Comments on FDA informed consent information sheet draft guidance from AllTrials campaign

Docket number: FDA-2006-D-0031

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The AllTrials campaign was launched in January 2013 to call for all clinical trials to be registered and results reported. It is an initiative of Bad Science, BMJ, Centre for Evidence-based Medicine, Cochrane Collaboration, James Lind Initiative, PLOS and Sense About Science. It is supported by nearly 80,000 people and over 500 organisations including regulators; medical schools and universities; medical bodies and Royal Colleges; research funders and more than 200 patient groups from across the world.

We support the section on "reporting aggregate results of the clinical investigation" (Section V.K.). People who have participated in clinical trials have told us that they expect to be given the results of the trial(s) they participated in and that those results will be shared publicly. We agree with providing participants with aggregate results in a "clear and comprehensible manner."

The draft guidance doesn't include anything on allowing trial sponsors to share anonymised data from the trial participants. Some pharmaceutical companies already claim that they can't share more information from their clinical trials because their consent forms didn't explicitly include this. Not encouraging people running trials to include a note on sharing information, which patients want and actually expect to happen, is a betrayal of the patients' trust and might even damage medical research.

The value of sharing individual patient data has been proven time and again. Scientists have been reviewing patient data from trials since the 1970s[1] and those reviews have led to many medical advances including better survival rates from chemotherapy[2], improved heart disease treatments[3] and higher childhood cancer survival rates[4]. See Annex 1 for a list of ten studies that demonstrate the importance of individual patient data meta-analyses.

Some pharmaceutical companies have already begun to allow independent researchers to access data from their clinical trials. Johnson & Johnson announced in January that they were giving all of their data to researchers at Yale University[5]. Bristol-Meyers Squibb announced a collaboration with researchers at Duke University to grant access to its clinical trial data in June[6]. Bayer, Boehringer Ingelheim, GSK, Lilly, Novartis, Roche, Sanofi, Takeda, UCB and ViiV Healthcare share data through ClinicalStudyDataRequest.com[7].

The guidance needs to include an element informing patients that clinical investigators will be able to share non-identifiable data from their trials with other researchers.

Signed by

Síle Lane
Director of Campaigns

Sense About Science
14A Clerkenwell Green
London EC1R ODP
United Kingdom
Tel +44 (0) 207 490 9590
slane@senseaboutscience.org

References

[1] Collaborative analysis of long-term anticoagulant administration after acute myocardial infarction. An international anticoagulant review group. Lancet. 1970 Jan 31;1(7640):203-9.

[2] Chemotherapy in adult high-grade glioma: a systematic review and meta-analysis of individual patient data from 12 randomised trials. Glioma Meta-analysis Trialists. Lancet [2002, 359(9311):1011-1018.

[3] Antiplatelet Trialists' collaboration. Collaborative overview of randomised trials of antiplatelet therapy--I: Prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. BMJ. 1994 Jan 8;308(6921):81-106.

[4] Duration and intensity of maintenance chemotherapy in acute lymphoblastic leukaemia: overview of 42 trials involving 12 000 randomised children. Childhood ALL Collaborative Group. Lancet. 1996 Jun 29;347(9018):1783-8.

[5] Johnson & Johnson announces clinical trial data sharing agreement with Yale School of Medicine. 2014 Jan 30. http://www.jnj.com/news/all/johnson-and-johnson-announces-clinical-trial-data-sharing-agreement-with-yale-school-of-medicine

[6] Bristol-Myers Squibb expands access to clinical trial data through collaboration with academic research institute. 2014 Jun 24. http://news.bms.com/press-release/bristol-myers-squibb-expands-access-clinical-trial-data-through-collaboration-academic

[7] ClinicalStudyDataRequest.com https://clinicalstudydatarequest.com

Annex 1: Ten studies that demonstrate the importance of IPD meta-analysis and the global impact on care across a wide spectrum of patients and diseases.

IPD Study	Result	Issue
Chemotherapy in adult high-grade glioma: a systematic review and meta-analysis of individual patient data from 12 randomised trials. Glioma Meta-analysis Trialists. Lancet [2002, 359(9311):1011-1018	Results showed significant prolongation of survival associated with chemotherapy.	Small but clear improvement in survival from chemotherapy encouraged further studies of drug treatment of these tumors.
Antiplatelet Trialists' collaboration. Collaborative overview of randomised trials of antiplatelet therapy--I: Prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients BMJ. 1994 Jan 8;308(6921):81-106.	In each of four main high-risk categories of patients antiplatelet therapy was definitely protective.	One of three IPD met-analyses that widely influenced the treatment of patients with ischemic heart disease.
Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. Cholesterol Treatment Trialists' (CTT) Collaborators. Lancet. 2005 Oct 8;366(9493):1267-78.	Statin therapy reduces the 5-year incidence of major coronary events, coronary revascularisation, and stroke by about one fifth per mmol/L reduction in LDL cholesterol.	Impacted worldwide on how cholesterol therapy is used across low and high-risk individuals.
Effects of adjuvant tamoxifen and of cytotoxic therapy on mortality in early breast cancer. An overview of 61 randomized trials among 28,896 women. Early Breast Cancer Trialists' Collaborative Group. N Engl J Med. 1988 Dec 29;319(26):1681-92	The overview was able to demonstrate particularly clearly that both tamoxifen and cytotoxic therapy can reduce five-year mortality.	Meta-analysis that guides chemotherapy choices in breast cancer today.
Collaborative analysis of long-term anticoagulant administration after acute myocardial infarction. An international anticoagulant review group. Lancet. 1970 Jan 31;1(7640):203-9	The mortality experience of " anticoagulant " and " comparative " series, which were shown to be alike in relevant clinical characteristics, was significantly lower (by 20%) in males given anticoagulants.	Illustration that IPD meta-analysis been around for a long time and consent forms really should have caught up by now:
McCormack K, Grant A, Scott N. Value of updating a systematic review in surgery using individual patient data. Br J Surg2004;91:495-9.	Hernia surgery trials showed laparoscopic repair significantly reduced persistent pain compared with open repair, OR 0.54, 95% CI 0.46 to 0.64).	Contradicted an earlier meta-analysis of published data alone, which indicated a statistically significant benefit in favour of open repair. OR 2.03 (95% CI 1.03 to 4.01). *
Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. Lancet. 1994,343.311-*322*	Fibrinolytic therapy was associated with an excess of deaths during days 0-1 (especially among patients presenting more than 12 h after symptom onset, and in the elderly) but this was outweighed by a much larger benefit during days 2-35.	Indicated that fibrinolytic therapy was beneficial in a much wider range of patients than were receiving treatment routinely at the time.
Duration and intensity of maintenance chemotherapy in acute lymphoblastic leukaemia: overview of 42 trials involving 12 000 randomised children. Childhood ALL Collaborative Group Lancet. 1996 Jun 29;347(9018):1783-8.	Intensive re-induction chemotherapy produced an absolute improvement of about 4% percent in long-term survival	Showed important findings of IPD in childhood cancers.

Effect of antihypertensive drug treatment on cardiovascular outcomes in women and men. A meta-analysis of individual patient data from randomized, controlled trials. The INDANA Investigators. Ann Intern Med. 1997 May 15;126(10):761-7.	In terms of relative risk, treatment benefit did not differ between women and men.	At the time it was not clear whether treatment benefit was similar for both sexes as many more men had participated in the trials.

***** *Jeng GT, Scott JR, Burmeister LF. A comparison of meta-analytic results using literature vs individual patient data. Paternal cell immunization for recurrent miscarriage. JAMA1995;274:830-6.*