

INITIAL STATEMENT OF REASONS

Summary of Proposal

The purpose of these proposed regulations is to implement Assembly Bill (AB) 2599 (Stats. 2008, Chapter 680). Health and Safety Code (HSC) Section 125002(e), requires that regulations be adopted that specify the protocols and conditions under which requests for biospecimens for research will be approved and released. The standards in these proposed regulations are limited to the release of biospecimens and/or data to approved researchers. They shall further set forth a request process, reasons for denial, and fee structure for biospecimens, related data, data linkage, data processing, and additional related services. Existing California Department of Public Health (Department) regulations do not address the provisions specified in AB 2599.

Policy Statement Overview

Problem Statement: The Department must establish guidelines for invoicing, charging and collecting fees from approved researchers that are in an amount that is necessary to cover expenses associated with research requests for biospecimens and/or data and to make these biospecimens and/or data available to approved researchers. The Governor signed into law AB 2599 which requires the Department to implement, interpret, or make specific enacted provisions by regulations that specify the protocols and conditions under which requests for the biospecimens and/or data will be approved and released to researchers.

Objectives: The broad objectives of this proposed regulatory action are to:

- Provide guidelines for invoicing, charging and collecting fees, in an amount that will cover expenses associated with research requests.
- Specify the protocols and conditions under which requests for research will be approved and released.
- Specify the protocols and conditions for biospecimen retrieval, re-inventory, and shipping.

Benefits: Anticipated benefits from this proposed regulatory action are:

- Approved researchers will be allowed use of biospecimens and/or data to develop and evaluate screening tests, prevention strategies and treatments, and identify risk factors, for women and children's diseases.
- A uniform system will be established for releasing biospecimens and/or data to approved researchers.
- Specific guidance will be provided to approved researchers identifying the procedures and costs associated with the release of biospecimens and/or data from the Department.

The nonmonetary benefits to the protection of public health and safety, worker safety, or the environment, the prevention of discrimination, the promotion of fairness or social equity, and the increase in openness and transparency in business and government, of releasing biospecimens and/or data to approved researchers is impossible to determine, but they have the potential to be significant in terms of the possible advances in the screening, prevention and treatment of diseases. Early identification and successful treatment of disease may result in a very significant increase in the financial well-being, health and welfare of the people of California.

Evaluation as to whether the proposed regulations are inconsistent or incompatible with existing state regulations

The Department evaluated this proposal as to whether the proposed regulations are inconsistent or incompatible with existing state regulations. This evaluation included a review of the Department's existing state regulations and those regulations specific to the implementation of the California Biobank Program (CBP). An internet search of other state agency regulations was also performed, and it was determined that no other state regulation addressed the same subject matter and that this proposal was not inconsistent or incompatible with other state regulations. Therefore, the Department has determined that this proposal, if adopted, would not be inconsistent or incompatible with existing state regulations.

Background

The Legislature of the State of California has found and declared that the California Birth Defects Monitoring Program (CBDMP), the Genetic Disease Screening Program (GDSP), and the Maternal Child and Adolescent Health Program (MCAH) are mandated to store, analyze and share biospecimens for research purposes. The Department maintains a large and diverse repository of over 17.5 million prenatal and newborn biospecimens (and associated databases), GDSP data, and CBDMP registry data. It also links these biospecimens and data to the State Registrar of Vital Statistics including fetal death, live birth and death data. Research requests involve biospecimen retrieval, re-inventory, and shipping as well as data requests in association with the biospecimens. Data requests involve processing, data linkage, data entry, and related data management.

Detailed Discussion of Each Regulation

The regulations interpreting, specifying, or implementing provisions of AB 2599 are in Title 17 California Code of Regulations (CCR), Division 1, Chapter 4, Subchapter 9. The justifications for the proposed regulations are as follows:

Adopt the title **Group 6. California Biobank Program** to reflect the content of the articles within the group. This is a nonsubstantial change.

Adopt the title **Article 1. Definitions** to reflect the content of sections within the article. This is a nonsubstantial change.

