Considerations and Recommendations for a National Policy Regarding the Retention and Use of Dried Blood Spot Specimens after Newborn Screening

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Draft ‘White’ Paper for ACHDNC Work Group

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Process for Paper Preparation

- Prepared draft outline for review by ACHDNC
- ACHDNC approved outline and recommended working group
- Reviewed and validated current State storage times
- Completed background literature review
- Work group members prepared various sections of paper building on literature extracts provided by workgroup chairs
- Chairs assimilated material into working draft, executive summary, and recommendations
- Three webinars of 1 – 1.5 hrs held with over 350 participants
- Work group provided input and approval of final editions of paper, summary and recommendations

Community Input

- Three Webinars with Stakeholders
- Webinars designed to provide the newborn screening stakeholder community with information about a subject of special interest to the ACHDNC and to solicit outside input into the preparation of a discussion 'white paper' that may lead to further ACHDNC actions.
- Participation
  - Genetic Alliance
    - 106 participants logged into the webinar
  - Regional Collaboratives – Principal Investigators, etc.
    - 38 participants logged into the webinar
  - Association of Public Health Laboratories
    - 220 participants from 49 states

Questions/Comments Received

- Three types of questions and comments
  - Technical
  - Education
  - Policy

Questions/Comments Received

1. Technical in nature
   - What is the temperature of the biobank?
   - What should be done with unsatisfactory specimens with respect to biobanking?
   - Do you have support from prenatal providers for improving education materials about newborn screening and the use of residual specimens?

Questions/Comments Received

2. Public Education

- Will you discuss the possibility that more parents will opt out due to fear of research on their child's DNA?
- What is the likelihood the prenatal care providers will follow through with an educational mandate?
- Do you have support from prenatal providers for improving education materials about newborn screening and the use of residual specimens?
- In accordance with the recommendation that States need to be more proactive in prenatal NBS education, it would be helpful if the ACHDNC would make a similar recommendation to professional organizations.

Questions/Comments Received

3. Policy
   - Are any of the states that don't keep blood spots very long considering changing their policies to store specimens for longer periods?
   - Are you aware of any states that use a Scientific Advisory Committee in addition to an IRB to discuss study proposals using dried blood spots?
   - Would you comment on the added costs that come from requiring the duties to be expanded for collection staff to explain the retention and storage policy to parents?

General Questions

- Do these policies address the issues pertaining to the de-identification of the stored samples?
- What type of policy and recommendations can you speculate are needed (or are already included in the report) if DNA sequencing of the newborn genome is incorporated as the screening panel in the future?
- Is there a potential for a recommendation regarding what researchers can do regarding anonymous findings that might be of interest to the newborn.?

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 (1996).

Therrell BL, Hannon WH, Pass KA, et al., Biochem Molec Med 1996;57:116-24.

BIOCHEMICAL AND MOLECULAR MEDICINE 57, 116–124 (1996)
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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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Storing Newborn Blood Spots: Modern Controversies (2004)

Kharaboyan L, Avard D, Knoppers BM, J Law Med Ethics 2004;32(4): 741-8.

Storing Newborn Blood Spots: Modern Controversies

Linda Kharaboyan, Denise Avard, and Bartha Maria Knoppers

Though in existence for over thirty-five years, due to the increasing panoply of possible tests. Newborn screening programs are drawing public attention. Many jurisdictions have mandatory newborn screening programs for treatable disorders. Disorders are detected through tests on blood spots drawn from a newborn's heel soon after birth and verified through a diagnostic test with follow-up. Unbeknownst to most parents, these blood spot cards are also stored thereafter. Indeed, while dried blood spots (DBSs) are primarily used for screening for health problems, experience demonstrates that they can be made useful in various contexts unrelated to screening.

Newborn dried blood spots have taken on a new life as a result of developments in genetics and the increasing ability of bioinformatics to link DNA information with clinical data. Additionally, storage and secondary uses have been documented to occur without parental consent. In the absence of uniform guidelines, there is an urgent need to develop policies that address the issue of dried blood spot storage, secondary use and the ensuing ethical, legal, and social dilemmas.

