

## **THE OSTEOARTHRITIS INITIATIVE (OAI) APPLICATION GUIDE FOR STUDIES REQUESTING EXISTING CORE BIOSPECIMENS**

This document outlines the process by which requests for access to existing biospecimens from the OAI resource are processed, evaluated and approved.

### **Types of specimen available**

<b><u>Type of Specimen</u></b>	<b><u>Maximum allowable specimen per study</u></b>
Serum	0.15 ml (total of serum and plasma per study)
EDTA plasma	0.15 ml (total of serum and plasma per study)
Citrate plasma	0.15 ml (total of serum and plasma per study)
DNA	500 ng
RNA	To Be Determined
Urine	2 ml

*Whole blood is not available.*

### **Review and approval process**

Individuals who have agreed to serve on the Biospecimen Review and Allocation Committee (BRAC) will be asked to make recommendations to NIAMS regarding approval of proposals that request OAI biospecimens. BRAC review panels will consist of at least 3 voting members appointed by the NIAMS Project Office (PO) as well as one non-voting member of the OAI Steering Committee. The OAI Steering Committee representative will serve as the liaison between the BRAC and the OAI Steering Committee and will change periodically.

Proposals will be reviewed for feasibility (i.e., availability of the type and amount of specimen(s) requested), for scientific merit based on modified NIH criteria, and for consistency with the objectives and goals of the OAI. Priority for proposals requesting serum or plasma will be given to those proposing longitudinal measurements of biomarkers.

Proposals that are approved by the BRAC will be forwarded to the OAI Data Coordinating Center for informational purposes. Any investigator whose proposal adds additional burden to OAI participants must also complete an application for an ancillary proposal (see the OAI Web Site; Ancillary Studies procedures). The NIAMS PO will issue a letter of approval after reviews are completed. The release of the biospecimens will be contingent on verification of funding. A diagram of the application and review process is attached to these guidelines. The PI will be expected to provide sufficient funds to cover costs of sample pulling and shipping when such services are rendered.

## **How to Apply:**

1. Complete the “Application Form for Request of OAI Core Biospecimens”
2. Submit the application form, narrative proposal (see details on the next page), and any required attachments to KAI, Inc., the administrator for the BRAC, by email to [OAIbiospecimens@kai-research.com](mailto:OAIbiospecimens@kai-research.com). *Electronic versions of documents are the preferred method of submission.*
3. **The full review process will take 6-10 weeks.** The principal investigator (PI) may receive questions from the BRAC through KAI to clarify the proposal further. Once the BRAC reviews the proposal, it will be forwarded to the NIAMS PO for review and possible approval. The NIAMS PO will provide the final notification of approval to the PI through KAI. If the proposal is not accepted, a written explanation of the reasons for declining the request will be provided. If these can be effectively addressed, a proposal may be revised and resubmitted.

Once the request is approved, requested specimens will be set aside but will not be dispensed until a letter from the funding agency (sponsor) is provided to the NIAMS PO to confirm that the study will be funded. Samples will be provided in a blinded manner to the PI. The investigator must submit the data to the NIAMS PO for un-blinding. However these data will not be released to the OAI website until at least one year after the originating investigator has received the un-blinding documentation with OAI participant IDs attached from the NIAMS PO. Access to biospecimens will only be provided with the understanding that data generated through the study proposal will be submitted to the OAI public web site within a reasonable timeline not to exceed one year post un-blinding.

The PI is responsible for the costs of pulling, aliquoting, and shipping of the samples and any costs associated with follow up inventory. A maximum of 18 months may lapse between protocol approval and confirmation of funding. If funding confirmation or a status update concerning funding is not provide to the NIAMS PO within 18 months, the hold will be dropped and the samples will be made available to other requests.

## **Application Form for Request of OAI Core Biospecimens**

### ***Proposal Format***

The narrative proposal format should conform to the following specifications:

- Maximum of 10 pages (including abstract, tables and figures); references may be additional. The PI should to be as concise as possible. Proposals that are longer than 10 pages will be returned for editing.
- Minimum font size of 11 pt (12 pt is preferred).
- Express amount of specimen requested as follows (it is imperative to justify sample size and amount of specimen requested; see limitations above):
  - Serum, EDTA and citrate plasma in milliliters (ml)
  - DNA in nanograms (ng)
  - Urine in ml
  - RNA in micrograms or nanograms (not currently extracted)
- List genes to be studied by gene name followed by HUGO Gene Nomenclature Committee gene symbol (see <http://www.gene.ucl.ac.uk/nomenclature>) in parenthesis - e.g. low density lipoprotein receptor (LDLR), estrogen receptor 1 (ESR1).

