Sjögren's International Collaborative Clinical Alliance (SICCA)
***Biorepository* #HHSN26S201300057C**
SICCA Dissemination Plan

Applications will be reviewed 3 times per year, according to the following schedule:

Application Cycle	Letter of Intent (LOI) Deadline	Approximate Review Completion Date
1	February 1	May 1
2	June 1	September 1
3	October 1	January 1 (of next year)

A. Letter of Intent

The applicant should submit a 1-2 page letter of intent (LOI) to Annie Chou (annie.chou@ucsf.edu) with the following information:

1) Name of the PI and Co-PIs (where applicable)
2) Location (s) and institutions (s) where research will take place
3) Hypothesis, specific aims, and *brief* relevant background and significance
4) Requirements for the types and numbers of specimens and associated data
5) Will you need analysis support from the SICCA team?
6) Existing or future support for conduct of the research
7) How did you learn of the SICCA Registry?

2. The LOI will be reviewed by the SICCA Project Directors. If the request appears reasonable and the requested specimen type and number and associated data are available, the LOI will be forwarded to the NIDCR Contracting Officer's Technical Representative (COTR) for approval. If the LOI is approved, the investigator will be contacted within 4 weeks to submit a full application (documents are posted on the SICCA website). If the request does not appear reasonable or the requested specimens and associated data are not available, the applicant will be notified in writing of the basis for non-approval and a revised LOI will be requested. All revisions must show in HIGHLIGHTED font, and a separate point-by-point description of changes made according to the reviewer's comments must be submitted.

B. Full Application

Two weeks from the date the LOI is approved, a completed SICCA Full Application should be submitted to the SICCA Coordinating Center using the following application forms from the SICCA website:
https://sicca-online.ucsf.edu/dissemination
SICCA Agreement Form

SICCA Application Cover Sheet
SICCA Dissemination Study Protocol
SICCA Data Request Form (*if applicable*)
SICCA Specimen Request Form (*if applicable*)

The completed application should be emailed to Annie Chou (annie.chou@ucsf.edu).

C. Review and Approval of Applications

1. The application will first be reviewed by SICCA staff to ensure that all necessary information is included. If the application is incomplete, it will be returned to the lead investigator, for completion and re-submission.

2. The SICCA Directors will review the application and assign two members of the International Review Panel to review the application. If the application requires modification, the applicant(s) will be contacted and the application will need to be resubmitted. A third reviewer maybe contacted if there is disagreement between the two reviewers.

3. If revisions are requested, all revisions must show in HIGHLIGHTED font, and a separate point-by-point description of changes made according to the reviewer's comments must be included for resubmission.

4. The reviewers will use standardized criteria (draft form is on page 5 and 6) for evaluation.

5. After receipt of the reviewer's comments, the application will be forwarded to the NIDCR COTR for final approval. Ultimate authority for approval rests with the SICCA Directors and Project Officer.

6. SICCA will contact the lead investigator regarding the outcome of review (e.g. approval, modification, or disapproval).

7. Specimens or data will not be released until documentation of local Institutional Review Board (IRB) approval has been provided along with a Federal wide Assurance (FWA) number for foreign collaborators and a signed and approved MTA agreement (see section D, below).

D. Publication Guidelines

1. **ALL** abstracts and manuscripts **MUST** be submitted to the SICCA Directors two weeks before they are submitted to a journal, conference workshop or other meeting. Abstracts and manuscripts will be reviewed for accuracy. Feedback will be given about any factual errors that need to be corrected before publication.

2. All publications and presentations of studies utilizing samples and/or data must acknowledge the SICCA registry. The suggested form for acknowledgment is:

Data and specimens used in this manuscript are from the Sjögren's International Collaborative Clinical Alliance (SICCA) Biorepository, funded under contract #HHSN26S201300057C by the National Institute of Dental and Craniofacial Research. This manuscript/presentation was prepared using a publicly available SICCA data set and does not necessarily reflect the opinions or views of the SICCA investigators, the NIH or NIDCR.

3. The question of co-authorship (if any) by members of SICCA Coordinating Center and Research Group members will be negotiated individually for each project. Manuscripts resulting from collaborative studies must be reviewed by all SICCA investigators who are co-authors and the NIDCR Program Officer. Sufficient time for revision should be allowed before submission to a journal. Final revisions also must be available to co-authors for review before resubmission.

4. An electronic copy of all published manuscripts should be sent to Annie Chou (annie.chou@ucsf.edu to provide an archival record of work resulting from the study.

