Initial Review Submission Packet (Version 1.1)

1.0 Initial Review Submission Packet

1.1 Today's Date:

01/29/2013

1.2 Study Title:

Humanized Mouse Models for HIV Therapeutics Development

1.3 IRB #:

1.4 Principal Investigator:

[redacted]

1.5 * Lay summary (1 to 3 brief sentences):

Human fetal tissues will be implanted into immunodeficient mice to generate humanized mice for HIV infection and drug efficacy studies.

1.6 * This submission is a:

- (•) New study (never been approved before)
- ( ) Currently approved study due for continuing review (also submit a Continuing Review application in iMedRIS)
- ( ) Currently approved study that is being modified (also submit a Modification application in iMedRIS)
- ( ) Currently approved study not due for continuing review with no modifications

1.7 For currently approved studies, provide the CHR approval number:

1.8 Special processing instructions or information about the submission:

2.0 CHR Application Form

2.1 * Attach the IRB application you completed for this protocol:

Edit/ View	Version	Title
	1.1	Study Application (Version 1.1) - Attached

3.0 Other Study Documents

3.1 Attach the other study documents (e.g. protocol, investigators brochure, recruitment materials, instruments, case report forms, study handouts or other miscellaneous documents):

Version	Sponsor Version	Title	Category	Expiration Date	Document Outcome	View Document
1.0		Human subjects description	Grant (pertinent portion of)		Approved	581.30 KB

Initial Review Submission Packet (Version 1.0)

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01/29/2013

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Version	Sponsor Version	Title	Category	Expiration Date	Document Outcome	View Document
No Document(s) have been attached to this form.						

Review Response Submission Form (Version 1.1)

1.0 Review Response Submission Form

You have received this form either during the administrative pre-review process or after formal review by the committee. This form allows you to respond to recommendations, stipulations, or other issues identified during this review process. Make the appropriate revisions to your submission and attach the new versions in the Revised Submission Materials section.

TIP: We recommend saving this form frequently to avoid loss of work due to being timed out of your session. To save the form, change all the drop down answers in the stipulations to "Yes," "No," or "N/A" and click "Save Form."

2.0 General Information

2.1 Principal Investigator:

[redacted]

2.2 Study Title:

Humanized Mouse Models for HIV Therapeutics Development

2.3 Study Number:

13-10683

2.4 Study Alias:

Humanized mice

3.0 Stipulations and Comments

3.1 To address each stipulation, you need to update the Study Application, submission form or document to which the stipulation is linked. To do so, click "Add Revision" the first time you revise the item or click the component name if you have already added a revision. For help, click the Help section in the upper right-hand corner and read the "Responding to Requests for Submission Corrections" quick guide. Please also write your responses to each of the stipulations in the Details fields rather than at the end of the form. (The system keeps a history of stipulations and responses and it doesn't work if it's not used right.)

Stipulations that must be addressed:

⚠ **Stipulation 1 out of 5:**

Description:

Sections 13.1-13.1 of the CHR application: Please list a single number in these sections for the total sample size for this study. In section13.4 you should break down the number to describe how many per year. It is not clear from this application how many years this study will be active.

Stipulation Type: **(Stipulation must be addressed)**

Do you accept this Stipulation?	○ **N/A** ● **Yes** ○ **No**
Provide an explanation on how you addressed this Stipulation:	

Stipulation 2 out of 5:

Description:

Sections 13.6-13.7: Please list the inclusion/exclusion criteria for the individuals whose fetal tissue will be used for this study.

Stipulation Type: **(Stipulation must be addressed)**

Do you accept this Stipulation?	○ **N/A** ● **Yes** ○ **No**
Provide an explanation on how you addressed this Stipulation:	

Stipulation 3 out of 5:

Description:

Section 13.8: Please check "yes" since it is assumed that one inclusion criteria for this group is that they would be women.

Stipulation Type: **(Stipulation must be addressed)**

Do you accept this Stipulation?	○ **N/A** ● **Yes** ○ **No**
Provide an explanation on how you addressed this Stipulation:	

Stipulation 4 out of 5:

Description:

Section 17.4: Please check "no" and uncheck "names" since you indicate in section 17.7 that identifiers, including names, will not be recorded.

Stipulation Type: **(Stipulation must be addressed)**

Do you accept this Stipulation?	○ **N/A** ● **Yes** ○ **No**
Provide an explanation on how you addressed this Stipulation:	

Stipulation 5 out of 5:

Description:

Section 17.5: Please remove the text from the box since the person collecting the tissue is an investigator on this study.

Stipulation Type: **(Stipulation must be addressed)**

Do you accept this Stipulation?	○ **N/A** ● **Yes** ○ **No**
Provide an explanation on how you addressed this Stipulation:	

Comments That Must Be Addressed With Follow-up Deadlines:

No Stipulation entered.

Comments:

No Stipulation entered.

4.0 Unresolved Stipulations/Comments

4.1

No Stipulation is outstanding.

5.0 Revised Submission Materials

5.1 A copy of the materials you submitted most recently as part of this submission is attached. Click the green bar to access these items, make changes, and attach new or revised documents.

6.0 Response Comments

6.1 Additional comments about this response:

Review Response Submission Form (Version 1.0)

1.0 Review Response Submission Form

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2.0 General Information

2.1 Principal Investigator:

[redacted]

2.2 Study Title:

Humanized Mouse Models for HIV Therapeutics Development

2.3 Study Number:

13-10683

2.4 Study Alias:

Humanized mice

3.0 Stipulations and Comments

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Stipulations that must be addressed:

Stipulation 1 out of 2:

Description:

You have checked in section 7.3 of the CHR application that you are attaching the section of the federal proposal that describes human subjects work. Please attach this as an additional study document with this application.

Stipulation Type: **(Stipulation must be addressed)**

Do you accept this Stipulation?	○ **N/A** ● **Yes** ○ **No**
Provide an explanation on how you addressed this Stipulation:	The section of the federal proposal that describes human subjects work is attached.

Stipulation 2 out of 2:

Description:

In section 11.4 of the application you state that "human fetal tissues will be obtained after termination of pregnancy…" You have previously checked in section 11.2 that the biological specimens have already been collected. Please clarify in 11.4 that these tissues have already been obtained. Otherwise this study would not qualify for "Exempt".

Stipulation Type: **(Stipulation must be addressed)**

Do you accept this Stipulation?	○ **N/A** ○ **Yes** ● **No**
Provide an explanation on how you addressed this Stipulation:	The human fetal tissues to be implanted into immunodeficient mice have not already been collected because they must be freshly obtained for successful engraftment. These tissues would otherwise be discarded.

Comments That Must Be Addressed With Follow-up Deadlines:

No Stipulation entered.

Comments:

No Stipulation entered.

4.0 Unresolved Stipulations/Comments

4.1

No Stipulation is outstanding.	

5.0 Revised Submission Materials

5.1 A copy of the materials you submitted most recently as part of this submission is attached. Click the green bar to access these items, make changes, and attach new or revised documents.

6.0 Response Comments

6.1 Additional comments about this response:

Initial Review Submission Packet (Version 1.2)

1.0 Initial Review Submission Packet

1.1 Today's Date:

01/29/2013

1.2 Study Title:

Humanized Mouse Models for HIV Therapeutics Development

1.3 IRB #:

1.4 Principal Investigator:

[redacted]

1.5 * Lay summary (1 to 3 brief sentences):

Human fetal tissues will be implanted into immunodeficient mice to generate humanized mice for HIV infection and drug efficacy studies.

1.6 * This submission is a:

- (•) New study (never been approved before)
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1.7 For currently approved studies, provide the CHR approval number:

1.8 Special processing instructions or information about the submission:

2.0 CHR Application Form

2.1 * Attach the IRB application you completed for this protocol:

Edit/ View	Version	Title
	1.2	Study Application (Version 1.2) - Attached

3.0 Other Study Documents

3.1 Attach the other study documents (e.g. protocol, investigators brochure, recruitment materials, instruments, case report forms, study handouts or other miscellaneous documents):

Version	Sponsor Version	Title	Category	Expiration Date	Document Outcome	View Document
1.0		Human subjects description	Grant (pertinent portion of)		Approved	581.30 KB

Study Application (Version 1.2)

1.0 General Information

***Enter the full title of your study:**

Humanized Mouse Models for HIV Therapeutics Development

***Enter the study alias:**

Humanized mice
* This field allows you to enter an abbreviated version of the Study Title to quickly identify this study.