***To assure an efficient review process, these points should be clearly and fully described in your submission (while staying within the 10 page limit):***

- 1) A 200-word abstract that can be used to communicate the key objectives.
- 2) Specific Aims
- 3) Background and significance, including the potential to contribute to the health of OA patients

- 4) Methods, including all of the following that are applicable:
  - a) Sample type (citratated plasma, EDTA plasma, serum, urine, DNA, RNA), volume, and study years for which samples are being requested (refer to OAI Biospecimen Request Form)
  - b) Requirements for frozen versus previously thawed samples and, if the latter, any limitations on number of freeze thaw cycles
  - c) Description of study participants from whom samples are being requested (number and characteristics)
  - d) Statistical design, analyses and power calculations
  - e) Assays planned (be specific; for SNA, attach list of genes and SNPs following nomenclature described above)
  - f) Methodology description (include references or a detailed description if not yet published) and rationale for the selection of the biomarker assays
  - g) Specificity, sensitivity, and precision for each proposed assay
- 5) Projected timeline for a) pulling & shipping; b) sample analysis; c) return of sample, if applicable
- 6) How will the study be funded? If applying for a grant, who is the sponsor and what is the time line for funding
- 7) Investigator qualifications and involvement in OA research
- 8) Environment (expertise and capabilities to be able to conduct proposed research)
- 9) Do you anticipate using the data to file an application for a patent, to the FDA, or for other similar purposes?
- 10) Is DNA to be used? If so, include a plan for addressing any relevant clinical, ethical, legal, or social implications of the findings.
- 11) Data sharing plan (it is essential that the data generated from use of the biospecimens be returned to the NIAMS PO within one year of un-blinding for posting on the OAI Online website.

**Application Submission Deadlines**

<b><u>OAI Biospecimen Application Submitted to KAI</u></b>	<b><u>BRAC Review Intervals</u></b>	<b><u>Corresponding NIH Application Receipt Dates</u></b>
Jan 15	—————→ Feb/March	—————→ June/July
May 15	—————→ June/July	—————→ Oct/Nov
Sept 15	—————→ Oct/Nov	—————→ Feb/March

## Review Criteria

*Scoring note: 5 = outstanding, 4 = excellent, 3 = good, 2 = acceptable, 1 = poor, 0 = unacceptable*

<b>I. Scientific Review (Scored 0-5)</b>	
<b>Significance:</b> Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge or clinical practice be advanced? What will be the effect of these studies on the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?	
<b>Approach:</b> Are the conceptual or clinical framework, design, methods, and analyses adequately developed, well integrated, well reasoned, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics?	
<b>Innovation:</b> Is the project original and innovative? For example: Does the project challenge existing paradigms or clinical practice; address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools, or technologies for this area?	
<b>Investigator:</b> Are the investigators appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and other researchers? Does the investigative team bring complementary and integrated expertise to the project (if applicable)?	
<b>Environment:</b> Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed studies benefit from unique features of the scientific environment, or subject populations, or employ useful collaborative arrangements? Is there evidence of institutional support?	
<b>II. OAI Priorities and Policy (scored 0-5)</b>	
Potential for contributing to the health of osteoarthritis patients or understanding of disease	
Draws on unique characteristics of the OAI	
Efficient use of biologic specimens (volume of specimen; number of genotypes/ phenotypes tested; use of high throughput facilities; need for ad hoc thawing)	
Complements the current portfolio of existing studies	
Value of scientific resources that will be contributed to the OAI	
<b>III. Operational Criteria (not scored)</b>	<b>Meets Criterion?</b>
If necessary, has the proposed use of biologic specimens been submitted for IRB approval?	Y / N / NA
Is notification of study results required? If so, is there an appropriate plan to notify participants?	Y / N / NA
Is there an appropriate plan for disposition of unused samples?	Y / N / NA
Is there an appropriate plan for disposition of study data (e.g., publication, use in larger grant application, etc.) and is there a time line for submission of data to NIAMS for addition to OAI data base?	Y / N / NA

## Application and Approval Process for Studies Involving OAI Core Biospecimens

*Please note – the stages outlined below assume approval at every review stage. However, at any stage in this review process, the application may be sent back to the PI for revisions or more information may be requested*

The application process and deadlines will be posted on the OAI website hosted by UCSF and also posted on the NIAMS website.

See “OAI Study Application Guide for Studies Involving Core Specimens.”

The PI submits application and supporting documents to KAI for NIAMS by the January 15, May 15 and September 15 deadline(s). See attached for application receipt/review dates.

The Biospecimen Review and Allocation Committee (BRAC) will consist of voting members appointed by the NIAMS Project Officer and one non-voting member of the OAI Steering Committee. Each application will be reviewed by 2-6 individuals out of the pool of reviewers that make up the BRAC, based on their willingness to serve and affirmation of no conflict of interest.

KAI compiles and summarizes the BRAC reviews and provides them to the NIAMS PO for further evaluation. Reviewed applications and scores will be evaluated and final decisions for approval of access to biospecimens will be made.

Approval letters will be sent to the PI from NIAMS. Specimens will be released only when funding is approved. The PI of approved application provides proof of funding to NIAMS PO prior to releasing specimens. The letter is valid for 18 months.

OR

Rejection letters will be sent to the PI from NIAMS with explanation for rejection.

Once proof of funding is provided to the NIAMS PO, PI will complete biospecimens request form and samples will be released.

If PI does not apply for funding within 18 months, he/she will have to reapply for approval. It is the responsibility of the PI to keep the NIAMS PO informed of status of funding requests.