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# Guidelines for the Retention, Storage, and Use of Residual Dried Blood Spot Samples after Newborn Screening Analysis: Statement of the Council of Regional Networks for Genetic Services

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**These guidelines provide scientific information for policy development by state health departments considering appropriate use of newborn screening specimens after screening tests are finished. Information was collected, debated, and formulated into a policy statement by the Newborn Screening Committee of the Council of Regional Networks for Genetic Services (CORN), a federally funded national consortium of representatives from 10 regional genetics networks. Newborn screening programs vary widely in approaches and policies concerning residual dried blood spot samples (DBS) collected for newborn screening. Recognition of the epidemiological utility of DBS samples for HIV seroprevalence surveys and a growing interest in DBSs for DNA analysis has intensified consideration of issues regarding retention, storage, and use of residual DBS samples. Potentially these samples provide a genetic material "bank" for all newborns nationwide. Their value as a resource for other uses has already been recognized by scientists, administrators, and judicial officials. Programs should promulgate rules for retention and use of residual newborn screening DBS samples based on scientifically valid information. Banking of newborn samples as sources of genetic material should be considered in light of potential benefit or harm to society.** 

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## BACKGROUND

The Council of Regional Networks for Genetic Services (CORN) is a federally funded project to improve the quantity, quality, and availability of cost-effective genetic services in the United States. CORN was developed in 1985 in response to the need for an organization that could coordinate activities among federally funded genetic service networks encompassing the entire United States and could implement programs of national significance that emerge from regional initiatives in priority areas such as quality assurance, data collection, and education. Two delegates from each of the 10 defined networks serve on the CORN steering committee with additional representation from the Alliance for Genetic Support Groups, national sickle cell disease programs, and certain other organizations involved in genetic services. CORN members constitute a unique organization of genetic service providers, public health personnel, and consumers. In its goals



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and activities, the organization focuses on the public health components of genetic services.

The Newborn Screening Committee of CORN was formed in 1987 to address national and regional issues about newborn screening. A major goal of the committee is to provide guidance in the resolution of universal problems and concerns that affect the public health community conducting newborn screening programs. Previously, the committee developed guidelines for newborn screening systems (1). The guidelines presented here are intended to help newborn screening programs make decisions about developing protocols and justifications for length of retention of residual dried blood spots (DBSs) once the newborn screening process has been completed. These guidelines provide specific information about (1) duration and conditions of storage, (2) elements associated with sample release and use, and (3) concerns with the potential DNA banking of samples. In all cases, newborn screening programs should have written procedures for storing, releasing, and using residual samples.

## INTRODUCTION

Currently, most newborn screening programs destroy all residual DBS samples within a year after the newborn screening analytical process has been completed. However, some programs save some or all of their samples for a number of years on the basis of potential public health needs and concerns, acknowledging that these samples could be subpoenaed for forensic or other legal purposes (e.g., analysis in a lawsuit for failure to detect a specific screening disorder). A widely disseminated belief is that saved samples can only negatively impact a program's legal liability by providing evidence of an analyte that "should" have been detected. The decision to save residual DBSs should be justified, and related protocols developed, using scientific reasoning and all available information. A decision not to save the DBSs beyond a certain time should likewise be carefully weighed against all information. The program's advisors (see Section 1.3 in ref. 1) should participate in any decisions and policy developments concerning residual DBSs.

Decisions concerning the length of retention of residual DBSs should be made on the basis of the stability of the analytes of interest, the potential use of the DBS samples, and technical issues concerning proper storage and ease of retrieval. An extensive search of the literature concerning stability of analytes in DBSs was performed, but was of minimal value in making decisions about long-term storage. Table 1 gives a review of the most recent or the most comprehensive published data for stability of newborn screening analytes in DBSs. These stability studies were performed using a variety of procedures and conditions, and most did not result in meaningful conclusions about long-term storage outcomes. The storage studies were performed over relatively short periods and provided sufficient data relevant only to the testing environment for identifying disorders among newborns. Interpretation of stability data was inconsistent and included evaluations based on analyte concentration either for disease classification or for recovery level. Elution schemes for DBSs were usually carried out for fixed time intervals; therefore, data from samples that eluted slowly could be misinterpreted as resulting from sample instability. Analytical reference points for assessing stability were often weak. The general conclusion from these published studies was that data are not available for predicting stability outcomes from long-term storage of DBSs and that, for maximum stability of most analytes, DBSs should be stored at low temperature and controlled low humidity.