Lead authors are responsible for complying with NIH Public Access Policy, that peer-reviewed manuscripts arising from NIH funding and accepted for publication on or after April 7, 2008 are deposited in PubMed Central (PMC). The PMCID or NIH Manuscript Submission Reference Number (NIHMSID) should be sent to Annie Chou along with two copies of the published manuscript.

5. **Specimens or data provided by SICCA are intended *exclusively* for the purpose of performing SICCA-approved research. These specimens and data *may not* be shared with other investigators or used for additional projects without the written consent of the SICCA Directors.**

E. Material Transfer Agreement (MTA)

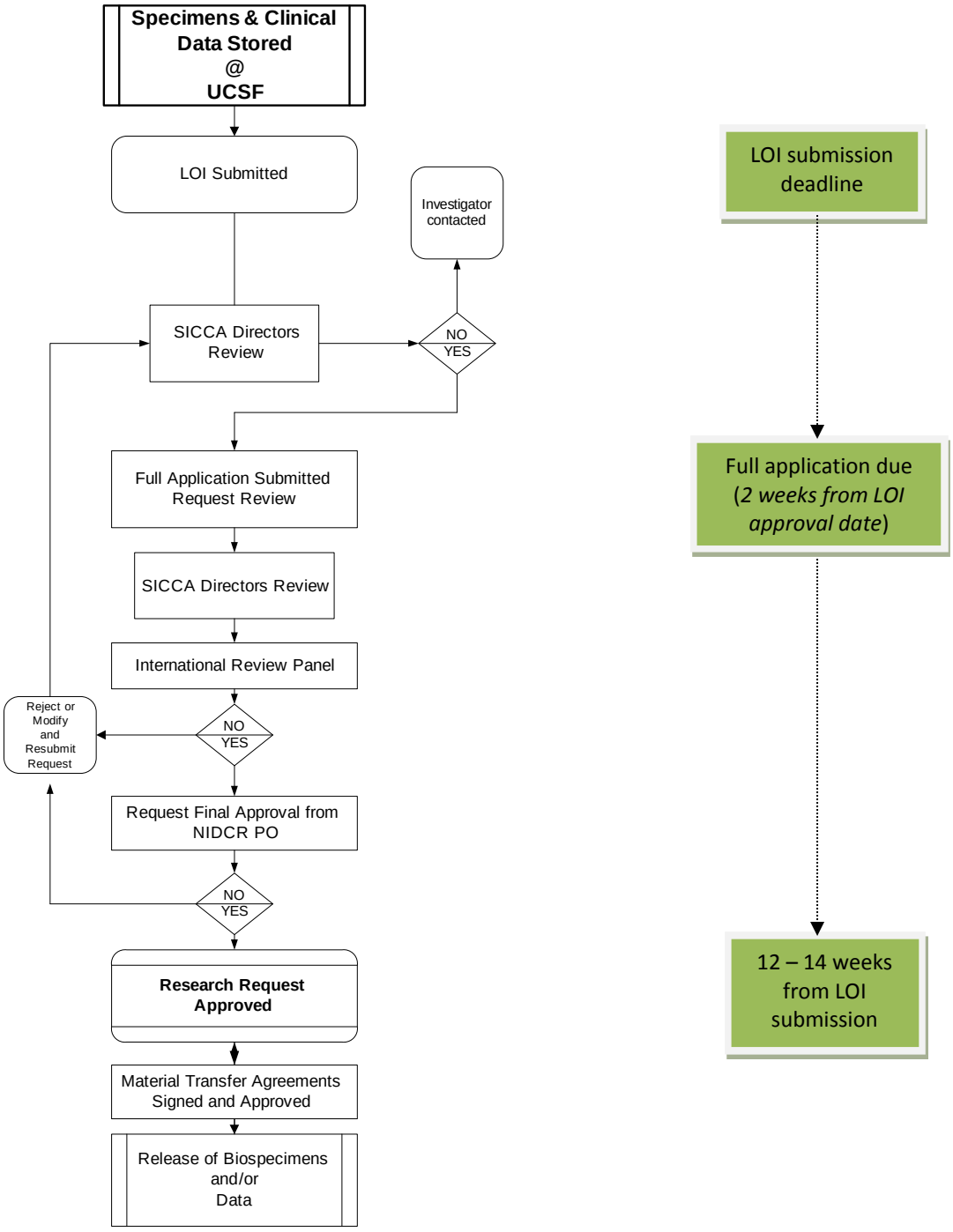
1. Annie Chou will contact the PI of this application to fill out a MTA questionnaire.