Internationally, regionally, and nationally, governmental, professional, and consumer organizations have contributed to the debate on the storage and retention of newborn screening residual blood samples. Despite all these efforts, a consensus of opinion on any one issue has yet to be reached. We will compare current guidelines and policy documents that apply to banking DBSs and assess the similarities and differences as concerns consent to storage, length of storage, and access to stored samples. Our comparison examines countries from different regions of the world and offers different socio-political contexts for examining the rationale for storage and issues of confidentiality and consent. As novel uses of newborn spots emerge,[1] and as researchers and public officials contemplate mechanisms for the retention of DBSs by newborn screening laboratories[2], it is crucial to outline current purposes and lengths of storage and adequate consent requirements for the secondary uses of archived bloodspots in research or otherwise.

Banking Residual DBSs: Purpose and Length?

Purpose of Storing

Since the late 1960s, newborn screening to detect congenital metabolic disorders has been standard paediatric procedure in newborn care in most industrialized countries. Early detection of pre-symptomatic disorders such as Phenylketonuria (PKU) and Congenital hypothyroidism (CH) has prevented chil-

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Danish Biobank

Established in 1993
Institutionalized in 2004

Bent Norgaard-Pedersen
Statens Serum Institut
Copenhagen, Denmark

"A biobank is … a structured collection of human biological material which is accessible under certain criteria, and where information contained in the biological material can be traced back to individuals."

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Policy Statements
Residual Newborn Dried Blood Spots

- AAP Task Force 2000 [Pediatrics 2000; 106 (suppl)]
  - Develop policies for unlinked/linked residual samples in research/surveillance
  - Organize collaborative efforts to develop minimum standards for storage of residual samples at state level
  - Consider creating national or multi-state population-based specimen resource for research

APHL Position / Policy Statement -- 2005

Residual Newborn Screening (NBS) Specimens

A statement of position:

"There may be other reasons (*other than QA*) to save DBS specimens, including test development, research, and forensic identification. To retain DBSs for such purposes requires clear guidelines that are incorporated into national consensus policies that state health departments follow in carrying out their authorized NBS programs."

APHL ASSOCIATION OF PUBLIC HEALTH LABORATORIES

APHL Position/Policy Statement

Residual Newborn Screening (NBS) Specimens

A. Statement of Position

APHL supports the development of national consensus policies, procedures, and standards for retaining residual dried blood spot (DBS) specimens following NBS analysis. These policies and procedures must recognize existing federal regulations for clinical testing, state laws, professional guidelines, and ethical and legal precedents. The policies should also allow for introduction of new analytes and techniques into the NBS laboratory arena. To meet recognized laboratory quality assurance practices, DBS specimens must be retained for a time period and under conditions that permits analytical validation [1]. There may be other reasons to save DBS specimens, including test development, research, and forensic identification. To retain DBSs for such purposes requires clear guidelines that are incorporated into national consensus policies that state public health departments can follow in carrying out their authorized NBS programs.

B. Background

A survey of state NBS programs found large variations in policies regarding retention of specimens, extending from a few weeks to 21 years or longer [2]. In 1996, the Council of Regional Networks for Genetic Services (CORN) issued guidelines for the retention, storage, and use of DBSs following NBS analysis [3]. As this report noted, the length or retention of residual DBS specimens should be made on the basis of the stability of the analytes of interest, the potential use of the DBS specimens, and technical issues concerning proper storage and ease of retrieval. While methods for analyzing DNA from DBSs continue to improve and provide a mechanism for performing multiple molecular techniques from a single DBS, additional issues are raised concerning the availability of genetic information from these potential DNA banks.