Advances in techniques for obtaining DNA from DBSs and refinements in applying polymerase chain reaction (PCR) technology have provided an analytical mechanism for generating numerous genetic tests from a single DBS. Scientific and forensic concerns have accelerated interest in the potential use of existing DBS sources for these genetic studies.

**TABLE 1**
**Stability[a] (months) of Analytes in Dried Blood on Filter Paper**

| Analyte | −20°C | 4°C | Ambient | Reference |
|---|---|---|---|---|
| Apo A-1 | 43 days | 1 day (25 days) | 1 day | 3 (4) |
| Apo B | 7 days | 3 days (1) | 3 days | 5 (4) |
| β-Globin DNA | — | — | 1 year | 6 |
| Biotinidase | — | — | <2 days | 7 |
| Galactose | — | 1.5 | 1 week | 8 |
| Galactose-1-phosphate | — | 2 | 1 week | 8 |
| G-1-P uridyltransferase | — | — | <15 days | 9 |
| Hemoglobins—F.A.S.C | 3 | — | –(1) | 10(11) |
| hepatitis B antigen | 6 | 6 | 6 | 12 |
| HIV-1 antibodies | 6[b] (5) | 6[b] (5) | 2[b] (1,5) | 13(14) |
| HIV-1 proviral DNA | 3,5[b] | — | 3.5 | 15 |
| Leucine | 5 | 5 | 2 weeks | 16 |
| Methionine | 5 years[b]) | 5 | 5 | 16 |
| Phenylalanine | (2 yr) | 5 | 5 | 16(17) |
| 17α-hydroxyprogesteron | — | 7[b] | 7 | 18 |
| Thyrotropin (TSH) | 1 | 1,(1 year[b]) | 1 | 19(20) |
| Thyroxine ($T_4$) | — | 5,(1 year[b]) | 5 | 21(20) |

*Note.* References in parentheses refer to corresponding stability times in parentheses.

[a] Maximum stability may be greater than indicated but is limited to length of experiment.

[b] Desiccated conditions.

Whole blood absorbed into filter paper and then dried offers an excellent means for creating a repository (bank) of samples for DNA investigations. Such a storage system is already in use for biological "dog tags" for military personnel (2). Some researchers and public officials are considering mechanisms to require the retention of DBSs by newborn screening laboratories as a foundation for future DNA banks. Many issues have arisen surrounding the need for DBS sample banking: the potential public health value; other possible uses; appropriate sample release procedures; personal privacy issues; and other ethical, moral, social, and legal concerns. The value of national DNA sample banks for all newborns has been debated in many scientific discussions. The impact of decisions from vested interest groups on current newborn screening systems is unclear and the final decisions may ultimately be made with little consultation from newborn screening programs.

## 1. SCIENTIFIC ISSUES

### *1.1 Retention of Samples*

*How long are DBSs currently retained by screening programs?* Among the state newborn screening programs, the length of time for storage of residual samples varies: 10 programs save samples for 21 years or more; 6 programs, for >5 to 7 years; 2 programs, for >1 to 3 years; 6 programs, for >6 to 12 months; 21 programs, for >1 to 6 months; 5 programs, for 1 to 4 weeks; and for 3 programs retention information is not available (22). Only one program is known to save residual samples at low temperature (−20°C) in sealed bags containing a desiccant. A few states have retained in excess of a million residual samples. Some states have indicated that saved residual DBSs may become a permanent collection. The cost estimates for low-temperature storage or any other storage systems have not been reported. In addition, no detailed information is available on the various storage systems used by the various programs.

*Why save DBSs after newborn screening is complete?* Clinical laboratories do not usually retain residual serum or blood samples after the results have been reported for the test for which the samples were originally collected. If questions arise regarding test results, fresh samples are collected to ensure integrity of the sample, and the analysis is repeated. Analogous to some newborn screening programs, pathology laboratories do retain autopsy samples for some extended periods. When a laboratory sample is retained, it should be stored carefully and appropriately for an intended purpose. The duration of storage should meet the defined purpose.

