, where permitted by applicable law and regulation, seek a waiver of informed consent from an appropriate IRB/IEC as defined above.

If the donor's identity cannot be determined (e.g., because the specimens have been stripped of identifying information to protect donor privacy), Pfizer will, where permitted by applicable law, rule and/or regulation, seek a waiver of informed consent and approval for the proposed new research from an appropriate IRB/IEC as defined above.

If appropriate, additional data protection measures may be applied to the biospecimens before use, for example, in accordance with the new informed consent (and assent, where appropriate) or IRB/IEC waiver requirements.

5. VERSION HISTORY AND APPROVAL

Version	Effective Date	Change Type (New, Revise, Admin)	Summary of Revisions
2.0	01-Jul-2016	Admin	Administrative change - No new requirements added or process changes made. Updated to new policy template. Removed and revised CMCD references. Removed TMF section as this is covered in new CT29-GSOP-01 *Biospecimen Management During a Study*.
1.0	01-Apr-2013	New	New policy replaces CT29 *Policy On The Use of Human Tissue dated* 01-Apr-2010. Updated to new policy template per GSOP ADM01; changed policy title; changed retained pharmacogenomic samples to banked biospecimens; added Appendix to clarify requirements for obtaining IRB/IEC approval for new uses of biological specimens; added references to associated Work Instructions.

CT29-POL Version 2.0 administrative change:

CMCD Author	Brucker, Jacqueline

Required approver(s):

Head of SOPs	Lu-Chi, Greig

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CT29-POL	2.0	USE OF HUMAN BIOLOGICAL SPECIMENS	01-Jul-2016

CT29-POL Version 1.0:

CMCD Author	Karounis, Lynn

Required approvers:

BPO/SME	Kropp, Anne
BPO/SME	Powell, Coralie
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Head of SOPs	Maziarz, Mary Ann