Currently, the Genetic Services Branch of the Maternal and Child Health Bureau, Health Resources and Services Administration, Department of Health and Human Services, in addition to supporting the National Newborn Screening and Genetics Resource Center, has funded two contracts to develop model policies and procedures for NBS programs (American College of Medical Genetics, UCLA Center for Society, the Individual and Genetics). Both organizations held conferences on these topics in late 2002 to consider the feasibility of establishing a multi-state or central DBS bank for the purpose of providing a resource for obtaining population-based data on prevalence of gene variants of public health significance, and the association of gene variants with disease and risk factors. At the meetings, consensus was not reached on these complex ethical, public education, and scientific issues.

Professional societies have also examined these issues [4]. Until such time that recognized national policies and procedures are in place, individual states will have to address a number of technical, legal, and ethical issues regarding retention of DBSs and other specimens for potential genetic, epidemiologic, research, test development, liability, or forensic purposes. As noted in the CORN report [2], these include: 1) the stability of analytes; 2) the length of time that specimens should be retained and for what purposes; 3) the requirement of legal consent; 4) a Human Subjects Review process; 5) the removal of identifiers; and 6) the ownership of the specimens.

Source: http://www.aphl.org

National Newborn Screening and Genetics Resource Center NNSGRC

ACMG Position / Policy Statement -- 2009

Residual Newborn Screening (NBS) Specimens

A statement of position:

- Residual Dried blood spots are a valuable national resource that can contribute significantly to the health of children.
- NBS blood spots are stored with rigorous control and respect for privacy and confidentiality.
- Parents should have the option to have their child's specimen stored in a national repository for research."

American College of Medical Genetics
Medical Genetics: Translating Genes Into Health®

Position Statement on Importance of Residual Newborn Screening Dried Blood Spots

State newborn screening programs are highly valued by the public for their ability to detect newborns that are at high risk for developing diseases with high morbidity and mortality. Newborn screening provides early detection and, thereby, allows for timely treatment with proven clinical interventions that are effective in minimizing disease development. The great majority of the conditions for which newborns are screened are genetic. The dried blood spot card that is collected from the vast majority of the 4.2 million U.S. newborns each year is central to such public health-based newborn screening activities. The American College of Medical Genetics (ACMG) believes that these are invaluable resources for the improvement of newborn screening and, therefore, the health of our children. In addition to their immediate use in screening babies, dried blood spots have considerable additional value. They are essential for quality improvement of newborn screening tests and are critical in the development of new screening tests.

A newborn screening test cannot be introduced into the general population until pilot studies are done in the population. The full spectrum of a specific genetic disease cannot be known until it has been assessed in a general population. This permits determination of the range of severity of the disease, its incidence and genetic etiology in the general population and in subpopulations, as well as the performance characteristics of both the screening and diagnostic tests and the response to interventions.

The only source of material available to carry out such pilot studies and answer many of these questions is the dried blood spot. Many of these questions can be answered by use of either anonymized (no individual identifying link is retained) or deidentified (individual identity link retained and privacy and confidentiality maintained under the stewardship of the public health programs) dried blood spots. When the identity of the individual is needed, as occurs when it is necessary to test a dried blood spot to determine if a disease for which an individual has been diagnosed might be amenable to newborn screening, investigators seek typical informed consent from those involved.

A very small but very vocal minority has begun to argue for the destruction of residual newborn screening dried blood spot filter cards after screening has been completed. Their arguments are based on unsubstantiated and highly exaggerated privacy concerns. Such destruction of dried blood spots would significantly and negatively impact the quality and development of newborn screening programs.

