**NASH CRN**

# SP - Study Proposal

**Purpose:** To describe the participants, design, methods, and resources of the proposed ancillary study.
**When:** Whenever an ancillary study is proposed that involves NASH CRN patients, NASH CRN staff, or other NASH CRN resources.
**Completed by:** Investigator proposing an ancillary study.
**Instructions:** This form should be completed by the proposing investigator and signed by the proposing investigator. The liaison (who must be a NASH CRN Steering Committee member) must also review and sign the form. Electronic signatures are acceptable. This form should be completed electronically by typing into the space provided for the items below. Completed forms (along with any supporting materials) should be emailed to Katherine Yates (kyates1@jh.edu) and Peggy Adamo (madamo1@jhu.edu ) at the DCC.

## A. Administrative Information

**1.** Name, institution, and contact information (telephone and email) for principal investigator of the proposed study:

**2.** List other collaborators (name, email, institution, state/country):

**3.** NASH CRN liaison (must be a NASH CRN Steering Committee member):

**4.** There must be no significant overlap or conflict with ongoing studies involving NASH CRN patients. Before completing the remainder of this study proposal, you and the NASH CRN liaison should review the objectives of all ongoing NASH CRN studies and all currently active ancillary study proposals to be sure that there is no substantial overlap or conflict with your proposed study. Also, you should review ancillary study proposals that were disapproved in order to avoid submitting a similar study proposal, which would likely be disapproved. The full list of all study proposals is available on the NASH CRN website: www.nashcrn.com on the Ancillary Studies web page (link). At the end of this study proposal you will be required to sign to certify that you have completed these reviews and have found no substantial overlap or conflict, or that any potential overlap or conflict has been discussed with the co-chairs of the Ancillary Studies Committee and has been resolved to the degree that the proposal may be submitted for review. By continuing with this proposal I attest that I understand the foregoing. NASH CRN liaison initial here:

**5. Assurance that all collaborators have reviewed and approved the study proposal:**

a. Signature of proposing investigator:
*(An electronic signature is acceptable.)*

b. Signature of NASH CRN liaison (must be a NASH CRN Steering Committee member):
(*An electronic signature is acceptable.)*

**B. Study Design**

**6.** Study title:

**7.** Study objective:

**8.** Primary outcome:

**9.** Estimated start and end dates of study:

**10.** NASH CRN population to be used *(check all that apply)*

( ) PIVENS
( ) TONIC
( ) NAFLD Database
( ) NAFLD Adult Database 2
( ) NAFLD Pediatric Database 2
( ) FLINT
( ) CyNCh
( ) STOP-NAFLD
( ) NAFLD Database 3
( ) VEDS
( ) Other *(describe below)*:

**11.** Concept sheet: Describe concisely the research design and methods for achieving the study objectives. This abstract is meant to serve as a succinct and accurate description of the proposed work. **DO NOT EXCEED THE 2 PAGES PROVIDED. References can be submitted as a separate attachment to the study proposal form.**

**12.** Sample size justification: specify 1. type I and type II error rates, 2. primary outcome variable, 3. minimum clinically meaningful difference (in units), and 4. method of analysis for the primary outcome variable, and 5. the statistical software used for the sample size justification.

**13.** Will the data generated from this study be required to be deposited in a public-use repository? If so, the principal investigator is responsible for fulfilling this requirement.

Yes ( ) No ( )

**14.**

## C. NASH CRN Resources

**14.** Does the study require new data (questionnaires, measurements, specimens) to be collected on NASH CRN patients?

Yes ( ) No ( )

**15.**

If Yes, specify the types of data to be collected, the collection procedures, and the frequencies of collection. Specify the impact on NASH CRN staff and patients and whether the new data interfere with data collection for the main studies.

