Identifying risks of SARS-CoV-2 outbreaks in work settings and the implications for control measures

(i) Study design

This is a 5-year study comprising of a randomized controlled trial (RCT), a longitudinal quantitative study, a longitudinal qualitative study and a longitudinal workplace hygiene study in 3 selected non-healthcare work settings (i.e., non-office, mobile and office). The RCT will be implemented at the earliest stage of the project and completed in the first 2 years to generate short-term impact of research and inform policy. The 3 parallel longitudinal studies will be commenced in the 1.5th year and completed in the timeline of 4.5th year, and thus they would provide both the short-term and long-term impact of the research. The layout of overall study design and workflow chart is shown in **Figure 1**.

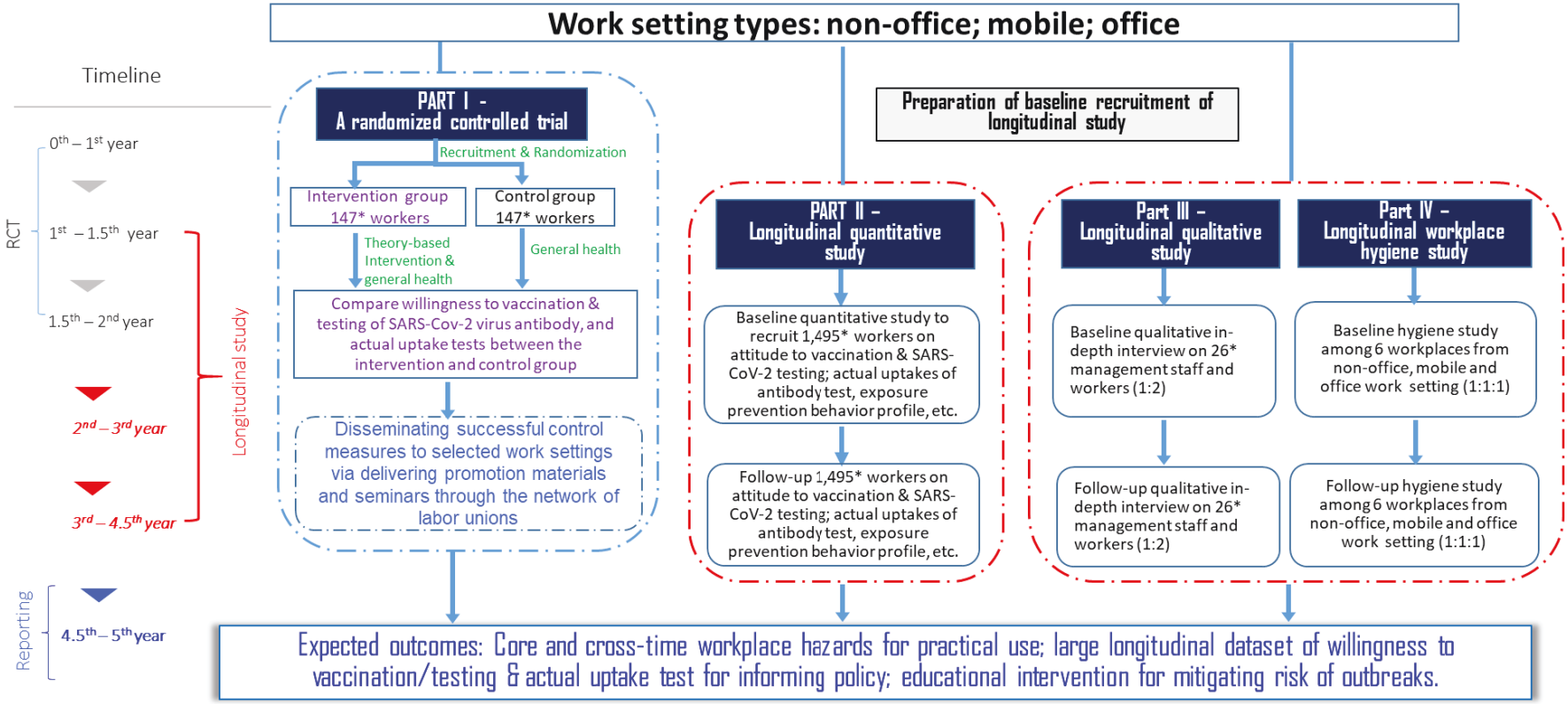
The choice of longitudinally repeated measurement using a mixed method of both quantitative and qualitative methods is made for the purpose of exploration of the possible new phenomenon of awareness and uptake of vaccination of virus tests over time among Hong Kong workers. Results from the longitudinally repeated workplace hygiene studies (e.g., airflow rate/direction, change volume of fresh air, etc.) would provide timely evidence on informing and enhancing the series of repeated quantitative surveys among workers over time.

