Completing the Regulatory Documents

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When might you need to be involved in completing or submitting regulatory documents?

- You want to undertake a research project at your CF Centre
- Your CF Centre is going to be a site in a multi-centre clinical trial co-ordinated by someone else
- You want to be Chief Investigator on a multi-centre research project

How do people feel about regulatory documents?

Outline

- What are the common regulatory documents?
- Why are they important?
- Which regulatory documents are you likely to need?
- Tips for completing them successfully

Common Regulatory Documents

- Ethical Approval Forms

- Clinical Trial Approval Forms
  - EudraCT Registration Number
  - National / European Medicines Agency Clinical Trial Authorisation Approvals

- Institutional Approval Forms

The order that these forms are completed may vary depending on the study, the number of trial sites, and your base country

Why are these documents important?

- Ensure ICH-GCP standards
  - the rights, safety, and well being of trial subjects are paramount, and are more important than the interests of science or society

Josef Mengele
Auschwitz 1942-1945

The Tuskegee Syphilis Study
USA 1932-1972

The Willowbrook School Study
USA 1955-1970

Which Regulatory Documents ?

Study Type	Characteristics	Approvals required
Research	is designed and conducted to generate new knowledge and should follow the systems for approval of Clinical Research	Ethical Approval (EudraCT registration) (Clinical Trial Authorisation) Institutional Approval
Audit	is designed to answer the question "Does this service reach a predetermined standard?"	Institutional Approval
Service Evaluation	is designed to answer the question "what standard does this service achieve?"	Institutional Approval

Ethical Approval Forms

Ethical Approval Forms

Welcome to the Integrated Research Application System

IRAS Project Filter

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

Please enter a short title for this project (maximum 70 characters)
Clinical progress over time in children with PCD

1. Is your project research?

(•) Yes ( ) No

2. Select one category from the list below:

- ( ) Clinical trial of an investigational medicinal product
- ( ) Clinical investigation or other study of a medical device
- ( ) Combined trial of an investigational medicinal product and an investigational medical device
- ( ) Other clinical trial or clinical investigation
- (•) Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
- ( ) Study involving qualitative methods only
- ( ) Study limited to working with human tissue samples, other human biological samples and/or data *(specific project only)*
- ( ) Research tissue bank
- ( ) Research database

If your work does not fit any of these categories, select the option below:

- ( ) Other study

2. OVERVIEW OF THE RESEARCH

To provide all the information required by review bodies and research information systems, we ask a number of specific questions. This section invites you to give an overview using language comprehensible to lay reviewers and members of the public. Please read the guidance notes for advice on this section.

A6-1. Summary of the study. *Please provide a brief summary of the research (maximum 300 words) using language easily understood by lay reviewers and members of the public. This summary will be published on the website of the National Research Ethics Service following the ethical review.*

I aim to review a cohort of patients in the Yorkshire area with Primary Ciliary Dyskinesia (PCD) that were studied by Dr Louise Blackburn in 2002. The initial study in 2002 looked at areas such as the patient's growth, respiratory symptoms and signs, lung function tests, microbiological infection/colonisation, and evidence of nutritional deficiencies on blood testing. The aim is to look at the change over the last 8 years in the clinical parameters of these patients looking specifically at growth, lung function, exacerbations, and current treatment of these patients.

The aim of the study is to answer the following questions:
1. What is the clinical progress over time in the lung function of the individuals with PCD?
2. What is the change in growth over time in individuals with PCD?
3. What symptoms and functional status do individuals with PCD have?
4. Does the child's ethnic background influence clinical progress?
5. Does the age at diagnosis influence clinical progress?
6. Does the type of cilia abnormality influence clinical progress?
7. What is the quality of life of patients with PCD?

This study will be a case series looking at a population of patients initially studied by Dr Louise Blackburn in 2002. In that study the aim was to look at paediatric patients (<18yrs of age) who have a diagnosis of PCD in the Yorkshire region, it is possible that some of these patients are now no longer children and are adults and thus would be under the care of adult physicians.

There were a total of 28 children in Dr Louise Blackburn's initial study and I aim to recruit all if these patients.

A6-2. Summary of main issues. *Please summarise the main ethical and design issues arising from the study and say how you have addressed them.*

Consent:
- All participants will be approached individually and asked to participate. Participants will be informed that if they do not participate in the study they will not incur any penalties and that their responses would be treated with the strictest of confidence.
- With regard to informed consent, as some participants will be below the age of 18 their parents or guardians will be approached for consent. All participants or parents of participants will have to read and sign a consent form.