Some reasons for retaining residual DBSs include: legal accountability (e.g., number of punches taken for analysis, the existence of a sample and its adequate collection), future DNA testing, reconfirmation of newborn screening analytical results, new method evaluations and comparisons, epidemiological or other public health surveys, special health-related studies for patient or family, and forensic studies.

Some reasons for discarding residual DBSs include: lack or uncertainty of analyte stability, high storage cost, unavailability of suitable storage space, no defined justification for future use, no mechanism for easy retrieval, no quality assurance system to ensure integrity of stored samples, lack of informed consent, and the failure to contribute positively to legal liabilities.

*Why retain residual DBSs for possible DNA testing?* A policy of retaining samples for possible DNA analysis may be questioned on the basis of its expense and the unknown demand for use of the samples. Locating a specific DBS within a sample storage facility, potentially containing millions of samples, may be a problem if retrieval procedures are not carefully planned. Ownership of the DNA in a residual DBS is also an issue, especially given the current informed consent process used by most programs (i.e., legally required with attention given only to dissent). Without informed consent about specific sample use, DNA ownership and use is an issue. Sample ownership and use may be an issue even with informed consent. Saving DBSs for use in the identification of a person may ultimately infringe on the rights of the individual (see Section 2.3).

*What are the concerns when using residual DBSs in method studies and evaluations?* For validating new analytical methods or for comparing methods, studies usually require samples of a collection age closely approximating the age of samples intended for use in the proposed method. Compromised or potentially compromised samples from uncontrolled storage are usually not scientifically suited for method evaluations or comparisons.

*What is the appropriate means for disposing of residual DBSs?* When the length of storage specified by the program's policy on use and storage of residual DBSs is reached, samples should be inciner-

ated or otherwise safely destroyed. If samples must be transported off site for incineration or destruction, precautions should be taken to assure that confidentiality of samples during transportation and destruction is maintained and that appropriate disposal of samples is achieved (i.e., no identifying information should be attached). The program's specified length of retention for DBSs should be consistently met. All information about disposal of residual samples should be documented.

### *1.2 Storage of Samples*

*Usage of retained DBSs is directly impacted by the concern and care applied to their storage.* If a newborn screening program elects to store residual DBSs for an extended period of time, a scientifically sound and justifiable approach to storage should be taken and there should be careful planning. A storage policy should be developed and advice and consultation should be obtained from programs experienced in long-term storage of DBSs and from other organizations maintaining sample banks [e.g., the military, Centers for Disease Control and Prevention (CDC)]. Flow charting the process and using barcodes or other electronic media identification should be considered in the cataloging process. Systems for easy access and retrieval should be carefully designed, and storage conditions should be maintained with careful documentation (23). Additionally, the long-term cost and technical logistics of maintaining a sample bank should be anticipated.

*Optimal operation of a DBS storage facility requires that storage be carefully planned and that storage conditions be specified and monitored.* If the purpose for saving samples involves future analysis, screening programs should use data that address the stability of various analytes when making decisions about storage conditions (see Table 1). The defined purpose of storing samples should dictate the environmental parameters for storage. Ideally, residual DBSs should be stored frozen (preferably at –20°C) in sealed bags of low gas permeability containing a desiccant and a humidity indicator. Samples retained only for DNA testing may be stored refrigerated (preferably at 4°C) in sealed bags of low gas permeability and contain a desiccant for humidity control. In all storage situations, precautions should be taken to ensure that possible contamination from sample-to-sample contact is not a problem. During storage, a humidity indicator should be periodically monitored and appropriate action taken to reactivate the desiccant when humidity exceeds 30% (13, 17) or some other designated level of action. Every DBS should be properly identified. An index or catalog should be maintained so that any individual sample can be easily located. Whenever a sample is retrieved, documentation should be kept indicating: (1) who had access to the sample; (2) the purpose for which the sample was accessed; (3) the authorizing authority; (4) the chain-of-custody from retrieval to analysis; (5) the amount of sample released; (6) the results of any analysis of the sample; and (7) changes to any demographic or descriptive data. Appropriate and secured records should be maintained in a manner similar to that required for maintaining legal evidence in forensic laboratories. A quality assurance system is necessary for documenting the integrity of the stored DBS. At least two newborn screening programs have recently developed detailed sample storage policies and planned storage systems.

