The BPSU Study Application Handbook - Guide to BPSU Phase 1 study application process

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BPSU parent bodies:

Public Health England

RCPCH Royal College of Paediatrics and Child Health *Leading the way in Children's Health*

UCL GREAT ORMOND STREET INSTITUTE OF CHILD HEALTH

with support from:

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Overview

This document provides a step-by-step guide to getting approval for your study from the BPSU Scientific Committee (BPSU SC), the multi-centre research ethics committee (REC), the Confidentiality Advisory Group (CAG) of the Health Research Authority (HRA), the Scottish Public Benefit and Privacy Panel for Health (PBPP) and Social Care and your local NHS Trust Research and Development (R&D) Department.

This guide includes a list of key contacts, abbreviations and a flowchart of the application process. Additional helpful documents which may be found on the BPSU website www.rcpch.ac.uk/bpsu are also referenced in this document.

The Scientific Coordinator and Research Facilitator are the first points of contact for general enquiries, including operational and process matters, meeting dates and press releases. Initial enquiries about undertaking a BPSU study should be directed to the BPSU office.

For advice on the development of an application, such as details of surveillance methodology, ethics or questionnaires, contact should be made with the relevant medical adviser (for communicable or non-communicable diseases) or the scientific coordinator. Contact details for medical advisers can be provided by the BPSU office. Medical advisers correspond with applicants and convey the views of the committee regarding research proposals.

The Chair of the BPSU SC may be contacted directly; however this would not usually be necessary during the course of an application.

Key contacts

BPSU Chair

Dr Shamez Ladhani, Chair of the BPSU Scientific Committee
Email: shamez.ladhani@phe.gov.uk

BPSU Medical Advisers

Dr James Lopez Bernal, Medical Adviser
Email: james.lopezbernal@gmail.com

Dr Jonathan Fok, Medical Adviser (communicable disease)
Email: jonathan.fok@phe.gov.uk

Dr Lamiya Samad, Medical Advisor (non-communicable disease)
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BPSU Office

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Abbreviations

BPSU SC	British Paediatric Surveillance Unit Scientific Committee
CAG	Confidentiality Advisory Group
HRA	Health Research Authority
IG Toolkit	Information Governance Toolkit
(M)REC	(Multi-centre) Research Ethics Committee
NRES	National Research Ethics Service
MRC	Medical Research Council
Section 251	NHS Act 2006 provision for unconsented data use
R&D	Research and Development (Department within NHS Trusts)
IRAS	Integrated Research Application System
PAC	Privacy Advisory Committee (Northern Ireland)
PBPP	Public Benefit and Privacy Panel for Health and Social Care (Scotland)

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1: Introduction - Making an enquiry to the BPSU

Applications for inclusion of a study on the reporting cards are considered by the BPSU scientific committee (BSC), which meets every two months. As the success of the BPSU methodology relies entirely on the willingness of consultant paediatricians to complete and return the monthly Orange Card and study questionnaires – referred to as proformas, it is essential that BPSU studies are scientifically robust, adequately resourced and contribute to clinical and public health practice without putting too great a burden on reporting doctors. The application process has been developed to reflect these responsibilities.

There is a two-stage application procedure. **Phase 1** (P1) is an outline application to establish if the study meets the BPSU criteria. Applications should be submitted on the P1 application form. If the P1 is accepted by the BSC, a more detailed **Phase 2** (P2) application will be invited – see (www.rcpch.ac.uk/bpsu/resources).

Unfortunately some applications will be unsuccessful however good the research idea may be. Applications are most often turned down because the BSC considers that the study is not suited to BPSU surveillance methodology.

