"Study To Assess Hepatitis Risk (STAHR)"

List of deliverables from call (this is not meant to be a comprehensive list):
Upload IRB approval (UCSD) and the approved protocol into ROCIS

I have attached the UCSD IRB approval and the approved protocol.

Include in supporting statement:

Describe CDC's vision for the long-term, national surveillance system (we talked about it being annual with a substantially shorter questionnaire, cross-sectional analysis, link to services, incentives, etc...) that this pilot is going to form the foundation for and, (1) specifically identify the types of questions that CDC is most interested for the larger system and (2) describe the anticipated implementation of whatever recruitment strategy is identified to be the most effective.

HCV is among the 60 national notifiable diseases that are reported through the National Notifiable Disease Surveillance System. Through this passive system fewer than a 1000 cases of acute hepatitis C virus (HCV) infection are reported each year. Since blood transfusion is no longer a risk, many of these are putatively injection drug users (IDUs); however, this information is usually not collected at the local level and even less frequently reported to CDC.

In the absence of additional efforts to reach hard-to-reach at-risk population, passive surveillance for hepatitis C infection will never reach its full potential of representing all persons at risk for hepatitis C and will continue to under-represent the burden of hepatitis in young IDUs. Data from STAHR will be used to develop surveillance strategies that state and local health departments can implement without extraordinary effort. Using serial cross-sectional seroprevalence surveys, CDC and local health departments will be better able to estimate the magnitude and trends of acute HCV infection in this population.
Accordingly, the long-term intent of the STAHR project is to provide a framework for active national surveillance for HCV in IDUs as part of an expanded national hepatitis surveillance system. Through the STAHR, national surveillance will expand case-finding methods among drug users to provide more realistic estimates of acute HCV in this vulnerable population. That is, the methods and serial surveillance developed by this project can be applied nationwide at the local level to assess incidence of HCV among drug users. In turn, this project will increase access and understanding of this marginalized and hard-to-reach population and inform targeted vaccinations, prevention messages, and care. We anticipate that one or more of the three recruitment methods used in STAHR--street outreach method, respondent-driven sampling method, and venue based recruitment method--will be suitable for use in serial cross-sectional seroprevalence surveys among IDUs when serial surveillance becomes integrated into the local health departments' hepatitis surveillance. Findings from these focused, intensive investigations, in turn, will facilitate larger surveys that can be generalized to broader populations of young IDUs.

Further, we anticipate that the automated computer-assisted self interview ('ACASI') used in STAHR will become part of the health department survey tool. For national HCV surveillance, the ACASI survey will be shortened but still include questions about drug-use and sexual behaviors behaviors, use of injection paraphernalia, etc. Many of the questions will focus on barriers to hepatitis care or to getting treatment for drug addiction. The choice of the questions ultimately used in each module might vary with the location, the venue where the young IDUs are reached and the comfort level of the IDUs with the health department survey staff charged with HCV surveillance.

Incentives are integral part of studies involving any hard-to-reach population. Projects that target IDUs have given incentives to increase participation. e anticipate that incentivizing participation for certain hard-to-reach groups such as the young IDUs will be explored when the national surveillance is implemented.

Active serial surveillance for viral hepatitis in IDUs is a new strategy that will require trained staff with extra resources in order to be implemented in a routine fashion by the local health departments. Thus, the STAHR project will also identify the personnel, training, and additional resources essential to integrate serial surveillance as a component of the notifiable disease surveillance at the state or local health departments. Eventually, serial surveillance may be extended by the local health departments to infections other than HCV.

CDC is most interested in finding ways of incorporating not only HCV and other infectious disease surveillance into its surveillance systems, but improving and expanding its behavioral surveillance projects. The detailed questionnaire used in STAHR is expected to identify the questions that are relevant to effective behavioral surveillance among IDUs. In particular, STAHR would identify the questions and information most likely to delineate drug use behavior, access to health care and drug treatment and other information that can then be targeted for intervention.

HCV testing will be the pillar of the long-term surveillance project for blood-borne infections. In this pilot we intend to test the ease or complexity of sample collection by different recruitment methods and to determine the prevalence of HCV by the different recruitment methods. This will be accomplished by merging this information to the survey data—i.e., determine the proportion of participants who learn their HCV status first time during this survey, and estimate the baseline seroprevalence for the serial cross-sectional seroprevalence survey.

