FDA Approves First Racially Targeted Drug

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Until recently, the prototype subject for clinical research in the United States has been the single white male.1 Because of our uneasiness with race and ethnicity, medicine has been reluctant to address the relevance of race or ethnicity to the diagnosis and treatment of disease, except in the most obvious cases.2 Specialists note, however, that diseases and conditions once thought to be ethnically neutral express themselves differently and vary in incidence among ethnic groups.3

There is some medical evidence that certain drugs respond quite differently in some racial and ethnic groups. To the limited extent such knowledge exists, a physician must consider race and ethnicity when making treatment decisions. For example, African Americans with high blood pressure typically respond to diuretics much better than whites, and Asians respond to some anti-psychotic drugs at a dosage of one-tenth that required for whites.4 However, the exclusion of minorities from clinical trials has resulted in huge gaps in medical knowledge, with physicians increasingly uncomfortable with being forced to extrapolate from all-white-male data when making treatment decisions.5

In designing therapeutic regimens, it is important to understand variations in drug response and metabolism.6 Factors such as age, diet, underlying disease, and interactions with other drugs, are recognized as variables that must be accounted for in understanding a patient’s response to and disposition of drugs.7 Race is a less-appreciated and less-understood variable although medical evidence is mounting of substantial racial differences in drug response and disposition, either due to differences in the rate of drug metabolism, pharmacologic response, or underlying mechanisms of the disease being treated.8

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1 Rebecca Dresser, Wanted Single, White Male for Medical Research, 22 HASTINGS CENTER REP. 24 (Jan-Feb. 1992).
3 Id.
4 Id.
7 Id.
8 Id.
As early as 1929, researchers noted racial differences in drug response to ephedrine.\textsuperscript{9} Numerous studies have since demonstrated that black patients do not respond as well as white patients to the antihypertensive effects of β-blockers.\textsuperscript{10} Some research has simply noted the differences in response to a drug between various racial or ethnic groups. Researchers in some cases, however, are beginning to understand the reasons behind the different responses, and the answers have not necessarily been as expected. As noted above, black hypertensive patients require larger doses of β-blockers than do whites. Data from the Beta-blocker Heart Attack Trial suggests that serum concentrations of the β-blocker propranolol are lower in blacks compared with whites when both groups receive the same doses.\textsuperscript{11}

Historically, minorities were overrepresented as research subjects because they could be easily exploited, and minority health was studied to improve the health of the majority population.\textsuperscript{12} African Americans were particularly and consistently exploited first as slaves, and again when emancipation of slaves raised concerns about the spread of diseases to the white population.\textsuperscript{13} Research ethics has been described as “born in scandal and reared in protectionism.”\textsuperscript{14} In the 1970s, research ethics literature tended to characterize participation in clinical trials as a risky endeavor, with much focus on the protection of “vulnerable” populations, including racial and ethnic minorities.\textsuperscript{15} This philosophy of protection resulted in riskier research being done on middle-aged males with middle-class incomes. Where Institutional Review Boards (IRBs) addressed the issue of subject selection at all, the focus was on limiting the scope of subjects allowed to participate on the basis that certain populations were too vulnerable to be included.\textsuperscript{16}

By the 1980s, the public’s perception of the benefits of clinical research to individual subjects had radically changed, with patients clamoring for access to clinical trials and to experimental drugs, driven largely by AIDS activism.\textsuperscript{17} The focus of ethicists shifted from protecting potential subjects, or classes of subjects, to questioning the exclusion of patients from clinical trials.\textsuperscript{18}

By the early 1990s, IRBs were being required to justify the exclusion of groups from clinical trials based on the ethical principle of justice, i.e., the fair distribution of anticipated benefits to the subjects.\textsuperscript{19} The IRB Guidebook for 1993 even asked researchers to question whether the selection process overprotected subjects considered...
vulnerable.\textsuperscript{20} A further issue began to emerge in the 1990s: If the results of research are to be of maximum benefit to society, then subjects must be representative of the population, with the ethical focus shifting to beneficence rather than justice.\textsuperscript{21} The regulatory response to this shift in thinking is evidenced by the 1994 National Institutes of Health (NIH) guidelines requiring the inclusion of women and minorities as subjects in clinical research for NIH-supported research.\textsuperscript{22}

In June 2005 the U.S Food and Drug Administration (FDA) approved BiDil, a heart failure drug specifically targeted to black patients. Such approval “marks the first time that the agency has approved a drug for a specific racial group.”\textsuperscript{23} Previous studies suggested that BiDil might benefit black patients even though the drug did not appear to benefit white patients.\textsuperscript{24} The FDA approved the drug based on a third clinical trial, the African-American Heart Failure Trial (A-HeFT). This trial tested black patients who were undergoing other therapies.\textsuperscript{25} The results “strongly suggested that there were differences between blacks and whites in response to this medicine.”\textsuperscript{26} Researchers believe that “[d]ifferences may be related to environmental, social, lifestyle, or genetic factors or to interactions among all of these factors.”\textsuperscript{27} Whatever the reasons, researchers found that “BiDil dramatically reduces death and hospitalization in blacks.”\textsuperscript{28}

Some will correctly argue that there are numerous problems with, and arguments against, using race and ethnicity in epidemiological studies, at least in the manner it has routinely been used.\textsuperscript{29} Nonetheless, the FDA was correct in approving BiDil given the evidence from the clinical trials of the drug. The National Medical Association expressed approval for the FDA’s action, but suggested that “…a larger clinical trial involving other populations would also be helpful.”\textsuperscript{30} The approval of BiDil is also a direct consequence of changes in research ethics over a 40-year period.

December 2005

\textsuperscript{20} Id.
\textsuperscript{21} Weijer, supra note 14, at 340.
\textsuperscript{24} Id.
\textsuperscript{25} Id.
\textsuperscript{26} Id.
\textsuperscript{27} Id.
\textsuperscript{28} Id.
\textsuperscript{30} Meadows, supra note 23.