Important considerations before applying

- Make sure your study meets the BPSU eligibility criteria (see Eligibility Criteria, p.7). Please discuss your application with a medical adviser or the Scientific Coordinator beforehand if these are unclear.
- Study aims must be appropriate for national surveillance methodology, for example, to establish incidence of a rare disorder or to investigate variations in clinical management.
- You must consider patient and public involvement (PPI) in preparation for your Phase 1 application. Undertaking research without patients' knowledge or consent and in children with rare diseases raises ethical concerns. PPI enables researchers to invite contributions from patient groups and consult on the acceptability of their approach. We would expect that you have identified PPI groups, discussed the study with them and you should, if possible, provide a letter of support for your application.
- It can take several months to complete the application process as revisions to the methodology and questionnaires are often required. Our fast-track process; is usually reserved for those conditions considered public health emergencies.
- Applications should reach the BPSU office at least four weeks prior to the BSC meeting to allow the scientific coordinator / medical advisers to comment on the application and revisions to be made prior to committee papers being sent out. Deadlines for forthcoming meetings are available from the BPSU office or on the BPSU website (www.rcpch.ac.uk/bpsu/apply).
- The study surveillance period is usually 13 months though this can be extended if it is felt that additional case ascertainment is required to address the study objectives.
- There is a contribution charge for undertaking a study through the BPSU. The charge being **£15,000** in the first year (for 13 months of surveillance) and **£10,000** a year for subsequent years, these amounts will be invoiced for at the start of each year of surveillance. Any additional printing required will be charged to the applicant following communication. Please note the full

economic cost of a study is £25,000 and this should be sought when approaching commercial funders.

Enquiring about undertaking a BPSU study

An enquiry about undertaking a study through the BPSU can be made by telephone, e-mail or in person to the BPSU office.

Any interest in a particular topic is recorded by the BPSU alongside the enquirer's name and contact details. The earliest enquiry about a specific topic is given precedence. If after 12 months, an enquiry has not been followed up by a P1 application, then the BPSU office would contact you to discuss removing your name from the enquiry list and to give you an opportunity to make a formal application before any action is taken.