*A quality assurance system should be designed to ensure validity of stored samples for their intended purpose.* If the analytes for which the DBSs are being saved are known, then appropriate assayed DBS quality control samples should be included in the storage. All control samples must be handled and maintained under identical processing conditions to the stored samples. In order to prevent location bias, control samples should be randomized in the storage system. Compromised or potentially compromised samples have limited scientific value.

### *1.3 Use of Stored Samples*

*What studies and applications have been identified for using stored residual DBSs?* The DBS material remaining after newborn screening has been completed can be used effectively for epidemiological studies and for analytical method development, comparison, and validation. Such uses are generally considered to be important public health applications for these residual samples. For example, the HIV seroprevalence survey among childbearing women (24) that provides important public health data on the spread of HIV infections was predicated on the use of residual DBSs. Each use entails specific requirements [e.g., the need for fresh samples (within a short time after collection) and the need for specific demographic information linked to the sample]. To date, few studies have required samples older than a few months. Because requests for samples for studies of these types have been limited,

most screening programs have no laws or regulations governing the use of residual DBSs (see Section 2.3). Each request is reviewed for individual merit and release decisions are made accordingly.

*Should residual DBS samples be provided for public health epidemiological studies, for assessing their use in detecting new disorders, and for the validations of new methods?* Screening programs should establish a review process to be followed for all DBS requests and to ensure valid use of these samples before their release. The laboratory should have a written policy for release of residual DBSs (see Section 2.3). Samples should not be released from the laboratory with personal identifying data (or demographic data that could potentially identify a person) without appropriate signed consent (e.g., from the parents of the newborn). Further, all studies using residual DBSs should be reviewed and cleared by a Human Subjects Review process. The screening program's advisors (see Section 1.3 in ref. 1) should be involved in the decision process. When samples are released, the recipient of the sample should be advised that, although low in potential biological hazards, DBSs are nevertheless biological materials and appropriate precautions should be exercised in their handling.

### *1.4 Financial and Professional Considerations*

*Costs are associated with storage and retrieval of DBS samples.* Most epidemiological studies and method evaluations have support funds available, and the storage laboratory should carefully consider reimbursement for costs in cataloging, storing, and retrieving samples, including any specialized processing such as removing personal identification, retrieving special sample sets of specific categories, and providing demographic databases. Reimbursement should also be considered for provision of DBSs to commercial manufacturers for research applications. Small numbers of anonymous residual DBSs might be provided free of charge to individual researchers at the discretion of the program director. Funds generated from stored samples should be used for cost offsets to the storage program. Authorships or professional acknowledgments related to sample use should be agreed in advance of any publication. Such items as time and work related to sample access, difficulty in information retrieval, and related analytical or demographic information used might be included in these considerations.

## 2 LEGAL AND ETHICAL ISSUES

### *2.1 Retention of Samples*

*When appropriately used, retained DBSs may be valuable resources with potential benefits for individuals and society.* Solutions to the legal and ethical concerns about the retention of residual DBSs are unclear. As more and more screening programs consider retaining DBSs and as the use of DNA technology in detecting genetic disorders rapidly expands, a more formal approach to legal and ethical concerns should be taken. Some of the questions to be addressed include: (1) the stability and suitability of analytes in DBSs (see Table 1); (2) the length of time DBSs should be retained and for what purposes; (3) the requirement of legal consent; (4) the removal of identifiers; (5) a Human Subjects Review process; and (6) the ownership of the DBS. A recently published review (2) describes both the importance of retaining sample collection cards and the importance of DNA banks. The existence of these unplanned DNA banks for newborns has raised concerns regarding the privacy of medical records because of an increase in the amount of DNA information available (such as disease susceptibility) through technologic advancements (2).

*An ethical concern is retaining DBSs with the capability of linking them to patient information.* Currently, the trend is for states either to retain DBSs for longer periods or to be increasingly concerned about destroying them in a specified period. Because of the claimed value of these samples, it is becoming more difficult to justify not retaining and storing them for longer periods. However, in a recent Institute of Medicine report, the statement is made that DBSs should be made available for research "only if identifiers have been removed" (25). This concern for confidentiality continues to fuel the ethical debate over public health benefits versus personal privacy.

