Sjögren's International Collaborative Clinical Alliance (SICCA)
***Next Generation Studies* #1U01DE028891-01A1**
SICCA Dissemination Plan
Full Application Guidelines & Packet 2023

A. Letter of Intent

The applicant should submit a 1-2 page letter of intent (LOI) to Caroline Shiboski, SICCA Principal Investigator (PI), at caroline.shiboski@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

Upon receiving LOI:

1) PI will review LOI (as primary reviewer), and assign an internal Secondary Reviewer
2) Discuss via email/phone
3) Pose specimen feasibility questions to Data Manager
4) Consult and address any concerns with NIDCR as needed
5) Send compiled comments to requesting investigator within 2 weeks of receipt of the LOI
6) If request described in LOI is deemed feasible by primary and secondary reviewers, the applicant(s) will be invited to submit a full application.

B. Full Application

Two weeks from the date the LOI is approved, a completed SICCA Full Application should be submitted by e-mail to caroline.shiboski@ucsf.edu . It should include:

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

Revised Full Application Review Procedure for 2023

1) Full Application received by SICCA PI

2) Full Application will be sent to 2 internal Reviewers with *Full Application Review Form* to fill out
    - Discuss via email/phone
    - Pose any remaining specimen questions to Data Manager.
    - Primary and Secondary internal Reviewers will discuss with PI which External Reviewer has most relevant background an expertise to revienw FA
    - PI will email External Reviewer a request to complete the Full Application review within 1-2 weeks
3) Completed *Full Application Review Forms* are due **2 weeks from date sent to reviewers**.
4) Compiled reviewers comments (and approval or request for revision) from Internal Primary, Secondary, and External Reviewers will be sent to investigator(s) after consultation with NIDCR Project Officer Preethi Chander as needed

C. 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 of SICCA information. Feedback will be given about any factual errors regarding SICCA cohort and study design 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) Next Generation Studies, funded under contract #1U01DE028891-01A1 (and previously under N01 DE-32636 and #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 as needed. 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 Caroline Shiboski, at caroline.shiboski@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 SICCA PI 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 PI.

D. Material Transfer Agreement (MTA)

- Applicant will be requested to fill out a MTA questionnaire.
- The MTA questionnaire is submitted to UCSF's Office of Sponsored Research (OSR) after review by the SICCA PI
- A representative from OSR will contact the applicant and forward a copy ofthe 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

E. 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.

F. 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 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) Next Generation Studies, funded under contract #1U01DE028891-01A1 (and previously under N01 DE-32636 and #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.

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.

NAME OF PRINCIPAL INVESTIGATOR

_____

SIGNATURE: _____

DATE: _____

Please sign and email to Caroline Shiboski, at caroline.shiboski@ucsf.edu

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:

_____

_____

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 Caroline Shiboski, at caroline.shiboski@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-NextGen

Study Protocol Outline (Limit of 5 pages)

Use the following format to present your study plan (font no smaller than 11). 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(s)** *(Please formulate specific research question(s) that include a primary outcome/dependent variable, and one of more predictor/independent variables)*
4. **Hypothesis** *(Please state the hypothesis behind each 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** *(The SICCA cohort comprises 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 2016 ACR-EULAR Classification Criteria for Sjögren's Syndrome[1]*
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)*
8. **Statistical analysis plan and sample size justification/power calculations** *(This section should include a plan of the statistical analyses proposed for this protocol, and who will perform the analysis. 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).*
9. **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)*
10. **Timeline** *for completion of study (include manuscript preparation and publication)*
11. **Cited References**
12. **NIH style biosketch:** *Please submit a copy of your and statistician's (if applicable) NIH bio*
13. **Existing** or **potential funding source:** *please specify funding source (and period) for the proposed project*
14. If you have been invited to submit a revised application please summarize the changes you made and show revisions in your revised application.