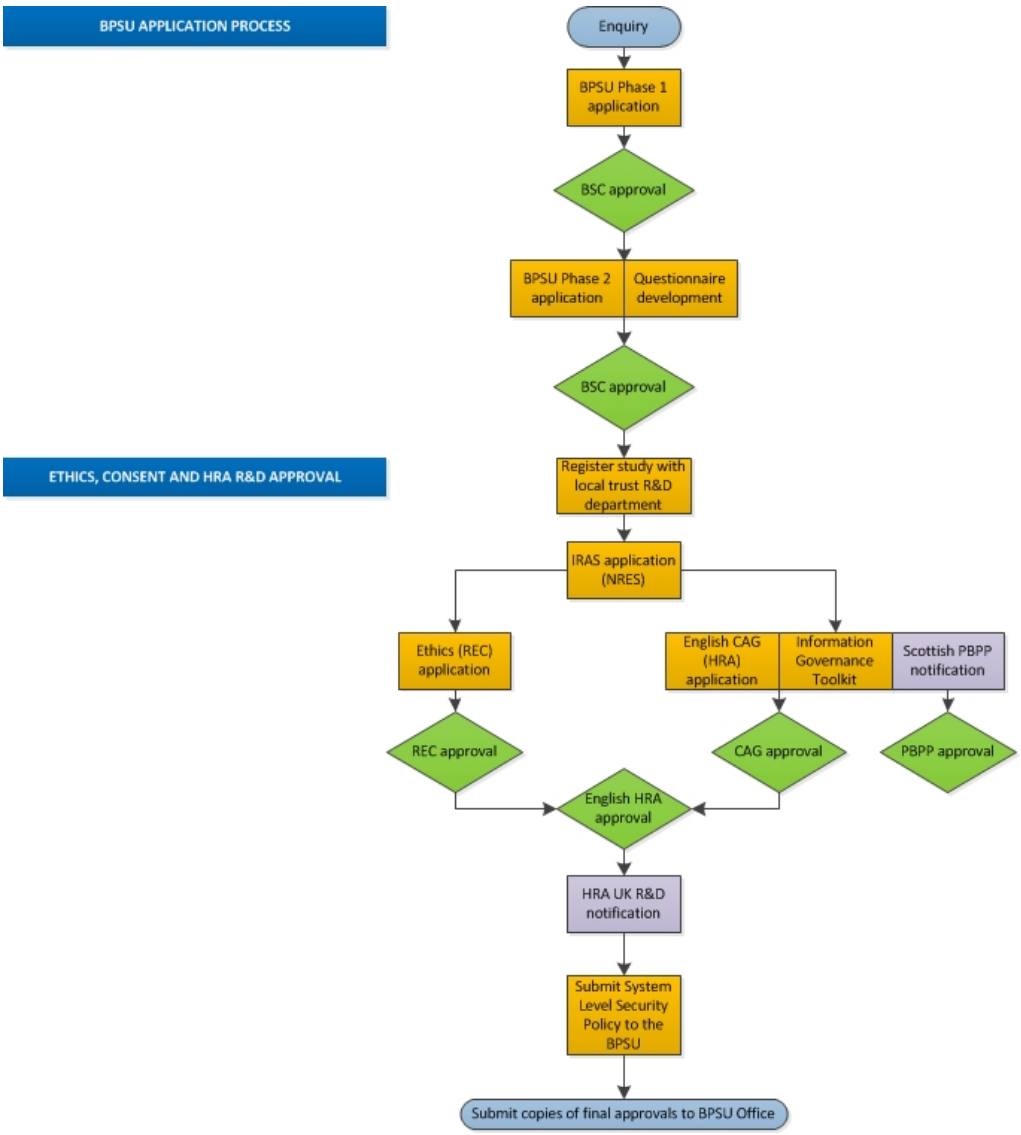

Figure 1: The full BPSU study application process

2: The BPSU Phase 1 Application

Eligibility Criteria

Studies considered eligible to be undertaken through the BPSU are those where:

- the condition is a relatively rare childhood disorder or a rare complication of a more common disease of such low incidence or prevalence as to require ascertainment of cases on a national scale in order to generate sufficient numbers for study. In practice, the condition studied should have an expected incidence in the UK of normally *no more than 360 cases per year*
- the majority of cases are expected to be seen by seen by paediatricians
- cases can be easily identified and defined using a clear case definition
- study data is easily accessible from the normal clinical notes
- approval to collect unconsented identifiable data is sought from the CAG of the HRA and PBPP.

Examples of studies which would **not** normally be eligible for study through the BPSU are those which:

- are interventional studies
- require controls
- can be undertaken through a regional study
- can be undertaken though a study involving specialist clinicians only
- require retrospective reporting,
- involve any additional clinical intervention for reported cases (other than the results of diagnostic tests on samples collected during routine clinical management).

Outcomes from a Phase 1 application

Following consideration of the P1 application you will be contacted by letter to inform you of the outcome. The following outcomes are possible:

1) The P1 accepted and a P2 sought with/without specific clarifications.
2) Further details and a revised P1 application may be sought before a decision is made.
3) You may be asked to attend and discuss your application with the BSC before a final decision is made.
4) The application may be rejected.

NB: **Acceptance of the P1 does not imply that the P2 will be approved.**

Once a P1 application has been accepted the BSC expect submission of a P2 application within 6 months. If a P2 application is not forthcoming then the BPSU Office will contact you to discuss removing your submission from the application process. The BPSU office will give you the opportunity to make a formal P2 application before any action is taken.

Completing the Phase 1 application form

Please read these details carefully before completing your P1 application. Failure to do so could lead to delay or even rejection of the application.

Prospective applicants are advised to submit their application at least twelve months before the proposed starting date.

Please check that you are using the current version of the P1 application form, which is available to download from the BPSU website.

Guidance on individual questions in the Phase 1 Application

1. Title of the study

Please provide the full title of the study. You may wish to provide an alternate brief title if the full title is long or complex, but please avoid using abbreviations or acronyms.

2. Investigators

Please list all investigators involved in the study, their contribution to this study, job title, affiliation, and. Please also indicate clearly the principal contact for correspondence on this application, giving a full contact address, e-mail address and telephone number. Please indicate also the individual who is the designated Principal Investigator – this person will be responsible for research governance. At least one of the study investigators should be a paediatrician receiving the Orange Card.

3. Describe the study

This should explain in LAY TERMS:

a) the condition to be studied,
b) the background to the study proposal, including current knowledge about incidence and prevalence,
c) the public health and scientific importance of the study,
d) the study methodology, and
e) the expected benefits of the study.

This explanation should be easily understood by a lay person as the BSC includes lay and medical reviewers.

4. Research questions/surveillance objectives

Give a clear statement of the specific research questions that will be investigated by this study. These usually fall into the categories of 1) estimating incidence/birth prevalence; 2) describing the clinical features at presentation; 3) describing management and outcomes.