American College of Medical Genetics • American College of Medical Genetics Foundation
9650 Rockville Pike, Bethesda, MD 20814 Telephone 301-634-7127 Fax 301-634-7275

Source: http://www.acmg.net

National Newborn Screening and Genetics Resource Center
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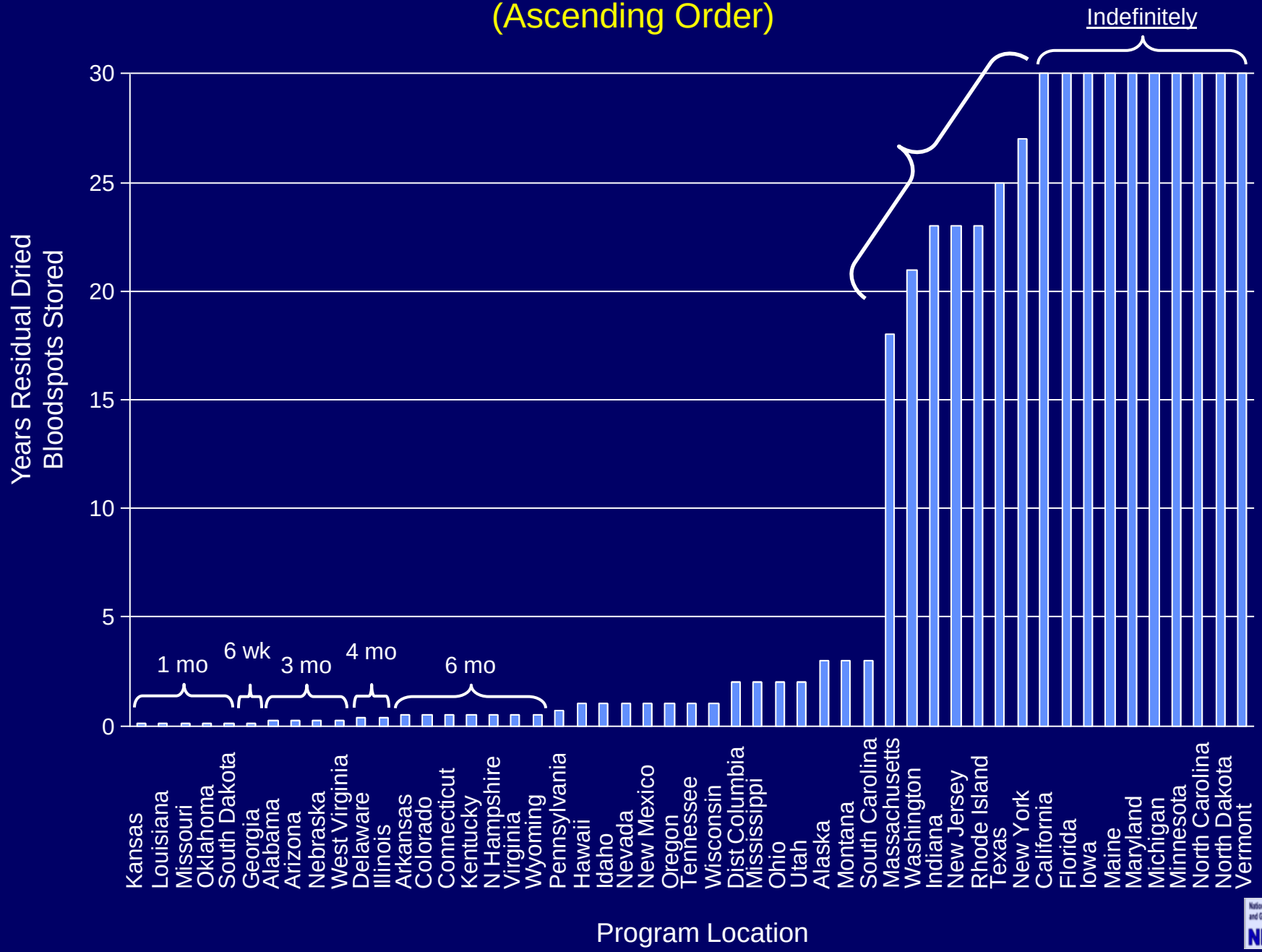
Reported Residual Bloodspot Storage – 8/1/2009

(Ascending Order)



