User Guidance

a. What is an investigator sponsored study?

i. An investigator sponsored study is a research effort where the sponsor of the work is an investigator, healthcare institution, or some form of medical network external to GSK and is seeking support from GSK to conduct the work.

b. What types of support can be provided by GSK?

i. GSK support of approved proposals can be in the form of funding and/or study materials (including GSK products, adjuvant for vaccines, placebo, or other medicinal products necessary for the research)

ii. In exceptional circumstances where the study requires a specialized capability to perform a specific activity (e.g. assays in the case of vaccines or biomarker research) that the sponsor does not have and cannot feasibly retain an appropriate vendor; GSK may perform the specific activity as part of GSK's support. Any GSK funding for the study will reflect the fact that GSK is providing this support.

c. What are GSKs current areas of interest?

i. Allergy

ii. Bone

iii. CV

iv. Consumer Health Care

v. Dermatology

vi. Gastrointestinal

vii. Immunology

viii. Infectious Disease

ix. Metabolic

x. Neuroscience

xi. Oncology

xii. Rare Diseases

xiii. Respiratory (updated 20th March 2017)

Asthma

- Intra-class comparisons of the effect of ICS/LABAs e.g. stable vs. flexible dosing on patient-related outcomes; night time awakenings, health care utilization, QoL, including health economic/cost effectiveness analyses based on the above across treatments
- Studies aiming to characterize asthma patient archetypes and associated burden, priorities and implications for treatment

- Studies to evaluate approaches to prevent or attenuate the development of (severe) asthma
- Studies to uncover markers of disease progression in severe asthma
- Studies assessing sleep disturbances and/or night-time awakenings in asthmatics
- Studies assessing sensitivity to allergens and environmental triggers
- Innovative studies in smaller scale, using registries or databases to track patients' journey through the health system to look at differences between ICS/LABAs and other treatment regimens
- Inhaler comparisons (ease-of-use, patient preference, critical errors) that have not yet been undertaken
- Correct inhaler use/errors in patients with disabilities
- Impact of the microbiome on asthma exacerbations
- Studies to characterize the inflammatory profile / phenotype of asthma exacerbations.
- Studies to clarify the positioning of inhaled triple therapy (ICS/LABA/LAMA) in asthma
- Further elucidate the positioning of ICS/LABA vs. triple vs. biological in the asthma treatment pathway
- Studies linking improved adherence with improved outcomes in asthma patients e.g.
    - Interventions with Apps and other tools
    - Identifying subsets of non-adherent patients and tailor interventions
    - Educational interventions including shared decision-making between physician and patient
- Genetic studies to identify subgroups that respond better/don't respond to ICS/LABA
- Biomarkers to better characterize asthma pheno- and endotypes of (severe) asthma.
- Biomarkers to monitor and assess the therapeutic effect of targeted asthma treatment
- Pheno- and genotypic sub-characterization of patients with severe eosinophilic asthma and treatment responses

Paediatric asthma

- Childhood origins of adult asthma
- Correct inhaler use/errors in children and teenagers with asthma
- Studies assessing sleep disturbances and/or night-time awakenings in children with asthma
- Impact of the microbiome on asthma exacerbations
- Studies aiming to characterize asthma patient archetypes and associated burden, priorities and implications for treatment
- Studies linking improved adherence with improved outcomes in asthma patients e.g.
    - Interventions with Apps and other tools
    - Identifying subsets of non-adherent patients and tailor interventions

    - Educational interventions including shared decision-making between physician and patient
- Innovative studies in smaller scale, using registries or databases to track patients' journey through the health system to look at differences between ICS/LABAs and other treatment regimens
- Studies assessing sensitivity to allergens and environmental triggers

COPD

- Translating lung function improvement to patient centric outcomes e.g. dyspnea
- Medium/long-term benefits of early use of dual vs. mono-bronchodilation
- Effects of pharmacotherapy for patients with COPD on physical activity in the setting of a rehabilitation/motivational scheme
- Understanding composite measures of COPD stability (Clinically Important Deterioration) and linkage of short term measures to longer term outcomes
- Adherence and Dosing: Impact of inhaler characteristics, dosing frequency, ease of use, etc.
- Epidemiological studies of hyperinflation by GOLD stage in COPD
- COPD App for COPD monitoring
- Determine the most appropriate patient for ICS/LABA vs. LAMA/LABA vs. Triple in early COPD
- Cardiac benefits of improved hyperinflation/dual bronchodilation
- Benefits of dual bronchodilation on other co-morbidities
- Effects of pharmacotherapy including dual bronchodilation on sleep quality and morning symptoms
- Cost-effectiveness and health economic analyses for and across treatments
- Improving understanding of exacerbation phenotypes and their differential responses to treatment
- Understanding utility of blood eosinophil count as a potential biomarker of responsiveness to inhaled steroids and mepolizumab
- Determination of the mechanistic link between blood eosinophil count and COPD exacerbations
- Improved understanding of rapid disease progressors, including predictors and surrogate markers
- COPD understanding in Japanese patients
- Rate of decline in FEV and factors that predict more accelerated decline
- Childhood origins of COPD