**15.** Does this study require access to previously collected NASH CRN data items?

Yes ( ) No ( )

**16.**

If Yes, specify the relevant study, data forms, and specific items. Specify the time frame for which data are needed (e.g., baseline data needed or specific follow-up data points or both).

| Study | Visit | Form | Items |
|---|---|---|---|
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**16.** Does this study require access to NASH CRN specimens or liver biopsy slides?

Yes ( ) No ( )

**17.**

**17.** Unstained liver tissue slides

a. Does this study require access to unstained liver tissue slides?

Yes ( ) No ( )

**18.**

b. Number of unstained liver tissue slides requested:
**Note: All slides must be returned to the DCC upon study completion.**

| | NAFLD Database | | | PIVENS | | | TONIC | | | NAFLD Adult Database 2 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | # of patients | # of slides per patient | total # of slides | # of patients | # of slides per patient | total # of slides | # of patients | # of slides per patient | total # of slides | # of patients | # of slides per patient | total # of slides |
| Baseline | | | | | | | | | | | | |
| Follow-up | | | | | | | | | | | | |

| | NAFLD Pediatric Database 2 | | | FLINT | | | CyNCh | | | STOP-NAFLD | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | # of patients | # of slides per patient | total # of slides | # of patients | # of slides per patient | total # of slides | # of patients | # of slides per patient | total # of slides | # of patients | # of slides per patient | total # of slides |
| Baseline | | | | | | | | | | | | |
| Follow-up | | | | | | | | | | n/a | n/a | n/a |

| | NAFLD Database 3 | | |
|---|---|---|---|
| | # of patients | # of slides per patient | total # of slides |
| Baseline | | | |
| Follow-up | | | |

c. Justify the number of unstained slides requested in the box below. In addition, include any specifications for unstained slides (describe any special requirements for slides, e.g., obtained within 3 months of serum specimen, baseline and follow-up slides must be paired):

| |
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**18.** Stained liver tissue slides

a. Do you want to borrow centrally stained liver tissue slides?

Yes ( ) No ( )

**19.** ←

b. Number of patients and types of stained liver tissue slides requested:
**Note: All slides must be returned to the DCC upon study completion.**

| | | # of patients | | | | |
|---|---|---|---|---|---|---|
| | | NAFLD Database | PIVENS | TONIC | NAFLD Adult Database 2 | NAFLD Pediatric Database 2 |
| Baseline | H & E | | | | | |
| | Trichrome | | | | | |
| | Iron | | | | | |
| Follow-up | H & E | | | | | |
| | Trichrome | | | | | |
| | Iron | | | | | |
| Total # of slides | | | | | | |

| | | # of patients | | | |
|---|---|---|---|---|---|
| | | FLINT | CyNCh | STOP-NAFLD | NAFLD Database 3 |
| Baseline | H & E | | | | |
| | Trichrome | | | | |
| | Iron | | | | |
| Follow-up | H & E | | | n/a | |
| | Trichrome | | | n/a | |
| | Iron | | | n/a | |
| Total # of slides | | | | | |

c. Justify the number of stained slides requested in the box below. In addition, include any specifications for stained slides (describe any special requirements for slides, e.g., obtained within 3 months of serum specimen, baseline and follow-up slides must be paired):

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**19.** Serum specimens

a. Does the study require access to serum specimens?

Yes ( ) No ( )

**20.** ←

b. Number of serum specimens requested:

| **NAFLD Database** | Baseline | f048 | f096 | f144 | f192 |
|---|---|---|---|---|---|
| # of patients | | | | | |
| # of 0.5mL aliquots per patient-visit | | | | | |
| Total # of aliquots | | | | | |

| **PIVENS** | Baseline | f016 | f032 | f048 | f064 | f080 | f096 | f120 |
|---|---|---|---|---|---|---|---|---|
| # of patients | | | | | | | | |
| # of 0.5mL aliquots per patient-visit | | | | | | | | |
| Total # of aliquots | | | | | | | | |

| **TONIC** | Baseline | f024 | f048 | f072 | f096 |
|---|---|---|---|---|---|
| # of patients | | | | | |
| # of 0.5mL aliquots per patient-visit | | | | | |
| Total # of aliquots | | | | | |