*Retained DBSs may be useful in certain legal situations.* Because of the proliferation of DNA studies, DBSs are increasingly considered for DNA analysis. One of the main areas of consideration is forensic use. Some states are enacting or have enacted legislation in this area and two reviews have recently been published on this subject (26, 27). Some state, territorial, or federal law enforcement agencies may maintain their own DNA banks. Nevertheless, residual newborn screening samples or

other potential DNA samples collected for public health purposes should be used only after careful consideration in any legal cases. These samples should be released only after consultation with legal counsel and only if the requesters can show that there is no suitable alternative source.

### *2.2 Privacy Protection*

*Formal procedures, documentation, and written policies should be considered when planning for DBS sample storage.* Because of the increasing number of requests for DBSs, the procedures and regulations regarding the release and use of DBSs should be formalized (28). In a previously cited study (2), only 13% of the states indicated that there were written regulations from state departments of health about third party access to samples. Of all state laboratories reporting, 19% had some internal written policies (2). One state has established rules and regulations requiring that all requests for samples should be in writing and should include information about project goals and intended use of results. A committee within the state agency is required to review all requests before acceptance or rejection. Most newborn screening programs lack sample storage systems or policies for DBSs that meet the legal chain-of-custody requirements for samples of potential use for forensic purposes. Programs should ensure that sample storage procedures are appropriate for the samples' intended uses.

### *2.3 Use of Samples*

*Appropriate consent is an important issue.* Most state screening programs use informed refusal, or dissent, meaning that parents may refuse the DBS collection and subsequent screening tests which are otherwise required by law. In one state, agreeing to the test also implies consent to use the residual DBSs for anonymous program evaluation and research, in addition to all tests required to complete the original screening intent. With the proliferation of other uses for samples, the type of consent or refusal obtained should be clarified (29). The collection form and educational material for parents could indicate that the sample becomes the property of the state and that, unless the parents object in writing, the sample may be used without personal identifiers in studies related to preventing birth defects and disorders of the newborn or for protecting the public's health. In such cases, a protocol for obtaining parental consent for any studies that are not anonymous may be needed. Some legal experts have proposed, on the other hand, that proper informed consent is impossible since it is not possible to adequately inform or educate a parent about all potential uses and outcomes associated with the consent.

Release of identifying information should only occur after thorough review by a Human Subjects Review Board and should require written consent if there is any possibility for the identification of adverse outcomes. Whenever DBSs are released, only a minimum quantity of sample should be released and at least one spot should always be retained for program purposes. The use of this remaining spot should be a matter of program policy. A possible acceptable use might be for further testing (at the family's request) when clinical problems exist relating to patient or family health. When providing residual DBSs for any use, the screening program, its advisors (see Section 1.3 in ref. 1), or its review board must be cognizant of any local or state laws or regulations that take precedence for sample use.

The issue of counseling parents when test results are released should be addressed. DBSs should not be released to the parents; however, with the parent's written permission, the samples may be released directly to a laboratory or a physician. This suggestion is justified on the basis of possible contamination of the sample in the hands of the parent, a situation that would complicate the clinical picture. Therefore, a state agency cannot protect itself from legal problems if DBSs are released directly to parents. Limited, aggregate demographic data may be considered for release in epidemiological studies, on anonymous samples, with the approval of a Human Subjects Review Board. Care should be taken with unlinked studies to ensure that small cell sizes of demographic data cannot lead to personal identification through such data. Anonymous test results directly related to the screening program itself may not require such review.

*Many different types of requests for DBSs should be anticipated by the newborn screening program.* One board category of requests for residual DBSs includes special studies for which significant numbers of samples are requested. A second category includes individual requests from families or family physicians in order to identify a possible disorder contributing to a family member's morbidity or mortality. If identifiers are required for a study,

or contact of patients or families is needed, there should be no release of DBSs or data without using an approved Human Subjects Review protocol, including consent, terms of release, and confidentiality protection. Strict documentation should be applied for all uses of DBSs, including to whom and for what purpose the samples were released and whether or not special consent was obtained. Some examples of specific types of requests are cited below:

*Subpoena.* In most instances, a subpoena should be required for all releases of DBSs or test results relating to a legal case, especially where chain-of-custody must be documented. However, there may be some instances in which a mutual agreement between the screening program and the requester leads to release of a DBS without a subpoena.