Both serological and molecular testing will be conducted on samples collected from consenting individuals in the STAHR project. The serological test results will be used to determine the prevalence of markers of HCV infection. The molecular testing (HCV RNA) that will be completed on HCV-seronegative samples will be used to determine possible early HCV infection (acute infection).

Finally, STAHR data may be used to assess progress in performance goals of CDC's National Center for HIV/AIDS, viral hepatitis, STD, and TB Prevention (NCHHSTP) to: 1) increase the proportion of people who consistently engage in behaviors that reduce risk of hepatitis transmission or acquisition; 2) track the prevalence of disease; 3) monitor behaviors that increase the risk of hepatitis C infection (among those who are not infected); and 4) provide locally relevant data for community planning.

Include a justification for the various question "modules" found in the questionnaire (e.g. border Qs, friends Qs) and for the number of response categories (we discussed how this level of detail, while burdensome, increases the utility of the study and takes advantage of access to respondents)

The following considerations were made in the decision to include such a lengthy survey instrument. The questionnaire is estimated to take about 45 minute to 1 hour. The survey administration is simplified by having the questions on a computer which will properly administer skip patterns depending on responses to screener questions usually at the beginning of each module. The survey is close ended and attempts have been made not to include any open ended questions and self entry of response to minimize the effect of such entry to the quality of data and to enjoy the ease of coded response in analysis. Additionally, by adding a more extensive list of response options to some of the questions, this pilot study seeks to inform the larger national surveillance study by having more comprehensive options and narrowing the response options for the larger surveillance study.

The following is justification for the various questions by module.

Injection network: This module describes the injection related relationships and networks. This is important for understanding injection networks and how transmission occurs. These data will also help to interpret differences between samples obtained from the three different recruitment strategies.

Alcohol and non injection drug use: In addition to injecting drugs, IDUs also use drugs and alcohol through non-injected routes, which can impact their cognitive function, decision making, and personal risk profiles. These factors have been found to be useful in understanding risk factors for HCV infection in other studies.

Injection drug use: This module addresses the specifics of the injected agents, preparation of drugs, sharing of drugs and injection paraphernalia, frequency of injection, place of injection. This section is important for understanding injection networks and history of injection drug use. These questions will also be analyzed with lab results in hopes of learning risky behavior linked to transmission.

Sharing works: This module is supplementary to the “injection drug use” module. This module describes prevalence of injection related risk behavior for transmission of HCV. This module also examines in depth the knowledge of injection partners as well as HCV and HIV status of people they share needles with. Data from this module will be used in analysis to identify characteristics of needle sharing.

Syringe Exchange Programs: This module addresses the use of the San Diego Syringe Exchange Program to exchange clean needles. We seek to learn more about participant’s knowledge about the program as well as get detailed information of their use and barriers to practicing safe injecting behaviors. Data from this module will be used in the analysis of clean needle availability.

Abscess Questions: This module seeks to learn about history of abscesses and treatment options. These questions will be linked to risk behaviors.

Overdose: This module of only 3 questions asks participants for overdose history. This data will be used to capture overdose trends of IDU as well as linking current drug use.

Law Enforcement Interactions: This module is designed to measure the effect law enforcement interactions has on participants risk behaviors. Previous studies have found a link between law enforcement interactions to high risk behaviors among IDUs.

Injection Correlates: This module of 3 questions is linked to the sharing works module and tries to quantify frequency of syringe sharing with main injecting partner. Data from this module will also be included in the analysis of sharing patterns.

HCV transmission beliefs and HCV testing: This module addresses participants' beliefs, medication and HCV testing history. We will use this data in the analysis portion of the study.

HIV transmission beliefs and HIV testing: This module is identical to the HCV transmission beliefs and testing with focus on HIV beliefs and medical history for HIV. This module will also be used in the analysis portion of the study.

Drug treatment: This module is designed to address any history of current or past participation in drug treatment programs. The use of these questions will aid analysis by identifying potential barriers or cofounders in the results. San Diego is very distinct in it population characteristics mainly due to it's proximity to Tijuana, Mexico. Because this is a pilot study that will be used to inform the larger national surveillance study, we want to make sure we don't misinterpret the results. We decided to include a question that captures the use of drug treatment programs in the US or Mexico.

