INDIANA UNIVERSITY

CENTER FOR BIOETHICS

Data points on the growth of international human subjects research

1. Global number of clinical trials

Not including phase IV, medical device and non-medicinal trials, the number of clinical trials have risen from 40,000 in 2000 to 59,000 in 2006. (CenterWatch 2009, p. 118)

On February 22, 2011, The WHO's "International Clinical Trials Registry Platform" listed a total of 127,042 registered trials; 52,960 were associated with the term "United States". (Data source: http://apps.who.int/trialsearch/)

On February 22, 2011, a search for all trials registered in ClinicalTrials.gov returned 103,266 studies; 36,498 of these were actively recruiting new subjects. Of these active studies, 17,858 were located in the United States. (Data source: http://clinicaltrials.gov)

2. Number of investigators

The number of U.S. clinical investigators has declined in recent years (from 15,687 in 2000 to 13,439 in 2007), while the number of non-U.S. investigators has doubled (from 4,451 in 2000 to 9,449 in 2007). (CenterWatch 2009, p. 340)

3. International investigators increasing (FDA 1572 forms)

“Since 2002, the number of U.S.-based clinical investigators filing new Forms FDA 1572 has declined by 5.5% annually. During the same period, the number of active FDA regulated investigators based outside the United States has grown by 15% annually.” (Getz 2007, p. 42)

The frequency of foreign-based studies, as evidenced from FDA 1572 forms, has increased from 16.3% (in 2001) to 35.5% (in 2007) of all studies. (CenterWatch 2009, p. 488)

U.S.-based trials decreased from a high of 32,027 (in 2001) to 24,654 (in 2007); in the same years, non-U.S.-based trials increased from 6,226 to 12,402. In 2007 a total 99 countries submitted FDA 1572 forms. (CenterWatch 2009, p. 489, 491)

4. Domestic vs. international growth reflected in clinicaltrials.gov

“In terms of growth rates, 24 of the fastest growing 25 countries are from emerging regions ..., while 19 of the 25 slowest growing top 50 countries are from traditional regions.” (Thiers FA, Sinskey AJ, and Berndt ER 2007, p. 1)

Jere Odell. Data points on the growth of international human subjects research. Indiana University Center for Bioethics. February 23, 2011.

“Emerging regions grew from less than 8% in the BCTs [biopharmaceutical clinical trials] initiating recruitment in 2002 to 20% of BCT sites that became active in 2006. (Thiers FA, Sinskey AJ, and Berndt ER 2007, p. 1)

5. Percentage of foreign clinical researchers submitting Investigational New Drug (IND) Applications to the FDA

“The percentage of foreign clinical investigators conducting clinical trials under INDs has more than doubled over the past decade.” Having increased from under 15% in 1998 to over 30% in 2008, the recent rise in applications suggests that foreign clinical trials will increase in the coming years. (OIG 2010, p. 13-14)

“If a sponsor has not submitted an IND or consulted with FDA in some other way about its foreign clinical trials, FDA has no way of knowing whether and where clinical trials are taking place.” (OIG 2010, p. 17)

6. International research contributing to applications for FDA marketing approvals in 2008

"Eighty percent of approved marketing applications for drugs and biologics contained data from foreign clinical trials.” (OIG 2010, p. 8)

7. Increase of international research measured in publications, 1995 - 2005

Based on 300 articles published in NEJM, Lancet, and JAMA: “[T]he number of countries serving as trial sites outside the United States more than doubled in 10 years, whereas the proportion of trials conducted in the United States and Western Europe decreased.” (Glickman SW, et al. 2009, p. 816)

8. Number of subjects enrolled in other countries

Based on data from the European Medicines Agency (EMA) from 2005 to 2009, about 35% of all subjects enrolled in trials were from nontraditional (non-European, non-North American) research countries. This number has more than doubled in the last five years (from 21,653 in 2005 to 64,101 in 2008 and 46,059 in 2009). EMA totals for the five years by region--Europe: 162,702; North America: 209, 705; "Rest of the World": 221,092. (SOMO 2011, p. 93)

“Seventy-eight percent of all subjects who participated in clinical trials were enrolled at foreign sites; 54 percent of all trial sites were foreign.” (OIG 2010, p. 10)

"Western Europe accounted for 58 percent of subjects enrolled at foreign sites ... Central and South America also enrolled a significant number. This region contained 26 percent of all subjects enrolled at foreign trial sites." Note: Trials in Central and South America have been very large--averaging 10 times larger than enrollments in Western Europe. (OIG 2010, p. 11-13)