2.0 Add departments

2.1 and Specify Research Location:

Is Primary?	Department Name
◉	[redacted]

3.0 List the key study personnel: (Note: external and affiliated collaborators who are not in the UCSF directory can be identified later in the Qualifications of Key Study Personnel section at the end of the form)

3.1 *Please add a Principal Investigator for the study:

[redacted]

Select if applicable

☐ Department Chair ☐ Resident

☐ Fellow

If the Principal Investigator is a Fellow, the name of the Faculty Advisor must be supplied below.

3.2 If applicable, please select the Research Staff personnel

A) Additional Investigators

B) Research Support Staff

[redacted]

3.3 *Please add a Study Contact

[redacted]

The Study Contact(s) will receive all important system notifications along with the Principal Investigator. (e.g. The project contact(s) are typically either the Study Coordinator or the Principal Investigator themselves).

3.4 If applicable, please add a Faculty Advisor/Mentor:

3.5 If applicable, please select the Designated Department Approval(s)

[redacted]

Add the name of the individual authorized to approve and sign off on this protocol from your Department (e.g. the Department Chair or Dean).

4.0 Qualifications of Key Study Personnel

4.1 List the study responsibilities and qualifications of any individuals who qualify as Key Study Personnel (KSP) at UCSF and affiliated sites ONLY by clicking the "Add a new row" button: NOTE: This information is required and your application will be considered incomplete without it.

KSP Name	Description of Study Responsibilities	Qualifications
[redacted]		

5.0 Initial Screening Questions

5.1 * This study involves human stem cells (including iPS cells and adult stem cells), gametes or embryos:

- (•) No
- ( ) Yes, and requires CHR and GESCR review
- ( ) Yes, and requires GESCR review, but NOT CHR review

5.2 * This application involves a Humanitarian Use Device:

- (●) No
- ( ) Yes, and it includes a research component
- ( ) Yes, and it involves clinical care ONLY

5.3 * This is a CIRB study (e.g. the NCI CIRB will be the IRB of record):

( ) Yes (●) No

5.4 * This application includes a request to rely on another IRB (other than NCI CIRB):

( ) Yes (●) No

Note: If this request is approved, the CHR will **NOT** review and approve this study. Another institution will be the IRB of record.

6.0 Application Type

6.1 * This research involves:

- (●) Minimal risk
- ( ) Greater than minimal risk

6.2 * This application is:

- ( ) Full Committee
- (●) Expedited
- ( ) Exempt

6.3 If you think this study qualifies for expedited review, select the regulatory category(ies) that the research falls under:

- [ ] Category 1: A very limited number of studies of approved drugs and devices
- [ ] Category 2: Blood sampling
- [ ] Category 3: Noninvasive specimen collection (e.g. buccal swabs, urine, hair and nail clippings, etc.)
- [ ] Category 4: Noninvasive clinical procedures (e.g. physical sensors such as pulse oximeters, MRI, EKG, EEG, ultrasound, moderate exercise testing, etc.)
- [x] Category 5: Research involving materials (data, documents, records, or specimens) that were previously collected for either nonresearch or research purposes
- [ ] Category 6: Use of recordings (voice, video, digital or image)
- [ ] Category 7: Low risk behavioral research or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies
- [ ] Category 8: Continuing review of previously approved full committee research that is essentially complete
- [ ] Category 9: Continuing review of research NOT involving an IND or IDE where the IRB has determined that the research poses no greater than minimal risk

6.4 * This study involves:

- ( ) Subject contact (including phone, email or web contact)
- (●) No subject contact (limited to medical records review, biological specimen analysis, and/or data analysis)

7.0 Funding

7.1 Identify all sponsors and provide the funding details. If funding comes from a Subcontract, please list only the Prime Sponsor:

External Sponsor:

View Details	Sponsor Name	Sponsor Type	Awardee Institution:	Contract Type:	Project Number	UCSF RAS System Award Number ("A" + 6 digits)
⊟	NIH Natl Inst Allergy & Infectious Dis.	01	UCSF	Contract		A118823

Sponsor Name:	NIH Natl Inst Allergy & Infectious Dis.
Sponsor Type:	01
Sponsor Role:	Funding
CFDA Number:	
Grant/Contract Number:	
Awardee Institution::	UCSF
Is Institution the Primary Grant Holder:	Yes
Contract Type:	Contract
Project Number:	
UCSF RAS System Award Number ("A" + 6 digits):	A118823
Grant Number for Studies Not Funded thru UCSF:	
Grant Title:	Tissue-based Small Animal Model for HIV Drug Discovery
PI Name: (If PI is not the same as identified on the study.)	
Explain Any Significant Discrepancy:	

Gift, Program, or Internal Funding (check all that apply):

- ☐ Funded by gift (specify source below)
- ☐ Funded by UCSF or UC-wide program (specify source below)
- ☐ Specific departmental funding (specify source below, if applicable)
- ☐ Unfunded (miscellaneous departmental funding)
- ☐ Unfunded student project

List the gift, program, or departmental funding source:

7.2 If you tried to add a sponsor in the question above and it was not in the list, follow these steps:

- **If funding has already been awarded or the contract is being processed by the Contracts and Grants or Industry Contracts unit, your sponsor is already in the system and the project has a UCSF RAS System Proposal or Award number. Check with your department's Research Services**

Analyst (RSA) to ask how the sponsor is listed in the UC sponsor list and what the Proposal or Award number is.

- **If you need additional assistance, contact the Contracts and Grants Award Team at CGAwardTeam@ucsf.edu and list the sponsor in the box below.**

○ Sponsor not in list

Only if your sponsor is not yet in the list, type the sponsor's name:

If the funding is administered by the UCSF Office of Sponsored Research, your study will not receive CHR approval until the sponsor and funding details have been added to your application.

7.3 * This study is supported in whole or in part by Federal funding:

◉ Yes ○ No

If **yes**, indicate which portion of your grant you will be attaching:

- ☐ The Research Plan, including the Human Subjects Section of your NIH grant or subcontract
- ☑ For other federal proposals (contracts or grants), the section of the proposal describing human subjects work
- ☐ The section of your progress report if it provides the most current information about your human subjects work
- ☐ The grant is not attached. The study is funded by an award that does not describe specific plans for human subjects, such as career development awards (K awards), cooperative agreements, program projects, and training grants (T32 awards)

8.0 Statement of Financial Interest

8.1 * The Principal Investigator and/or one or more of the key study personnel has financial interests related to this study:

○ Yes ◉ No

If **Yes**, the Conflict of Interest Advisory Committee (COIAC) office may contact you for additional information.

9.0 Sites

9.1 Institutions (check all that apply):

- ☑ UCSF
- ☐ China Basin
- ☐ Helen Diller Family Comprehensive Cancer Center
- ☐ Mission Bay
- ☐ Mount Zion
- ☑ San Francisco General Hospital (SFGH)
- ☐ SF VA Medical Center (SF VAMC)
- ☐ Blood Centers of the Pacific (BCP)
- ☐ Blood Systems Research Institute (BSRI)
- ☐ Fresno (Community Medical Center)

- [ ] Gallo
- [ ] Gladstone
- [ ] Institute on Aging (IOA)
- [ ] Jewish Home
- [ ] SF Dept of Public Health (DPH)

9.2 Check all the other types of sites not affiliated with UCSF with which you are cooperating or collaborating on this project:

- [ ] Other UC Campus
- [ ] Other institution
- [ ] Other community-based site
- [ ] Foreign Country

List the foreign country/ies:

9.3 * This is a multicenter study:

- ( ) Yes
- (•) No

9.4 Check any research programs this study is associated with:

- [ ] Cancer Center
- [ ] Center for AIDS Prevention Sciences (CAPS)
- [ ] Global Health Sciences
- [ ] Immune Tolerance Network (ITN)
- [ ] Neurosciences Clinical Research Unit (NCRU)
- [ ] Osher Center
- [ ] Positive Health Program

10.0 Study Design

10.1 * Study design:

Human fetal tissue specimens (which would otherwise be discarded) will be retrieved from products of conception obtained
from induced abortions at the Women's Option Center at SFGH. Tissues will be collected only if informed consent has been obtained agreeing that the tissue may be saved for future study.

