

REPORT OF THE COUNCIL ON ETHICAL AND JUDICIAL AFFAIRS*

CEJA Report 6-A-11

Subject: Informed Consent in Research Involving Stored Human Biological Materials
(Resolution 1-A-10)
Presented by: John W. McMahon, Sr., MD, Chair
Referred to: Reference Committee on Amendments to Constitution and Bylaws
(Patricia L. Austin, MD, Chair)

1 This report responds to Resolution 1-A-10, “Patient Confidentiality in Biobanks” which asked the
2 American Medical Association (AMA) to support the development and use of a universal consent
3 form for research that involves a participant’s stored biological materials. The resolution further
4 asked the AMA to adopt as policy certain specific disclosures as part of the informed consent
5 process for such research.
6

7 Based on its review of the data available, relevant federal and international policy, and the ethical
8 analysis that informs current AMA policies, CEJA concludes that a universal consent form would
9 not achieve the purpose intended by the directive—specifically, would not ensure that participants
10 who provide samples of tissue, blood, cells, or DNA (“biospecimens”) fully understand that their
11 biological materials may be pooled and stored for potential future research. Moreover, the Council
12 concludes that the salient ethical issues central to the specific disclosures proposed for a universal
13 consent form are appropriately addressed in existing policy.
14

15 RESEARCH WITH STORED HUMAN BIOLOGICAL MATERIALS

16
17 More than 300 million human biospecimens are stored in the United States in public and private
18 repositories known as biobanks.^{1,2} Biospecimens are collected in a variety of settings, including
19 routine clinical and surgical procedures, medical and academic research, pharmaceutical treatment
20 and device trials and judiciary proceedings.^{2,3} The specimens are stored according to type of sample
21 and the setting from which they were collected, creating biobanks that range from small collections
22 of a single type of sample in academic or hospital settings to large-scale, national repositories of
23 diverse samples. Biobanks vary in terms of the quality of specimens and potential to support
24 further uses.³ They also vary with respect to whether their parent institutions are public or private
25 and for profit or nonprofit, as well as their policies and practices regarding access to specimens and
26 the extent to which specimens can be traced to the donor (i.e., whether they are identified, de-
27 identified, or coded).³ This wide variation is a result of the many purposes for which biospecimens
28 are collected and maintained.
29

30 Biospecimens contain genetic material that can be analyzed to identify gene variants associated
31 with human diseases.² For this reason, they are an increasingly important tool for research into
32 human diseases and their genetic and physiological causes.¹ When linked with demographic and

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1 environmental information, biospecimens can support population level research into gene-gene and
2 gene-environment interactions for understanding disease.¹ Three-fourths of clinical trials submitted
3 to the FDA for approval now include a provision for sampling and storing human tissue for future
4 genetic analysis.¹

5
6 Growing ethical and regulatory interest, especially in regards to large biobanks, has been prompted
7 by ongoing innovation in molecular biology and genomics including advances in techniques and
8 computational capabilities, systematic approaches to genomics, and increasing exchange of
9 specimens and information among researchers.³ This has resulted in a large number of guidelines
10 from professional societies, including the AMA,⁴ as well as national and international regulatory
11 bodies. Multiple policies and regulations now address privacy and confidentiality, disclosure of
12 research results, intellectual property, benefit sharing, biobank governance, and, most importantly
13 for the present analysis, informed consent.^{1,2,3}

14 15 DISCLOSURE & INFORMED CONSENT IN BIOBANKING

16
17 Informed consent is a foundational ethical principle in research that involves human participants,
18 just as it is in clinical medicine. In the research setting, the ultimate goal of the informed consent
19 process is to respect human subjects as persons and protect their autonomy by ensuring that
20 sufficient information is provided to enable prospective research subjects to make voluntary, well-
21 informed decisions whether to participate or not.⁵ Participants should “have the opportunity to be
22 informed about, evaluate, and consent to the goals of the intended research.”⁶

23
24 The nature and scope of consent has been a key focus of debate with respect to research involving
25 biospecimens, particularly in light of the fact that biobanks are intended to maintain specimens
26 long term and to support multiple research activities over time. Questions have been raised about
27 what kinds of information must be disclosed and, importantly, whether individuals can
28 meaningfully consent to future, as yet undesigned, research with their stored specimens. At the
29 time specimens are collected, researchers may not be able to provide specifics about the potential
30 risks, benefits, or other aspects of future research.⁷ Consent that is not specific to the research to be
31 carried out is not ethically sufficient.

32
33 A variety of professional societies and agencies in the United States have addressed the need for
34 guidelines for informed consent in the context of biobanking, including the American Society for
35 Human Genetics,⁸ the Office for Human Research Protections,⁹ the Food and Drug
36 Administration,¹⁰ and the National Cancer Institute (NCI),⁷ as has the World Medical
37 Association.¹¹ Such guidelines are meant to supplement and/or clarify existing regulatory
38 requirements for informed consent (45 CFR 46.116) to address the distinctive issues raised in
39 research with biospecimens.