Asthma, COPD and other Respiratory Diseases

- Studies assessing novel endpoints across the disease spectrum in paediatric and adult patients with respiratory disease, including asthma and COPD
- Characterization of different inflammatory pathways across the respiratory disease spectrum, including asthma and COPD.
- Characterization of eosinophil function and activation status in difference body compartment (blood, tissue, sputum) of the patient with respiratory disease, including asthma and COPD
- Studies to characterize airway remodeling and potential surrogate markers to evaluate the impact of treatment in asthma and COPD patients
- Areas where the eosinophil plays a critical role in the pathophysiology of the disease
- Use of mepolizumab in very early asthma disease to reduce/prevent disease progression
- Understanding similarities and differences of anti-IL5 and anti-IL5 receptor approaches
- Combination use of different mode of action monoclonal antibodies in specific asthma subtypes
- Smoking in respiratory disease and association with steroid resistance

xiv. Thrombosis

xv. Urology

xvi. Vaccines (updated 20th March 2017)

Across Diseases & Technologies, General Vaccine Science

- Studies on societal and economic barriers for providers and population to vaccine uptake (in particular for adolescents, adults and elderly)
- Innovative solutions for educational activities aiming to increase vaccine awareness and acceptance in adolescents, adults and elderly
- Studies on the aging parameters of the immune system and how they impact the immune response to vaccines of elderly vs young people
- Health Technology Assessment studies assessing the role and value of vaccine solutions beyond the simple cost/benefit assessment of vaccines
- Studies measuring the impact of communication interventions on vaccination delivered in a digital format
- Studies on understanding the immune responses during pregnancy and how that relates to vaccination
- Health Economic and Epidemiological studies on methodology evaluations across multiple vaccines and age ranges

Study Areas of no interest:

- *For Health Economic and Epidemiological studies referring to specific vaccines. , e.g. flu coverage in elderly, Tdap coverage in adults, etc. please refer to product and diseases specific sections*
- *Studies or programmes to develop generic digital delivery platforms or applications*

Adjuvant System & Immunostimulant

- Studies to increase knowledge of Adjuvant Systems and other immunostimulants mode of action

Study Areas of no interest:

- First in Human study proposals aiming to assess a new antigen formulated with a GSK's Adjuvant Systems

Diphtheria, Tetanus, Pertussis, *Haemophilus influenzae* type b (HiB), Poliomyelitis

- Impact/effectiveness studies in relation with maternal immunisation
- Prevalence/burden of disease of Pertussis in elderly
- Impact/effectiveness studies of Tdap (Diphtheria, Tetanus, Pertussis) vaccines in Elderly

Hepatitis A

- Long term impact and immunogenicity of Hepatitis A vaccine
- Impact of Hepatitis A universal mass vaccinations on burden of disease
- Hepatitis A virus seroprevalence data and model epidemiological dynamics to predict endemicity shift

Hepatitis B

Studies in populations at increased risk:

- Impact of Hepatitis B vaccination on type 2 diabetes disease outcomes
- Incidence of Hepatitis B infection in type 2 diabetes patients outside of the US
- Observational studies to assess vaccine coverage and awareness of risk of Hepatitis B infection among Chronic Kidney Disease patients and their Health Care providers

Herpes Zoster

- Burden of shingles, Postherpetic Neuralgia (PHN) and other Herpes Zoster (HZ) complications in overall elderly or immunocompromised populations (HIV infected patients, medically immunosuppressed patients, etc.) .

- Observational studies to assess awareness of the risk of shingles, PHN and other HZ complications among elderly patients and Health Care Providers.
- Observational & database analysis studies to assess the local incidence, impact on Quality of Life (QoL) and cost of herpes zoster complications in elderly or immunocompromised population.
- Prospective and longitudinal health outcomes studies on QoL measures, role of caregivers, interference on daily activities, health care costs, etc.
- Observational and database studies assessing comorbidities in patients following the diagnosis of herpes zoster.
- Vaccines immunogenicity and safety comparative clinical studies in elderly population.

Human Papillomavirus (HPV)

- Real life effectiveness/impact of HPV vaccines against vaccine and non-vaccine types and duration of cross protection
- Real life effectiveness of Cervarix on non-cervical cancers and pre-cancerous lesions/infections
- Implementation studies, e.g. generate data on resource utilization
- Alternative schedules for HPV vaccines (eg. mixed schedule, 1-dose)
- Impact of adjuvant in HPV vaccines on humoral and cellular immune responses.
- Immunogenicity, efficacy, safety in specific populations (immunocompromised, males etc.)