2. The MTA questionnaire is submitted to UCSF's Office of Sponsored Research (OSR).

3. A representative from OSR will contact the applicant and forward a copy of the Simple Letter Agreement (SLA) for Transfer of Non-Propriety Biological Material for signature. Along with the SLA a SICCA agreement form will be sent for the applicant's (PI) signature.

A process flow chart for the dissemination plan follows.

Dissemination Plan Flow Process



SICCA DISSEMINATION REQUEST REVIEW FORM FOR
UCSF SICCA DIRECTORS AND INTERNATIONAL EXTERNAL REVIEWERS

SCIENTIFIC CONCEPT SHEET REVIEW FORM
Submission Type Initial _____ Revised _____
Title of Study:

Investigator/Contact:

IRB Approval
Does this site have IRB/IEC approval? Yes _____ No _____
IRB/IEC approval number: _____
If a foreign institution – what is the FWA number _____

Does this proposal require specimens? Yes _____ No _____

Does this proposal require data? Yes _____ No _____

Reviewer's Name:

Date Completed:

I. GENERAL COMMENTS:	**YES**	**NO**	**N/A; COMMENTS:**
Is the hypothesis clearly defined?			
Is there sufficient background to justify the hypothesis?			
Are the specific aims clearly defined and feasible?			
Are the hypotheses significant?			
Is the study design appropriate?			
Are the methods to be employed appropriate?			
Is the type and volume of specimen requested appropriate for the methodology			

suggested? Do the aims and importance of the study justify the use of SICCA biospecimens and data? Is the time frame realistic?			

II. COMMENTS:

Issues to be addressed by the proposing investigator

III. SCORE	**IV. RECOMMENDED ACTION**
1	**Approve** with no changes
2	Approve with **minor changes** (comments required)
3	**Major revision required** (to be returned to author and re-submitted)
4	**Reject**

F. Distribution Process

Specimens - The SICCA Repository staff will receive the approved request for specimens and make arrangements with the receiving laboratory to ensure they are ready to receive specimens.

Material Transfer Agreements (MTAs) must be on file with UCSF's Office of Sponsored Research. The MTA is comprised of a simple letter agreement (SLA) that UCSF's Office of Sponsored Research and the recipient or their institute's contract officer must sign. To expedite this process, SICCA staff will complete an MTA questionnaire for each request and email it to UCSF's Office of Sponsored Research.

All specimens with the exception of DNA will be shipped from the SICCA Repository. The UCSF DNA Bank is responsible for extracting DNA from whole blood and shipping the samples to the investigator. During subsequent phases of the dissemination plan DNA samples from blood relatives collected using Oragene collection kits will be made available.

All specimens will be shipped on dry ice with the exception of paraffin slides. The UCSF SICCA Repository staff are trained and certified to ship specimens worldwide on dry ice. They have been trained according to IATA regulations. The investigator will provide the SICCA Repository with a Federal Express account number to pay for all shipping charges.

Data – A core dataset with a description of variables will be made available to applicants who have provided a detailed plan of the proposed statistical analysis, and evidence that a statistician will be performing these analyses (biosketch required). The applicant is expected to provide a list of variables required for their proposal. The applicants would also need to be able provide data analyses outputs as needed for quality control by the SICCA Statistical team.

If applicants do not have access to local statistical support, they would need to collaborate with the UCSF SICCA team for analyses to be performed by the SICCA Statistical team.

G. Expenses

There are expenses that will be generated due to the dissemination of specimens and data, which will be the responsibility of the investigator.

Examples of these expenses are:

- Preparation and shipment of specimens by SICCA Repository (charges will apply based on the number of specimens requested)
- DNA normalization and aliquoting if investigator requires a format other than a 96 well plate

- Shipments of DNA
- Paraffin or cryosectioning of LSG specimens

SICCA *Sjögren's International Collaborative Clinical Alliance*

SICCA AGREEMENT FORM

This form must be included along with your proposed research plan.

1. I/we agree that that all results derived from studies using the clinical data, and or biological specimens shall be reported to the Sjögren's Syndrome Registry and Repository for the NIDCR**.** I/we agree that the biological material and/or data received will not be further distributed to others or used for studies other than the one proposed. All publications and presentations of studies utilizing samples and/or data supplied by the SICCA will acknowledge both the contribution of samples and or data and the SICCA registry itself. The following materials are considered to be publications: a) articles in journals, b) abstracts and presentations in meetings, conferences, and symposia, and c) books and book chapters.