Reported Residual Bloodspot Storage – 8/1/2009

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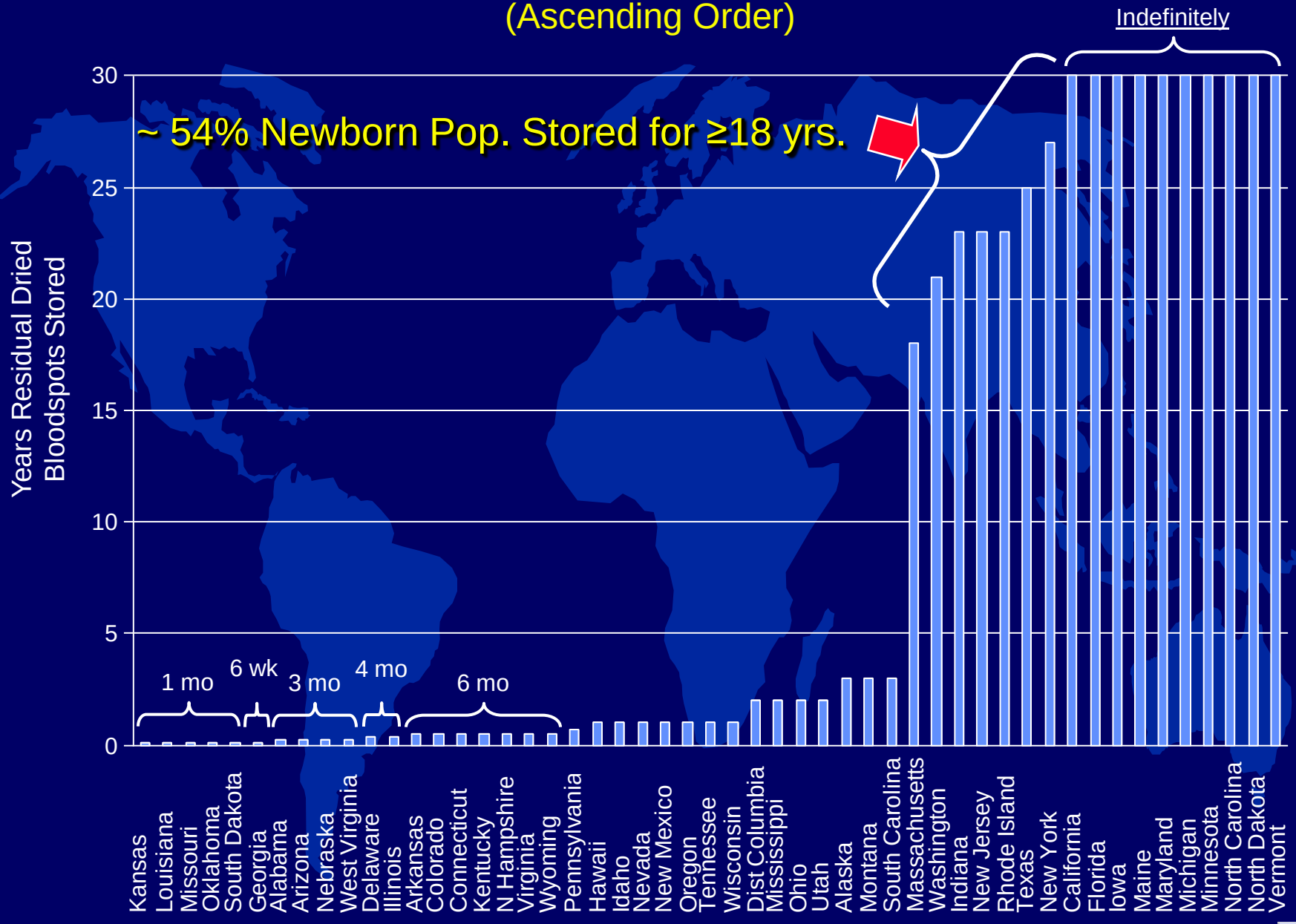

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Reported Residual Bloodspot Storage – 8/1/2009

