

# Clinical Trials Disclosure Requirements: Too Much of a Good Thing?

By Christine P. Bump and Anne Marie Murphy

The demand to register and disclose the results of clinical trials in a publicly accessible forum is gathering momentum in the US and around the world. Congress, state legislatures and the international scientific community are among those demanding greater public access to clinical research information. It has been posited that registering and disclosing clinical trial results will help maintain industry accountability, advance public health and restore public trust in pharmaceutical research.<sup>1</sup> Although the pharmaceutical industry, largely of its own accord, posts clinical trial results in databases, federal and state legislation would expand existing clinical trials registration and disclosure requirements.

The medical community also has an interest in greater public access to clinical research information. The American Medical Association (AMA) has requested that the US Department of Health and Human Services (DHHS) establish a comprehensive registry for all clinical trials conducted in the US.<sup>2</sup> The World Health Organization (WHO) has proposed international standards for clinical trials registries and members of the International Committee of Medical Journals Editors (ICMJE) will publish reports of clinical trials only if they are registered in conformance with the WHO standards.

While the desire for such public access is laudable, requiring disclosure of clinical research may create unintended consequences and prove problematic for both the pharmaceutical industry and the public. Moreover, legislation is probably not even necessary in light of the ICMJE requirement to register or face the inability to publish in member journals.

## Clinical Trials Registries: Background and Legislation

Clinical trials registries provide a public record of ongoing clinical trials but do not typically disclose results. Registries are intended to inform patients (and their physicians) of clinical trials in which they may wish to participate. While such information is valuable, currently, there is no single registry that provides complete information about all ongoing US clinical trials.<sup>3</sup>

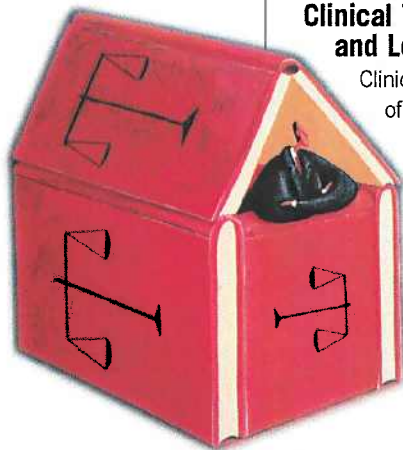
## Federal Legislation

Section 113 of the *Food and Drug Administration Modernization Act* of 1997 (*FDAMA*) introduced clinical trials registries by mandating that DHHS, through the National Institutes of Health (NIH), establish a "data bank of information on clinical trials for drugs for serious or life-threatening diseases and conditions."<sup>4</sup> This registry was intended to provide, in a form "readily understood by members of the public," a description of each experimental drug's purpose, eligibility criteria for participation in the trial, trial site locations and a point of contact.<sup>5</sup> To comply with section 113 of *FDAMA*, the National Library of Medicine developed ClinicalTrials.gov, an online registry of clinical trials for NIH. ClinicalTrials.gov provides regularly updated information about federally and privately supported ongoing clinical trials that are open and recruiting patients.

Until recently, total registration of drug trials for serious and life-threatening conditions was low. In 2002, FDA concluded that only 30% of drug trials required to register on ClinicalTrials.gov were, in fact, registered.<sup>6</sup> In July 2004, FDA revealed that 76% of cancer drug clinical trials required to register on the site were, in fact, registered.<sup>7</sup>

In February 2005, Senator Christopher J. Dodd proposed additional legislation, the *Fair Access to Clinical Trials Act* of 2005 (the *FACT Act*), which would extend *FDAMA*'s requirement for registration of clinical trials. Under the *FACT Act*, the requirement to register clinical trials would be expanded to include biological products and medical devices. Sponsors would also be required to include details about the outcome measures to be used in the trials.<sup>8</sup> The bill was referred to the Senate's Committee on Health, Education, Labor, and Pensions on 28 February 2005. As of 15 November 2005, it was still in committee; no further action had been taken. Other bills relating to clinical trials registration have been introduced and more may be proposed. For example, Senator Judd Gregg has announced that he is drafting legislation that would "expand the types of trials to be registered, so that information on marketed drugs would be available to consumers."<sup>9</sup>

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## State Legislation

In addition to activity at the federal level, more than 20 states have proposed registration requirements for clinical drug trials that occur within their borders.<sup>10</sup> Though the states' goals appear to be increased transparency, their approaches are not consistent. Some states simply want clinical trials to register on [ClinicalTrials.gov](http://ClinicalTrials.gov).<sup>11</sup> Others seek to require clinical trials within the state to register with state departments and agencies,<sup>12</sup> and some states plan to limit registration requirements to trials that are funded by the state.<sup>13</sup> State proposals have, to date, neglected to specify whether all trials, regardless of phase, are subject to proposed registration requirements.