The suggested form for acknowledgment is:

Data and specimens used in this manuscript are from the Sjögren's International Collaborative Clinical Alliance [SICCA], funded under contract N01 DE-32636 by the National Institute of Dental and Craniofacial Research, with funding support from the National Eye Institute and Office for Research in Women's Health.

2. All abstracts and manuscripts are requested to be submitted to the SICCA Directors and NIDCR Contracting Officer's Technical Representative (COTR) for review and comment.

3. I/we assure that the use of all data and specimens will not lead to the violation of the privacy of patient information.

4. If the data and/or specimens collected from SICCA are used for a funded project, a copy of the annual progress report will be submitted to the SICCA Coordinating Center.

5. I/we have submitted proof of local IRB approval for this study.

6. For all studies in which SICCA data and/or biospecimens are used, SICCA-based data will not be merged with similar data from other sources. Thus, resulting analyses will reflect SICCA data only, or if increasing a sample size is critical to study results, a second analysis may be performed with merged data. In such a case, both data sources and analyses must be described and included, both separately and merged, in all forms of communication, including abstract, presentations, papers and grant proposals.

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NAME OF PRINCIPAL INVESTIGATOR

_____

SIGNATURE: _____

DATE: _____

Please sign and email to Annie Chou (annie.chou@ucsf.edu).

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SICCA Data/Biospecimen Application Form Cover Sheet

One of the goals of SICCA is to provide data and biospecimens from Sjögren's syndrome patients and controls to investigators studying this disease. The research projects should represent cutting-edge concepts and technology that will move the field of Sjögren's research forward and help to improve prevention and management of this disease.

A. General Information

1. Date: _____

2. Submission Type: ☐ Initial ☐ Revised

3. Study name:

_____

_____

_____

_____

4. Investigator(s):

_____

_____

5. Institution(s):

_____

_____

6. Address of Principal Investigator:

_____

_____

_____

7. Phone Number(s):

_____

_____

8. Fax number:

_____

9. Email Address:

_____

_____

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10. Contact Person (if different from principal investigator):

_____

Phone Number: _____ Fax number: _____

Email address: _____

11. Does this proposal involve a R01 submission or other extramural grant?

☐ Yes ☐ No

If yes, please specify funding agency or grant number.

_____

12. IRB Approval:

Does this project have local IRB approval? ☐ Yes ☐ No
If no IRB approval what is the anticipated approval date?_____
IRB Approval Number: _____

If study site is located outside the United States, please provide
FWA Number: _____
Expiration Date of FWA: _____

13. For application review purposes, do you have:
Conflicts of interest with any investigators: _____

Recommendations for reviewers: _____

The completed SICCA Data/Biospecimens Application Form should be sent electronically (as a PDF) to Annie Chou at annie.chou@ucsf.edu

For Internal Use Only

Date of Receipt _____

Reviewers: SICCA Directors:_____Approved for external review_____ Rejected _____
Review panel – Name of Reviewers_____
_____

☐ Approved ☐ Approved with comments

☐ Revision Requested ☐ Rejected

Comments:_____
_____
_____

NIDCR PO: ☐ Approved ☐ Rejected

SICCA *Sjögren's International Collaborative Clinical Alliance*

Study Protocol (Limit of 5 pages)

Use the following format to present your study plan. Complete in 12-point font only. Please submit electronic copies in .pdf format.

1) Lay language summary (provide a one paragraph summary of the study)

2) Background (a brief description of the rationale for the study including references)

3) Research Question (Please formulate a specific research question that includes a primary outcome/dependent variable, and one of more predictor/independent variables – e.g., is there an association between variable(s) X, Y, Z, and outcome W in a defined subgroup of the SICCA cohort)

4) **Hypothesis** (Please state the hypothesis behind your research question)

5) Study design (While the SICCA study design is a prospective cohort study with participants seen a 2 time points, you may wish to conduct a nested study with a different design such as a nested case-control study or other. Please specify your study design, and how it can be adapted to the SICCA cohort)

6) Study population (SICCA is a well defined population of adult men and women, from various countries and continents, with signs and symptoms that may be suggestive of Sjögren's syndrome. However, you may wish to identify a target population that would be a sub-group within the SICCA cohort. Please define the target population to whom you wish to be able to infer your study results. Please review Case Definition based on the new American College of Rheumatology Classification Criteria for Sjögren's syndrome (Shiboski et al, 2012) on the following page)

7) Variables and Measures, including laboratory assays (Please define each outcome and predictor variable you wish to include in the analysis you will perform to answer your research question. A list of available variables can be derived from the data collection forms on the SICCA website. If your proposal includes new assays to be performed on SICCA specimens, please describe each assay and the variable that would result from each assay – e.g., assay X will be defined as a continuous variable expressed in mg/mL).