Sexual Behavior: This module was designed to assess HCV risk behaviors by differentiating steady vs. non-steady partners. Previous studies have found differences between risk behaviors people engage in with a steady vs. non -steady partner. Even though this module looks very lengthy, we have strategically ordered questions so that the main questions are asked first and if the questions don't apply to them (i.e. they did not have sex with a female) they will skip all the female sex questions.

Past Sexual History: This module asks participant for age of first sexual encounter as well as sex trading history. These factors have been found to be useful in understanding risk factors for HCV infection in other studies.

Sex Correlates and General Correlates: These two modules address condom use, child and adult sexual and physical abuse and HIV and HCV knowledge. These factors will be used in the analysis to identify and correlate to risk behaviors.

Vaccination History: As mentioned in our call, this is module is of interest to the CDC because we want to capture history of Hepatitis A and B vaccines in our population. Additionally, this will also be included in the analysis and will inform the larger national surveillance study if there is a greater need for Hepatitis A and B education.

Social Support: This module consists of 3 questions which tries to target the level of support the participants feel they have. These questions will also be included in the analysis.

Tuberculosis: This module assesses tuberculosis history. This data will be help to identify co-infections of HCV and HIV with TB. TB has been linked to these diseases by previous studies.

STI questions: These six questions will assess other potential sexually transmitted infections commonly linked to high risk behaviors. This data will also be included in the analysis of co-infections.

Hepatitis Questions: These questions try to assess actual history of Hepatitis infections diagnosed by a doctor. This will be correlated with other variables in the study.

RDS Questions: This module describes the recruiter (seed) who gave them a coupon. This section will be skipped if participant was not in the RDS phase of the study. These data will also help to interpret differences between samples obtained from the three different recruitment strategies as well as identifying characteristics of the seeds and recruiter.

Cross border questions: Tijuana, Mexico and San Diego, California share the world's busiest land border crossing. Due to its proximity to the U.S. there is a unique comingling effect of drug use between people that go back and forth between borders. This is one of the reasons we would like to assess risk behaviors that occur in Tijuana and the US and provide appropriate data results for the larger national surveillance stud. This data will also be included in the analysis.

Include a brief justification for the "sub-studies" (blood testing (acute/chronic) at CDC and vaccination uptake)

As the main objective of this project is to determine incidence of HCV infection serological testing for HCV and HCV RNA testing will be performed. The serological testing will be performed at the public health laboratory of the San Diego County in order to have the results available on time to return to the participants. Samples will also be stored at CDC to be tested by the most sensitive method to detect acute HCV infection. Considerations were also made to the fact that this high risk behavior exposes individuals to other blood borne viral infections like HIV. Therefore, participants will be offered to be screened for HIV and be given the necessary referral to care or prevention counseling. As part of NCHHSTP, DVH is committed to integrating scientific and service provision efforts for viral hepatitis and other infections that disproportionately affect our target populations (e.g., IDUs) such as HIV. Thus, we make every effort to incorporate HIV activities into our work on HCV among IDUs. HIV testing as part of this project supports the CDC National Center for HIV, Viral hepatitis, STD, and TB Prevention's goal of program collaboration and service integration (PCSI).

Completion of vaccination series is crucial to achieve the full benefits of HAV and HBV vaccines. Understanding the factors associated with vaccination uptake is important to develop strategies for increasing the series completion rates. In order to overcome the complexities related to obtaining vaccination status and related data from facilities where such service was obtained by study participants, incentive of $5.00 is given to participants every time they come to the study coordinator with evidence of vaccination receipt. The analysis of these data will include the proportion of participants who received only one or two doses or the complete three dose series and the predictors of completing the vaccination series. Based on the findings of this component of the project, the study will offer information to local health authorities about how to deal with vaccination uptake issues at the local level.

Correct language on incentives so that it does not sound like respondents are being compensated for their time.

We have consistently used the word "incentive" in Supporting Statement A.9.

There are a few more smaller items that I will send through in a track changes document before the end of the week. Please send revised documents (track changes) to me for review prior to uploading clean versions into ROCIS. When clean versions are uploaded, please remember to rename so that the revised version is easily identified.