The problems that I may encounter include:
- Failure to gain consent.
- Unable to access participants for reasons such as participants may have moved out of region.
- Some of the participants are now adults and will have moved onto adult services and thus accessing their information may be more difficult. I have liased with the adult respiratory team that looks after patients with PCD and they are willing to help me as long as I have ethics approval.
- I will need to get some help managing the statistics and I hope to get some help via the university and from senior colleagues.

UK NRES: 29 pages

Lots of examples and help on IRAS website
https://www.myresearchproject.org.uk/Help/UsingIRAS.aspx

Tips to successful completion: Ethical Approval Documents

- Don’t be put off by the length
- Much can be cut and pasted from documents you already have
- Read the guidance and follow it
- Try and look at a previous example
- Use approved structure for subject information leaflets; consent forms etc

Ethics forms tips (2)

- Once you have filled in the 70-80% you can do yourself, ask your Institution for advice
- Then get it submitted! It will hardly ever sail through first time however long you spend on it
- Wait 4-8 weeks (UK IRAS 60 days), but ask the administrator for the date it will be reviewed
- If possible attend the meeting (might save you another 4-6 weeks)

Clinical Trial Registration and Authorisation Forms

EudraCT Registration

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

- EudraCT (European Union Drug Regulating Authorities Clinical Trials)
- Number required **earlY** for any clinical trial involving investigational medicinal product (including pharmacokinetic studies)
- Will need medically qualified chief investigator
- Apply on-line (https://eudract.ema.europa.eu/index.html)

Clinical Trial Authorisation

- Needed for each country where there will be study sites ~ 30 day assessment period
- In United Kingdom: 

- Application form on EudraCT website
- Simple studies may need “Notification” only (eg Some Phase 4 measuring drug levels/side effects of drugs in routine clinical use)
- Fees apply (Euros 330.00 – 5305.00)
- Phase 1-3 applications very complex and not for the faint hearted

Approval by your own Institution (also known as R&D Approval)

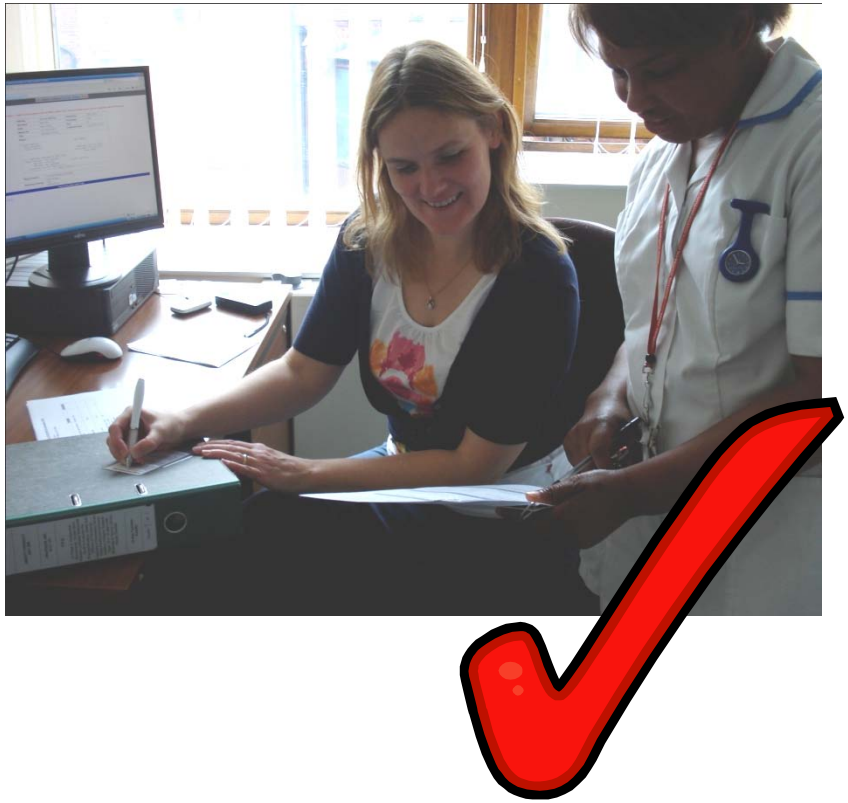
Approval by your own Institution

- Institution needs to clarify costs; income; and responsibility/liability

- In UK this is performed using a “Site-Specific Information Form (SSI)” generated from the Ethics Form

Tips to efficient Institutional Approval:

1. Get the signatures you need in person



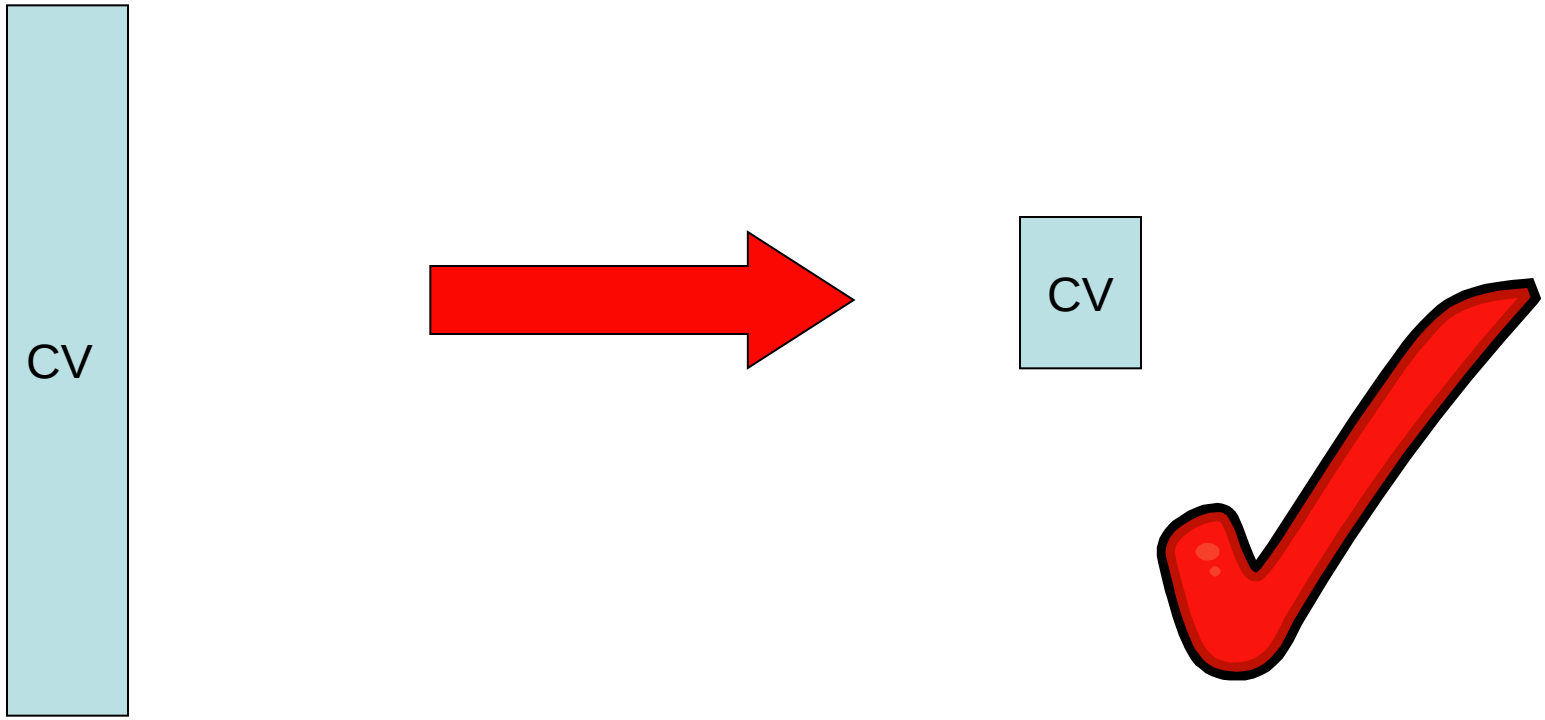
Tips to efficient Institutional Approval:

2. Use the Institution's checklist to ensure you have all the forms and documents you need

- "Site-Specific Information Form (SSI)"
- Brief 2 page CV of each investigator
- GCP certificate for each investigator
- Approval from each relevant department (eg x-ray; pharmacy; laboratories; management)

Tips to efficient Institutional Approval:

3. Make a short CV from an Investigator's long CV (don't wait for them to do it)



Tips to efficient Institutional Approval:

4. Go to the Approvals Department in person and check through with them that you have submitted all the relevant documents

Tips to efficient Institutional Approval:

5. Check how long approval will take (~30 days) and keep in touch till approval granted

After approval

- Wait till you have all the approvals in writing
- Follow the approved protocol
- Remember any paperwork may be audited (In UK about 1 in 3 studies undergo a full audit)
- Remember your responsibilities as an Investigator

Summary: Completing the Regulatory Documents

Summary

- Regulatory documents are important to protect study subjects and ensure worthwhile research
- Plan carefully what forms you will need
- Don’t be put off by the length of the forms
- Minimise delays by being pro-active
- If you are stuck, ask advice: Lots of support on the Web or from your own Institution
- It is not as hard as you think!

Parental Permission obtained

Thank you!