Disparate registration requirements and numerous registration sites will make compliance difficult and will not enable patients and physicians to access information easily. Moreover, many clinical trials—especially phase 3 trials—are conducted at multiple sites across state lines. Sponsors and investigators may face conflicting requirements for registration at each trial site, which may ultimately impede the public's ability to learn about clinical trials.

## Clinical Trials Registries: WHO and ICMJE Requirements

The international scientific community is also demanding registration of clinical trials. In April 2004, WHO's registration advisory group identified 20 items relating to investigational clinical trials—a "minimal data set"—that should be included in registration.<sup>14</sup> WHO revised its minimal data set (partly in response to public comments) and published a revision on 21 October 2005 with a request for additional comments.<sup>15</sup> This revised registration data set includes the name of the primary register, a trial identification number, funding source(s), primary and secondary

sponsors, a description of the condition being studied, a description of the study and comparison/control intervention(s), key inclusion and exclusion criteria, primary outcomes and key secondary outcomes.<sup>16</sup>

In an effort to foster comprehensive publicly available clinical trial information, the ICMJE adopted WHO's April 2004 minimal data set for its new requirement for publication in member journals. In September 2004, members of the ICMJE (which include the *New England Journal of Medicine* and the *Journal of the American Medical Association*) stated in a joint editorial that member journals will consider a trial for publication only if it was registered on an accepted online trial registry before the first patient was enrolled, and only if the registration includes information that satisfies all 20 fields in WHO's minimal data set.<sup>17</sup> In October 2005, the ICMJE published an updated version of its uniform requirements for manuscripts submitted to biomedical journals, reiterating its September 2004 announcement.<sup>18</sup>

The ICMJE's policy applies to phase 3 trials that started recruiting on or after 1 July 2005; phase 3 trials that were ongoing before that date must have been registered by 13 September 2005 in order to be considered for publication. Phase 1 trials are specifically excluded from the registration requirement, but each ICMJE journal editor is to determine on a case-by-case basis whether to apply the registration requirement to trials whose "prespecified goal is to investigate the biology of disease or to provide preliminary data that may lead to larger, clinically directive trials."<sup>19</sup> The ICMJE does not advocate one particular registry, but requires clinical trials to appear on registries that are not-for-profit, electronically searchable, accessible to the public at no charge, open to all registrants and verifiable.<sup>20</sup>

## Clinical Trials Results Databases

While clinical trials registries provide a public record of clinical trials, results databases are public postings of clinical trial findings—including negative findings and adverse side effects. In October 2004, the pharmaceutical industry, through the Pharmaceutical Research and Manufacturers of America (PhRMA), launched its own web-based clinical study results database, [ClinicalStudyResults.org](http://ClinicalStudyResults.org). This results database is a "central, standardized repository for published and unpublished clinical studies that have already been completed,"<sup>21</sup> and should contain the results from all "hypothesis-testing" clinical studies (mainly phase 3 and phase 4 studies) completed since 1 October 2002 for drug products approved in the US.<sup>22</sup> Additionally, many individual pharmaceutical companies post their clinical study results on their websites. GlaxoSmithKline, for example, has its

own database that provides the results of all completed phase 1 through phase 4 clinical trials of its marketed drugs.<sup>23</sup>

Industry leaders have noted several potential problems associated with clinical trials results databases, especially if they include data from exploratory studies. One potential problem is that publicly disseminating these results may cause confusion or create false hope for patients.<sup>24</sup> Conclusions about a product's safety and efficacy, for example, cannot be drawn from exploratory study results. Additionally, providing information about exploratory studies or unapproved compounds may pose threats to intellectual property rights and competition.<sup>25</sup> While the objective of publicly disseminating important clinical trials results is commendable, more attention needs to be given to the manner and context in which such information is provided.<sup>26</sup> Otherwise, a glut of information may simply overwhelm the public.

## Conclusion

Continued legislation at both the federal and state levels has the potential to produce many different standards for registries and results reporting. Already, proposed clinical trials registries and results databases vary in the type of information that will be required to be registered or reported, the format for registration and reporting and the means by which compliance with requirements will be monitored and enforced. State registration requirements may not be consistent with respect to the clinical trial phases required to be registered or the types of diseases or health conditions under investigation. Various clinical trials results databases will also differ in the phase and scope of the clinical trials for which results must be reported, as well as the amount and type of information required to be reported.

Disparate sources of information related to clinical trials may result in an excess of publicly available information about them, in that there may be conflicting and inconsistent information disseminated about treatments and their availability to patients. Unless standardized, the volume of information presented in different forums with different requirements may confuse or even mislead the public. Therefore, clear, uniform standards for clinical trials registries and results databases are needed. The WHO, ICMJE and pharmaceutical industry itself are well on the way to achieving this goal. Federal and state legislatures' objectives may be best served by deferring to these efforts. ■

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