8) Statistical analysis plan and sample size justification/power calculations (This section should include a plan of the statistical analyses proposed for this protocol. The sample size calculation should include an expected effect size the applicant wishes to detect with a justification on how this effect size was determined, the level of significance (alpha), whether a 1 or 2 sided test will be used, and the desired level of power for the analysis; 80% is standard).

8) **QA/QC procedures** (for studies generating new laboratory data, summarize laboratory QA/QC procedures, participation in recognized program, past publication, etc., relevant to the proposed investigations or testing)

9) **Timeline** for completion of study (include manuscript preparation and publication)

10) **Cited References**

11) Please submit a copy of your **NIH style biosketch** (go to http://grants.nih.gov/grants/funding/phs398/phs398.html) and **Other Support** with publications listed that are relevant to this proposal and SICCA's objectives .

12) **Existing** or **potential funding source, please specify:** pending application, planned application or funded project, and dates of funded period.

13) If you are requested to submit a revised application please summarize the changes you made and show revisions in your revised application.

SJÖGREN'S SYNDROME PROVISIONAL CASE DEFINITION: based on the new American College of Rheumatology Classification Criteria for Sjögren's syndrome (Shiboski et al, 2012)*

A "case" is defined as having two out of three of the following objective tests:

- Serology positive for anti-SSA and/or SSB antibodies **OR** (positive rheumatoid factor **and** ANA titer $\geq$1:320).
- Ocular staining score ≥3
- Presence of focal lymphocytic sialadenitis with a focus score $\geq$ 1 focus/4 mm^2;

A "control" may be defined as being negative for all objective tests included in the case definition above, however, applicants may also wish to propose an alternative definition for a control in their proposal.

* Shiboski SC, Shiboski CH, Criswell LA, Baer AN, Challacombe S, Lanfranchi H, *et al*. American college of rheumatology classification criteria for Sjogren's syndrome: a data-driven, expert consensus approach in the Sjogren's international collaborative clinical alliance cohort. *Arthritis Care Res* 2012;64:475-487.

SICCA Sjögren's International Collaborative Clinical Alliance

Data Request Form

Annie Chou, UCSF, 513 Parnassus Avenue, San Francisco, CA 94143-0500
415-502-7052 (voice) • 415-476-9370 (fax) • annie.chou@ucsf.edu

SJÖGREN'S SYNDROME CASE DEFINITION: based on the new American College of Rheumatology Classification Criteria for Sjögren's syndrome (Shiboski et al, 2012)*

A "case" is defined as having two out of three of the following objective tests:

- Serology positive for anti-SSA and/or SSB antibodies **OR** (positive rheumatoid factor **and** ANA titer ≥1:320).
- Ocular staining score ≥3
- Presence of focal lymphocytic sialadenitis with a focus score ≥ 1 focus/4 mm^2;

A "control" *may* be defined as being negative for all objective tests included in the case definition above, however, applicants may wish to propose an alternative definition for a control in their proposed plan.

Please check data requested.

☐ Case status (ACR SS phenotype versus control phenotype)

☐ Race/ethnicity (see list below)

Caucasian, Native American, Asian or Pacific Islander, Hispanic/Latino African-American, Afro-Caribbean or other African Heritage

☐ Age ☐ Gender

☐ Labial salivary gland (LSG) biopsy diagnosis

☐ LSG biopsy Focus Score (0 - 12) ☐ Ocular Staining Score (0 – 12)

☐ SSA (negative or positive)

☐ SSB (negative or positive)

☐ ANA (negative or positive, if positive, includes titer and pattern)

☐ Rheumatoid factor (negative or positive)

☐ Recruitment site (Argentina, China, Denmark, India, Japan, UK, US)

☐ Other, please explore our data collection forms on the SICCA website: https://sicca-online.ucsf.edu/

**This data request form has a limited number of variables. Additional variables are available for dissemination. These can be explored by using the Data Services section of our website: https://sicca-online.ucsf.edu/

A detailed plan of the proposed statistical analysis and evidence that a statistician will be performing these analyses must be included in the proposal. The applicant would also need to be able to provide data analyses output as needed for quality control by the SICCA Statistical team. If the applicant does not have access to local statistical support, they would need to collaborate with the UCSF SICCA team for analyses to be performed by the SICCA Statistical team.