It must be possible to address these questions:

a) without direct contact with patients,

b) without seeking investigations that would normally not have been undertaken by the paediatrician, and
c) without a separate comparison (control) group.

Consider how you will ask suitable questions in the proforma to gather information to answer your research objectives. Consider if you will have a sufficiently large sample size to address your objectives, for example regional variations in incidence could not usually be addressed by a BPSU study as the sample size would be too small. Please note also that the BPSU surveillance methodology is not suitable for identifying causal relationships, as the frequency of 'risk' factors identified amongst notified cases cannot be compared with the frequency of these factors in unaffected 'control' children.

5. Case definition

Give a clear case definition for the condition of interest. The ***surveillance case definition*** is a case definition which may be wider than the analytic case definition in order to ensure cases are not missed. For example, the surveillance case definition will often include suspected cases where confirmation is awaited. The ***analytic case definition*** describes very carefully those children who will be included in the study, i.e. will become your 'confirmed cases' for further analysis. Examples of case definitions used in previous studies are provided in Appendix 2: Case Definition – Development and Examples.

In many studies, the age range for cases will include ages from birth up to but not including 16 years. Please consider if children in the upper age range will be seen by paediatricians for this condition.

6. Expected numbers

Please supply an estimate of the number of cases expected each year i.e. yearly incidence rate, AND indicates the sources that you have used to estimate this. More than 360 cases per year (or 30 per month) would normally be considered too high for the BPSU due to the monthly volume of notifications and the fact that regional studies may be sufficient. Please note that there are often duplicate reports so that the number of cases reported might be considerably higher than the number of true cases included in the analysis.

Indicate the source of denominator data for calculating incidence. This is often a routine data source, such as the following:

- England and Wales - Office for National Statistics mid-year population estimates or birth statistics (www.statistics.gov.uk).
- Northern Ireland – Northern Ireland Statistics and Research Agency (www.nisra.gov.uk).
- Republic of Ireland – Central Statistics Office (www.cso.ie).
- Scotland – ISD Scotland (www.isdscotland.org).

7. Alternative sources of data

Are there other clinicians besides paediatricians who are likely to see cases? If so, it is essential to consider whether to involve these clinical specialists in case reporting as this improves ascertainment and reduces bias. Please list any additional sources of case reporting that you are currently considering. Further details of these will be required in a P2 application.

8. Proposed level and nature of public involvement

You will be expected to engage with public or patient organisations relevant to your study as early as possible. We would expect that you have identified PPI groups, discussed the study with them and you should. In seeking a PPI letter of support please inform them of the BPSU methodology – the BPSU office can advise you on the appropriate wording. Submission of a letter of support which includes an acknowledgement that the BPSU methodology involves data collection without consent is advisable.

It is important to read the "PPI guidance for researchers" document (available at www.rcpch.ac.uk/bpsu/patientsandpublic) in order to understand the essential nature of PPI in BPSU studies. The minimum requirements the BPSU expects are summarised as follows:-

- Early contact with patients/patient representatives/members of the public.
- Involvement in producing the lay summary for the BPSU application forms.
- Involvement in producing the public information leaflet.
- Commitment to keeping those involved informed as the study progresses.
- Involvement in producing a lay summary for the findings for dissemination.

Please state which organisations you would be likely to approach and how you plan to engage with them. You may also ask for advice from the BPSU office.

9. Proposed territorial coverage

The Orange Card is sent via an email link to paediatricians in England, Wales, Scotland, Northern Ireland, Channel Islands and Ireland. If you wish to exclude any of these countries, then you must state this and provide justification. This will only be permitted in exceptional circumstances, for example when another Paediatric Surveillance Unit is already conducting a similar study.

10. Funding, personnel and resource arrangements

Please confirm that you are arranging or applying for funds to undertake the study, even if these are not yet confirmed. Please name any bodies to which a grant application has been submitted or for whom one is being prepared. If funding is already in place, please state whether this is from a commercial source or whether you are personally in receipt of funds to undertake the research. If funding is from a commercial source, you may be expected to demonstrate, for example through a contract with the funders, that this will not influence the reporting of results. Contribution costs stand at **£15,000** for a 13 month study plus an additional **£8,500** for each further 12 months. Note the Full Economic Cost (FEC) for the BPSU for running a 13 month study is £25,000. **If your funding is via a commercial source the FEC figure should be stated in any application.**

In planning the administration of your study you need to be aware that the bulk of these costs are often consumables, such as postage and questionnaires and most importantly staff time. You will need to make sure you have enough administrative support as administrative burden is often a lot greater than first thought. The burden can be reduced by collecting data electronically but this in itself may have cost implications. We estimate that it costs £50,000 to run a study processing around 350 cases (500 reports).

