

DATABASES AND SAMPLE BANKS: NEW ISSUES

BACKGROUND:

For decades, databases and sample banks have been maintained as a way of conducting retrospective research of a number of types. They have been helpful in allowing centers to pool results; they have been helpful in gaining long-term follow-up data; they have been helpful in testing new diagnostic tests or classification schemes. As a simple example out of many, the current lymphoma classification was largely developed through retrospective review of thousands of stored biopsy specimens in the light of newer pathophysiologic knowledge, then comparing the observations with the clinical outcomes in the patients. For another, the frequency of HIV's introduction into our population was confirmed by retrospective testing of stored plasma samples from hemophiliacs.

At a technical level, many such databases and sample banks have operated in violation of either confidentiality law or ethical principles related to patient confidentiality. However, this has not been a matter of burning concern, because the risks of confidentiality breaches were small and the research and public health utility of the repositories were significant.

Several factors have combined to occasion a higher level of scrutiny; these include (but are not limited to):

- 1) The ability to detect information that would be embarrassing, that the subject may or may not wish to know (e.g. misassigned paternity);
- 2) The ability to detect genetic or other markers of disease susceptibility, which persons other than the subject may wish to know;
- 3) Attempts by employers and insurers to gain access to research data, specifically for the purpose of denying employment, denying insurance or rating insurance higher;
- 4) Commercial developments involving stored samples, in which there might be ownership issues;
- 5) Use of stored samples for research or other purposes which the donors have found objectionable;
- 6) A generally increasing sense of patient/subject autonomy ("respect for persons" as it is termed in the Belmont Report)
- 7) Concern for the limited legal durability of consent for release of medical records;
- 8) Concern for the invalidity of parental consent for a minor who has since consent reached majority.

In short, the risk of having data or samples in a repository can no longer be assumed to be trivial. A higher standard is clearly in order, but consensus is still building as to exactly what that standard should be; even thornier is the question how to handle the transition with respect to samples and data collected/retained under a confidentiality standard now found wanting.

GENERAL PRINCIPLES:

- 1) Under ordinary circumstances, a physician is ethically enjoined from releasing diagnostic information or other personal data about patients to someone who is not involved in the patient's care;
- 2) Under ordinary circumstances, the patient/subject has the right to give or deny consent for the research use of data or materials obtained from him/her; this right is very strong when the data or materials retain identifiers linking them to the patient/subject;
- 3) A research subject has the right to know the nature of the research in which his or her participation is sought;

- 4) A research subject has the right to know the risks of research participation; this extends to risk of breach of confidentiality;
- 5) research subject has the right to withdraw from participation in research at any time; this includes the right to withdraw from durable confidentiality risks;
- 6) Use of donated materials for a purpose other than that for which they were donated may create a burden of renewed consent;
- 7) Approaching patients/subjects for renewed consent may create its own risk of breach of confidentiality and may itself be intrusive.

INTERIM RECOMMENDATIONS:

- 1) The best single step for researchers entering data or samples into banks is to get a forthright consent from the donor, in a process which discloses:
 - a) The nature of the planned research, including enough broad description that it does not narrowly restrict the investigators' ability to use the resource. The basic idea here is to find out if there is any type of research to which the subject might object (e.g. some conservative Catholics may not wish to contribute to research involving manipulation of fertility). Because the precise use of a sample bank or databank ten years hence is speculative, one should be pretty broad;
 - b) The nature of the confidentiality risk; What sort of identifiers will be on the material; who can have access and how; how long will the material be held; where will it be held?
 - c) The severity of the confidentiality risk; How sensitive is the information likely to be generated?
 - d) The voluntariness of participation;
 - e) The freedom to withdraw; How will the confidentiality risk be terminated?
 - f) The degree to which ongoing access to medical records is being sought for correlative information, and the duration of such access; Note that the ethically-allowable interval may be longer than the legally-valid durability of consent, so this can get sticky";
 - g) Whether or not it is anticipated that the subject might be approached for follow-up information or follow-up samples in the future (a process to which the subject should have the opportunity to give or deny consent)
- 2) The best way to deal with the confidentiality risk is to eliminate it by stripping the samples or data of all identifiers which can be linked to the original patient/subject/donor. For waste samples or clinical data, this may allow exempt status and very likely will allow expedited IRB review.
- 3) The utility of the sample bank or database may depend on the ability to make a link to the original source, in order to correlate with clinical outcomes and the like. In this case, the sample should bear a code, the code should be secure and there should be limited access to the code. The sample should bear no identifiers which can be traced to the source in the absence of the code.
- 4) If data or samples from a child are entered in a bank on the strength of parental consent, that consent ceases to be valid when the child reaches majority. This transition should be specifically planned for in studies involving long-term follow-up of children.
- 5) If data or samples are to be used in a manner qualitatively different from that to which consent has been given, renewed consent may be necessary. Because this can be intrusive and create confidentiality risks of its own, this should be avoided through broad but forthright consent

discussions with the donor at the time of banking. It is expected that IRBs or Ethics Committees may have to review such cases to decide when re-consent is appropriate.

- 6) If a subject decides to withdraw from participation in the tissue bank or database, the subject has that right. Such withdrawal must include the opportunity to withdraw from the continuing confidentiality risk; that implies that the subject has the right to demand the breakage of any identification links to his or her samples or data; some IRBs have held that it extends to a right to demand destruction of the samples or data.
- 7) Consent wordings for "routine disposition" of tissue samples and for "teaching use" of data and samples are not adequate to address the risk as currently perceived. Improved wording in surgical consent forms and general care consent forms may help, but explicit consent forms aimed at satisfaction of current concerns are far better.
- 8) For data and samples collected prior to 1996 [the date of passage of a Minnesota patient privacy law], there is unlikely to be an adequate record of consent; yet it may be burdensome for the investigator and intrusive to the subject to seek a 1996-style consent from the old subjects & moreover, many of them may be dead or be unable to be located. Rather than discard useful material in response to changing standards, it seems reasonable instead to:
 - a) remove identifiers wherever it is consistent with the planned use of the material;
 - b) use a secure code linking identifiers to code-labeled samples where a link is required;
 - c) submit IRB approval requests for new uses, expecting many of them to be approved easily.

COMMENTS:

It is expected (from experiences at the few centers who have kept track) that most patients/subjects will happily give very broad consent. Of those who do not, most will give some sort of restricted consent. It is therefore expected that this will have only a very modest impact on subject accrual. The big issues, here, are being absolutely frank with the subjects/patients/donors and containing the confidentiality risk in an effective manner.

IRBs will be increasingly asking for information as to the manner in which these issues have been addressed. If that is set forth in the original application, it will save a lot of hassle and may avoid the need for multiple passes through the Committee in order to gain approval.

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