Adopt **Section 6550. California Biobank Program Definitions** to both address the problems and realize the benefits as stated regarding this regulatory action and identify, and define terms used within this proposal and existing regulations for clarity as follows:

Subsection (a) is necessary to define the term “batch” to clarify how specific biospecimens may be requested by a researcher and because the fee structure specified in Section 6557 is based in part on whether biospecimens can be accessed by batches or not. Biospecimen retrieval from within batches takes less staff time and effort than retrieval from a range of biospecimen locations, and therefore the retrieval cost will reflect the degree of effort required to pull the biospecimens.

Subsection (b) is necessary to define the term “Biospecimen”, this identifies that biospecimens are blood samples.

Subsection (c) is necessary to define the term “California Biobank Program” and acronym “CBP” to identify the entity that maintains the biospecimens and related GDSP and CBDMP related data and is the program to which researchers must submit applications in order to obtain the biospecimens and/or data they require for research projects.

Subsection (d) is necessary to define the term “California Birth Defects Monitoring Program” and the acronym “CBDMP.” This definition is needed to identify the California Birth Defects Monitoring Program as part of the Maternal Child and Adolescent Health Program because it is one of the three programs within the Center for Family Health (CFH) that will provide biospecimens and/or data to researchers through the CBP.

Subsection (e) is necessary to define the term “case biospecimen”. To clarify how specific biospecimens may be requested by a researcher. It is also necessary to understand how the fee structure specified in Section 6557 is calculated for specific types of biospecimens.

Subsection (f) is necessary to define the term “control biospecimen” because it indicates that controls are specific biospecimen(s) requested by the researcher. The term control also denotes where the biospecimen is stored, which directly effects the cost calculation for obtaining the biospecimen as specified in Section 6557. If the control is pulled from the same batch as the case, there is less staff time and effort required, so this type of request will cost less to obtain.

Subsection (g) is necessary to specify the term “Department” is specific to the Center for Family Health because the three programs which will make up the CBP reside within

the Department; these programs are the GDSP, CBDMP, and the MCAH. The Department will administer the CBP.

Subsection (h) is necessary to define the term “Genetic Disease Screening Program” and the acronym “GDSP” to indicate that GDSP is one of the three programs within the CFH that will provide biospecimens and/or data to researchers through the CBP.

Subsection (i) is necessary to define the term “Newborn Biospecimen” as one of the types of biospecimens that are stored by the CBP. A newborn biospecimen is one of the primary types of biospecimens that researchers will be requesting. It is also necessary to understand how the fees specified in Section 6557 are calculated for the newborn biospecimens

Subsection (j) is necessary to define GDSP’s “Newborn Screening Program” and the acronym “NBS”, which is administered by the Department and is mandated by HSC Sections 125000, 125001, and 125025 to provide organized quality-assured screening of all births in California for genetic disorders. Disorders mandated for testing are established in HSC Sections 124977, 125000, 125001 and 125025, and in Section 6501 Title 17 CCR. The Newborn Screening panel screens for over 80 disorders that include amino acid disorders such as phenylketonuria, organic acid disorders, fatty acid oxidation disorders, galactosemia, congenital hypothyroidism, congenital adrenal hyperplasia, sickle cell anemia, cystic fibrosis, and biotinidase deficiency and other hemoglobinopathies. Screening takes place in Department approved screening laboratories.

Subsection (k) is necessary to define the term “Newborn Screening Specimen Collection Filter Paper Card” which is the type of paper that newborn biospecimens are collected on and which will be available for researchers to purchase.

Subsection (l) is necessary to define the term “Prenatal Biospecimen” as one of the types of biospecimens that are stored by the CBP’s biobank. A prenatal biospecimen is one of the primary types of biospecimens that researchers will be requesting. It is also necessary to understand how the fees specified in Section 6557.1 are calculated for the two types of prenatal biospecimens. Screening takes place in Department approved screening laboratories.

Subsection (m) is necessary to define the GDSP’s “Prenatal Screening Program” and the acronym “PNS” which is authorized by the Department to screen for birth defects via the sequence of serum screening which is provided by Department approved prenatal birth defect screening laboratories. Serum screening consists of tests for pregnancy associated analytes in the first and/or second trimester.

Subsection (n) is necessary to define the term “Screening Information System” and the acronym “SIS” to identify the database and associated SIS screens that are used by the

researcher to request biospecimens and/or data from the CBP. In addition all applications and supporting documentation will be entered by research requestors into the SIS for consideration. Approval, denial or requests for additional information shall be communicated by the Department to the requestor via SIS. The Department will also use this system to manage the CBP's biospecimens and related data. All entries are stored in the CBP's SIS database.

Adopt the title **Article 2. Request Application Process** to reflect the content of sections within the article. This is a nonsubstantial change.

Adopt **Section 6551. Application Process for Requests for Biospecimens and/or Data** to both address the problems and realize the benefits as stated regarding this regulatory action and to establish an application process for obtaining biospecimens, pursuant to HSC Section 125002, as follows:

Subsection (a) is necessary to establish that the researcher must convey specific information in writing to staff of GDSP, CBDMP, or MCAH.

Subsection (a)(1) is necessary to set forth the requirement that the researcher provide the Department with a request for the specific biospecimens and/or data that are needed for the research project. This will allow the Department to determine early in the process if the research request requires biospecimens and/or data that the CBP does not possess or involves quantities that do not exist or cannot be provided without negatively impacting other research requests.

Subsection (a)(2) is necessary to set forth the requirement that the researcher describe the research project so that the Department may evaluate the request for approval or denial. A research request that does not meet the standards required by the regulations to obtain biospecimens and/or data may be denied, as described in Section 6553.

Subsection (a)(3) is necessary to establish the information about the researcher that the Department requires to begin the application process.

Subsection (b) is necessary to establish how the researcher will obtain information to securely access the SIS, into which all further information will be entered to complete the application process. Using the SIS process ensures that the confidentiality of the research request is maintained within a secure system and allows the Department to easily access all information regarding the request, which decreases staff time when evaluating and processing the request.

Subsection (c) is necessary to outline the documentation that must be transmitted into the SIS; all listed information must be received in order for the research request to be approved. It is in the public's interest that the information be uploaded into a secure system (SIS) to prevent any release of confidential information. It is in the Department's

interest that all documentation be entered into a central location, for ease of management and to decrease the cost of staff resources.

Subsection (c)(1) is necessary to allow the Department to evaluate the viability and feasibility of the request.

Subsection (c)(2) is necessary so that the Department may verify that the State Committee for the Protection of Human Subjects (CPHS) has approved the research request.

Subsection (c)(3) is necessary so that the Department may verify the researcher submitted an application to CPHS for the specific research request.

Subsection (c)(4) is necessary to establish that a signed and completed Biospecimen/Data Use and Confidentiality Agreement has been provided to demonstrate that researchers agree that their use of biospecimens and/or related data will comply as specified in the Agreement.

Subsection (c)(5) is necessary to establish that the methods used by the researcher to maintain confidentiality of the biospecimens and/or data meet established Department and statutory guidelines.

Subsection (c)(6) is a necessary means of determining whether the research is performed by persons who the Department has deemed have the appropriate expertise and training in their given discipline. Requests from researchers that do not meet the Department standards will not be approved. The researcher's curriculum vitae will provide the Department with the researcher's academic affiliations, and a bibliography of their research activities.

Subsection (c)(7) is necessary so the Department may verify that the researcher has obtained approval from the State Registrar of Vital Statistics for projects requiring Vital Statistics data (fetal death, live birth and death records) in accordance with HSC Sections 102430(a)(4) and 102430(c).

Subsection (c)(8) is necessary to allow the Department to assess whether the requested biospecimens are contained within the CBP's repository, and will reduce costs by eliminating projects that request biospecimens and/or data that are not available.

Subsection (c)(9) is necessary to allow the Department to assess whether the required data are contained within the CBP's databases, and will reduce costs by eliminating projects that require data that is not available.

Subsection (c)(10) is necessary because the Department needs to know where to ship the biospecimens. This will assist the Department to determine the appropriate method of shipping to meet the researcher's needs.

Subsection (c)(11) is necessary because there are several methods of packaging biospecimens. Obtaining this information in advance ensures that the method will maintain the quality of the biospecimens and that the Department will be able to comply with the packing requirements of the researcher. If the Department cannot accommodate the packing requirements of the requestor, the research request may not be approved.

Subsection (c)(12) is necessary because there are several methods of shipping that are available to the researcher. This will assist the Department to determine the appropriate method of shipping to meet the researcher's needs. If the Department cannot accommodate the shipping requirements of the requestor, the research request may not be approved.

Subsection (d) is necessary to outline the actions that must be taken by the researcher when the project has been completed. Failure to comply with this section will prevent the researcher from receiving any further biospecimens and/or data.

Subsection (d)(1) is necessary because the biospecimens are the property of the State as stated in Article 4, Section 6505(j), CCR, and it is the Department's responsibility to specify requirements that are consistent with protecting the confidentiality of such biospecimens.

Subsection (d)(2) is necessary because the Department data are the property of the State as stated in Article 4 Section 6505(j) CCR, and it is the Department's responsibility to specify requirements that are consistent with protecting the privacy and confidentiality of such data.

Subsection (d)(3) is necessary because the biospecimens are the property of the State as stated in Article 4 Section 6505(j) CCR, and it is the Department's responsibility to specify requirements that are consistent with protecting the confidentiality of such biospecimens including all residual products that are derived from the biospecimens.

Subsection (d)(4) is necessary because the Department's biospecimens and or the products thereof are the property of the State, and it is the Department's responsibility to specify requirements that are consistent with protecting the privacy and confidentiality of the individual from whom biospecimens are obtained.

Adopt the title **Article 3. Approval, Denial, and Revocation of Request** to reflect the content of sections within the article. This is a nonsubstantial change.

Adopt **Section 6553. Reasons for Denial** to both address the problems and realize the benefits as stated regarding this regulatory action, and establish under what circumstances a research request for biospecimens and/or data related to the biospecimens will not be approved. This section ensures the researcher is aware of the reasons a request may be denied.

Subsection (a) is necessary to identify the sections of the HSC which reference the CPHS requirements for protecting personal information held in agency databases. In addition, in the case where a research project may extend over several years, CPHS approval must be received for each subsequent annual renewal of the project otherwise the request will be denied and/or request approval will be revoked as stated in Section 6551(c)(2). This is also necessary because the Department cannot provide biospecimens to research projects that have not obtained the required CPHS approvals.

Subsection (b) is necessary to define the requirements under which the request will be denied or its approval revoked if it is found that biospecimens and/or data are to be, or have been used for any purposes other than those described in HSC Section 124991(g)(1)-(4). This section is added to provide to identify the section of the HSC which reference the CPHS and is necessary because it is the law that the biospecimens and/or data only be used for purposes described therein.

Subsection (c) is necessary to specify that biospecimens and/or data will be released only for research that advances the existing body of knowledge and that has significant impact on health. Research projects that repeat research that is well established in the field are unnecessary and will deplete limited biospecimen resources, occupy crucial staff time that could be allocated for processing research requests for non-repetitive projects, and may also limit the ability to provide specimens for future research requests that may advance public health. All requests will be reviewed by Department qualified research scientists.

Subsection (d) is necessary because fulfilling requests that exceed the staff resources of the Department may interfere with the ability of the Department to complete its essential daily activities.

Subsection (e) is necessary because the biospecimens are the property of the State as stated in Article 4, Section 6505(j) CCR, and it is the Department's responsibility to specify requirements that are consistent with protecting the confidentiality of such biospecimens.

Subsection (f) is necessary because the Department data are the property of the State as stated in Article 4, Section 6505(j), CCR, and it is the Department's responsibility to specify requirements that are consistent with protecting the privacy and confidentiality of such data.

Subsection (g) is necessary because the Department data are the property of the State as stated in Article 4, Section 6505(j), CCR, and it is the Department's responsibility to specify requirements that are consistent with protecting the privacy and confidentiality of such data.

Subsection (h) is necessary because the biospecimens are the property of the State as stated in Article 4, Section 6505(j), CCR, and it is the Department's responsibility to specify requirements that are consistent with protecting the confidentiality of such biospecimens including all residual products that are derived from the biospecimens.

Subsection (i) is necessary because the Department's biospecimens and the products thereof are the property of the State, and it is the Department's responsibility to specific requirements that are consistent with protecting the privacy and confidentiality of the individual from whom biospecimens are obtained.

Subsection (j) is necessary because peer review is the recognized industry standard by which scientific research projects are evaluated. Research projects that do not meet these standards may result in false or misleading conclusions and not significantly add to or improve the public's health.

Subsections (j)(1) and (j)(2) are necessary because they describe reasons that a research request may be scientifically flawed and therefore denied. Studies that do not employ sound research methodology or do not adequately address research aims may lead to incorrect or inadequate conclusions that may be challenged by the scientific community. Early evaluation of the research studies methodology by staff trained in these fields saves staff resources by excluding these types of projects.

Subsection (j)(3) is necessary because the biospecimens are a limited resource and need to be preserved for other critical purposes, such as evaluation of new testing methods and pilot studies of new disorders that may be added to the testing panel. The Department may deny research requests that would utilize more specimens and data than are needed to answer a particular research question.

Subsection (j)(4) is necessary because the Department will not release biospecimens for research that makes use of inappropriate statistical analysis, which may misrepresent the results of the study. Department qualified staff statisticians will evaluate the statistical methods used to ensure that the statistical methods used will not result in biased or inaccurate results.

Subsection (k) is necessary because it is vital that the Department maintain the public health and welfare by continuing to add new disorders to the screening panels and ensure that the most current and accurate testing methods are being used. The

Department reserves the right to deny requests for biospecimens that are needed for testing of new disorders and program development within the Department.

Subsection (l) is necessary because researchers must have State Registrar of Vital Statistics approval prior to the release of information from live birth, fetal death and death records.

Subsection (m) is necessary for the Department to ensure, as broad as possible, access is granted to qualifying researchers. Researchers who request excessive biospecimens could negatively impact such access.

Adopt **Section 6553.1. Revocation of Research Project** to both address the problems and realize the benefits as stated regarding this regulatory action, and to identify the reasons a research request may be revoked. It also informs the researcher that they must return all biospecimens and destroy all data upon revocation of the research request.

Subsection (a) is necessary to ensure that the researcher obtains the necessary annual renewals, in compliance with Section 6553(a). The Department must comply with the statutes and regulations governing the Health and Human Services Agency Committee for the Protection of Human Subjects.

Subsection (b) is necessary because the program must collect fees to cover the cost of administering the CBP pursuant to HSC Sections 124977(b)(4)(A) and 124977(b)(5). If the Department is unable to collect fees from researchers, the program cannot continue to operate.

Subsection (c) is necessary to protect the confidentiality of the data and biospecimens as required in HSC Section 124980(j) and to prevent data and biospecimen misuse.

Subsection (d) is necessary to ensure that the researcher complies with the signed Department data use and confidentiality agreement for all projects that have been approved by the Department [in compliance with Section 6551 (c)(4)].

Subsection (e) is necessary to ensure that all biospecimens are returned by the researcher to the CBP upon completion or revocation of the research project [in compliance with Section 6551(d)(1)].

Subsections (f) and (g) are necessary to ensure that all biospecimens and/or data and the products thereof are destroyed by the researcher upon completion or revocation of the research project [in compliance with Section 6551(d)(2)].

Subsection (h) is necessary to protect the confidentiality of the biospecimens and the product thereof as required in HSC Section 124980(j) and to prevent data and biospecimen misuse project [in compliance with Section 6551(d)(3)].

Adopt the title **Article 4. Request for Citations upon Publication of Results** to reflect the content of sections within the article. This is a nonsubstantial change.

Adopt **Section 6555. Requirements for Citations upon Publication of Results** to both address the problems and realize the benefits as stated regarding this regulatory action and to establish the necessity of the Department to be apprised of publications that may influence which disorders the Department may screen for and provide insight into new treatment options for existing disorders, which furthers the health and welfare of the people of California. This is necessary to ensure that the Department is informed of the publications that are released that utilized biospecimens and/or data provided by the Department.

