

rent grade 3 or 4 fatigue. Prospective studies incorporating thyroid-function testing are under way to further define the incidence of sunitinib-induced hypothyroidism and its potential relationship to fatigue as reported by patients.

Robert J. Motzer, M.D.

Memorial Sloan-Kettering Cancer Center
New York, NY 10021
motzerr@mskcc.org

Trial Registration

TO THE EDITOR: In their editorial, Drazen and Zarin (Jan. 11 issue)¹ express optimism about the registration of commercially sponsored clinical trials. Citing the ClinicalTrials.gov database, they report that 8% of pharmaceutical-industry registrations between January 1, 2006, and December 1, 2006, were missing information on outcome measures (down from 26% of registrations before January 1, 2006).

Unfortunately, little is known about the trial-registration policies and practices of major pharmaceutical companies.² For example, although the registration standards advocated by the International Committee of Medical Journal Editors³ are steps in the right direction, they only encourage, rather than guarantee, complete trial registration. In the absence of legal mandates for registration of all clinical trials, including phase 1 and phase 2 studies as well as trial results, no examination of today's voluntary registries can definitively indicate whether transparency in clinical research has truly improved, since unregistered trials necessarily remain unaccounted for in any analysis.

Currently, the Fair Access to Clinical Trials Act promises this legal mandate⁴ yet continues to lie dormant in U.S. congressional committees.⁵ Enactment of this legislation, should it come to pass, will be true cause for cheer.

Jason P. Lott, M.A.

University of Pennsylvania
Philadelphia, PA 19104
lottj@mail.med.upenn.edu

1. Drazen JM, Zarin DA. Salvation by registration. *N Engl J Med* 2007;356:184-5.
2. Lott JP, Katz KA. Pharmaceutical companies' policies and practices regarding prospective registration of dermatology-related clinical trials. *Br J Dermatol* 2006;155:635-8.
3. De Angelis C, Drazen JM, Frizelle FA, et al. Clinical trial registration: a statement from the International Committee of Medical Journal Editors. *N Engl J Med* 2004;351:1250-1.
4. Steinbrook R. Registration of clinical trials — voluntary or mandatory? *N Engl J Med* 2004;351:1820-2.
5. Henderson JK, Cassady Q. Drug deals 2006: cutting edge legal and regulatory issues in the pharmaceutical industry. *Ann Health Law* 2006;15:107-49.

THE EDITOR REPLIES: I concur with Mr. Lott that we would be better served if data on all clinical trials were available in public databases; legislation is one way to achieve this goal. In addition to the Fair Access to Clinical Trials Act, the Kennedy–Enzi bill¹ was recently introduced, with many of the same broad goals of the Fair Access to Clinical Trials Act.

In the absence of legislation, investigators must be vigilant. It was not my goal to suggest that Dr. Motzer should have personally registered his clinical trial on the treatment of renal-cell carcinoma. Instead, I urge all investigators participating in a clinical trial to check the registration to be sure it is fair, accurate, and fully informative.

Jeffrey M. Drazen, M.D.

1. Kennedy-Enzi bill, S.484. (Accessed March 22, 2007, at [http://thomas.loc.gov/cgi-bin/bdquery/D?d110:464.:/list/bss/d110SN.lst::\[TOM:/bss/110search.html\]](http://thomas.loc.gov/cgi-bin/bdquery/D?d110:464.:/list/bss/d110SN.lst::[TOM:/bss/110search.html]).)

Five-Gene Signature in Non–Small-Cell Lung Cancer

TO THE EDITOR: Chen et al. (Jan. 4 issue)¹ state that their five-gene prognostic signature in non–small-cell lung cancer (NSCLC) was validated three times. However, validations 1 and 3 changed the measurement method that was used to define

the signature under validation. Correct validation of a signature requires a new series of patients, a consistent statistical method to define the signature, and the same measurement technique.² Validation 1 reused the original cohort and