(ii) Subjects to be included

Study subjects: In the Part I randomized controlled trial (RCT), 294 eligible workers from 3 non-healthcare work settings will be recruited, and randomized into intervention group (147 subjects) and control group (147 subjects). To be eligible to the Part I RCT, all participants are required to be aged 18 or above, who can read Chinese and currently being employed in three non-healthcare work settings from non-office, mobile, and office work environment in Hong Kong. We attempt to follow-up all participants of the RCT for 9 months to observe the effectiveness of the intervention on improving the primary outcomes, i.e., attitude to vaccination and SARS-CoV-2 testing.

In Part II longitudinal quantitative study, we plan to recruit a total of 1,495 workers who are aged 18 or above and currently working in non-office, mobile, or office work setting in Hong Kong. All eligible study subjects in Part II longitudinal/ prospective cohort study will be recruited in the timeline of 1.5th -3.5th year of the project and followed up for 2 years to observe the changes of attitude to vaccination and virus testing as well as risk profiles of workers towards outbreaks over time.

Figure 1. Workflow chart of hazard identification of outbreaks and control measures in work settings



** After considering a lost-to-follow-up rate of about 40%*

In the Part III longitudinal qualitative study, we plan to recruit an overall 26 management staff and frontline workers (in a ratio of 1:2) with same inclusion/exclusion criteria as the Part I & II study, i.e., aged 18 or above and currently being employed in three non-healthcare work settings from non-office, mobile, and office work environment in Hong Kong.

All above planned number of participants to be enrolled in the baseline of the Part I, II and III study have already considered a potential loss-to-follow-up rate of about 40%.

Settings: The 3 work settings are categorized by types as below according to their job nature and working environment:

(1) Non-office work: Workers normally carry out their jobs with a range of environment in an indoor or outdoor working space where close contact with the general public is frequent, and thus non-office work settings are considered at a higher risk of COVID-19 than the office work settings. Workers in non-office settings mainly include construction, accommodation and food service (e.g., hotel, restaurant), art/entertainment and recreation, professional bus drivers, outdoor instructor, real estate, wholesale and retail trades, etc.
(2) Mobile work: Workers who frequently move within or in and out of Hong Kong for conducting business that involves closer and more frequent contact with the general public than the non-office workers, thus their risks to contracting COVID-19 are regarded to be the highest among 3 selected work settings. Workers in mobile work settings mainly include taxi drivers, food delivery workers, courier delivery workers, police officer, etc.
(3) Office work: Workers normally carry out professional duties and administrative work in an indoor working space, such as an office or a room. Although the details of the job nature depend on the type of business to be involved, office work usually include using computers, communicating with others by telephone or fax, keeping records and files, etc. In general, office work offers relatively stable working environment where close contact with the general public is less frequent, and thus is considered having a low risk of contracting COVID-19 in the workplace. Workers in office work setting mainly include clerical workers, administrative workers, computer technicians, information and communication workers, etc.