DELIVERY INFORMATION

We will deliver data via a secure server to the recipient and email address specified below:

Recipient:_____

Email:_____

Phone:_____

* Shiboski SC, Shiboski CH, Criswell LA, Baer AN, Challacombe S, Lanfranchi H, *et al*. American college of rheumatology classification criteria for Sjogren's syndrome: a data-driven, expert consensus approach in the Sjogren's international collaborative clinical alliance cohort. *Arthritis Care Res* 2012;64:475-487.

SICCA *Sjögren's International Collaborative Clinical Alliance*
Specimen Request Form

Annie Chou, UCSF, 513 Parnassus Avenue, San Francisco, CA 94143-0500
415-502-7052 (voice) • 415-476-9370 (fax) • annie.chou@ucsf.edu

SJÖGREN'S SYNDROME CASE DEFINITION: based on the new American College of Rheumatology Classification Criteria for Sjögren's syndrome (Shiboski et al, 2012)*

A "case" is defined as having two out of three of the following objective tests:

- Serology positive for anti-SSA and/or SSB antibodies **OR** (positive rheumatoid factor **and** ANA titer ≥1:320).
- Ocular staining score ≥3
- Presence of focal lymphocytic sialadenitis with a focus score ≥ 1 focus/4 mm^2;

A "control" may be defined as being negative for all objective tests included in the case definition above, however, applicants may wish to propose an alternative definition for a control in their proposed plan.

Request for Biospecimens: **Please check all that apply and specify the minimum amount required for your assay. (ie: 25 µl). Note: write N/A if some of the options don't apply to your request**

☐ PBMC (maximum is 1 vial/case) (approximately *10 million cells/ml/vial)* # ACR SS phenotype: _____ # Controls :_____	☐ Plasma: # ACR SS phenotype: _____ µl/case: _____ # Controls :_____ µl/case:_____
☐ Saliva – Parotid # ACR SS phenotype: _____ µl/case: _____ # Controls :_____ µl/case:_____	☐ Saliva – Whole # ACR SS phenotype: _____ µl /case:. _____ # Controls :_____ µl/case:_____
☐ Serum # ACR SS phenotype: _____ µl/case. _____ # Controls :_____ µl/case:_____	☐ Tears on Schirmer Strips (half of a strip in a cryovial) # ACR SS phenotype: _____ # Controls :_____
☐ RNA Ocular Imprints (on mixed cellulose ester membranes 13 millimeter in diameter, half circle in a cryovial) # ACR SS phenotype: _____ # Controls :_____	If you are requesting multiple specimens, do you require matched samples? (ie: sets of specimens from the same individuals) ☐ Yes ☐ No

☐ **DNA** Genomic DNA isolation is performed utilizing standardized and quality controlled Gentra Systems' PureGene DNA isolation system or Qiagen kits . Check format ☐ 96-well plate _____ #of wells/case ☐ 2 ml microfuge tube DNA Concentration _____ Final DNA volume (µl) _____ # ACR SS phenotype: _____ # Controls :_____	☐ **Labial salivary glands** ☐ **Paraffin-embedded**: # ACR SS phenotype: _____ No. of slides per case: _____ No. of 5 µm sections/slide:_____ # Controls :_____ No. of slides per case: _____ No. of 5 µm sections/slide:_____ ☐ **Frozen glands:** # ACR SS phenotypes: _____ # Controls :_____

SHIPPING INFORMATION

We will ship your specimens via Federal Express. Please provide recipient's name and exact shipping address and phone number.

Recipient's Name:_____

Address (please include exact street address, room number, city, state, zip code and country):

_____

_____

_____

Phone Number(s):

_____

Email address:

_____

To cover the cost of shipping please provide your Federal Express Account number:

_____

_____

* Shiboski SC, Shiboski CH, Criswell LA, Baer AN, Challacombe S, Lanfranchi H, *et al*. American college of rheumatology classification criteria for Sjogren's syndrome: a data-driven, expert consensus approach in the Sjogren's international collaborative clinical alliance cohort. *Arthritis Care Res* 2012;64:475-487.

Please note that any leftover specimens cannot be returned to the SICCA repository without prior approval by the SICCA Coordinating Center.