| **NAFLD Adult Database 2** | Baseline | t048 | t096 | t144 | t192 |
|---|---|---|---|---|---|
| # of patients | | | | | |
| # of 0.5mL aliquots per patient-visit | | | | | |
| Total # of aliquots | | | | | |

| **NAFLD Pediatric Database 2** | Baseline | t048 | t096 | t144 | t192 |
|---|---|---|---|---|---|
| # of patients | | | | | |
| # of 0.5mL aliquots per patient-visit | | | | | |
| Total # of aliquots | | | | | |

| **FLINT** | Baseline | f12 | f24 | f36 | f48 | f60 | f72 | f96 |
|---|---|---|---|---|---|---|---|---|
| # of patients | | | | | | | | |
| # of 0.5mL aliquots per patient-visit | | | | | | | | |
| Total # of aliquots | | | | | | | | |

| **CyNCh** | Baseline | f12 | f24 | f36 | f52 | f76 |
|---|---|---|---|---|---|---|
| # of patients | | | | | | |
| # of 0.5mL aliquots per patient-visit | | | | | | |
| Total # of aliquots | | | | | | |

| **STOP-NAFLD** | Baseline | f12 | f24 | f36 |
|---|---|---|---|---|
| # of patients | | | | |
| # of 0.5mL aliquots per patient-visit | | | | |
| Total # of aliquots | | | | |

| **NAFLD Database 3** | Baseline | v048 | v096 | v144 | v192 |
|---|---|---|---|---|---|
| # of patients | | | | | |
| # of 0.5mL aliquots per patient-visit | | | | | |
| Total # of aliquots | | | | | |

| **VEDS** | Baseline | f12 | f24 | f48 |
|---|---|---|---|---|
| # of patients | | | | |
| # of 0.5mL aliquots per patient-visit | | | | |
| Total # of aliquots | | | | |

c. Justify the volume of serum requested in the box below. In addition, include any specifications for serum specimens (describe any special requirements for specimens, e.g., obtained within 3 months of liver biopsy, baseline and follow-up specimens must be paired):

**20.** Plasma specimens

a. Does the study require access to plasma specimens?

Yes ( ) No ( )

→ **21.**

b. Number of plasma specimens requested:

| **NAFLD Database** | Baseline | f048 | f096 | f144 | f192 |
|---|---|---|---|---|---|
| # of patients | | | | | |
| # of 0.5mL aliquots per patient-visit | | | | | |
| Total # of aliquots | | | | | |

| **PIVENS** | Baseline | f048 | f096 | f120 |
|---|---|---|---|---|
| # of patients | | | | |
| # of 0.5mL aliquots per patient-visit | | | | |
| Total # of aliquots | | | | |

| **TONIC** | Baseline | f048 | f096 |
|---|---|---|---|
| # of patients | | | |
| # of 0.5mL aliquots per patient-visit | | | |
| Total # of aliquots | | | |

| **NAFLD Adult Database 2** | Baseline | t048 | t096 | t144 | t192 |
|---|---|---|---|---|---|
| # of patients | | | | | |
| # of 0.5mL aliquots per patient-visit | | | | | |
| Total # of aliquots | | | | | |

| **NAFLD Pediatric Database 2** | Baseline | t048 | t096 | t144 | t192 |
|---|---|---|---|---|---|
| # of patients | | | | | |
| # of 0.5mL aliquots per patient-visit | | | | | |
| Total # of aliquots | | | | | |

| **FLINT** | Baseline | f12 | f24 | f36 | f48 | f60 | f72 | f96 |
|---|---|---|---|---|---|---|---|---|
| # of patients | | | | | | | | |
| # of 0.5mL aliquots per patient-visit | | | | | | | | |
| Total # of aliquots | | | | | | | | |