10.2 Check all that apply:

- [ ] Phase I
- [ ] Phase II
- [ ] Phase III
- [ ] Phase IV

11.0 Scientific Considerations

11.1 Hypothesis:

This study has a hypothesis:

○ Yes ◉ No

If yes, state the hypothesis or hypotheses:

11.2 * List the specific aims:

Human fetal tissues will be implanted into immunodeficient mice to make them susceptible to infection with HIV so that the efficacy of new antiviral drugs can be evaluated.

11.3 Statistical analysis:

Cohorts of 50 mice will be generated from each set of fetal tissues, which permits 7 groups of 7 mice each. Viral loads will be compared between treated and untreated mice by the Mann-Whitney U test, and P values ≤0.05 will be considered statistically significant.

11.4 * This is an investigator-initiated study:

◉ Yes ○ No

11.5 This study has received scientific or scholarly review from (check all that apply): * Please note that effective January 2, 2013 both Feasibility and Scientific Merit Review are required for all interventional clinical trials *prior* to IRB review.

☐ Cancer Center Protocol Review Committee (PRC) (Full approval or contingent PRC approval is required prior to final CHR approval for cancer-related protocols.)
☐ CTSI Clinical Research Center (CRC) advisory committee
☐ Departmental scientific review
☐ Other:

Specify **Other**:

If required, attach the Feasibility and Scientific Review forms in the Other Study Documents section of the Initial Review Submission Packet.

12.0 Background

12.1 Background:

The ultimate goal of this Contract is to speed the development of new therapies for HIV
infection. Besides supplying key information for in vivo safety and efficacy, preclinical evaluation
in small animal models can enable (1) head-to-head comparisons of antiviral potency for
chemical lead selection, (2) proof-of-principle data for drugs with novel mechanisms of action,
(3) information on tissue reservoirs of HIV infection that cannot be readily obtained from human
patients, and (4) study of potential toxicities prior to Phase I clinical trials. The scope of this

contract for Humanized Mouse Models for HIV Therapeutics Development is to conduct studies in vitro and in humanized mouse models, to improve the SCID-hu Thy/Liv model and a second model with human leukocyte reconstitution in gut-associated lymphoid tissue, and to adapt other existing or newly discovered models, all for the purpose of developing novel therapies for HIV disease. As we have done for this Contract since 1995, we will employ state-of-the-art techniques and technologies in these models for evaluating promising therapies and other interventions for HIV/AIDS. The SCID-hu Thy/Liv mouse, pioneered by McCune and colleagues, is generated by implanting pieces of human fetal thymus and liver together under the kidney capsule of CB-17-*scid* mice. In a highly reproducible manner, these organs fuse, become vascularized, and grow into a stable organoid termed "Thy/Liv," reaching a total mass of 100–300 x 10^6 human cells in 18 weeks. The Thy/Liv implant reproduces the differentiation, proliferation, and function of human hematopoietic progenitor cells derived from the fetal liver within the human thymus. The implants possess histologically normal cortical and medullary compartments that sustain multilineage human hematopoiesis for 6–12 months, generating a continuous source of CD4-expressing thymocytes that can serve as target cells for HIV infection and replication.

12.2 Preliminary studies:

We have generated appoximately 1,200 humanized mice per year since 2000 with human fetal tissues obtained from Advanced Bioscience Resources (ABR). Sometimes ABR cannot supply these tissues, so we are seeking approval to collect them from [redacted].

12.3 References:

If you have a separate bibliography, attach it to the submission with your other study documents.

13.0 Sample Size and Eligibility

13.1 Number of subjects that will be enrolled at UCSF and affiliated institutions:

168

13.2 Total number of subjects that will be enrolled at all sites:

168

13.3 Estimated number of people that you will need to consent and screen here (but not necessarily enroll) to get the needed subjects:

336

13.4 Explain how and why the number of subjects was chosen:

Tissues from each subject will be used to make one cohort of humanized mice, and 24 mouse cohorts will be made per year for a period of 7 years.

13.5 * Eligible age range(s):

- [ ] 0-6 years
- [ ] 7-12 years
- [ ] 13-17 years
- [x] 18+ years

13.6 Inclusion criteria:

Termination of pregnancy at 20–24 gestational weeks.

13.7 Exclusion criteria:

Termination of pregnancy before 19 gestational weeks.

13.8 There are inclusion or exclusion criteria based on gender, race or ethnicity:

(•) Yes ( ) No

If **yes**, please explain the nature and rationale for the restrictions:

The subjects are women.

14.0 Use of In Vitro Diagnostics in Studies Not Involving Subject Contact

14.1 * This study involves the investigational use of an in vitro diagnostic device:

( ) Yes (•) No

15.0 Other Approvals and Registrations

15.1 * This is a clinical trial:

( ) Yes (•) No

Clinical Trial Registration
"NCT" number for this trial:

15.2 * Do any study activities take place on patient care units:

○ Yes ◉ No

If **Yes**, attach a letter of support for the study from the involved patient care manager(s).

15.3 * Data from this study will be submitted to NIH for Genome-Wide Association Studies (GWAS):

○ Yes ◉ No

15.4 * This study involves administration of vaccines produced using recombinant DNA technologies to human subjects:

○ Yes ◉ No

15.5 * This study involves human gene transfer (NOTE: Requires NIH Recombinant DNA Advisory Committee (RAC) review prior to CHR approval):

○ Yes ◉ No

15.6 * The UCSF Radiation Safety Committee requires review of your protocol if it includes administration of radiation as part of standard of care OR research exposures. Does your protocol involve any radiation exposure to patients/subjects:

○ Yes ◉ No

15.7 This study involves other regulated materials and requires approval and/or authorization from the following regulatory committees:

☑ Institutional Biological Safety Committee (IBC)

Specify BUA #:

BU000793-02B (PI: [redacted]

☑ Institutional Animal Care and Use Committee (IACUC)

Specify IACUC #:

AN089843-01C

☐ Radiation Safety Committee

Specify RUA #:

☐ Radioactive Drug Research Committee (RDRC)

Specify RDRC #:

☑ Controlled Substances

16.0 Procedures: No Subject Contact

16.1 Check all that apply:

- ☐ Retrospective Chart Review
- ☑ Biological Specimen Analysis
- ☐ Specimen Banking for Future Research
- ☐ Data Analysis
- ☐ UCSF is serving as the Coordinating Center only

16.2 Source:

[redacted]. [redacted] and [redacted] in my lab will collect the tissues from the specimen containers.

16.3 The source obtained consent from subjects to use the biological specimens or data for the research proposed in this study:

◉ Yes ○ No

If **no**, explain:

16.4 The source has IRB Approval to obtain and possess the biological specimens or data:

◉ Yes ○ No

If **no,** explain:

16.5 Type of records, biological specimens, and data:

Human fetal tissues.

16.6 Dates for the records, biological specimens, or data that will be used:

From:

To:

OR

☑ Indefinite (for repositories and other ongoing research resources)

16.7 Variables that will be abstracted from the records or received with the biological specimens or data set:

None.

17.0 Confidentiality and Privacy

17.1 Plans for maintaining privacy in the research setting:

17.2 Possible consequences to subjects resulting from a loss of privacy:

17.3 Study data are:

- [ ] Derived from the Integrated Data Repository (IDR) or The Health Record Data Service (THREDS) at SFGH
- [ ] Derived from a medical record (identify source below)
- [ ] Added to the hospital or clinical medical record
- [x] Created or collected as part of health care
- [ ] Used to make health care decisions
- [x] Obtained from the subject, including interviews, questionnaires
- [ ] Obtained from a foreign country or countries only
- [ ] Obtained from records open to the public
- [ ] Obtained from existing research records
- [ ] None of the above

If **derived from a medical record**, identify source:

17.4 Identifiers may be included in research records:

- ( ) Yes (•) No

If **yes**, check all the identifiers that may be included:

- [ ] Names
- [ ] Dates
- [ ] Postal addresses
- [ ] Phone numbers
- [ ] Fax numbers
- [ ] Email addresses
- [ ] Social Security Numbers*
- [ ] Medical record numbers
- [ ] Health plan numbers
- [ ] Account numbers
- [ ] License or certificate numbers
- [ ] Vehicle ID numbers
- [ ] Device identifiers or serial numbers
- [ ] Web URLs
- [ ] IP address numbers
- [ ] Biometric identifiers
- [ ] Facial photos or other identifiable images
- [ ] Any other unique identifier

* Required for studies conducted at the VAMC

17.5 Identifiable information might be disclosed as part of study activities:

- ( ) Yes (•) No

If **yes**, indicate to whom identifiable information may be disclosed:

- [ ] The subject's medical record
- [ ] The study sponsor
- [ ] Collaborators

- [ ] The US Food & Drug Administration (FDA)
- [ ] Others (specify below)
- [ ] A Foreign Country or Countries (specify below)

If **Others**, specify:

17.6 Indicate how data are kept secure and protected from improper use and disclosure (check all that apply): NOTE: Whenever possible, do not store subject identifiers on laptops, PDAs, or other portable devices. If you collect subject identifiers on portable devices, you MUST encrypt the devices.