SJÖGREN'S SYNDROME CASE DEFINITION[1]:

A "case" is defined as any SICCA participant who has a score ≥ 4 when summing the weights from the following items:

Item	Weight / Score
LSG with FLS and FS ≥ 1[3]	3
Anti-SSA (Ro) +	3
OSS ≥ 5 (or VB ≥ 4) on at least one eye[4]	1
Schirmer ≤ 5 mm/5min on at least one eye	1
UWS[5] flow rate ≤ 0.1 ml/min	1

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.

1. **Shiboski CH**, Shiboski SC, Seror R, Criswell LA, Labetoulle M, Lietman TM, Rasmussen A, Scofield H, Vitali C, Bowman SJ, Mariette X and the International SS Criteria Working Group. 2016 ACR-EULAR Classification Criteria for primary Sjögren's Syndrome: A Consensus and Data-Driven Methodology Involving Three International Patient Cohorts. Arthritis & Rheum 2017;69(1):35-45

Data Request Form

Caroline Shiboski, at caroline.shiboski@ucsf.edu

SJÖGREN'S SYNDROME CASE DEFINITION: based on the 2016 ACR-EULAR Classification Criteria for Sjögren's syndrome (Shiboski et al, 2017).*

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

Item	Weight / Score
LSG with FLS and FS ≥ 1[3]	3
Anti-SSA (Ro) +	3
OSS ≥ 5 (or VB ≥ 4) on at least one eye[4]	1
Schirmer ≤ 5 mm/5min on at least one eye	1
UWS[5] flow rate ≤ 0.1 ml/min	1

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://siccaonline.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://siccaonline.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 CH**, Shiboski SC, Seror R, Criswell LA, Labetoulle M, Lietman TM, Rasmussen A, Scofield H, Vitali C, Bowman SJ, Mariette X and the International SS Criteria Working Group. 2016 ACR-EULAR Classification Criteria for primary Sjögren's Syndrome: A Consensus and Data-Driven Methodology Involving Three International Patient Cohorts. *Arthritis & Rheum* 2017;69(1):35-45

Specimen Request Form

Caroline Shiboski, at caroline.shiboski@ucsf.edu

SJÖGREN'S SYNDROME CASE DEFINITION: based on the 2016 ACR-EULAR Classification Criteria for Sjögren's syndrome (Shiboski et al, 2017).*

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

Item	Weight / Score
LSG with FLS and FS ≥ 1[3]	3
Anti-SSA (Ro) +	3
OSS ≥ 5 (or VB ≥ 4) on at least one eye[4]	1
Schirmer ≤ 5 mm/5min on at least one eye	1
UWS[5] flow rate ≤ 0.1 ml/min	1

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-EULAR SS phenotype: __ # Controls:___	☐ Plasma: # ACR-EULAR SS phenotype:__µl/case:____ # Controls :_____µl/case:_____
☐ Saliva – Parotid # ACR-EULAR SS phenotype:__µl/case:____ # Controls :_____µl/case:_____	☐ Saliva – Whole # ACR-EULAR SS phenotype:__µl /case:. ____ # Controls :_____µl/case:_____
☐ Serum # ACR-EULAR SS phenotype:___µl/case. __ # Controls :_____µl/case:_____	☐ Tears on Schirmer Strips (half of a strip in a cryovial) # ACR-EULAR 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/EULAR SS phenotype: _____

Controls :_____

☐ **Labial salivary glands**

☐ **Paraffin-embedded**:

ACR/EULAR 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-EULAR 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 CH, Shiboski SC, Seror R, Criswell LA, Labetoulle M, Lietman TM, Rasmussen A, Scofield H, Vitali C, Bowman SJ, Mariette X and the International SS Criteria Working Group. 2016 ACR-EULAR Classification Criteria for primary Sjögren's Syndrome: A Consensus and Data-Driven Methodology Involving Three International Patient Cohorts. Arthritis & Rheum 2017;69(1):35-45

Please note that any leftover specimens cannot be returned to the SICCA repository without prior approval by the SICCA Specimen Bank