Sample size: We estimated sample size for the Part I – Randomized controlled trial according to two independent proportions power analysis. As there is no relevant data of willingness to vaccination on our target subjects to guide the sample size calculation regarding an educational intervention against COVID-19, we employed a conservative assumption that the intervention will make a 20% change for worker's attitude to vaccination/virus test, sample size for both groups/arms will be 124, 130, 124, 109 and 79 for the proportion of willingness to vaccination/virus test of 30%, 40%, 50%, 60%, and 70%, respectively, with a 90% G-power. Therefore, a minimal 79 pairs subjects are required to achieve the primary objective (RCT) of this proposal project; if further assuming a loss-to-follow-up rate of about 40%, then an overall 222 participants with 111 subjects in the intervention group and 111 subjects in the control group are required. However, if given the most conservative sample size estimation with 40% loss-to-

follow-up rate, a total of 364 subjects with 182 subjects in each arm of RCT (130*1.4) are required. Therefore, the overall sample size for RCT could reasonably range from 222 to 364 to satisfy the primary research objective of this proposal project. In the proposed RCT, we considered taking the mean of the "most-least conservative" sample sizes of 294 [(222+364)/2] from G-power as a reasonable sample size with 147 subjects in each arm, and this sample size (i.e., 294) has already taken into consideration a potential loss-to-follow-up rate of about 40%.

We estimated sample size for the Part II – Longitudinal/prospective cohort study (quantitative survey) according to the formula for cohort studies. As there is no relevant publication for a reference, a conservative estimation is used to calculate the sample size for Part II study. For the estimation of the maximum sample size of longitudinally quantitative survey for the Part II study, the presumed population proportion is set as 0.5, which means that half of the workers have positive attitude to vaccination or willingness of SARS-Cov-2 virus testing in the selected work settings. It is estimated that a minimum of 1,068 workers is required for the longitudinal/prospective cohort study to accept an absolute sample error of 3.0% at 95% confidence level. Currently, there is not enough guideline for choosing an appropriate absolute error, and an absolute error of 5% is generally recommended in many studies. So, an absolute error of 3.0% employed in the project is more conservative than many other studies for sample size estimation. Although the required sample size is getting larger with the increase of population size, it will not change much when the population size is larger than 20,000. According to the latest statistics of the Census and Statistics Department of Hong Kong, the employed persons during 12/2020 - 2/2021 in Hong Kong are about 3.6 million, and therefore, it is appropriate to adopt this method of sample size calculation for a population-based cohort study in Hong Kong working settings. Assuming a potential loss-to-follow-up rate of about 40%, 1,495 workers are suggested to be recruited in the baseline survey for the Part II study.

While there is no established requirement for sample size estimation for the Part III and IV study which only involve qualitative approach and workplace hygiene measurement, it usually desires a reasonable sample size with representative sample. We plan to recruit 26 (18*1.4) eligible subjects at the baseline from 3 defined work settings to participate in the Part III qualitative study and 6 representative workplaces for the Part IV study that are regarded as reasonable. We set the sample size according to number of participants/workplaces estimated to reach data saturation.

(iii)<u>Methods</u>

This project includes **FOUR parts** – Part I randomized control trial, Part II longitudinal quantitative study (i.e., prospective cohort study), Part III longitudinal qualitative study, and Part IV longitudinal workplace hygiene study.

(iii.1) Procedure of Part I study

Part I is a 9-month **randomized controlled trial** to be conducted with single blinding and concealment during Year 1-2 (as shown in **Figure 1**).

Study subjects of the RCT: Two hundred ninety four workers from non-office, mobile and office work settings will be invited to participate in the RCT. The aim of the RCT is to test the hypothesis that a 9-month intervention program improves primarily the attitude towards vaccination and COVID-19 testing, with impact on the improving the actual uptake of COVID-19 testing and risk profile toward outbreaks at workplace.

***Procedures of the RCT*:** All 294 participants will be randomized to intervention group and control group. Intervention group will receive theory-based educational intervention using the Theory of Planned Behaviours (TPB) PLUS general health information, while the control group will receive only general health information. As this RCT will investigate factors that can explain worker's intention to vaccination and virus testing, the theoretical framework using the theory for planned behavior (i.e., TPB) is a proper approach for improving workers' attitude toward SARS-CoV-2 and raise their intention to vaccination and virus testing. The intervention will be implemented at the baseline with measurements repeated at the 3rd month, 6th month and 9th month. The standardized mode of intervention includes face-to-face/online seminar (depends on the COVID-19 situation), message via mobile phone, promotion pamphlet, etc.

Primary outcomes of the RCT include attitude to vaccination and virus testing, and the secondary outcomes of the RCT are actual uptakes of virus antibody testing and changes of risk profile toward outbreaks in the workplace.