Influenza

- Evaluation of moderate to severe influenza illness and endpoint in children as of 6 month of age, and in elderly population
- Influenza B Epidemiology & burden in children and at-risk groups (e.g.: Respiratory / Cardiac Metabolic…)
- Flu vaccine (QIV) effectiveness and herd effect evaluation in children 6 month of age onward studies
- Flu vaccination coverage and uptake in children (as of 6months in Europe and international and in at-risk groups (e.g.: Respiratory / Cardiac/ Metabolic) and elderly populations

Study Areas of <u>no</u> interest:

- *Alternate vaccination routes*
- *head-to-head flu vaccine (QIV and QIV-LAIV) efficacy studies*

Malaria

- Safety and effectiveness of RTS,S/AS01 in real life settings, including different immunization schedules and co-administration regimen

- Country specific Health Economics studies
- Assessment of safety and efficacy/effectiveness of RTS,S/AS01 in older children (beyond 17 months of age), adolescents and adults in regions where this would be justified by the *P. falciparum* disease burden.
- Assessment of safety and efficacy/effectiveness of RTS,S/AS01 outside sub-Saharan Africa where this would be justified by the *P. falciparum* disease burden.
- Perceptions of communities on malaria and malaria intervention programs, and assessment of the impact of RTS,S/AS01 implementation on these perceptions
- Projects to strengthen pharmacovigilance in sub-Saharan Africa

Study Areas of no interest:

- *Country-specific randomized controlled efficacy trials or safety studies*
- *Prospective study with RTS,S/AS01 without other recommended malaria interventions*

Measles, Mumps, Rubella, Varicella (chicken pox)

- Varicella epidemiology
- Varicella burden of disease
- Varicella prevention

Neisseria Meningitidis, Meningococcal Disease

- Innovative approaches to cost-effectiveness and health economic analyses
- Impact/Effectiveness studies for Meningococcal vaccine
- Impact on meningococcal carriage

Pneumoccocal Disease, Streptococcus pneumoniae

- Comparison of impact between Synflorix and PCV13
- Impact of Synflorix on carriage, replacement disease and herd protection (all ages)
- Mechanism of action of Synflorix. Can include NTHi transmission and disease in children, carriage studies or modeling, helping understand impact on herd protection and replacement disease
- Impact of Synflorix on pneumonia, otitis media or antibiotic prescription
- Studies in at risk populations <18 years of age

Study Areas of no interest:

- *Burden of disease studies, except for selected, well designed studies in developing countries*
- *Immunogenicity of mixed schedules and vaccine interchangeability*
- *Studies in older age groups (>5 years of age)*

Rabies

- Studies that evaluate rabies burden of disease and access to treatment in endemic countries
- Studies evaluating the impact of educational interventions about rabies on Health Care Professionals and general public behavior
- Novel vaccination schedules including changes to number of doses, mode of administration or timing
- Co-administration studies
- Studies to examine long term impact on disease and/or immunogenicity

Rotavirus

- Impact and effectiveness of rotavirus vaccination in different settings (e.g. long term effectiveness, compliance, herd effect, early protection)

Travel Vaccines

- Observational studies, including Knowledge Attitude and Practices (KAP) surveys, to assess acceptance of travel vaccination, vaccine coverage and disease awareness (Hep A/B, Typhoid fever, Rabies and Tick Borne Encephalitis) amongst travelers and Health Care Professionals
- Hepatitis A and Hepatitis B seroprevalence in specific traveler populations (e.g Visiting Friends & Relatives (VFR); immigrants etc)

Tick Borne Encephalitis

- Understand changing epidemiology of Tick Borne Encephalitis (TBE)
- Long Term immunogenicity in children vaccinated with Encepur to assess the long term persistence and need for boosters
- Tick Borne Encephalitis (TBE) seroprotection levels after partial and full vaccination to assess the percentage of protected individuals and speed of protection.