- [ ] Data are stored securely in My Research
- [ ] Data are coded; data key is destroyed at end of study
- [ ] Data are coded; data key is kept separately and securely
- [ ] Data are kept in a locked file cabinet
- [ ] Data are kept in a locked office or suite
- [ ] Electronic data are protected with a password
- [ ] Data are stored on a secure network
- [ ] Data are collected/stored using REDCap or REDCap Survey

17.7 Additional measures to assure confidentiality and protect identifiers from improper use and disclosure, if any:

Patient identifiers (names on specimen containers) are not recorded by the personnel in my lab ([redacted] and [redacted] who will collect the fetal tissues from the specimen containers a [redacted]

17.8 This study may collect information that State or Federal law requires to be reported to other officials or ethically requires action:

- ○ Yes
- ◉ No

Explain:

17.9 This study will be issued a Certificate of Confidentiality:

- ○ Yes
- ◉ No

18.0 Subjects

18.1 Check all types of subjects that may be enrolled:

- [ ] Inpatients
- [x] Outpatients
- [ ] Healthy volunteers
- [ ] Staff of UCSF or affiliated institutions

18.2 Additional vulnerable populations:

- [ ] Children
- [ ] Subjects unable to consent for themselves
- [ ] Subjects unable to consent for themselves (emergency setting)

- [ ] Subjects with diminished capacity to consent
- [ ] Subjects unable to read, speak or understand English
- [ ] Pregnant women
- [ ] Fetuses
- [ ] Neonates
- [ ] Prisoners
- [ ] Economically or educationally disadvantaged persons
- [ ] Investigators' staff
- [ ] Students

Explain why it is appropriate to include the types of subjects checked above in this particular study:

Describe the additional safeguards that have been included in the study to protect the rights and welfare of these subjects and minimize coercion or undue influence:

19.0 Waiver of Consent/Authorization for Minimal Risk Research

19.1 * Waiving consent/authorization will not adversely affect subjects' rights and welfare:

- (•) Yes

If **no**, a waiver of consent/authorization can NOT be granted.

19.2 * It is not practicable to conduct the research without the waiver, nor is it practicable to conduct the research without access to the requested information:

- (•) Yes

If **no**, a waiver of consent/authorization can NOT be granted.

Provide rationale:

Tissue is obtained only from patients who have consented to the pregnancy tissue being used anonymously for medical research.

19.3 * Subjects will be provided with additional pertinent information after their participation:

- ( ) Yes (•) No

If yes, describe the process and attach any post-enrollment information sheets or consent forms for review:

19.4 * If you are recording identifiers, describe your plan to destroy the identifiers at the earliest opportunity consistent with the research or provide a health or research justification for retaining the identifiers, or indicate and explain that retention is required by law:

No identifiers will be recorded.

20.0 CTSI Screening Questions

20.1 * **This study will be carried out at one of the UCSF Clinical Research Services (CRS) units or will utilize CRS services:**

○ Yes ◉ No

20.2 This project involves community-based research:

○ Yes ◉ No

20.3 This project involves practice-based research:

○ Yes ◉ No

21.0 End of Study Application

21.1

End of Study Application Form

To continue working on the Study Application: Click on the section you need to edit in the left-hand menu. Remember to save through the entire Study Application after making changes. If you are done working on the Study Application: Click Save and Continue. If this is a new study, you will automatically enter the Initial Review Submission Packet form, where you can attach consent forms or other study documents. Review the Initial Review Submission Checklist for a list of required attachments. Answer all questions and attach all required documents to speed up your approval. * Please note that effective January 2, 2013 both Feasibility and Scientific Merit Review are required for all interventional clinical trials *prior* to IRB review. If required, your application will NOT be considered complete if the Feasibility and Scientific Review forms are not attached in the Other Study Documents section.

Study Application (Version 1.1)

1.0 General Information

***Enter the full title of your study:**

Humanized Mouse Models for HIV Therapeutics Development

***Enter the study alias:**

Humanized mice
* This field allows you to enter an abbreviated version of the Study Title to quickly identify this study.

2.0 Add departments

2.1 and Specify Research Location:

Is Primary?	Department Name
◉	[redacted]

3.0 List the key study personnel: (Note: external and affiliated collaborators who are not in the UCSF directory can be identified later in the Qualifications of Key Study Personnel section at the end of the form)

3.1 *Please add a Principal Investigator for the study:

[redacted]

Select if applicable

☐ Department Chair ☐ Resident

☐ Fellow

If the Principal Investigator is a Fellow, the name of the Faculty Advisor must be supplied below.

3.2 If applicable, please select the Research Staff personnel

A) Additional Investigators

B) Research Support Staff

[redacted]

3.3 *Please add a Study Contact

[redacted]

The Study Contact(s) will receive all important system notifications along with the Principal Investigator. (e.g. The project contact(s) are typically either the Study Coordinator or the Principal Investigator themselves).

3.4 If applicable, please add a Faculty Advisor/Mentor:

3.5 If applicable, please select the Designated Department Approval(s)

[redacted]

Add the name of the individual authorized to approve and sign off on this protocol from your Department (e.g. the Department Chair or Dean).

4.0 Qualifications of Key Study Personnel

4.1 List the study responsibilities and qualifications of any individuals who qualify as Key Study Personnel (KSP) at UCSF and affiliated sites ONLY by clicking the "Add a new row" button: NOTE: This information is required and your application will be considered incomplete without it.

KSP Name	Description of Study Responsibilities	Qualifications
[redacted]		

5.0 Initial Screening Questions

5.1 * This study involves human stem cells (including iPS cells and adult stem cells), gametes or embryos:

- (•) No
- ( ) Yes, and requires CHR and GESCR review
- ( ) Yes, and requires GESCR review, but NOT CHR review

5.2 * This application involves a Humanitarian Use Device:

- (●) No
- ( ) Yes, and it includes a research component
- ( ) Yes, and it involves clinical care ONLY

5.3 * This is a CIRB study (e.g. the NCI CIRB will be the IRB of record):

( ) Yes (●) No

5.4 * This application includes a request to rely on another IRB (other than NCI CIRB):

( ) Yes (●) No

Note: If this request is approved, the CHR will **NOT** review and approve this study. Another institution will be the IRB of record.

6.0 Application Type

6.1 * This research involves:

- (●) Minimal risk
- ( ) Greater than minimal risk

6.2 * This application is:

- ( ) Full Committee
- (●) Expedited
- ( ) Exempt

6.3 If you think this study qualifies for expedited review, select the regulatory category(ies) that the research falls under:

- [ ] Category 1: A very limited number of studies of approved drugs and devices
- [ ] Category 2: Blood sampling
- [ ] Category 3: Noninvasive specimen collection (e.g. buccal swabs, urine, hair and nail clippings, etc.)
- [ ] Category 4: Noninvasive clinical procedures (e.g. physical sensors such as pulse oximeters, MRI, EKG, EEG, ultrasound, moderate exercise testing, etc.)
- [x] Category 5: Research involving materials (data, documents, records, or specimens) that were previously collected for either nonresearch or research purposes
- [ ] Category 6: Use of recordings (voice, video, digital or image)
- [ ] Category 7: Low risk behavioral research or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies
- [ ] Category 8: Continuing review of previously approved full committee research that is essentially complete
- [ ] Category 9: Continuing review of research NOT involving an IND or IDE where the IRB has determined that the research poses no greater than minimal risk

6.4 * This study involves:

- ( ) Subject contact (including phone, email or web contact)
- (●) No subject contact (limited to medical records review, biological specimen analysis, and/or data analysis)

7.0 Funding

7.1 Identify all sponsors and provide the funding details. If funding comes from a Subcontract, please list only the Prime Sponsor:

External Sponsor:

View Details	Sponsor Name	Sponsor Type	Awardee Institution:	Contract Type:	Project Number	UCSF RAS System Award Number ("A" + 6 digits)
⊟	NIH Natl Inst Allergy & Infectious Dis.	01	UCSF	Contract		A118823

Sponsor Name:	NIH Natl Inst Allergy & Infectious Dis.
Sponsor Type:	01
Sponsor Role:	Funding
CFDA Number:	
Grant/Contract Number:	
Awardee Institution::	UCSF
Is Institution the Primary Grant Holder:	Yes
Contract Type:	Contract
Project Number:	
UCSF RAS System Award Number ("A" + 6 digits):	A118823
Grant Number for Studies Not Funded thru UCSF:	
Grant Title:	Tissue-based Small Animal Model for HIV Drug Discovery
PI Name: (If PI is not the same as identified on the study.)	
Explain Any Significant Discrepancy:	

Gift, Program, or Internal Funding (check all that apply):

- ☐ Funded by gift (specify source below)
- ☐ Funded by UCSF or UC-wide program (specify source below)
- ☐ Specific departmental funding (specify source below, if applicable)
- ☐ Unfunded (miscellaneous departmental funding)
- ☐ Unfunded student project

List the gift, program, or departmental funding source:

7.2 If you tried to add a sponsor in the question above and it was not in the list, follow these steps:

- **If funding has already been awarded or the contract is being processed by the Contracts and Grants or Industry Contracts unit, your sponsor is already in the system and the project has a UCSF RAS System Proposal or Award number. Check with your department's Research Services**

Analyst (RSA) to ask how the sponsor is listed in the UC sponsor list and what the Proposal or Award number is.

- **If you need additional assistance, contact the Contracts and Grants Award Team at CGAwardTeam@ucsf.edu and list the sponsor in the box below.**

○ Sponsor not in list

Only if your sponsor is not yet in the list, type the sponsor's name:

If the funding is administered by the UCSF Office of Sponsored Research, your study will not receive CHR approval until the sponsor and funding details have been added to your application.

7.3 * This study is supported in whole or in part by Federal funding:

◉ Yes ○ No

If **yes**, indicate which portion of your grant you will be attaching:

- ☐ The Research Plan, including the Human Subjects Section of your NIH grant or subcontract
- ☑ For other federal proposals (contracts or grants), the section of the proposal describing human subjects work
- ☐ The section of your progress report if it provides the most current information about your human subjects work
- ☐ The grant is not attached. The study is funded by an award that does not describe specific plans for human subjects, such as career development awards (K awards), cooperative agreements, program projects, and training grants (T32 awards)

8.0 Statement of Financial Interest

8.1 * The Principal Investigator and/or one or more of the key study personnel has financial interests related to this study:

○ Yes ◉ No

If **Yes**, the Conflict of Interest Advisory Committee (COIAC) office may contact you for additional information.

9.0 Sites

9.1 Institutions (check all that apply):

- ☑ UCSF
- ☐ China Basin
- ☐ Helen Diller Family Comprehensive Cancer Center
- ☐ Mission Bay
- ☐ Mount Zion
- ☑ San Francisco General Hospital (SFGH)
- ☐ SF VA Medical Center (SF VAMC)
- ☐ Blood Centers of the Pacific (BCP)
- ☐ Blood Systems Research Institute (BSRI)
- ☐ Fresno (Community Medical Center)

- [ ] Gallo
- [ ] Gladstone
- [ ] Institute on Aging (IOA)
- [ ] Jewish Home
- [ ] SF Dept of Public Health (DPH)

9.2 Check all the other types of sites not affiliated with UCSF with which you are cooperating or collaborating on this project:

- [ ] Other UC Campus
- [ ] Other institution
- [ ] Other community-based site
- [ ] Foreign Country

List the foreign country/ies:

9.3 * This is a multicenter study:

- ( ) Yes
- (•) No

9.4 Check any research programs this study is associated with:

- [ ] Cancer Center
- [ ] Center for AIDS Prevention Sciences (CAPS)
- [ ] Global Health Sciences
- [ ] Immune Tolerance Network (ITN)
- [ ] Neurosciences Clinical Research Unit (NCRU)
- [ ] Osher Center
- [ ] Positive Health Program

10.0 Study Design

10.1 * Study design:

Human fetal tissue specimens (which would otherwise be discarded) will be retrieved from products of conception obtained
from induced abortions at [redacted]. Tissues will be collected only if informed consent has been obtained agreeing that the tissue may be saved for future study.

10.2 Check all that apply:

- [ ] Phase I
- [ ] Phase II
- [ ] Phase III
- [ ] Phase IV

11.0 Scientific Considerations

11.1 Hypothesis:

This study has a hypothesis:

○ Yes ◉ No

If yes, state the hypothesis or hypotheses:

11.2 * List the specific aims:

Human fetal tissues will be implanted into immunodeficient mice to make them susceptible to infection with HIV so that the efficacy of new antiviral drugs can be evaluated.

11.3 Statistical analysis:

Cohorts of 50 mice will be generated from each set of fetal tissues, which permits 7 groups of 7 mice each. Viral loads will be compared between treated and untreated mice by the Mann-Whitney U test, and P values ≤0.05 will be considered statistically significant.

11.4 * This is an investigator-initiated study:

◉ Yes ○ No

11.5 This study has received scientific or scholarly review from (check all that apply): * Please note that effective January 2, 2013 both Feasibility and Scientific Merit Review are required for all interventional clinical trials *prior* to IRB review.

☐ Cancer Center Protocol Review Committee (PRC) (Full approval or contingent PRC approval is required prior to final CHR approval for cancer-related protocols.)
☐ CTSI Clinical Research Center (CRC) advisory committee
☐ Departmental scientific review
☐ Other:

Specify **Other**:

If required, attach the Feasibility and Scientific Review forms in the Other Study Documents section of the Initial Review Submission Packet.

12.0 Background

12.1 Background:

The ultimate goal of this Contract is to speed the development of new therapies for HIV
infection. Besides supplying key information for in vivo safety and efficacy, preclinical evaluation
in small animal models can enable (1) head-to-head comparisons of antiviral potency for
chemical lead selection, (2) proof-of-principle data for drugs with novel mechanisms of action,
(3) information on tissue reservoirs of HIV infection that cannot be readily obtained from human
patients, and (4) study of potential toxicities prior to Phase I clinical trials. The scope of this

contract for Humanized Mouse Models for HIV Therapeutics Development is to conduct studies in vitro and in humanized mouse models, to improve the SCID-hu Thy/Liv model and a second model with human leukocyte reconstitution in gut-associated lymphoid tissue, and to adapt other existing or newly discovered models, all for the purpose of developing novel therapies for HIV disease. As we have done for this Contract since 1995, we will employ state-of-the-art techniques and technologies in these models for evaluating promising therapies and other interventions for HIV/AIDS. The SCID-hu Thy/Liv mouse, pioneered by McCune and colleagues, is generated by implanting pieces of human fetal thymus and liver together under the kidney capsule of CB-17-*scid* mice. In a highly reproducible manner, these organs fuse, become vascularized, and grow into a stable organoid termed "Thy/Liv," reaching a total mass of 100–300 x 10^6 human cells in 18 weeks. The Thy/Liv implant reproduces the differentiation, proliferation, and function of human hematopoietic progenitor cells derived from the fetal liver within the human thymus. The implants possess histologically normal cortical and medullary compartments that sustain multilineage human hematopoiesis for 6–12 months, generating a continuous source of CD4-expressing thymocytes that can serve as target cells for HIV infection and replication.

12.2 Preliminary studies:

We have generated appoximately 1,200 humanized mice per year since 2000 with human fetal tissues obtained from Advanced Bioscience Resources (ABR). Sometimes ABR cannot supply these tissues, so we are seeking approval to collect them from [redacted]

12.3 References:

If you have a separate bibliography, attach it to the submission with your other study documents.