9. Domestic vs. international FDA inspections in 2008

"FDA was 16 times more likely to inspect a clinical investigator at a domestic site than a foreign site." (OIG 2010, p. 16)

10. U.S. Investment sources in health R&D

Compared to other sources, total U.S. government spending on health R&D was static from 2004 to 2008. U.S. government spending increased in 2009, rising from about 39 billion in 2008 to 46.8 billion in 2009, in large part reflecting ARRA stimulus spending. In contrast, from 2001 to 2008 both industry spending (from roughly 45 to 65.3 billion) and philanthropic spending (from roughly 10 to 17.8 billion) increased steadily, but leveled off in 2009 (possibly reflecting the impact of the financial crisis). Health R&D spending from all U.S. sources increased steadily from about 80 billion in 2001 to 139 billion in 2009. However, in the last ten years total U.S. spending on health R&D (from all sources) accounts for less than 6% of all health costs. (Research!America 2010)

11. Spending, NIH

Although the number of awards to foreign sites has declined in 2009 and 2010, funds awarded to foreign sites doubled between 2004 and 2009. (Data source: NIH Awards by Location and Organization - NIH Research Portfolio Online Reporting Tools (RePORT). Accessed 18 Feb 2011 at: http://report.nih.gov)

All NIH grants to foreign countries increased from $69.6 million in 2000 to a high of $352.6 million in 2004; in recent years NIH spending abroad has leveled off at $196.7 and $212.4 million in 2007 and 2008 respectively. (CenterWatch 2009, p. 103)

12. R&D abroad, PhRMA member companies

Although decreasing in 2002 (-13.9%) and in 2009 (-7.1%), annual R&D abroad has risen from 4.22 billion (1999) to 10.99 billion in 2009. (PhRMA 2010, p. 44)

13. Spending, NGOs

"Total overseas health expenditures channeled through US NGOs" have increased from 1.32 (1990) to 2.16 billion (2010)--with a high of 3.1 billion in 2008 (in 2008 US Dollars). A recent, modest decline probably reflects the decline in the global economy. (IHME 2010, p. 24)

14. Spending, Bill and Melinda Gates Foundation (BMGF)

BMGF has steadily increased global funding for health research from roughly 64.19 million in 1999 to 528.6 million in 2009 (in 2008 U.S. dollars). Research institutions receive the largest portion of BMGF's donation, over a third of all of BMGF's health research donations. (IHME 2010, p. 92-94)

15. Spending, governments of "developed" countries

Official Development Aid (ODA) from "developed" to "developing" countries (only a small portion of which is for health research) has increased from .22% (1997) to .3% (2008). This is a recovery to levels of ODA in the early 90s—at roughly .33% from 1990 to 1992. (GFH 2009, p. 179)

16. Global pharmaceutical market share

Although the market share has changed very little in recent years (U.S. decreased from 49% in 2003 to 46% in 2007), Asia/Africa/Australia (13.9% CAGR 2004-2009) and Latin America (10.9% CAGR 2004-2009) are the fastest growing markets for pharmaceuticals. In contrast, the North American market grew by only 1.9% (CAGR 2004-2009). (CenterWatch 2009, p. 51; IMS Health Market Prognosis, March 2010)

17. On the globalization of clinical research industry

Two trends in the past 15 years: “Between 1995 and 2002, the landscape--primarily concentrated in North America and Western Europe—saw the emergence of new investigative site operating models (e.g., Site Management Organizations, Investigative Site Networks, Trial Management Organizations) and consolidation by well-capitalized companies. The years 2003 through 2010 can be best characterized as a period of intense globalization and the emergence and growth of investigative sites based in more remote regions of the globe.” (Getz and Zuckerman 2010, p. 34.)

“The typical late stage clinical study—sponsored by small, mid-size, and large companies—is conducted in an average of 34 countries today, more than 70 countries on average for the top 20 sponsor companies.” (Getz and Zuckerman 2010, p. 34.)

“[W]hile investigative sites in the European Union and North America reported flat annual growth in industry sponsored clinical trials during 2006 and 2008, sites in ascending regions reported a 17% annual increase in industry sponsored clinical trial volumes during the same period.” (Getz and Zuckerman 2010, p. 36)

17. Increase in non-clinical research

A bibliometric analysis of the ISI's Science and Social Science Indexes indicates found: "The annual number of public health publications rose by 55% over the 10-years." (Clarke A, et al. 2007, p. 44)

In a portrait of one region, funding for public health research increased dramatically (even when compared with biomedical and clinical research financing) in Argentina (+90.6%), Bolivia (+348.8%), Chile (+11.7%) and Paraguay (+3.4%) between 2004 and 2006. (GFH 2009, p. 32)

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