Key contents of intervention would include:

- TPB intervention: building positive attitudes towards COVID-19 related preventive behaviour (e.g., good compliance with infection control measures, encouraging uptake of testing and vaccination), subjective norms (tackling strategies for perceived social pressure from others or normative beliefs), and improving perceived behavioural control towards risks of outbreaks in workplace.
- Other necessary information: basic knowledge of SARS-CoV-2, chain of infection, health and social consequences of infection, general infection control measures, workplace engineering and administrative control measures.

(iii.2) Procedure of Part II study

Part II study includes longitudinal quantitative study (i.e., prospective cohort study) from the timeline of 1.5th – 4.5th year involving an overall 1,495 workers recruited at the baseline survey from non-office, mobile and office work settings. At the baseline survey, 1,495 workers from 3 studied work settings will be invited to respond to a standardized questionnaire on exposure,

prevention and attitude towards outbreaks, and willingness to be tested for COVID-19 and receiving vaccination. Results obtained from the baseline and follow-up surveys will be compared to understand the changes of attitudes, awareness, willingness to vaccination and virus test, and workplace risk profile of workers towards prevention and control of COVID-19.

Cohort enumeration at baseline and follow-up:

A two-stage sampling method will be employed to recruit 1,495 eligible cohort members at the baseline survey for the Part II longitudinal quantitative study (i.e., prospective cohort study) in the timeline of 1.5^{th}-2.5^{th} year. In stage one, we plan to invite local workers unions with non-office, mobile and office work settings through our networks and connections, such as the Federation of Hong Kong and Kowloon Labour Unions (FLU). There are more than 150 local worker unions under the network of FLU, covering a variety of types of worker unions including restaurants, transportation, construction, telephone and communication, etc. In stage two, we will then recruit about 1,495 workers from the worker unions who agree to participate in the Part II study of our project. However, the baseline recruitment of Part II study subjects will be stopped if the required sample size of workers is reached.

All eligible subjects recruited at the baseline will be invited to participate in the follow-up survey in the timeline of 3.5^{th}- 4.5^{th} year to compare the changes of attitude to vaccination and virus testing as well as risk profile toward infection control in the workplace through various means (e.g., telephone, email, worker unions). Any loss-to-follow-up will be recorded.

Participants who complete the whole questionnaire of the baseline or follow-up quantitative survey will receive 200HKD fast food restaurant / supermarket coupon, and if the participant completes both the baseline and follow-up quantitative questionnaire survey, she/he will receive a total of $400 fast food restaurant / supermarket coupon as a token of appreciation.

Questionnaire development:

A standardized questionnaire is designed to capture each participant's information on knowledge, attitude and awareness towards SARS-Cov-2, exposure prevention behaviour, and willingness to vaccination and virus testing, with key items on –

- General introduction
- Employment status, industry background and occupation, job nature and tasks, demographics
- Worker's exposure and prevention profile towards risks of outbreaks, including knowledge of engineering and administrative control measures (e.g., proper utility of personal protective equipment, social distancing), safety culture, types of occupational hazards/hazardous process
- Attitude and willingness to vaccination and SARS-CoV-2 testing, and barriers
- Previous work and related exposure behaviour and behaviour intention towards prevention of infectious diseases in the workplace

(iii.3) Procedure of Part III study

Part III study includes longitudinal qualitative studies in the timeline of 1.5^{th} – 4.5^{th} year involving an overall 26 management and frontline workers recruited at the baseline survey from non-office, mobile and office work settings. Part III study aims at understanding the level of administrative controls in workplace, awareness of virus testing and vaccination and barriers of the selected workplaces over time. At the baseline of longitudinal qualitative study, a total of 26 management staff and frontline workers (in a ratio of 1:2, and after considering a potential loss-to-follow-up rate of about 40%) will be simultaneously invited to participate in in-depth interviews using qualitative approach to understand the measures of administrative controls of their workplaces using a standardized checklist questionnaire developed according to scientific literature and documentation review from international organizations, e.g., OSHA, NIOSH, ILO. The developed checklist questionnaire will be used as international benchmark to evaluate level of measures of control achieved by the respective work settings. In addition, their barriers and challenges in getting COVID-19 vaccination and testing will also be investigated. The value of qualitative inquiries is to suffix an in-depth understanding of the reasons of the views they hold, and the vaccine decision making that are more complex in real life. It will also be useful to capture factors attributable to vaccine rejection, hesitancy or acceptance. The insights generated from the qualitative study (e.g., detailed barriers and attitudes) will inform questionnaire design in the longitudinal quantitative study and also help to explain the results from other parts of this proposed project.

Recruitment of longitudinal qualitative study and follow-up: At the baseline of longitudinal qualitative study, we target a total quota of 26 (18*1.4) management staff and frontline workers (in ratio of 1:2) selected from the studied work settings using the same eligible criteria as the Part II quantitative surveys, assuming a potential loss-to-follow-up rate of about 40%. In general, two workplaces from each of the selected work setting will be invited. The rationale of the choice of workplaces is based on their relevance to selected settings, *for example*:

- Group (1) Non-office: waiters/waitresses from catering companies, construction workers from construction companies
- Group (2) Mobile: taxi drivers, delivery men, social care workers who pay visit to individuals and families to provide social care, and international transport workers, such as air crew members, seafarers, and cross-border drivers)
- Group (3) Office: office assistants, clerks, and officers

Subjects in Group (1), (2) and (3) will be recruited through Workers' Union that have access to members who are our targeted work settings and occupations. Recruitment will be completed when data saturation is reached.

All eligible subjects recruited at the baseline (1.5^{th}-2.5^{th}) of longitudinal qualitative study will be invited to participate in the follow-up survey in the timeline of 3.5^{th}- 4.5^{th} year, in parallel

with the Part II longitudinal quantitative study and Part IV longitudinal workplace hygiene study. Any loss-to-follow-up will be recorded.

Interview guide and data collection for longitudinal qualitative study: In addition to a short questionnaire enquiring the personal profile of participants, a semi-structured 60-min interview guide asking open-ended questions will be developed based on literature reviews and expert advice from our multidisciplinary research team.

A trained Research Assistant with good knowledge of the subject area and qualitative interview skills will conduct the interview with written consent obtained in prior. Each will last around 45-60 minutes, be audio-taped and held at the meeting room of our research centre or Workers' Union, with privacy maintained. Each participant will receive HK$200 fast food restaurant / supermarket coupon; and if he/she complete either the baseline or follow-up qualitative interview, and if the participant completes both the baseline and follow-up qualitative interview, then she/he will receive a total of $400 fast food restaurant / supermarket coupon as a token of appreciation.

(iii.4) Procedure of Part IV study

Part IV includes a longitudinal workplace hygiene study in parallel with the **Part II and Part III** study during the timeline 1.5^{th} – 4.5^{th}, aiming at conducting repeated workplace hygiene study and assessment in selected work settings to systematically identify workplace hazards and/or hazardous process related to infection, and evaluating the existing control measures according to occupational health hazard evaluation.

The longitudinally repeated workplace hygiene study will focus on different indoor microenvironments of overall 18 workplaces from 3 selected work settings in Hong Kong industries over 5-year timeline, i.e., 6 workplaces from non-office, 6 workplaces from mobile and 6 workplaces from office work setting. Direct contact is one of the important transmission pathways for SARS-CoV-2, but how to use ventilation to improve aerosol/droplets transmission is our major task. Data collection and timeline of this longitudinal workplace hygiene study will follow the workflow chart of **Figure 1**. We will measure the geometry and thermo-fluid boundary conditions in indoor microenvironments. A 3D digital model will be built with several heated manikins to simulate different scenarios with different numbers of people/workers in indoor. The airflow, turbulence, and temperature distributions will be calculated using the RNG k-ε turbulence model. This model has the best overall performance among all Reynolds-averaged Navier-Stokes (RANS) models for enclosed environments. The transient exhaled pathogen transport will be calculated using the Lagrangian tracking method. The Lagrangian method calculates the trajectories of individual pathogen-containing particles on the basis of Newton's law. The discrete random walk (DRW) model will be used to calculate the turbulence dispersion.