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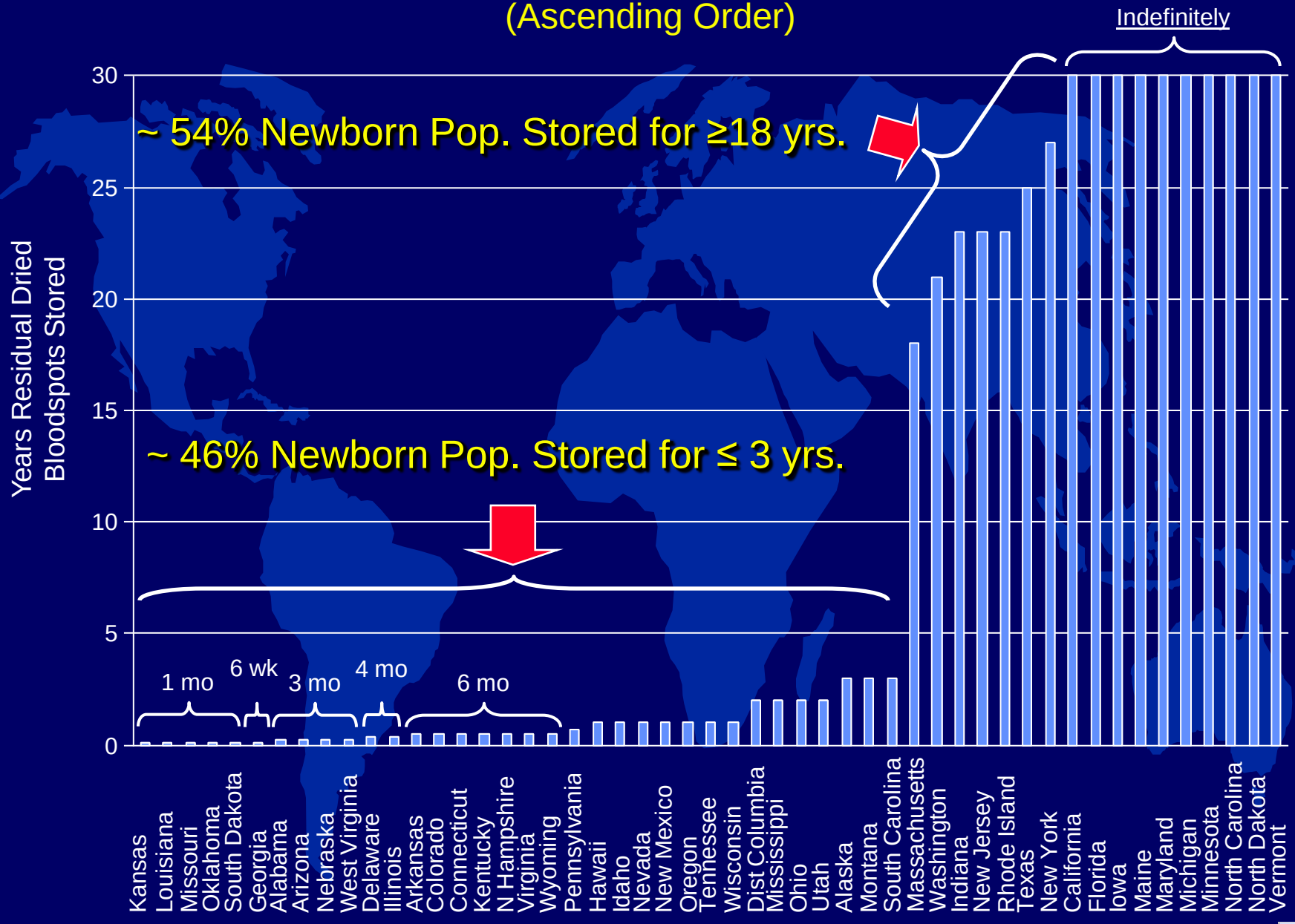

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Recommendation 1

1) *All state newborn screening programs should have a legally reviewed and accepted policy addressing the disposition of dried blood specimens remaining after newborn screening testing is complete and the screening results have been validated.*

Caveat to Recommendation 1

1) Multidisciplinary input, including consumers, should be solicited and thoughtfully considered in developing such a policy. This specimen disposition policy should include the length of time for which specimens will be stored and storage conditions. Compliance with storage processes included in NCCLS/CLSI Standard LA4-A5 or its current edition is recommended. Any data linkages should be carefully addressed and privacy and confidentiality assured.