I have attached the documents with the suggested revisions.

Addition to the list above would be:
1. Clearer discussion of recruitment strategies,

Respondent driven sampling (RDS): At least 250 participants will be recruited using RDS, a chain referral sampling approach that uses mathematical modeling to produce prevalence estimates that are unbiased by selecting initial participants or "seeds" in a non-random way.[1] Briefly, a diverse group of seeds (heterogeneous in age, gender, drug of choice, and recruitment venue) will be selected to initiate the process. Seeds will be current IDUs who project staff members identify as having large social networks and are popular among their peers. Although individuals tend to recruit participants similar to themselves, studies of RDS show that equilibrium is reached within approximately 4 to 5 waves of recruitment eliminating bias introduced by non-random seed selection.[1] After providing informed consent, seeds undergo the study procedures described previously and are then asked to refer their peers using three uniquely coded coupons containing the study name, interview locations, and a brief explanation of the study. For each new participant who is recruited by bringing back a coupon, the seed will receive $10. Recruitment waves continue as those recruited by coupons are given 3 coupons to recruit members of their own social network. Exclusion of individuals who have participated in the study through other recruitment methods could disrupt the natural propagation of RDS recruitment chains; therefore, RDS recruitment will be completed before initiating the other recruitment methods.

We will keep a "Coupon Tracking Log" to record the following: 1) each coupon's number, 2) the date a coupon was given to a participant for distribution, 3) the study ID number of the participant to whom the coupon was given for distribution, 4) the date each coupon was returned, 5) whether the person returning a coupon meet the study enrollment criteria of current injection and age between 18-30 years old and, if that person enrolls in the study, 6) the new participant's study number, 7) whether payment was provided to the participant who distributed the coupon, 8) biometric measures, and 9) personal identifiers such as gender and tattoos. The coupon tracking log will not include participants names and will be maintained on a password protected laptop computer in a separately password protected file. This computer will not contain any of the interview or test results data.

Venue based recruiting: At least 250 participants each will be recruited from two different venues that are accessed by IDUs. The syringe exchange program (SEP) run by Family Health Services of San Diego and sexually transmitted disease (STD) clinics operated by the San Diego County Department of Health Services (SDCDHS). Between July 2006 and June 2007, the SEP enrolled 442 new IDUs in the Downtown and North Park areas of San Diego with 3,628 client visits during that time. During 2000-2006, the main county STD clinic on Rosecrans Street

averaged 445 IDU clients per year; 145/year were <30 years old. Overall, 31% of IDUs were anti-HCV positive, of which 12% of those were <30 years old. Thus, a second STD clinic in the North Park neighborhood that serves a population with a high prevalence of drug use will be included. If necessary to meet our recruitment goals, recruitment may also take place at other STD clinics operated by Family Health Services of San Diego.

Street outreach: At least 250 plus participants will be recruited by having outreach workers pass out recruitment cards, leaving posters and leaflets at recruitment locations, and encouraging current study participants to inform their peers about the study. Outreach workers will approach individuals in neighborhoods, streets, bars, and other "hang-outs" where young IDUs are known to frequent. During these encounters, the outreach worker will attempt to engage individuals in conversation by offering HCV/HIV prevention materials (i.e., bleach kits, condoms and personal lubricant, and educational pamphlets). During these encounters, the outreach worker will also hand out recruitment cards with information about the study. In order to avoid requiring disclosure of the individuals' injection status, they will be told that they can take the card for themselves or someone they know who might be interested in the study.

Outreach workers will receive extensive training in how to approach and engage potential participants in these community settings. Ethical guidelines regarding professional conduct will be enforced for all outreach workers. Outreach workers will work in pairs to ensure their safety and adherence to the study protocol. Outreach workers will be able to provide information and directions to the study site or pre-screening when appropriate.

Recruitment sites are located in well-known areas of high drug traffic or drug use or where young injectors are known to congregate. Possible recruitment locations have been previously identified and mapped through ethnographic methods or through community contacts, key informants and a Community Advisory Board (CAB). In addition to recruiting participants directly from these recruitment areas, some participants may be indirectly referred to the study by friends who have participated in the study or who heard about the study but were ineligible. In these cases, participants will not identify their friends to study staff but will tell their friends about the study and encourage them to be screened for eligibility (respondent driven sampling – described above). When necessary, permission to recruit around business establishments will be secured prior to initiating recruitment.