40
41 For example, the NCI’s *Best Practices for Biospecimen Research* notes that “[r]espect for
42 individuals who have provided data or biospecimens for research is of paramount importance” and
43 that their preferences should be considered in seeking consent, within the provisions of applicable
44 law.⁷ NCI further notes that the consent document should clearly address use of biospecimens or
45 data by private or for-profit entities, the possibility that the research will lead to commercial
46 products, whether individual or aggregate results will be released and to whom, how data will be
47 stored and used (including whether and how it will be coded and whether it will be linked to
48 clinical data in the individual’s medical record), whether and with what oversight specimens or
49 data will be shared, and potential risks of genetic sequencing or analysis (if applicable). Guidelines

1 further recommend that, as appropriate for study design and resources of the biobank, participants
2 be allowed to specify types of research for which their specimens may be used and whether they
3 are willing to be contacted regarding research in the future. Finally, the consent guidelines
4 recommend that biobanks develop mechanisms to track the records of participants who withdraw
5 and that the consent process “highlight the human subject’s ability to discontinue participation and
6 describe what will take place should this occur.” (*Best Practices* also addresses technical and
7 operational issues for biobanks, as well as principles of responsible custodianship, privacy, access
8 to specimens and data, and intellectual property and resource sharing.)
9

10 As the introduction to *Best Practices* acknowledges, the many varying types of research that
11 depend on biobanks, its recommendations “are intended to be adapted, as appropriate, based on the
12 mission and scientific needs of individual biospecimen resources.”⁷ Entities that conduct research
13 with stored specimens under the auspices of the NCE or other agencies are expected to uphold
14 agency guidelines.
15

16 Notably, some countries allow for a blanket or general consent process to be utilized, while in the
17 US a tiered or tailored consent form is usually preferred. A tailored consent form offers specific
18 possible uses (such as research specifically related to the individual’s original disease or other
19 named diseases; any further specified research, requiring a separate consent form; or, commercial
20 uses) and asks the donor to select their preferences.¹² However, this can become problematic when
21 the biospecimens are intended to be used for a broad range of research, in which case providing a
22 list of potential types of research would be burdensome and uninformative.¹³ Since biobanks have
23 global potential, the dichotomy noted is another impediment to the construction of a universally
24 accepted consent form.
25

26 RELEVANT AMA POLICY

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28 In addition to providing general guidance about informed consent in Opinion E-8.08, “Informed
29 Consent,” which recognizes that a patient’s “right of self-decision can be effectively exercised only
30 if the patient possesses enough information to enable an informed choice,”¹⁴ AMA ethics policy
31 specifically addresses consent (and other) issues in the research setting. For research intended
32 primarily to gain scientific knowledge (as is most research involving biospecimens), Opinion E-
33 2.07, “Clinical Investigation,” requires that physician-investigators obtain participant’s voluntary,
34 written consent following disclosure of relevant information—in the context of clinical research,
35 that the research involves an investigational drug or procedure and a reasonable explanation of the
36 nature of the drug or procedure.¹⁵ In the context of genomic research involving biospecimens, this
37 can be interpreted to require discussion of the goals of the study and nature of analyses to be
38 conducted, as well as any unique or unusual risks the study may pose for participants. Opinion E-
39 2.08, “Commercial Use of Human Tissue,” provides that physicians contemplating research use of
40 organs or tissues must disclose possible commercial applications of the research and obtain the
41 consent of the tissue donor prior to any commercial use.¹⁶
42

43 Opinion E-2.079, “Safeguards in the Use of DNA Databanks in Genetic Research,” provides that in
44 addition to standard informed consent requirements (those of applicable regulations and of E-2.07),
45 the physician-investigator must disclose the privacy standards that govern the study, i.e., whether
46 and how data/specimens will be coded and if so under what circumstances the subject can expect to
47 be contacted in the future. Subjects must also be informed that they can refuse to allow the use of
48 their biological material, whether investigators stand to gain financially from the research and
49 when and how stored data and specimens will be discarded.⁴ E-2.079 further provides that when

1 research is carried out in an “identifiable community” investigators should consult with the
2 community to address potential harms to the community in addition to obtaining consent from
3 individual participants. Finally, the opinion also recommends that to provide greater protection for
4 confidentiality, genomic research not be conducted with identifiable samples.

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7 Policies of the AMA House of Delegates do not specifically address biobanking but do provide for
8 informed consent and protection of confidentiality in clinical and research settings, including the
9 use of de-identified data (H-315.978, “Privacy and Confidentiality”; H-315.983, “Patient Privacy
10 and Confidentiality”). H-460.931, “Genetics Testing Legislation,” opposes legislation that would
11 “unduly restrict the ability to use stored tissue for medical research.” Where obtaining patient
12 consent for disclosure of personal health information is impracticable, as would be the case for
13 subsequent research with de-identified biospecimens, H-315.983 endorses the oversight and
14 accountability provided by an IRB.

15 16 CONCLUSION

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18 Given regulatory injunctions to tailor disclosure during the informed consent process to the
19 particulars of the research for which a prospective participant’s consent is sought and existing
20 guidance from CEJA and the House of Delegates, CEJA does not support the creation of a
21 universal consent form to be used in all studies involving stored human biological materials.
22 Certain common elements would likely be necessary in any consent for such research; however, a
23 universal form alone cannot sufficiently provide the study-specific information on which
24 adequately informed consent must be based.

25
26 CEJA further holds that existing ethics and House policy already require the types of disclosure
27 called for in Resolution 1-A-10. That is, that individuals asked to provide biological samples
28 should be informed about (a) de-identification; (b) specimen pooling; (c) sharing of specimens
29 outside of the organization conducting the research study; (d) the selling or exchanging of
30 specimens; (e) future commercial use of specimens, and; (f) access, use or consideration by outside
31 entities.

32 33 RECOMMENDATION

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35 For the foregoing reasons, the Council recommends that E-2.07, “Clinical Investigation”; E-2.079,
36 “Safeguards in the Use of DNA Databanks in Genomic Research”; E-2.08, “Commercial Use of
37 Human Tissue”; E-8.08, “Informed Consent”; H-315.978, “Privacy and Confidentiality”; H-
38 315.983, “Patient Privacy and Confidentiality”; and H-460.931, “Genetics Testing Legislation” be
39 reaffirmed in lieu of Resolution 1-A-10 and that the remainder of this report be filed. (Reaffirm
40 HOD/CEJA Policy)

Fiscal Note: Staff cost estimated at less than \$500 to implement.

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