| **CyNCh** | Baseline | f12 | f24 | f36 | f52 | f76 |
|---|---|---|---|---|---|---|
| # of patients | | | | | | |
| # of 0.5mL aliquots per patient-visit | | | | | | |
| Total # of aliquots | | | | | | |

| **STOP-NAFLD** | Baseline | f12 | f24 | f36 |
|---|---|---|---|---|
| # of patients | | | | |
| # of 0.5mL aliquots per patient-visit | | | | |
| Total # of aliquots | | | | |

| **NAFLD Database 3** | Baseline | v048 | v096 | v144 | v192 |
|---|---|---|---|---|---|
| # of patients | | | | | |
| # of 0.5mL aliquots per patient-visit | | | | | |
| Total # of aliquots | | | | | |

| **VEDS** | Baseline | f12 | f24 | f48 |
|---|---|---|---|---|
| # of patients | | | | |
| # of 0.5mL aliquots per patient-visit | | | | |
| Total # of aliquots | | | | |

c. Justify the volume of plasma requested in the box below. In addition, include any specifications for plasma specimens (describe any special requirements for specimens, e.g., obtained within 3 months of liver biopsy, baseline and follow-up specimens must be paired):

**21.** DNA specimens

a. Does the study require access to DNA specimens?

Yes ( ) No ( )

**22.**

b. Please specify the SMALLEST quantity of DNA in micrograms (µg) that your study requires per patient-sample:

____ ____ µg

c. Number of DNA specimens requested:

| # of DNA specimens requested | | | | |
|---|---|---|---|---|
| NAFLD Database | PIVENS | TONIC | NAFLD Adult Database 2 | NAFLD Pediatric Database 2 |
| | | | | |

| # of DNA specimens requested | | | |
|---|---|---|---|
| FLINT | CyNCh | STOP-NAFLD | NAFLD Database 3 |
| | | | |

d. Justify the volume of DNA requested in the box below. In addition, include any specifications for DNA specimens (describe any special requirements for specimens, e.g., DNA specimens paired with liver biopsy):

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**22.** Liver tissue specimens – cDNA

a. Does this study require access to cDNA?

Yes ( ) No ( ) → **23.**

b. Patients and visits with cDNA specimens needed:

| | | # of patients with cDNA specimens requested | | | | | |
|---|---|---|---|---|---|---|---|
| | NAFLD Database | PIVENS | TONIC | NAFLD Adult Database 2 | NAFLD Pediatric Database 2 | FLINT | CyNCh |
| Baseline | | | | | | | |
| Follow-up | | | | | | | |

c. Please specify the SMALLEST quantity of cDNA in micrograms (µg) that your study requires per patient-sample:

____ ____ . ____ µg

d. Justify the number of cDNA specimens requested in the box below. In addition, include any specifications for cDNA specimens (describe any special requirements for specimens, e.g., obtained within 3 months of serum specimen, baseline and follow-up specimens must be paired):

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**23.** Liver tissue specimens – frozen in RNA*later*

a. Does this study require access to liver tissue specimens?

Yes ( ) No ( )

**24.** ←

b. Patients and visits with liver tissue specimens needed:

| | # of patients with liver tissue specimens requested | | | | |
|---|---|---|---|---|---|
| | NAFLD Adult Database 2 | NAFLD Pediatric Database 2 | FLINT | CyNCh | NAFLD Database 3 |
| Baseline | | | | | |
| Follow-up | | | | | |

c. Justify the number of liver tissue specimens requested in the box below. In addition, include any specifications for liver tissue specimens (describe any special requirements for specimens, e.g., obtained within 3 months of serum specimen, baseline and follow-up specimens must be paired):

**24.** Does this study require analysis help by the DCC?

Yes ( ) No ( )

**25.** ←

If Yes, please explain, including how the DCC effort will be funded:

**25.** Does this study require any other NASH CRN resources, including staff, equipment, space, or use of the Histology Review Center?