*Special Cases/Family Studies.* A common altruistic type of release (with written permission of parents or closest living relative) involves testing a DBS from a deceased child to determine a previously unknown cause of death. For example, testing for Medium Chain Acyl-CoA Dehydrogenase Deficiency (MCADD) or Cystic Fibrosis (CF) may be requested. Knowledge of previous test results may be useful in making subsequent decisions about pregnancy or in treating living siblings. In one instances, a mother was unjustly charged with the murder of her child by poisoning the child with antifreeze when actually the infant died of methylmalonic acidemia (30). Only after the same diagnosis was made through testing of another of her children was the mother cleared of the charge. This unfortunate situation might have been avoided if a residual DBS had been available. In most of these instances, the screening program's advisors (see Section 1.3 in ref.1) should be consulted before a sample is released.

*Research Studies.* These studies may be an appropriate use of residual DBSs if the following criteria are met: (1) Anonymous testing — Anonymity appears to negate the need for obtaining parental consent since no possible physical or psychological harm to the parents or child could result and because the sample can provide population data that is important in public health studies. An argument might be made that under certain conditions, population studies may be detrimental. Controversy regarding anonymity may also arise when significant, treatable problems are found in the sample of a person who cannot then be identified. For example, many states are currently struggling with the issue of the anonymity of HIV testing of DBSs since research indicates that transmission of the virus can be reduced by up to 65% through infusions of zidovudine (3′-azido-3′-deoxythymidine, ZDV, AZT) during late pregnancy and delivery (31). By the time of testing, it is too late to affect the outcome (since corrective measures do not currently exist for completely eradicating the virus in the newborn), but releasing the information to a mother for use to prevent transmission during a subsequent pregnancy could be important. (2) Reanalysis — Retrieval of a sample may be useful in order to attempt confirmation of original analytical results. Confirmatory testing might contribute to the resolution of a legal issue (e.g., to attempt to prove misidentification of a sample by DNA testing, to confirm late onset of disease, or to verify an original test result) if the DBS was not compromised during storage (see Section 1.2). Absence or decreased concentration of an analyte, when confirming original results; must be carefully weighted against proven stability of the analyte and appropriate storage conditions. Specific samples may also be retrieved to verify the adequacy of storage conditions or to provide documentation for a quality assurance assessment of stored DBSs. (3) Limitations — Since the amount of stored blood spot material is limited and finite, its potential use should be of significant impact, especially when usage of large numbers of DBSs are required. Inherent in any proposed use of newborn screening DBSs should be some element of contribution to public or family health or some contribution to the goals of public health genetic screening. Prioritizing possible uses of DBSs should be considered by each screening program in its written procedures.

The following examples represent special types of requests for residual DBSs that have been received by some newborn screening programs:

*Individual Requests.* In one state, there were approximately 20 requests for access to individual DBSs for testing in 1 year. These are some specific examples of requests: to study MCADD and sudden infant death syndrome (SIDS), to rule out mitochondrial DNA mutations, to study carbohydrate-deficient glycoprotein syndrome, to confirm an initial negative $T_4$ value in a legal case, to perform Werdnig-Hoffman disease linkage analysis, to study DiGeorge's syndrome (transfused infant), and to rule out galactosemia after an original screening result was reported negative for the disorder (see Section 1.2).

*Large-Scale Requests for DBSs or Data Bases.* Most of the research studies requested fewer than 1000 samples of known cases and approximately

equal numbers of control samples. Studies for which large numbers of DBSs have been retrieved include these: MCADD, SIDS, HIV seroprevalence study, conotruncal heart malformations, oral cleft malformations, genetic basis for cerebral palsy, hypothyroidism (test results only), sickle cell trait and SIDS (test results only), childhood leukemia, cancer-gene studies, miscellaneous hemoglobin results for new test development, and folate-receptor variants.