Others

d. What is the role of the investigator-sponsor?

i. Design the protocol

ii. Develop and maintain the case report forms

iii. Initiate and monitor the study

iv. Understand and comply with any and all pertinent laws, regulations, and guidelines

v. Understand and comply with any and all requirements of institution(s) with which they are associated or in which research will occur

vi. Report safety data to regulatory authorities, the IRB/IEC, and GSK

e. What is the role of GSK?

i. Provide approved support as outlined in the legal agreement in a timely manner

ii. Provide any scientific/medical feedback to the investigator-sponsor at any point in time regarding the proposal, the protocol, or any aspect of study conduct where GSK has a concern about the scientific integrity of the study or patient well-being

f. How does the overall process work?

i. Everything begins with you registering in the GSK ISS system; you will find a link to the registration page on the top of this web site

ii. Once you have registered, you will then be able to submit research proposals to GSK

iii. Throughout this step and all phases of the process, the system will automatically notify you about various documentation requirements, such as your curriculum vitae, budget requests (if applicable), and milestone updates

iv. Once you have submitted a proposal, it will be reviewed by GSK ISS personnel; if there are any questions, you will receive notification from GSK for clarification or additional information

v. After this initial review and any needed follow up is complete, the proposal will move into our global ISS proposal review process where GSK medical personnel for the given product/therapy area will review the proposal and make an initial decision; this decision could be approval, decline, or a request for additional information

vi. If the proposal is approved, the process then moves into protocol development and review; once you have completed a draft protocol, GSK medical personnel will review the protocol in a similar fashion as the initial proposal review with a primary focus on the scientific integrity of the study design and overall patient well being; the end result will be a similar set of decision outcomes as the initial proposal

vii. If you submit a full draft protocol with the initial proposal (not required), then both the proposal and protocol review would occur in one review step versus two

viii. Once the protocol is approved, we will then finalize contractual terms of the GSK support being provided and expectations for you as the study sponsor

ix. After the contract is finalized and all supporting documentation has been obtained, we will then be ready to start the conduct of the study

x. Throughout study conduct, the system will notify you automatically for study progress reports and supporting documentation for any support payments, product shipment requests, etc.

xi. Once study conduct is complete, we will then move into closing out the study and enter the publications phase of the study (final deliverables from the study as defined in the contract)

xii. Per the contractual terms, GSK will request review of any defined deliverables from the study (abstracts, publications, etc.)

xiii. At any point, you will be able to go into your account in the system and see the status of your proposal(s) and/or study(s)

g. What do I need to do to submit a proposal after I have registered at this site?

i. The first step is to click on the “Submit my proposal” button

ii. This will take you to the first of two parts to the proposal submission process

iii. Part one is the on-line form that basically captures categorical information about your proposal; this information is collected directly in the system to enable the proper internal routing and classification of the proposal

iv. Part two of the process captures the detail of the actual study you are proposing, including aspects of the overall study design, target population, statistical analysis plan, etc.

1. There are two options in completing part two of the process:

- 1) You can download and complete the provided template or
- 2) You can submit your own full protocol

2. Regardless of which option you choose, you will attach the completed template or protocol into the system and the file will become part of your proposal file that will be reviewed by GSK personnel

v. After attaching the template or protocol, you can also submit any other needed attachments at this point or later in the process; this could include an itemized budget for funding support requested, your curriculum vitae, or other study related documentation

vi. After you have submitted your full proposal, you will receive an automatic notification from the system via e-mail confirming success of your submission

vii. At any time, you can then click on "My proposals" and check the status of the proposal, add additional attachments to the system, or review correspondence that you have received from GSK

g. What does GSK expect of the investigator-sponsor?

i. Conduct a high quality ethical study

ii. Register the protocol on a public web site

iii. Complete required documentation in a timely manner

iv. Meet applicable deadlines as defined in the legal agreement

v. Report any safety issues and adverse events in a timely fashion as defined in the legal agreement

vi. Disclose any affiliation or financial conflicts of interest

vii. Publish study results

viii. Ask questions whenever needed

h. What should the sponsor of the study expect from GSK?

i. Professional interactions with GSK employees who put patient needs first in all that they do

ii. Timely responses to any inquiries or requests coming from the sponsor, including decisions on completed proposals

iii. An easy to use ISS system

iv. Compliance with data protection laws with respect to the personally identifiable information of the sponsors/investigators

i. How are support decisions made within GSK?

i. Once reviewed for completeness, all proposals go through a global review process that is made up of key medical personnel for the given product/therapy area

ii. Decisions are made based primarily on the overall scientific rationale of the proposal; additional considerations include alignment with GSK's areas of scientific interest, qualifications of the proposal sponsor, availability of internal funding resources, a fair market value assessment of any funding requested, and evaluation if similar research is already being conducted or has been conducted around the globe

j. Useful Links

i. FDA Forms

ii. US W-9 tax form

iii. US W-9 Tax form instructions

iv. Federation of State Medical Boards – Medical Licensure Information

v. OIG Exclusions Database

vi. FDA Debarment list

vii. FDA Disqualified/Totally Restricted List for Clinical Investigators

viii. PHS Administrative Action Bulletin Board

k. How do I contact GSK if I have questions about this system or the overall process?

i. Contact GSK

l. Data Privacy Policy

i. Privacy

m. Cookie policy

i. Cookie policy