With the calculated exhaled pathogen-containing particle (aerosol/droplets) distribution, we can predict the "hotspots" (aerosol/droplets) with relatively high pathogen concentrations and understand how the exhaled pathogen-containing particles (aerosol/droplets) transport from the person to person. The information about these hotspots will be provided to the property management team for control strategies (e.g. ventilation control or disinfection "hotspots"). In order to reduce the person-to-person transmission in confined area, this project will propose several partitioning strategies for blocking aerosol/droplets transmission routes. The proposed partitioning strategies will also be assessed using the CFD model. The calculated results will reveal whether the intervention strategies are effective or not.

Findings from the longitudinal hygiene study will provide objective evidence to validate the self-report of workers from same work settings and inform management for engineering control and workstation modification.

(iii.5) SARS-CoV-2 antibody rapid test

All participants of the RCT who do not finish COVID-19 vaccination will be invited to take the SARS-CoV-2 antibody rapid test four times points during the study to observe their attitudes toward antibody tests and their actual updates of the testing and compare the differences between the intervention and control group, i.e., at baseline, 3rd month, 6th month and 9th month of the RCT. We are also interested in inviting and welcoming those already with complete vaccination to participate in the SARS-CoV-2 antibody rapid test to understand their attitudes towards antibody testing and actual uptakes, and same primary outcomes between the intervention and control arms will be compared. The self-sampling test kit will detect the IgG/IgM antibody of SARS-CoV-2 from whole blood with above 90% sensitivity and specificity, which is recommended by US FDA.

(iv) Data processing & analysis

For quantitative results, descriptive analysis and Chi-square will be used for baseline data to analyse the difference in exposure and prevention, willingness to vaccination/testing and actual uptake of tests between comparison groups (e.g., work settings). Paired t-test and covariance analysis will be performed to compare the longitudinal changes of scores of each exposure prevention behaviour factors, attitude and willingness to vaccination and virus testing over time. Structural equation modelling and multivariate regression logistic modelling will be used to analyze the structural relationship between measured variables and latent constructs, as well as examine the association of exposure profile with willingness to vaccination/testing or uptake testing. Effectiveness of intervention will be examined by multivariable linear (for continuous nature of outcome) or Cox proportional hazard models (for binary outcome). Loss-to-follow-up will be reported and intention-to-treat analysis will be used for addressing the loss-to-follow-

up issue of the RCT. All statistical analyses for longitudinal quantitative and RCT data will be conducted by SPSS Version 26 and/or SAS 9.4 (SAS Institute Inc., North Carolina). P-value of less than 0.05 is considered statistically significant.

For qualitative analysis, the tape-recorded individual interviews will be transcribed verbatim and thematically analysed using Grounded Theory approach. Data will be horizontally compared between participants, and longitudinally analysed, tracking and explaining attitudinal and behavioral changes of individuals across time. The qualitative data will be delineated to a typology of reasons for (1) accepting, delaying or refusal of COVID-19 vaccine, and (2) factors contributing to uptake of COVID-19 testing in the workplace, generated through thematic analysis.

(v) Ethic issue

The proposed study will be compliance with the Declaration of Helsinki.

All participants will provide written informed consent. The consent form describes the study objectives, requirements for participation, potential risks and benefits for participants, safeguards in place to protect participant confidentiality, the study policy that no results antibody tests would be revealed to any third party (such as insurance company or employer), that all data (whether questionnaire data or biological data) will be analyzed and reported only in aggregate form, the voluntary nature of participation and the freedom to withdraw from the study at any time, and mechanisms for contacting designated individuals from the study institutions to ask questions and obtain further information about their rights as study participants.

There are no known medical risks associated with completing a questionnaire at entry into this study, and the risk associated with antibody test will be minimal. Study subjects or their families may face c of confidentiality regarding their questionnaire or antibody tests. However, due to the maintenance of strict confidentiality measures and the policy of this study team that research data are not disclosed, any potential psychological and/or social harm that could be associated with the release of private information is minimized. In the planned database, all data will be identified with a study number, and identifying information is maintained in a separate protected database. The analytic datasets and biologic specimens will not include the name of the subject (or other personal identifying information), and all analyses and reports will be based on aggregate data, so that study subjects cannot be identified.