*2.4 Privacy and Other Ethical Concerns*

*The potential for permanent storage of DBSs in DNA banks and the availability of genetic information in DBSs raise ethical concerns.* Although significant benefits may be gained from the storage of DBSs for genetic testing, the general public still has many concerns. An uneasiness exists about the possible misuse of these samples leading to discrimination, psychological harm, identification of incorrect assignment of paternity, and potential social injustices (28). Widespread testing for genetic factors (e.g., susceptibility) is not recommended for newborns when no clear indication of disease exists or where no medical intervention is possible (32).

## CONCLUSION

Currently, most state and territorial newborn screening programs have few or no procedures for retaining, storing, retrieving, and using residual DBSs. In reaction to continued questions about these issues, some newborn screening programs have either avoided the questions or reacted on a case by case basis with little or no scientific basis for their actions. Few scientifically sound procedural systems for retention, storage, and use of DBSs remaining after newborn screening currently exist. Each state has its own opinions, laws, concerns, and rationale for handling residual DBSs, and most programs are seeking nationwide guidance from the screening community. The ethical concerns of the public and the judiciary about issues related to discrimination and privacy may ultimately dictate policies related to retaining or destroying residual DBSs. Since it is likely that conclusive decisions regarding DBS banking of samples from all newborns for possible DNA analysis will be determined by the judicial system (27), it is hoped that the basis for such decisions will be based on the potential benefit or harm to society. Any decisions should include reflections on the numerous considerations presented in this guideline. Newborn screening programs should begin now to promulgate policies and rules for retention and use of residual newborn screening DBS samples. These guidelines are intended to establish a groundwork for the decisions necessary in developing sound policies for retention, storage, and use of residual dried blood spot samples after newborn screening.

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## REFERENCES

1. Therrell BL, Panny SR, Davidson A, Eckman J, Hannon WH, Henson MA *et al.* U.S. Newborn Screening System Guidelines: Statement of the Council of Regional Networks for Genetic Services. *Screening* **1:**135–147, 1992.
2. McEwen JE, Reilly PR. Stored Guthrie cards as DNA banks. *Am J Hum Genet* **55:**196–200, 1994.
3. Wang XL, Dudman NPB, Blades BL, Wilcken DEL. Changes in the immunoreactivity of apo A-1 during storage. *Clin Chim Acta* **179:**285–1294, 1989.
4. Van Biervliet JP, Vinaimont N, Caster H, Rosseneu M, Belpaire F. A screening procedure for dyslipoproteinemia in the newborn. Apoprotein quantitation on dried blood spots. *Clin Chim Acta* **120:**191–200, 1982.
5. Micic S, Arends J, Norgaard-Pedersen B, Christoffersen K, Andersen GE. Simultaneous quantification by double rocket immunoelectrophoresis of apolipoproteins A-1 and B in blood spotted on filter paper. *Clin Chem* **34:**2452–2455, 1988.
6. Rubin EM, Andrews KA, Kan YW. Newborn screening by DNA analysis of dried blood spots. *Hum Genet* **82:**134–136, 1989.
7. Pettit DA, Amador PS, Wolf B. The quantitation of biotinidase activity in dried blood spots using microtiter transfer plates: Identification of biotinidase-deficient and heterozygous individuals. *Anal Biochem* **179:**371–374, 1989.
8. Orfanos AP, Jinks DC, Guthrie R. Microassay for estimation of galactose and galactose-1-phosphate in dried blood specimens. *Clin Biochem* **19:**225–228, 1986.
9. Frazier DM, Clemoins EH, Kirkman HN. Minimizing false positive diagnoses in newborn screening for galactosemia. *Biochem Med Metab Biol* **48:**199–211, 1992.

