

# “GETTING INVOLVED IN RESEARCH”

A guide for individuals, families  
and the groups that support them.

Produced by The European Alliance  
of patient and parent organisations  
for Genetic Services and innovation in medicine (EAGS).



## Introduction

For many people affected by genetic disorders which are either not curable at the moment, or for which treatments may be limited in scope or effectiveness, progress in medical research into “their” condition holds out the best hope of an improvement in their circumstances. Many patient support groups have come into existence to promote this research and to raise the funds necessary to support it. One result of this commitment from those affected by genetic conditions has been a substantial increase in understanding of the basic biological processes underpinning the condition and, in some cases at least, significant progress in its management for affected individuals.

Participation in research is not an unmixed blessing. It offers hope that the threat of genetic disease that currently hangs over millions of families throughout the world will be lifted, but it also has costs associated with it that may, if not anticipated and planned for, create stresses and strains for the individuals who take part in the research and for the groups which provide support for them.

This short guide has been written following a seminar organised by the European Alliance of patient and parent organisations for Genetic Services and innovation in medicine (EAGS) in Geneva on 31st May 1999. It was attended by representatives from patient groups, academic clinicians and industry and is intended to provide a stimulus to get involved in research and a guide for those who would like to participate in various research projects for whatever reasons.

## Different types of research:

### Different ways of getting involved

The first question to be asked by any groups thinking about getting involved in research is “What do we mean by research?” Research comes in many formats, seeks to ask a wide variety of different types of question, and provides different opportunities for involvement.

“Basic” research (also known as “fundamental” and/or biological research) is the investigation of the mechanisms in the body which cause the disease and determine its progress. It tends to be professionally driven, with the work undertaken by scientists or clinicians. Historically patients have tended to be limited in their involvement in basic research to being the “subjects” of research projects – providing the raw material for the professionals to work on. Patient groups too have had a limited role, usually that of providing the funding and recruitment of participants.

This is changing as patients and patient groups become more actively involved. One important difference is that patients are increasingly involving themselves in the formulation of research questions with the scientists, so that their efforts are addressed to the aspects of the condition which cause most problems for those affected (and not simply at those where change is easiest to measure).

“Applied clinical” research (sometimes known as “Health Services” research) looks at the management of the condition in affected individuals and families. It can include psychological and social issues, the effectiveness of different treatment regimes and the organisation of service delivery by health and social services.

In basic and in applied research a number of models of patient or user involvement have emerged which go beyond the very basic level of being a research participant. These include:-

- a) **Consultation** – where professionals ask patients what they think and then go off and carry out research which may or may not reflect the views expressed.
- b) **Collaboration** – where patients are involved in the management of the research, sitting on project steering committees, playing a role in the design and implementation of projects and involving themselves in dissemination of the results.
- c) **Control** – where patients steer the project, involving professionals only by invitation where they have specific skills to offer.

Each of these models demands different responses from patients and from patient groups. Right from the start it is essential to be clear about what the proposed level of involvement will demand and to be explicit about the costs as well as the benefits involved for those who take part. Time, energy, responsibility and resources must be considered, including the “hidden” costs: there can be psychological as well as physical costs to the participants and also to their families, such as:-

- the beneficiaries of the research may be in the future, not those who do the work now. (But they may derive other, intangible benefits from the experience of participating)
- the fact that the research may reveal things about participants they were not expecting and would rather not have known. These may also have an impact on the wider family.

- services or treatments created as part of a research programme may be withdrawn when the project ends.

Given proper preparation patient involvement in research of all kinds must improve the focus and the effectiveness of the work undertaken. Without this it is likely to increase stress on all concerned, slowing rather than hastening progress toward effective treatments as outcomes may not be relevant to patients or those who stand to benefit.

Patient involvement can add to the efficacy of research uptake by ensuring that the potential barriers for those who hope to benefit from the research (be it a clinical output, a new drug or whatever) are understood. Issues such as prescribing or reimbursement rules, and regulatory hurdles need to be identified clearly and acknowledged alongside more obvious pitfalls, such as the fact that the research may simply fail to produce the expected results. These can be disseminated more effectively when patients are an integral part of the process. The involvement of patients can also help to keep everyone’s feet on the ground, avoiding expectations which cannot be met building up as a result of poor or inappropriate communications (in the popular press for example).

Patient involvement does not stop when the actual project comes to an end. The impact of the results can be substantially enhanced if they are involved in other ways. Some possibilities include:-

- a) Producing newsletters charting progress.
- b) Assisting collaboration between researchers (remember

research is a competitive activity and people may not always share results if they think there may be a career or financial advantage to keeping them secret for the time being – although respecting genuinely confidential information is essential).

- c) Raising the implementation issues arising from the research with generalist doctors, health economists and planners – creating the pressure to see research translated into service delivery.
- d) Disseminating outcomes to patients, professionals and the wider public – through conferences, publications and via electronic means.
- e) Managing the media, so the right “spin” is put on the outcomes.

### **Basic Research**

Patient involvement in basic research has proved essential to progress in many ways. It has been particularly important when rare disorders are to be investigated

because :-

- a) Doctors are often wrong in their assumptions about the “natural history” of un-researched diseases.
- b) Patients, and their support groups have often generated considerable knowledge themselves regarding their disease and possibilities for progress.
- c) Patients may be able to work out practical solutions to problems, based on personal experience which otherwise might be difficult to address by professionals.

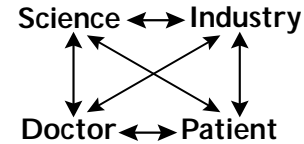
**“Getting Involved in Research”**

- d) Patients can put pressure on researchers to become involved in “their” condition (and offer incentives too!).
- e) Patient groups can collaborate with reputable researchers in obtaining data and so provide short cuts to data that might otherwise be hard to obtain.
- f) Patients can promote interdisciplinary collaboration and coordination, increasing the speed, quality and effectiveness of research in all its stages – from the initial description of the condition to the final marketing of effective products for treating the conditions.
- g) Patients can ensure that the research protocol is realistic and will be sensitive to the needs of other patients.
- h) Patients can help to interpret the results of data.
- i) Patients can help to produce relevant accessible written information about research for other potential participants.

The traditional model of research and development was a linear one :-

**Science → Industry → Doctor → Patient**

Today it is moving towards a model based on partnership, in which the contribution made by patients to the team effort needed to solve problems – especially those associated with rare diseases – is recognised :-



In this new model, patient groups are acting in a number of innovative roles:-

- i) as a pressure group on government and research funding councils to change funding priorities.
- ii) as a data bank for samples and information (including DNA, cells, tissues and information about the actual course of the disease in real life).
- iii) as significant sources of independent research funding.
- iv) as co-managers of research, advocacy groups or management committees
- v) as shareholders in research companies.
- vi) as participants in commercial ventures.
- vii) as watchdogs to ensure protection of participants in research.

Patients, and the groups which support them, are playing an increasingly active role in setting the basic research agenda. Through support groups, those who might have felt unable to influence research because they were isolated and affected by a “rare” disease are finding now this is not the case. Through the work of support groups, researchers and industry can feel the impact of those who are :-

- well diagnosed
- well organised
- well informed
- well connected
- enthusiastic
- committed

This can provide the driver for high quality basic research and also helps to ensure that its output moves from the laboratory into the next stages of the Research and Development process smoothly, efficiently and promptly.

### Research Registers

Registers of individuals and families affected by rare disorders have been a key tool in creating the “critical mass” necessary to stimulate research interest and make possible both fundamental biological research and the later undertaking of clinical trials.

Registers have taken a variety of forms and have been used for many different purposes. Before embarking on the creation of a register it is important to be absolutely clear about why one is needed, what it will contain, how it will be used, who will have access to it and how it is going to be maintained and kept up to date. Particularly important is the preservation of the confidentiality of those whose data is recorded on the register. People will not be happy to participate if they feel that information in the register might leak to those who might use it to their disadvantage - perhaps as a tool for

rationing health care, or for reducing their eligibility for insurance for example.

It is important to recognise that registers of patients with specific conditions have been set up for a range of different uses. If research is the primary purpose then much more detailed information may need to be held than would be the case if eligibility for services was to be the aim, for example.

Before embarking on the creation of a register, it is worth checking if one already exists elsewhere that the patient group can join with – or even “piggy-back” their own needs onto. This will avoid duplication, save energy and resources and in all probability help to ensure that the primary register is both more comprehensive and more up to date.

Being a patient on a register can create expectations about the benefits that may be accrued as a result. Individuals may expect access to information, priority in service provision, a degree of monitoring or other things that those operating the register had not anticipated. Unless the contract between the register holder and the patients and families registered is clear from the start, a breakdown of communication is almost inevitable. This undermines not only the effectiveness of the register to deliver against its stated goals, but also the productive relationship that is needed between patient support groups, their members, scientists and clinicians. Before giving their consent to join a register it is important that patients eligible are clear about all the pros and cons and have a realistic expectation of the likely costs and benefits.

## Clinical Trials

All patients, whether their condition is a common or a rare one, have a right to expect that the medicine they take will be safe, effective and reliable. In order to establish this a process of clinical trials has evolved over the last forty years. The process is tightly controlled by legislation and regulation and must be followed before a new drug is allowed to be put on the market and prescribed for general use by patients.

Much of the legislation is nationally biased. In addition there are a number of international measurers set up to ensure a consistent approach to establishing safety and effectiveness wherever the trial is undertaken. The International Conference on Harmonization (ICH), involving Europe, the USA and Japan has produced guidelines on Good Clinical Practice (GCP) considerations which must be met if clinical trials are to incorporate current best practice in their procedures. These GCP guidelines provide general standards, to ensure the protection of those taking part in trials from unnecessary risk or from exploitation. Other more specialised notes for guidance also give specific advice with respect to the particular design and conduct of trials for certain types of disease (e.g. cancer, heart disease) or population categories (e.g. children, the mentally ill) designed to protect those taking part in trials from unnecessary risk or from exploitation.

A clinical trial is a late step in the Research and Development process. It is established after a great deal of preliminary research in the laboratory and on animals. A detailed dossier has to be drawn

up prior to the trial which justifies the **need** for the trial and explains the **rationale** underpinning the proposed course of action. This information is scrutinised for its technical adequacy and also to ensure that it is ethically sound. If approval is given by the regulatory agencies in the country where it is proposed to hold the trial then it can proceed.

Clinical trials proceed by distinct stages which have to be completed satisfactorily before the next step can be taken:-

- Phase 1 is to look for the effect of the new substance (the drug) on the human body. This will normally involve a small number of healthy volunteers.
- Phase 2 looks at the question of the appropriate dose and the activity of the drug in people with the condition it is intended to treat. (This may include placebos where this is ethically justified). Phase 2 trials are usually undertaken with a few hundred patients participating. Phase 3 trials are usually carried out across many centres, often in different countries. This stage is to compare the new treatment with existing practice and it can involve several thousand patients.

Phases 1-3 may take 5-10 years. Once they are complete the drug is submitted to the regulatory agencies (e.g. the European agency for the Evaluation of Medical Products – EMEA) and if the authorities are satisfied then the new product is put on the market.

Phase 4 trials follow, monitoring the use of the product when administered according to its authorised therapeutic indications for patients, to increase knowledge of how the drug works in the

context of current medical practice, and to spot any previously undetected adverse consequences.

Central to the conduct of clinical trials is the fact that all patients are volunteers. They have the right to withdraw at any time and their access to other medical services must not be influenced by their participation, or nonparticipation in a clinical trial. Participants have the right to information about the trial, must not have their confidentiality compromised by their participation; and medical care during the trial must be provided.

Clinical trials always involve an element of uncertainty. If the outcome was known already, there would be no need for the trial.

These requirements and other issues to ensure trials are ethical and, as far as possible safe are laid down in the ICH guidelines. To give them the force of law and to standardise the proceedings for the conduct of clinical trials in Europe, the EU is currently bringing a new Directive into effect. This is not yet law. But when it is adopted, it is intended to ensure that the standards set throughout Europe are applied fairly and consistently and that adequate methods exist for inspection and verification of the procedures followed. It is hoped that a bureaucracy that will stifle research and slow drug development is not created. Ideally the approval of the protocol by the relevant Ethics Commission will remain the determining factor for allowing clinical trials to start.

One aspect of the traditional model for clinical trials will be immediately apparent to patient groups supporting families with rare genetic disorders – the numbers involved! A traditional clinical trial may involve several thousand patients – which may be more

than the total number of affected individuals in a country, or even in the whole of the EU. If the rules were to be applied rigidly this would inhibit or even prevent the development of products for the treatment of rare disorders, even if basic research produced promising results. Fortunately this paradox has been recognised and the dilemma of establishing efficacy whilst also demonstrating safety is being addressed through the Orphan Medicinal Products regulations.

The Orphan Medicinal Products Regulations give the European Agency for the Evaluation of Medical Products ( EMEA) the authority to advise on the conduct of clinical trials for products designed for use with rare disorders. This means that the nature and quality of evidence necessary to obtain permission for the new product to be put on the market can be established before the start of the clinical trial and the study designed in such a way that it can provide the necessary information in ways that reflect the needs of patients and the prevalence of the condition in the population.

Patient groups, scientists, clinicians and their industrial partners who are aware of the pending need to set up clinical trials for rare conditions should be in conversation with the relevant official of EMEA as soon as the need becomes apparent. This communication will ensure a smooth passage through the approval procedure and on to the market for the benefit of those affected.

## **Health Services Research**

Health services research is designed to ensure that scientific and clinical understanding of disease processes is applied by national health and social welfare systems in ways that really benefit patients to the maximum extent possible and which take account of the many and various factors integral to the experience of individuals and families living with chronic disease.

Patients should be involved in health services research for many reasons, including:-

- a) They can help to ensure that research identifies issues which are relevant to consumers and leads to developments in practice that would be feasible to introduce into their lives.
- b) They can access the views of people who are hard to reach, such as those from black and ethnic minority groups.
- c) They can help understand and interpret data by providing insights drawn from their own experience of illness and treatment.
- d) They can disseminate the results of research and work to ensure that changes in best practice are implemented.
- e) Patients are more likely to participate in research that they have been involved in planning and which addresses questions which they recognise as important.

Involving patients in health services research has been shown to be of benefit to professionals as well as patients and their families.

Among the principal gains experienced have been:-

- i) An increase in the wider perception of research as relevant and accessible to everyone involved in health care, not just the narrow community of academics and clinicians.
- ii) The introduction of the “reality check”.
- iii) A reduction in pomposity and jargon.

For patient groups, becoming empowered to participate in health services research as effective partners can be difficult and it often requires the group to develop mechanisms to support those of its membership who want to play an active role. Specific issues which need to be addressed if patient involvement is to be fully effective include:-

- 1) Training for patients and for professionals on working together.
- 2) Breaking down attitudinal barriers (on both sides)
- 3) Providing practical help to enable patients to participate in research planning and management – reimbursement of expenses, compensation for loss of earnings and access to child care or respite care are just three issues which may allow or inhibit patient participation.
- 4) Recognising expertise. Just as a clinician may want to use a statistician to help with some aspects of data analysis so patients will have particular areas where they are best equipped to make an expert contribution.

## Conclusion

Without the active involvement of patients in medical research at all stages from the preliminary categorisation of a disease and the framing of the first research question in the minds of academic scientists and clinicians through to the post-marketing surveillance of new drugs developed for use in the treatment of hitherto incurable genetic diseases medicine would still be in the dark ages.

"Getting involved" in medical research can be a daunting task for individuals and patient support groups supporting families with rare disorders about which not much is known. With preparation, foresight and planning the steps to involvement can be reduced in size, so that they can be seen to be manageable, logical and understandable by those who need and want to take them.

This short guide aims to identify some of the issues that patient groups have identified as important in helping them to take the plunge and get involved in research into "their" condition and the issues that affect the lives of the individuals and families they support. It is inevitably incomplete, it is probably partial and it raises more questions than it provides answers. In the context of a Europe with many different health care systems, and where patient groups have evolved in different ways and to different stages, this is inevitable. It is probably sensible too, in that any attempt to be prescriptive would fall foul of differing national, cultural and ethical traditions. Good practice must take account of these variations, embracing diversity without sacrificing quality.

The desire of patients is to have the threat that incurable genetic disease poses for them and their children. Properly targeted, high

quality research that seeks answers to the central questions regarding the management of their condition and of the other aspects of their lives must be respected so that they can gain and retain control over their lives.

This is a good thing!

For more information about getting involved in research you should contact

EAGS,  
c/o VSOP,  
Vredehofstraat 31,  
3761 HA Soestdijk,  
Netherlands;

Genetic Interest Group,  
Unit 4D,  
Leroy House,  
436 Essex Road,  
London N1 3QP, UK;

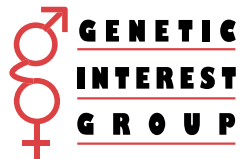
or  
Consumers in NHS Research Support Unit,  
Highcroft,  
Romsey Road,  
Winchester,  
Hampshire SO22 5DH, UK.



## **Acknowledgements**

The help and advice of many people has gone into this publication. Stephane Callewaert, John Dart and Ysbrand Poortman played particularly significant roles. Special mention must also be made of Bec Hanley and the Consumers in NHS Research Support Unit from whose publications a number of the examples quoted were lifted.

This publication was made possible as a result of a grant from GlaxoWellcome plc, whose support we gratefully acknowledge.



Unit 4D, Leroy House  
436 Essex Road  
London N1 3QP

Tel: (020) 7704 3141

Fax: (020) 7359 1447

Email: [mail@gig.org.uk](mailto:mail@gig.org.uk)

Website: [www.gig.org.uk](http://www.gig.org.uk)

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