Individuals who are willing to be contacted by the project staff to be reminded to come to the study site for eligibility screening will be asked for their name, telephone numbers where they can be reached, and whether a message may be left. All contact information obtained during such outreach encounters will be destroyed once potential participants have been found to be ineligible, participated in the study and completed both visits or they have indicated their desire not to participate. Individuals who are not asked contact information, or who do not wish to provide this information, will be given a number to contact the project staff.

1a. criteria that will be use to determine which recruitment strategy is most effective (metric),

The three different recruitment strategies will be compared for their effectiveness in terms of recruitment efficiency, logistics, sample demographics (demographic composition and injecting risk behaviors of the samples), ability to recruit more marginalized sections of the IDU community, time to recruit the target number of participants and safety of field workers.

1.b. and power to see differences.
(To do the power calculation would need to identify the size of the difference on the questionnaire factors that would likely be used in the national study.)

As STAHR is a project to pilot surveillance methods, the number of interviews has been set based on the estimated number of eligible persons, the time available for this pilot project, and the expected level of precision for a random sample. The two recruitment methods (RDS and street outreach method) will each attempt to complete a minimum of 250 interviews and the venue based method will recruit 250 each participants from two different venues (sexually transmitted disease clinic and needle exchange program). If the project meets the target number of interviews, at least 1,000 young IDUs will be interviewed during the project period.

Because STAHR is mainly descriptive, power calculations, which are used in sample size determinations for testing specific hypotheses, were not performed. Instead, the level of precision, i.e., the estimated 95% confidence interval half-width that can be expected was examined. The expected level of precision for a random sample was calculated for individual recruitment strategies (n = 250). The following table shows the expected level of precision for an estimate from these data, such as, for example, an estimate of the proportion of IDUs for whom heroin is the main drug injected. The CI half-widths in the table are the maximum that would be expected for estimates for total sample sizes of 250. The table below shows the level of precision to be expected not only for estimates for the entire population (column 2), but also for subpopulations (e.g. racial/ethnic groups) that comprise 50%, 25%, 15% and 10% of the total population (column 3, 4, 5, and 6, respectively).

	CI half-width	CI half-width	CI half-width	CI half-width	CI half-width
# interviews	total population	subpopn = 50%	subpopn = 25%	subpopn = 15%	subpopn = 10%
250	6.20%	8.77%	12.40%	16.01%	19.60%

CI half-widths for all the recruitment methods (n = 1000) are not included on the previous table because weighted analyses of the data aggregated across the different recruitment methods may be performed. Weighted analysis of the aggregated data is necessary because the selection probability will not be the same across recruitment methods. Having unequal selection probabilities means that variance estimates obtained from the aggregated sample will be larger than they would be for a simple random sample of the same size. This variance inflation is called design effect.

The following table shows 95% CI half-widths for estimates, given a sample size of 1000 for data from all methods combined. The table shows the level of precision to be expected not only for estimates for the entire population (column 2), but also for subpopulations that comprise 50%, 25%, 15% and 10% of the total population (column 3, 4, 5, and 6 respectively).

	CI half-width	CI half-width	CI half-width	CI half-width	CI half-width
# interviews	total population	subpopn = 50%	subpopn = 25%	subpopn = 15%	subpopn = 10%
1000	3.10%	4.38%	6.20%	8.00%	9.80%

It was decided that the minimum sample size that would be necessary for a project area to obtain total population estimates with an acceptable level of precision was 250.

The University of California, San Diego (UCSD) who will be implementing the information collection estimates that a convenience sample of 1000 respondents, (with sample sizes of 250 in each of the 4 groups), and an average HCV seroprevalence assumed to be between 0.15 and 0.40 based on existing estimates, a 0.05 significance level Chi-square test will have 80% power to detect a difference in HCV seroprevalence characterized by a variance of proportions between 0.001 and 0.003. Under the assumptions mentioned above, an effect size as small as 0.01 will be detectable. In addition, based on prior research the expected prevalence of high-risk injection practices is assumed to be between 0.30 and 0.75. Given the same assumptions as above this study will have 80% power to detect a difference in risk behavior prevalence across groups of at least 0.01.