13.0 Sample Size and Eligibility

13.1 Number of subjects that will be enrolled at UCSF and affiliated institutions:

24 per year

13.2 Total number of subjects that will be enrolled at all sites:

24 per year

13.3 Estimated number of people that you will need to consent and screen here (but not necessarily enroll) to get the needed subjects:

50 per year

13.4 Explain how and why the number of subjects was chosen:

Tissues from each subject will be used to make one cohort of humanized mice, and 24 mouse cohorts will be made per year.

13.5 * Eligible age range(s):

- [ ] 0-6 years
- [ ] 7-12 years
- [ ] 13-17 years
- [x] 18+ years

13.6 Inclusion criteria:

None.

13.7 Exclusion criteria:

None.

13.8 There are inclusion or exclusion criteria based on gender, race or ethnicity:

○ Yes ◉ No

If **yes**, please explain the nature and rationale for the restrictions:

14.0 Use of In Vitro Diagnostics in Studies Not Involving Subject Contact

14.1 * This study involves the investigational use of an in vitro diagnostic device:

○ Yes ◉ No

15.0 Other Approvals and Registrations

15.1 * This is a clinical trial:

○ Yes ◉ No

Clinical Trial Registration
"NCT" number for this trial:

15.2 * Do any study activities take place on patient care units:

○ Yes ◉ No

If **Yes**, attach a letter of support for the study from the involved patient care manager(s).

15.3 * Data from this study will be submitted to NIH for Genome-Wide Association Studies (GWAS):

○ Yes ◉ No

15.4 * This study involves administration of vaccines produced using recombinant DNA technologies to human subjects:

○ Yes ◉ No

15.5 * This study involves human gene transfer (NOTE: Requires NIH Recombinant DNA Advisory Committee (RAC) review prior to CHR approval):

○ Yes ◉ No

15.6 * The UCSF Radiation Safety Committee requires review of your protocol if it includes administration of radiation as part of standard of care OR research exposures. Does your protocol involve any radiation exposure to patients/subjects:

○ Yes ◉ No

15.7 This study involves other regulated materials and requires approval and/or authorization from the following regulatory committees:

☑ Institutional Biological Safety Committee (IBC)

Specify BUA #:

BU000793-02B (PI: [redacted]

☑ Institutional Animal Care and Use Committee (IACUC)

Specify IACUC #:

AN089843-01C

☐ Radiation Safety Committee

Specify RUA #:

☐ Radioactive Drug Research Committee (RDRC)

Specify RDRC #:

☑ Controlled Substances

16.0 Procedures: No Subject Contact

16.1 Check all that apply:

☐ Retrospective Chart Review
☑ Biological Specimen Analysis
☐ Specimen Banking for Future Research
☐ Data Analysis
☐ UCSF is serving as the Coordinating Center only

16.2 Source:

[redacted]. [redacted] and [redacted] in my lab will collect the tissues from the specimen containers.

16.3 The source obtained consent from subjects to use the biological specimens or data for the research proposed in this study:

◉ Yes ○ No

If **no**, explain:

16.4 The source has IRB Approval to obtain and possess the biological specimens or data:

◉ Yes ○ No

If **no,** explain:

16.5 Type of records, biological specimens, and data:

Human fetal tissues.

16.6 Dates for the records, biological specimens, or data that will be used:

From:

To:

OR

☑ Indefinite (for repositories and other ongoing research resources)

16.7 Variables that will be abstracted from the records or received with the biological specimens or data set:

None.

17.0 Confidentiality and Privacy

17.1 Plans for maintaining privacy in the research setting:

17.2 Possible consequences to subjects resulting from a loss of privacy:

17.3 Study data are:

- [ ] Derived from the Integrated Data Repository (IDR) or The Health Record Data Service (THREDS) at SFGH
- [ ] Derived from a medical record (identify source below)
- [ ] Added to the hospital or clinical medical record
- [x] Created or collected as part of health care
- [ ] Used to make health care decisions
- [x] Obtained from the subject, including interviews, questionnaires
- [ ] Obtained from a foreign country or countries only
- [ ] Obtained from records open to the public
- [ ] Obtained from existing research records
- [ ] None of the above

If **derived from a medical record**, identify source:

17.4 Identifiers may be included in research records:

- (•) Yes ( ) No

If **yes**, check all the identifiers that may be included:

- [x] Names
- [ ] Dates
- [ ] Postal addresses
- [ ] Phone numbers
- [ ] Fax numbers
- [ ] Email addresses
- [ ] Social Security Numbers*
- [ ] Medical record numbers
- [ ] Health plan numbers
- [ ] Account numbers
- [ ] License or certificate numbers
- [ ] Vehicle ID numbers
- [ ] Device identifiers or serial numbers
- [ ] Web URLs
- [ ] IP address numbers
- [ ] Biometric identifiers
- [ ] Facial photos or other identifiable images
- [ ] Any other unique identifier

* Required for studies conducted at the VAMC

17.5 Identifiable information might be disclosed as part of study activities:

- ( ) Yes (•) No

If **yes**, indicate to whom identifiable information may be disclosed:

- [ ] The subject's medical record
- [ ] The study sponsor
- [ ] Collaborators
- [ ] The US Food & Drug Administration (FDA)

☐ Others (specify below)
☐ A Foreign Country or Countries (specify below)

If **Others**, specify:

The person collecting the tissues may see name on specimen container.

17.6 Indicate how data are kept secure and protected from improper use and disclosure (check all that apply): NOTE: Whenever possible, do not store subject identifiers on laptops, PDAs, or other portable devices. If you collect subject identifiers on portable devices, you MUST encrypt the devices.

☐ Data are stored securely in My Research
☐ Data are coded; data key is destroyed at end of study
☐ Data are coded; data key is kept separately and securely
☐ Data are kept in a locked file cabinet
☐ Data are kept in a locked office or suite
☐ Electronic data are protected with a password
☐ Data are stored on a secure network
☐ Data are collected/stored using REDCap or REDCap Survey

17.7 Additional measures to assure confidentiality and protect identifiers from improper use and disclosure, if any:

Patient identifiers (names on specimen containers) are not recorded by the personnel in my lab ([redacted] and [redacted] who will collect the fetal tissues from the specimen containers at [redacted].

17.8 This study may collect information that State or Federal law requires to be reported to other officials or ethically requires action:

○ Yes ◉ No

Explain:

17.9 This study will be issued a Certificate of Confidentiality:

○ Yes ◉ No

18.0 Subjects

18.1 Check all types of subjects that may be enrolled:

☐ Inpatients
☑ Outpatients
☐ Healthy volunteers
☐ Staff of UCSF or affiliated institutions

18.2 Additional vulnerable populations:

☐ Children
☐ Subjects unable to consent for themselves
☐ Subjects unable to consent for themselves (emergency setting)
☐ Subjects with diminished capacity to consent

- [ ] Subjects unable to read, speak or understand English
- [ ] Pregnant women
- [ ] Fetuses
- [ ] Neonates
- [ ] Prisoners
- [ ] Economically or educationally disadvantaged persons
- [ ] Investigators' staff
- [ ] Students

Explain why it is appropriate to include the types of subjects checked above in this particular study:

Describe the additional safeguards that have been included in the study to protect the rights and welfare of these subjects and minimize coercion or undue influence:

19.0 Waiver of Consent/Authorization for Minimal Risk Research

19.1 * Waiving consent/authorization will not adversely affect subjects' rights and welfare:

- (•) Yes

If **no**, a waiver of consent/authorization can NOT be granted.

19.2 * It is not practicable to conduct the research without the waiver, nor is it practicable to conduct the research without access to the requested information:

- (•) Yes

If **no**, a waiver of consent/authorization can NOT be granted.

Provide rationale:

Tissue is obtained only from patients who have consented to the pregnancy tissue being used anonymously for medical research.

19.3 * Subjects will be provided with additional pertinent information after their participation:

- ( ) Yes (•) No

If yes, describe the process and attach any post-enrollment information sheets or consent forms for review:

19.4 * If you are recording identifiers, describe your plan to destroy the identifiers at the earliest opportunity consistent with the research or provide a health or research justification for retaining the identifiers, or indicate and explain that retention is required by law:

No identifiers will be recorded.

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20.1 * This study will be carried out at one of the UCSF Clinical Research Services (CRS) units or will

utilize CRS services:

○ Yes ◉ No	

20.2 This project involves community-based research:

○ Yes ◉ No	

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21.0 End of Study Application

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Study Application (Version 1.0)

1.0 General Information

***Enter the full title of your study:**

Humanized Mouse Models for HIV Therapeutics Development

***Enter the study alias:**

Humanized mice
* This field allows you to enter an abbreviated version of the Study Title to quickly identify this study.

2.0 Add departments

2.1 and Specify Research Location:

Is Primary?	Department Name
◉	[redacted]

3.0 List the key study personnel: (Note: external and affiliated collaborators who are not in the UCSF directory can be identified later in the Qualifications of Key Study Personnel section at the end of the form)

3.1 *Please add a Principal Investigator for the study:

[redacted]

Select if applicable

☐ Department Chair ☐ Resident

☐ Fellow

If the Principal Investigator is a Fellow, the name of the Faculty Advisor must be supplied below.

3.2 If applicable, please select the Research Staff personnel

A) Additional Investigators

B) Research Support Staff

[redacted]

3.3 *Please add a Study Contact

[redacted]

The Study Contact(s) will receive all important system notifications along with the Principal Investigator. (e.g. The project contact(s) are typically either the Study Coordinator or the Principal Investigator themselves).

3.4 If applicable, please add a Faculty Advisor/Mentor:

3.5 If applicable, please select the Designated Department Approval(s)

[redacted]

Add the name of the individual authorized to approve and sign off on this protocol from your Department (e.g. the Department Chair or Dean).

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- ( ) Yes, and requires GESCR review, but NOT CHR review

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- (●) No
- ( ) Yes, and it includes a research component
- ( ) Yes, and it involves clinical care ONLY

5.3 * This is a CIRB study (e.g. the NCI CIRB will be the IRB of record):

( ) Yes (●) No

5.4 * This application includes a request to rely on another IRB (other than NCI CIRB):

( ) Yes (●) No

Note: If this request is approved, the CHR will **NOT** review and approve this study. Another institution will be the IRB of record.

6.0 Application Type

6.1 * This research involves:

- (●) Minimal risk
- ( ) Greater than minimal risk

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- ( ) Full Committee
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Sponsor Name:	NIH Natl Inst Allergy & Infectious Dis.
Sponsor Type:	01
Sponsor Role:	Funding
CFDA Number:	
Grant/Contract Number:	
Awardee Institution::	UCSF
Is Institution the Primary Grant Holder:	Yes
Contract Type:	Contract
Project Number:	
UCSF RAS System Award Number ("A" + 6 digits):	A118823
Grant Number for Studies Not Funded thru UCSF:	
Grant Title:	Tissue-based Small Animal Model for HIV Drug Discovery
PI Name: (If PI is not the same as identified on the study.)	
Explain Any Significant Discrepancy:	

Gift, Program, or Internal Funding (check all that apply):

- ☐ Funded by gift (specify source below)
- ☐ Funded by UCSF or UC-wide program (specify source below)
- ☐ Specific departmental funding (specify source below, if applicable)
- ☐ Unfunded (miscellaneous departmental funding)
- ☐ Unfunded student project

List the gift, program, or departmental funding source:

7.2 If you tried to add a sponsor in the question above and it was not in the list, follow these steps:

- **If funding has already been awarded or the contract is being processed by the Contracts and Grants or Industry Contracts unit, your sponsor is already in the system and the project has a UCSF RAS System Proposal or Award number. Check with your department's Research Services**

Analyst (RSA) to ask how the sponsor is listed in the UC sponsor list and what the Proposal or Award number is.

- **If you need additional assistance, contact the Contracts and Grants Award Team at CGAwardTeam@ucsf.edu and list the sponsor in the box below.**

○ Sponsor not in list

Only if your sponsor is not yet in the list, type the sponsor's name:

If the funding is administered by the UCSF Office of Sponsored Research, your study will not receive CHR approval until the sponsor and funding details have been added to your application.

7.3 * This study is supported in whole or in part by Federal funding:

◉ Yes ○ No

If **yes**, indicate which portion of your grant you will be attaching:

- ☐ The Research Plan, including the Human Subjects Section of your NIH grant or subcontract
- ☑ For other federal proposals (contracts or grants), the section of the proposal describing human subjects work
- ☐ The section of your progress report if it provides the most current information about your human subjects work
- ☐ The grant is not attached. The study is funded by an award that does not describe specific plans for human subjects, such as career development awards (K awards), cooperative agreements, program projects, and training grants (T32 awards)

8.0 Statement of Financial Interest

8.1 * The Principal Investigator and/or one or more of the key study personnel has financial interests related to this study:

○ Yes ◉ No

If **Yes**, the Conflict of Interest Advisory Committee (COIAC) office may contact you for additional information.

9.0 Sites

9.1 Institutions (check all that apply):

- ☑ UCSF
- ☐ China Basin
- ☐ Helen Diller Family Comprehensive Cancer Center
- ☐ Mission Bay
- ☐ Mount Zion
- ☑ San Francisco General Hospital (SFGH)
- ☐ SF VA Medical Center (SF VAMC)
- ☐ Blood Centers of the Pacific (BCP)
- ☐ Blood Systems Research Institute (BSRI)
- ☐ Fresno (Community Medical Center)

- [ ] Gallo
- [ ] Gladstone
- [ ] Institute on Aging (IOA)
- [ ] Jewish Home
- [ ] SF Dept of Public Health (DPH)

9.2 Check all the other types of sites not affiliated with UCSF with which you are cooperating or collaborating on this project:

- [ ] Other UC Campus
- [ ] Other institution
- [ ] Other community-based site
- [ ] Foreign Country

List the foreign country/ies:

9.3 * This is a multicenter study:

- ( ) Yes
- (•) No

9.4 Check any research programs this study is associated with:

- [ ] Cancer Center
- [ ] Center for AIDS Prevention Sciences (CAPS)
- [ ] Global Health Sciences
- [ ] Immune Tolerance Network (ITN)
- [ ] Neurosciences Clinical Research Unit (NCRU)
- [ ] Osher Center
- [ ] Positive Health Program

10.0 Exempt Research Type

10.1 * Does this research involve access to Protected Health Information (i.e. medical or other health records)?

- (•) Yes
- ( ) No

If **Yes**, are you recording any identifiers in the research records at ANY point in time?

- (•) No

If **Yes**, this research is NOT Exempt. Return to the Application Type section and select "Expedited" or "Full Committee."

10.2 * This study involves:

- **Inpatients at UCSF or affiliated institutions**
- **Prisoners (other than incidental inclusion, e.g. in chart review studies)**

- (•) No

If **Yes**, this research is NOT Exempt. Go back and select "Expedited" or "Full Committee" in the Application Type section.

10.3 * This study involves:

- ☐ Category 1: Normal educational practices that are conducted in commonly accepted educational settings
- ☐ Category 2: Use of educational tests, surveys, interviews, or observations of public behavior
- ☐ Category 3: Use of educational tests, surveys, interviews, or observations of public behavior when the subjects are elected or appointed officials or candidates for public office, or if federal statute(s) require without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and therafter
- ☐ Category 4: Records review and/or data analysis (the study of already existing data, documents or records)
- ☑ Category 4: Biological specimen analysis (the study of already existing human biological specimens)

11.0 Exempt Category 4: Biological Specimen Analysis

11.1 There will be contact with the subjects:

- ◉ No

If **yes**, this research is NOT Exempt. Return to the Application Type section and select "Expedited" or "Full Committee."

11.2 The human biological specimens are pre-existing (collected prior to this research study):

- ◉ Yes

If **no**, this research is NOT Exempt. Return to the Application Type section and and select "Expedited" or "Full Committee."

11.3 Specimens were collected specifically for this proposed research project:

- ◉ No

If **yes**, this research is NOT Exempt. Return to the Application Type section and and select "Expedited" or "Full Committee."

11.4 * Describe the study purpose and activities:

Human fetal tissues will be obtained after termination of pregnancy and will be implanted into immunodeficient mice to generate humanized mice for HIV infection and drug efficacy studies.

11.5 The types of human biological specimens that will be studied are:

The tissue that will be collected includes specimens from organs that are part of the human immune system, including bone marrow, thymus, placental tissue, skin, lymph nodes, spleen, liver, intestine, and lung.

11.6 Source(s) of the human biological specimens:

- ☐ Historical samples (specify below)
- ☐ On-site or off-site repository/bank (specify below)
- ☑ Other (specify below)

If **Other**, specify:

[redacted]

Description of the source:

[redacted] offers high quality, sensitive, confidential abortion and family planning services; conducts clinical research to advance knowledge and improve abortion care; and trains future abortion care providers. The [redacted] serves as a premier clinical service and a model for hospitals and clinics throughout the country.

11.7 Access to identifiers:

- (•) The investigator has access to identifiers, but the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.
- ( ) The identifiers are maintained at the source only. The investigator receives de-identified specimens.

Note: Under **limited circumstances**, research involving only de-identified or coded private information or specimens is not human subjects research and does not need CHR review.

12.0 Waiver of Consent/Authorization for Minimal Risk Research

12.1 * Waiving consent/authorization will not adversely affect subjects' rights and welfare:

(•) Yes

If **no**, a waiver of consent/authorization can NOT be granted.

12.2 * It is not practicable to conduct the research without the waiver, nor is it practicable to conduct the research without access to the requested information:

(•) Yes

If **no**, a waiver of consent/authorization can NOT be granted.

Provide rationale:

Tissue is obtained only from patients who have consented to the pregnancy tissue being used anonymously for medical research.

12.3 * Subjects will be provided with additional pertinent information after their participation:

( ) Yes (•) No

If yes, describe the process and attach any post-enrollment information sheets or consent forms for review:

12.4 * If you are recording identifiers, describe your plan to destroy the identifiers at the earliest opportunity consistent with the research or provide a health or research justification for retaining the identifiers, or indicate and explain that retention is required by law:

No identifiers will be recorded.

13.0 CTSI Screening Questions

13.1 * **This study will be carried out at one of the UCSF Clinical Research Services (CRS) units or will utilize CRS services:**

○ Yes ◉ No

13.2 This project involves community-based research:

○ Yes ◉ No

13.3 This project involves practice-based research:

○ Yes ◉ No

14.0 End of Study Application

14.1

End of Study Application Form

To continue working on the Study Application: Click on the section you need to edit in the left-hand menu. Remember to save through the entire Study Application after making changes. If you are done working on the Study Application: Click Save and Continue. If this is a new study, you will automatically enter the Initial Review Submission Packet form, where you can attach consent forms or other study documents. Review the Initial Review Submission Checklist for a list of required attachments. Answer all questions and attach all required documents to speed up your approval. * Please note that effective January 2, 2013 both Feasibility and Scientific Merit Review are required for all interventional clinical trials *prior* to IRB review. If required, your application will NOT be considered complete if the Feasibility and Scientific Review forms are not attached in the Other Study Documents section.

University of California
San Francisco

Human Research Protection Program
Committee on Human Research

Notice of Exempt Certification

Principal Investigator [redacted] *Co-Principal Investigator*

Study Title: Humanized Mouse Models for HIV Therapeutics Development
IRB #: 13-10683
Reference #: 061685

Committee of Record: Parnassus Panel
Type of Submission: Submission Correction for Initial Review Submission Packet
Certification Date: 04/15/2013 **Expiration Date:** 04/14/2016

IRB Comments (if applicable):
Although this study was submitted on an expedited application, the CHR has determined that it qualifies for exempt category 4 and has certified the study as exempt.

This research qualifies as exempt under the following category:
(4) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

The requirement for individual HIPAA authorization is waived for all subjects. The use or disclosure of the requested information does not adversely affect the rights and welfare of the individuals and involves no more than a minimal risk to their privacy based on, at least, the presence of the following elements:

Modifications: For exempt research only, researchers can make *minor* changes to the study without notifying CHR. However, significant changes must be submitted to the CHR. The CHR website includes examples of minor vs. significant changes. All changes must follow UCSF guidance, and some changes are not allowed in the consent materials.

Expiration Notice: The iMedRIS system will generate an email notification eight weeks prior to the expiration of this study's approval. However, it is your responsibility to ensure that an application for continuing review approval has been submitted by the required time. In addition, you are required to submit a study closeout report at the completion of the project.

Approved Documents: To obtain a list of documents that were approved with this submission, follow these steps: Go to My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

For a list of all currently approved documents, follow these steps: Go to My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of

other approved documents.

San Francisco Veterans Affairs Medical Center (SFVAMC): If the SFVAMC is engaged in this research, you must secure approval of the VA Research & Development Committee in addition to CHR approval and follow all applicable VA and other federal requirements. The CHR website has more information.

Continuing Review Submission Form (Version 1.0)

1.0

Continuing Review Form

May 2019

NOTE: This form features dynamic show/hide functionality. Questions will appear and disappear as you complete the form. The form hides questions that are not relevant to your study. If the question numbers skip (e.g. 2.1, 2.4, 2.5, 2.8) it's because some questions are hidden. The form is functioning normally.

1.1 Principal Investigator:

[redacted]

1.2 Study Title:

Humanized Mouse Models for HIV Therapeutics Development

1.3 Study Number:

13-10683

1.5 * Preferred Contact Information: Please provide the best contact information (phone, pager or email) for both the PI and primary Study Contact in case the IRB needs to contact you directly:

[redacted]

1.6 Lay Summary:

Human fetal tissues will be implanted into immunodeficient mice to generate humanized mice for HIV infection and drug efficacy studies.

1.7 * NEW - Biospecimen Banks, Research Databases, and Recruitment Registries - Does this IRB approval ONLY cover activities such as biospecimen collection/banking, and/or collection of data in a research registry or recruitment database: (REQUIRED)

○ Yes ◉ No

1.8 * This is a: (REQUIRED)

◉ Continuing Review Only—no changes from last approval
○ Continuing Review and Minor Modification
○ Continuing Review and Major Modification

1.9 * Does this submission include personnel changes: (REQUIRED)

○ Yes ◉ No

1.16 * **Are there any changes in financial interests/conflicts related to this study for the PI or any other study personnel: (REQUIRED)**

○ Yes ◉ No

1.17 **Expiration Date: Hint: Click 'Refresh Constant Fields' to update the expiration date if this is a copied form.**

* **Has your study expired: (REQUIRED)**

○ Yes ◉ No

1.18 **Outstanding Stipulations:**

No Stipulation is outstanding.

2.0 Study Status for No Subject Contact Studies

Note: Investigators are no longer asked to provide the number of records and/or specimens reviewed since the last approval.

2.1 * **Study Status: (REQUIRED)**

○ Study activities have not yet commenced
◉ Study in progress - data or specimens are still being collected and/or analyzed
○ Final data analysis and/or manuscript preparation

2.2 * **Have you had any reportable incidents, including a breach of confidentiality (e.g. lost or stolen laptop or other machines/devices with study data on them, hacked networks or study records left in a public place): (REQUIRED)**

○ Yes ◉ No

University of California
San Francisco

Human Research Protection Program
Institutional Review Board (IRB)

Exempt Certification

Principal Investigator
[redacted]

Study Title: Humanized Mouse Models for HIV Therapeutics Development
IRB #: 13-10683
Reference #: 252589

Committee of Record: Parnassus Panel
Type of Submission: Continuing Review Submission Form
Certification Date: 05/23/2019

IRB Comments:

This research qualifies as exempt under the following Common Rule 1991 category:
(4) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

HIPAA Determinations:
The requirement for individual HIPAA authorization is waived for all subjects. The use or disclosure of the requested information does not adversely affect the rights and welfare of the individuals and involves no more than a minimal risk to their privacy based on, at least, the presence of the following elements: (1) an adequate plan to protect the identifiers from improper use and disclosure; (2) an adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or if such retention is otherwise required by law; (3) adequate written assurances that the requested information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the requested information would be permitted by the Privacy Rule; (4) the research could not practicably be conducted without the waiver; and (5) the research could not practicably be conducted without access to and use of the requested information.

Modifications: For exempt research only, researchers can make *minor* changes to the study without notifying UCSF IRB. However, significant changes must be submitted to the UCSF IRB. The UCSF IRB website includes examples of minor vs. significant changes. All changes must follow UCSF guidance, and

some changes are not allowed in the consent materials.

Study Closeout Report: This study does not have an expiration date. However, you are required to submit a study closeout report at the completion of the project.

For a list of all currently approved documents, follow these steps: Go to My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

San Francisco Veterans Affairs Medical Center (SFVAMC): If the SFVAMC is engaged in this research, you must secure approval of the VA Research & Development Committee in addition to UCSF IRB approval and follow all applicable VA and other federal requirements. The UCSF IRB website has more information.