11. References

A short list of any references relevant to the application should be included. If possible, attach copies of any papers which are not likely to be electronically available to the medical advisers.

Additional documents

Covering letter	Please attach a signed covering letter from the main contact/principal investigator for the study.
Supporting letters	Please attach any letters of support that you consider relevant for the committee to consider, for example award letters from funding bodies or letters confirming support by collaborating partners.
Signature	An electronic version of the application can be submitted directly to the BPSU office at bpsu@rcpch.ac.uk at least 4 weeks prior to the BSC meeting.

Appendix 1: Abbreviations and useful web addresses

Abbreviation	Organisation	Web links
CAG	Confidentiality Advisory Group (of the HRA)	www.hra.nhs.uk/resources/confidentiality-advisory-group/
GROS	General Register Office for Scotland	http://www.nrscotland.gov.uk/
HES	Hospital Episode Statistics	www.hesonline.nhs.uk
HRA	Health Research Authority	www.hra.nhs.uk http://www.hra.nhs.uk/resources/hra-approval-nhs-organisation-guidance/
HRA APT	HRA Approval Programme Team	hra.approvalprogramme@nhs.net
IC	NHS Information Centre	www.hscic.gov.uk
IGT	NHS Information Governance Toolkit	www.igt.hscic.gov.uk
IRAS	Integrated Research Applications System	www.myresearchproject.org.uk
	NHS Research Ethics Scotland	nhsg.nrspcc@nhs.net
ISD	Information and Statistics Division (Scotland's ONS)	www.isdscotland.org
MRIS	Medical Research Information Service (NHS Information Centre)	https://www.england.nhs.uk/2013/07/consultation-hosp-data/
ONS	Office for National Statistics	www.ons.gov.uk
PBPP	Public Benefit and Privacy Panel for Health and Social Care (Scotland only)	www.informationgovernance.scot.nhs.uk
PAC	Privacy Advisory Council (Northern Ireland)	http://www.privacyadvisorycommittee.hscni.net/
SLSP	System Level Security Policy	www.rcpch.ac.uk/bpsu/resources
UKCRC	UK Clinical Research Collaboration	www.ukcrc.org/regulation-governance
Other useful web links		
	Research database forms (and other example forms from IRAS) and e-learning module	www.ukcrc.org/regulation-governance/integrated-research-application-system
	MRC Data and Tissue Toolkit	www.dt-toolkit.ac.uk/home.cfm
	MRC Personal Information for Medical Research Guidance	www.mrc.ac.uk/pdf-pimr.pdf

Appendix 2: Case Definition – Development and Examples

Developing a case definition

The case definition along with the research objectives are often the most important factor in the success or failure of a surveillance study and may be the main reason for the BSC to require revisions to the application. Failure to be able to apply a clear unambiguous case definition will result in the application being rejected. Please give careful thought to the case definition and if necessary seek advice from the BPSU office.

If you are developing a case definition, consider which symptoms, signs and tests you use to make the diagnosis. Symptoms and signs, such as fatigue or fever, which are common to many conditions are unlikely to be useful elements of a case definition on their own, however they may be clearly diagnostic of a disorder when found in association with other specific symptoms or signs.

The surveillance case definition defines clinically the cases that investigators are aiming to identify. It should state the age range, clinical symptoms and signs and results of investigations which would indicate a child is definitely or is likely to be a case. The surveillance case definition may be broader (less specific) than the analytic case definition applied using information from the questionnaires. For example, the surveillance case definition may include suspected but unconfirmed cases, whilst the analytic case definition for incidence estimates should include confirmed cases only. The reporting instructions are based on the surveillance case definition and state simply which cases should be notified to the study by clinicians.

Example reporting instructions & case definitions

Vitamin D Deficiency