10. Garrick MD, Dembure P, Guthrie R. Sickle-cell anemia and other hemoglobinopathies: Procedures and strategy for screening employing spots of blood on filter paper as specimens. *N Engl J Med* **288:**1265–1268, 1973.
11. Henderson SJ, Fishlock K, Horn MEC, Oni L, Bellingham AJ. Neonatal screening for haemoglobin variants using filter paper-dried blood specimens. *Clin Lab Haematol* **13:**327–334, 1991.
12. Villa E, Cartolari R, Bellentani S, Rivasi P, Casolo G, Manenti F. Hepatitis B virus markers on dried blood spots. A new tool for epidemiological research. *J Clin Pathol* **34:**809–812, 1981.
13. Hannon WH, Henderson LO, Lewis DS, McGee SA. Preparation and characterization of human immunodeficiency virus seropositive dried blood-spot materials for quality control and performance evaluation of laboratories. In "Current Trends in Infant Screening" (Schmidt BJ, Diament AJ, Loghin-Grosso NS, Eds.). Proceedings of the Seventh International Screening Symposium; 1988 Nov 6–9; Sao Paulo, Brazil. Amsterdam: Elsevier, 1989, pp 31–63.
14. Behets F, Kashamuka M, Pappaioanou M, Green TA, Ryder RW, Batter V *et al.* Stability of human immunodeficiency virus type 1 antibodies in whole blood dried on filter paper and stored under various tropical conditions in Kinshasa, Zaire. *J Clin Microbiol* **30:**1179–1182, 1992.
15. Cassol S, Salas T, Gill MJ, Montpetit M, Rudnik J, O'ShaughnessySy CT, . Stability of dried blood spot specimens for detection of human immunodeficiency virus DNA by polymerase chain reaction. *J Clin Microbiol* **30:**3039–3042, 1992.
16. Lundsjö A, Hagelberg S, Palmér K, Lindblad BS. Amino acid profiles by HPLC after filter paper sampling: "Appropriate technology" for monitoring of nutritional status. *Clin Chim Acta* **191:**201–210, 1990.
17. Spierto FW, Hearn TL, Gardner FH, Hannon WH. Phenylalanine analyses of blood-spot control materials: Preparation of samples and evaluation of inter-laboratory performance. *Clin Chem* **31:**235–238, 1985.
18. Hofman LF, Klaniecki JE, Smith EK. Direct solid-phase radioimmunoassay for screening 17-hydroxyprogesterone in whole-blood samples from newborns. *Clin Chem* **31:**1127–1130, 1985.
19. Coombes EJ, Gamlen TR, Batstone GF. Effect of temperature on the stability of thyroid-stimulating hormone in dried blood spots. *Ann Clin Biochem* **20:**252–253, 1983.
20. Hearn TL, Hannon WH. Interlaboratory surveys of the quantitation of thyroxin and thyrotropin [thyroid-stimulating hormone] in dried blood spot specimens. *Clin Chem* **28:**2022–2025, 1982.
21. Kremer RD. Filter paper in clinical diagnostic screening. *Clin Lab Products* **11:**21–25, 1982.
22. Newborn Screening Committee. National Newborn Screening Report—1991. New York: The Council of Regional Networks for Genetic Services (CORN), 1994.
23. Michels R, Naber SP. Specimen storage and the use of a relational database. *JIFCC* **7:**67–69, 1995.
24. Pappaioanou M, George JR, Hannon WH, Gwinn M, Dondero TJ, Grady GF *et al.* HIV seroprevalence surveys of childbearing women—Objectives, methods, and uses of data. *Public Health Rep* **105:**147–152, 1990.
25. Andrews LB, Fullarton JE, Holtzman NA, Motulsky AG, editors. Assessing genetic risks: Implications for health and social policy. Washington DC: Committee on Assessing Genetics Risks, Ins of Med, Nat Acad Press, 1993.
26. Scheck B. DNA data banking: A cautionary tale. *Am J Hum Genet* **54:**931–933, 1994. [Editorial]
27. McEwen JE, Reilly PR. A review of state legislation on DNA forensic data banking. *Am J Hum Genet* **54:**941–958, 1994.
28. Annas GJ. Privacy rules for DNA databanks. *J Am Med Assoc* **270:**2346–2350, 1993.
29. Elias S, Annas GJ. Generic consent for genetic screening. *N Engl J Med* **330:**1611–1613, 1994.
30. Naber JM. Forensic application of newborn screening card in Michigan leads to murder conviction. Tenth National Neonatal Screening Symposium; 1994 Jun 7–10; Seattle, WA. [Abstract]
31. Connor EM, Sperling RS, Gelber R, Kiselev P, Scott G, O'Sullivan MJ *et al.* Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. *N Eng J Med* **331:**1173–1180, 1994.
32. Wertz DC, Fanos JH, Reilly PR. Genetic testing for children and adolescents: Who decides? *J Am Med Assoc* **272:**875–881, 1994.