Yes No

( ) ( )

**26.** ↵

If Yes, please list the resources required and how these resources will be funded:

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**D. Funding and IRB Approval**

**26.** Estimated budget:

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**27.** Will this study require a Letter of Support from the NASH CRN:

Yes No

( ) ( )

**28.** ↵

a. If yes, type of grant(s) being submitted:

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|---|
| |

b. Date that the Letter of Support is due: _____ _____ - _____ _____ _____ - _____ _____
day mon year

**28.** Status of funding:

( ) Funding is available (list source and amount):

| |
|---|
| |

( ) Request for added funding has been submitted (list agency approached for funding, amount requested, and date of expected action):

| |
|---|
| |

( ) Request for added funding will be submitted once a letter of support from the NASH CRN is available (list expected date of submission):

| |
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| |

**29.** Has this proposal been reviewed and approved by your IRB?:

Yes ( ) → **a.**

No ( ) → **b.**

a. If Yes, date approved: _____ _____ - _____ _____ _____ - _____ _____
day mon year

b. If No, status of IRB approval:

( ) Pending

( ) Not submitted (specify why not)

| |
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| |

c. Will the study have a consent statement?

Yes ( ) → Send a copy of your approved statement to the DCC once IRB approval is granted.

No ( )

**E. Primary investigator and NASH CRN liaison assurance to deposit any generated metabolomics, proteomic, genomic or other data from the ancillary study to the designated public-use repository as required by the NIH or other funding source(s) of the ancillary study (e.g. dbGaP for genomic data).**

**30.** Signature of proposing investigator:
*(An electronic signature is acceptable.)*

**31.** Signature of NASH CRN liaison (must be a NASH CRN Steering Committee member):
*(An electronic signature is acceptable.*)

**F. Study primary investigator and NASH CRN liaison assurance and sign off**

☐ I acknowledge that the NASH CRN Ancillary Studies Policy, including the policy on publications and presentations arising from ancillary studies, applies to the ancillary study proposed herein. These are located on the NASH CRN website (www.nashcrn.com) by clicking on the Publications or the Ancillary Studies menu options.

☐ I understand that **no clinical data will be provided to the investigator** until the DCC receives any generated data from the ancillary study with accompanying documentation.

☐ I understand that verification of data analyses may be required by the DCC prior to submission to any journal or meeting.

☐ I understand that any abstract/manuscripts resulting from this effort must be approved by the NASH CRN Publications Committee prior to submission to a meeting for presentation or to any journal.

☐ I understand that the NASH CRN Ancillary Studies Committee and the Publications Committee will make the final decision regarding authorship format and in cases of disagreement among co-authors, will decide the final author order.

☐ I have reviewed all NASH CRN protocols and ancillary studies listed on the NASH CRN website and certify that this study does not overlap or conflict with any active or completed study. Or, I certify that if potential conflict or overlap has been identified, that I have gained permission from the Ancillary Studies Committee co-chairs to submit this proposal for review.

☐ I understand that if there is a change to one or more of the aims or if additional NASH CRN resources are needed, I must gain approval from the Ancillary Studies Committee to proceed.

☐ I understand that the ancillary study must make its own arrangements for whatever repository, data collection, management, and analysis support that it needs.

☐ I will adhere to the confidentiality policies of the NASH CRN and associated IRB, which require that no identifying personal information be included in any abstract/manuscript or generated data sent to the DCC. In addition, no information available on the password-protected sections of the website will be disclosed to external investigators.

**32.** Date form submitted to NASH CRN: _____ _____ - _____ _____ _____ - _____ _____ _____ _____
day mon year

**33.** Signature of proposing investigator:
*(An electronic signature is acceptable.)*

**34.** Signature of NASH CRN liaison (must be a NASH CRN Steering Committee member):
*(An electronic signature is acceptable.*)

**G. Data Coordinating Center Use**

**35.** Date received at DCC:

_____ _____ - _____ _____ _____ - _____ _____
day mon year

**36.** DCC staff member: