#### REGISTERING CLINICAL TRIALS

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Patient trust and altruism are crucial to the conduct of research involving human subjects (1). Patients volunteer to be subjects for clinical studies because they believe that the results will benefit other patients. When the results of clinical trials are published, this is true. Indeed, clinical trials are crucial for advancing the quality of medicine because they provide the scientific evidence that supports sound clinical decision-making. For this contribution to the advancement of medicine, we owe our patients our gratitude. We also have an obligation to ensure that their participation makes a difference.

Unfortunately, not all clinical trials are published. Although investigators have an obligation to perform research ethically, and report the findings honestly, there are a number of factors that may determine whether or not the results of a clinical trial are ever published. Studies that provide equivocal or negative results may not be deemed suitable for publication by authors, editorial boards, and sponsors. But, the selective reporting of study results may do a disservice to our patients and violate their trust. Moreover, this may put future patient-subjects at needless risk because other investigators may unknowingly repeat studies that were completed, but not reported.

What does this mean to interventional pain management? As

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parties, including patients. As noted in a statement by the International Committee of Medical Journal Editors ICMJE (1), a clinical trials registry should be accessible to the public at no charge, be available to all investigators wishing to register, be managed by a nonprofit entity, and be searchable electronically. In addition, the registry should record specific types of information, including the study hypothesis and design, informed consent, outcomes measures, eligibility criteria, dates of the study, numbers of participants, funding sources and principal investigator contact information.

readers of recent guidelines and systematic

reviews published in Pain Physician know,

a single trial does not usually change the

way we practice medicine. Rather, it is

the accumulated body of evidence that

guides and changes the way we practice.

However, selective reporting of results can

adversely affect the validity of guidelines

and reviews, because unpublished studies

cannot influence medical thinking. This

can have negative consequences in terms

of medical policy-making, including

access to medical care and insurance

selective reporting is to require that

all clinical trials be registered with

some agency or reporting body, with

the database available to all interested

One remedy for the problem of

coverage for patients.

For purposes of registration, the ICMJE defined a clinical trial "as any research project that prospectively assigns human subjects to intervention or comparison groups to study the cause-and-effect relationship between a medical intervention and a health outcome" (1). Their revised definition included a requirement that there be a prospectively designated control or comparison group (2). Other types of studies, such as pharmacokinetics and toxicity studies,

observational studies with no concurrent control or comparative group, and Phase 1 studies are currently exempt from the need to register. However, any prospective trial whose chief purpose is to affect clinical practice should most likely be registered. Pain Physician has adopted this policy, which will be reviewed over the course of the next 24 months.

To be considered for publication in Pain Physician, the authors of a clinical trial must provide evidence of registration with a public trials registry. Trials must be registered at or before the onset of patient enrollment. This policy applies to any clinical trial beginning enrollment after July 1, 2005. For trials that started before this date, the Pain Physician journal will require registration by September 15, 2005. Although there may be some exceptions to this policy, arguments for exemption must be presented to the editorial board.

Benefits that may accrue from the registration of clinical trials include improved patient understanding about studies being done that may affect their medical care, and increased confidence that their contributions will be worthwhile. Clinicians also will have access to this information, which may improve their participation in the research process. Undeniably, we all have a stake in improving the quality of evidence-based medicine. Moreover, editors of journals will have to abide by the new requirements. Perhaps one result will be that more studies with negative or inconclusive results will be published.

The reasons for requiring registration of clinical trials are to protect the public trust and improve the quality of evidence-based medicine. We support this step forward.

For information about the topic of clinical trials, please see: http:

//www.clinicaltrials.gov. To learn about registering a clinical trial, see: http://prsinfo.clinicaltrials.gov. Web shots for both sites are shown in Figures 1 and 2. Examples of data collected in the ClinicalTrials.gov registry are shown in Table 1.

# Table 1. Example of data collected in the Clinical Trials.gov registry

- 1. Titles and Background Information
- 2. Investigational New Drug Application (IND)/Investigational Device Exemption (IDE) Information
- 3. Human Subjects Review
- 4. Sponsors
- 5. Study Description
- 6. Status Study Phase
- 7. Study Design
- 8. Interventions
- 9. Conditions and Keyword
- 10. Eligibility
- 11. Protocol Location, Contact and Investigator Information
- 12. Related Information

Full descriptions are available at: http://prsinfo.clinicaltrials.gov. PRS users provide and maintain information about their clinical trials ensuring the protocol records are correct and updated in a timely manner. The system allows users to create, modify, maintain and submit protocol records to ClinicalTrials.gov.

#### REFERENCES

- De Angelis C, Drazen JM, Frizelle FA, Haug C, Hoey J, Horton R, Kotzin S, Laine C, Marusic A, Overbeke AJPM, Schroeder TV, Sox HC, Van Der Weyden, MB. Clinical Trial Registration: A Statement from the International Committee of Medical Journal Editors. N Engl J Med 2004; 351:1250-1251.
- De Angelis C, Drazen JF, Frizelle FA, Haug C, Hoey J, Horton R, Kotzin S, Laine C, Marusic A, Overbeke AJPM, Schroeder TV, Sox HC, Van Der Weyden, MB. Is This Clinical Trial Fully Registered? A Statement From the International Committee of Medical Journal Editors. JAMA 2005; 293:2927-2929.

## Clinical Trials.gov



#### Home Search Browse Resources Help What's New About

ClinicalTrials.gov provides regularly updated information about federally and privately supported clinical research in human volunteers. ClinicalTrials.gov gives you information about a trial's purpose, who may participate, locations, and phone numbers for more details. Before searching, you may want to learn more about clinical trials.

INVESTIGATOR NOTE: Investigators wishing to register trials should refer to <a href="http://prsinfo.clinicaltrials.gov">http://prsinfo.clinicaltrials.gov</a>.

Search Clinical Trials

Search

Example: heart attack, Los Angeles

Search by Specific Information

Focused Search - search by disease, location, treatment, sponsor...

Browee

Browse by Condition - studies listed by disease or condition Browse by Sponsor - studies listed by funding organization Browse by Status - studies listed by recruitment status

Resource Information

Understanding Clinical Trials - information explaining and describing clinical trials

What's New - studies in the news

MedlinePlus - authoritative consumer health information

Genetics Home Reference - consumer information about genes and genetic conditions NIH Health Information - research supported by the National Institutes of Health

Fig. 1. Web site for topic of clinical trials: www.clinicaltrials.gov









### PRS Information

#### Registration of Clinical Trials

Clinical trials are registered with <u>ClinicalTrials.gov</u> via a web based data entry system called the Protocol Registration System (PRS).

 ${\bf Clinical Trials. gov\ allows\ the\ registration\ of\ trials\ that:}$ 

- are approved by a human subject review board (or equivalent) and
- conform to the regulations of the appropriate national health authorities.

Clinical Trials.gov facilitates registration of trials in accordance with the **International Committee of Medical Journal Editors (ICMJE)** initiative requiring prior entry of clinical trials in a public registry as a condition for publication.

Multi-site trials and multi-sponsor trials are susceptible to duplicate registration, thus care must be taken in how the trials are registered. For multi-sponsor trials it is the lead sponsor who should take responsibility for registration. It is critical that investigators and sponsors work together to ensure that a trial is registered once and only once.

#### Account Application Process

Organizations and investigators wishing to register trials must first apply for a PRS account via the links provided below. Within two business days, ClinicalTrials.gov will create the account and send email with instructions on how to login to the PRS, so that you can register your trials.

There are two types of PRS accounts:

- Organization accounts generally have multiple users and are used to register all the trials being conducted at an organization. <u>Apply for an organization account</u>
- Individual accounts are used to register trials conducted by a single investigator. Apply for an individual account

Questions? Contact us at register@clinicaltrials.gov

Fig. 2. Web site of The Protocol Registration System (PRS) http://prsinfo.clinicaltrials.gov.