Adopt the title **Article 5. California Biobank Program Biospecimen and Data Fees** to reflect the content of sections within the article. This is a nonsubstantial change.

Adopt **Section 6557. Newborn Biospecimen Fees** to both address the problems and realize the benefits as stated regarding this regulatory action and to implement the statutory requirements that the Department establish fees sufficient to cover the costs of the CBP.

Subsection (a) is necessary to set forth the cost for biospecimens that are identified by specific criteria. These biospecimens take the most staff time to pull because they are not stored in the same location. Staff must access various locations to collect the biospecimens, which increases the time it takes to collect them. The fee is based on the staff time needed to complete the request; the salaries, benefits and standard costs of staff that are responsible for pulling, processing and administering the biospecimens; related data analysis; direct costs associated with operating the CBP (e.g. freezers and lab equipment); and the Department overhead cost rates (e.g. Distributed Administration and Distributed IT).

Subsection (b) is necessary to set forth the cost for biospecimens if the researcher identifies case and control specimens. A portion of these biospecimens can be pulled from the same location which decreases the staff time needed to process such requests in comparison to those described in subsection (a). The fee is based on the staff time needed to complete the request; the salaries, benefits and standard costs of staff that are responsible for pulling, processing and administering the biospecimens; related data analysis; direct costs associated with operating the CBP (e.g. freezers and lab equipment); and the Department overhead cost rates (e.g. Distributed Administration and Distributed IT).

Subsection (c) is necessary to set forth the cost for biospecimens if the researcher does not request any individually identified biospecimens and the biospecimens can be accessed by batch. These biospecimens take less time than those in identified in subsection (b) because staff does not need to individually locate the biospecimens, but can provide a group that are stored together. The fee is based on the staff time needed to complete the request; the salaries, benefits and standard costs of staff that are responsible for pulling, processing and administering the biospecimens; related data analysis; direct costs associated with operating the CBP (e.g. freezers and lab equipment); and the Department overhead cost rates (e.g. Distributed Administration and Distributed IT).

Subsection (d) is necessary to set forth the cost for newborn screening specimen collection filter paper cards. This fee is based on the cost of manufacturing of the filter paper and is the standard charge as required in Article 4, Section 6508(b), CCR.

Adopt **Section 6557.1. Prenatal Biospecimen Fees** to both address the problems and realize the benefits as stated regarding this regulatory action and to define the fee for prenatal biospecimens. There is one fee for prenatal biospecimens. The fee is based on the staff time needed to complete the request; the salaries, benefits and standard costs of staff that are responsible for identifying appropriate specimens and administering the CBP; related data analysis; Department overhead cost rates (e.g. Distributed Administration and Distributed IT); and contractual cost of storing and shipping prenatal biospecimens.

Adopt **Section 6557.2. Fees Charged by the Department for GDSP Data Records Provided to Researchers** to both address the problems and realize the benefits as stated regarding this regulatory action and to establish the fee structure for the cost of data provided by GDSP. There is an hourly fee that is based on the total hourly cost (which includes salaries, benefits, standard costs and Department overhead) of the staff that will access, process, administer and maintain the GDSP data requested by researchers; and direct costs associated with maintaining the GDSP data base.

Adopt **Section 6557.3. CBDMP Data Fees** to both address the problems and realize the benefits as stated regarding this regulatory action and because it sets forth the fee to be charged for data provided by CBDMP. There is an hourly fee that is calculated by determining the total hourly cost (including salaries, benefits, standard costs, Department overhead) of the staff members who will be accessing, processing, and administering the CBDMP data requested by researchers.

Significant Statewide Adverse Economic Impact Directly Affecting Business, Including Ability to Compete

The requirement that biospecimens and data be made available to researchers will have no significant adverse economic impact on any business. There are no private companies, at this time, that have access to the number and types of biospecimens and

associated data that are contained within the CDPH/GDSP Biobank Program's repository. Thus, there will be no significant adverse economic impact on California businesses.

Document Relied Upon

Department of Public Health. "Economic Impact Assessment." January 16, 2014.