Recommendation 2

2) All state newborn screening programs should have a legally reviewed and accepted policy that specifies who may access and use dried blood specimens once they arrive at the state-designated newborn screening laboratory, including further access after newborn screening tests are completed.

Caveat to Recommendation 2

2) Multidisciplinary input, including consumers, should be solicited and thoughtfully considered in developing such a policy. This specimen access policy should include any uses prior to and after the newborn screening laboratory testing and validation process. If uses of dried blood spot specimens outside of newborn screening are allowed, then handling and disposition of the specimen should be addressed, and privacy and confidentiality of any associated patient information assured.

Recommendation 3

3) As part of the educational process of the newborn screening system, all state newborn screening programs should maintain and distribute educationally and culturally appropriate information that includes basic information about the use or potential use of the dried blood specimens.

Caveat to Recommendation 3

3) Where long-term storage policies or other options exist relative to storage of residual dried blood spots, such information should be included in prenatal education materials.

Recommendation 4

4) *All state newborn screening programs should work proactively to ensure that all families receiving prenatal care are educated about newborn screening.*

Caveat to Recommendation 4

4) This activity should include appropriate steps to inform and train prenatal care providers regarding their educational responsibilities within the newborn screening system. Processes should be in place to evaluate the extent, timing and understanding of prenatal education with an eye towards educational program improvement.

Recommendation 5

5) If residual blood specimens are to be available for any process outside of the legally required newborn screening process for which they were obtained, an indication of the parents' awareness and willingness to participate should exist in compliance with federal research requirements (45CFR46).

Caveat to Recommendation 5

5) A consent (opt in) or a dissent (opt out) process may meet this requirement depending on purposes for which specimens will be used. The use of residual specimens for program evaluation (e.g. repeat testing as a quality check) or process improvement (e.g. non-commercial, internal program new test development) are valid components of the newborn screening system and, therefore, should not require additional consent.

Recommendation 6

6) Newborn screening programs should assess the utility of any additional consent/dissent process implemented in order to better address issues of storage and use of residual dried blood specimens.

Caveat to Recommendation 6

6) The federal government is encouraged to consider this as a priority and to provide funding for utility assessment projects over the next 5 years.

Recommendation 7

7) The federal government is encouraged to provide administrative support and funding to develop:

a) Model consent/dissent processes for the use of residual NBS specimens;

b) Model educational programs for the general public on the importance of newborn screening and the potential uses of residual specimens to generate population-based knowledge about health and disease;

Recommendation 7

(Continued)

7) The federal government is encouraged to provide administrative support and funding to develop:

c) National data on the utility of any additional consent/dissent processes implemented relative to potential research uses of residual NBS specimens;

d) Educational materials with facts about potential uses of residual NBS specimens for both consumers and prenatal healthcare providers.

Optional Recommendation
(from vetting process)

Where state newborn screening programs elect to maintain a long-term newborn screening biobank of residual newborn screening specimens, a secure third party key holder system ("honest broker"), with appropriate consent, should be used to allow for emergency linkages in de-identified specimen studies.

Caveat for Optional Recommendation
(from vetting process)

The key holder would have the ability to reveal critical health information to a study subject should such information be discovered during the course of the research, and the ability to obtain and reveal personal information from a subject to a researcher, if such information were deemed to be of critical importance. In either case, consent from the study participant or appropriate parent or guardian would be required.