

# FDA Approval of BiDil: First Step to Pharmacogenomics or Detour into Race-based Medicine?

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According to the Food and Drug Administration [FDA], the goal of pharmacogenomics or “personalized medicine” is to tailor drug therapy to an individual’s unique genetic profile.<sup>1</sup> In order to facilitate the scientific exchange of information necessary to make advances in pharmacogenomic research, and provide guidance to industry on submission of genomic data, the FDA released the *Pharmacogenomic Data Submissions* in March 2005.<sup>2</sup> Three months later, the FDA approved BiDil, a heart failure medication marketed specifically for African-Americans and indicated for patients who “self-identify” as black,<sup>3</sup> referring to it as “a step toward the promise of personalized medicine”.<sup>4</sup> However, the trial on which the drug was approved did not include any genetic testing in an attempt to identify common genetic traits among the participants, it used race, the only available commonality.<sup>5</sup> While acknowledging race is an imperfect surrogate for genetic variation, Drs. Temple and Stockbridge, in their explanation of the FDA perspective, maintain it is a “useful proxy until the pathophysiologic bases for observed racial differences are better understood”.<sup>6</sup>

In approving BiDil on the basis of trials consisting only of African Americans, the FDA has condoned the use of race trials<sup>7</sup> and lends “the imprimatur of the state to the use of race as a biological category.”<sup>8</sup> In allowing researchers to utilize race as a convenient surrogate for genetics, the FDA is facilitating a trend towards race-based clinical trials resulting in the creation of “ethnic drugs” rather than individually tailored therapy. There is evidence that while initial research was aimed at tailoring drug therapy to individual genetic profiles, investigators are increasingly exploring group rather than individual genetic variability in drug response.<sup>9</sup> If drug approval can be obtained on race-based clinical trials, there is no economic incentive to undertake costly clinical testing to uncover the genetics basis of differential response or to develop pharmacological testing.

Pharmaceutical companies must abide by an elaborate FDA approval process, or face the rejection of their new drug application resulting in the loss of millions in research dollars. As Reul comments: “[t]he NDA [new drug application] process inherently places drug makers at the mercy of the FDA.”<sup>10</sup> The FDA can utilize this power, by creating regulations which promote strides in pharmacology while avoiding the creation of more “ethnic drugs”. Haga and Venter suggest promotion of a groups-based approach, in which the FDA refuses to accept race as proxy by passing guidelines requiring genomic analysis of large admixed populations to determine if distinct genetic variations between groups exist.<sup>11</sup> Alternatively, the FDA could incorporate a policy in which new drug applications utilizing race or ethnicity as “pseudo-biological variables”, include an explanation of why the particular racial group was selected and how classification was achieved.<sup>12</sup> This policy change is supported by the literature. According to Khan, researchers will use more care in using race, ensuring a distinction is maintained between the use of race as a social category and a biological category.<sup>13</sup> To justify the use of race the researchers must first show it serves a compelling interest, and then provide compelling scientific evidence supporting their assertion that race-specific genetic differences result in the relevant medical condition.<sup>14</sup> Finally, Ruel suggests regulations “explicitly authorizing race for surrogate research” in instances where scientific evidence supports using race as a proxy.<sup>15</sup> These regulations should specifically outline the uses of racial and genetic data, and penalties for discriminatory behavior.<sup>16</sup> In the case of BiDil, the FDA could have insisted the label indicate there appear to be more effective results in the specific population. Rather than approving the race-specific label and phase 4 post-marketing studies consisting of different racial groups a to look for differences in outcomes, and predictors of those differences such as genetic markers,<sup>17</sup> ensuring greater strides in pharmacologic research while approving the drug.



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1. Center for Drug Evaluation and Research, *Genomics at FDA: Background Information on Genomics*, online: U.S. Food and Drug Administration <http://www.fda.gov/cder/genomics/background.htm>.
2. U.S., Food and Drug Administration, *Guidance for Industry: Pharmacogenomic Data Submissions* (Rockville, Maryland, 2005), online: <http://www.fda.gov/CBER/gdlns/pharmdtasub.htm>.
3. BiDil, *Prescribing Information*, online: NitroMed <<http://www.bidil.com/hcp/>>.
4. U.S. Food and Drug Administration, New Release/Communiqué, P05-32, “FDA News: FDA Approves BiDil Heart Failure Drug for Black Patients” (23 June 2005), online: U.S. Food and Drug Administration <<http://www.fda.gov/bbs/topics/NEWS/2005/NEW01190.html>>.
5. LaVera Crawley, “The Paradox of Race in the BiDil Debate” (2007) 99:7 *Journal of the National Medical Association* 821.
6. Robert Temple & Norman L. Stockbridge, “BiDil for Heart Failure in Black Patients: The U.S. Food and Drug Administration Perspective” (2007) 146:1 *Annals of Internal Medicine* 57 at 58.
7. Michael D. Ruel, “Using Race in Clinical Research to Develop Tailored Medications: Is the FDA Encouraging Discrimination or Eliminating Traditional Disparities in Health Care for African Americans” (2006) 27:2 *Journal of Legal Medicine* 225 at 236.
8. Jonathan Kahn, “How a Drug Becomes ‘Ethnic’: Law, Commerce, and the Production of Racial Categories in Medicine” (2004) 4 *Yale Journal of Health Policy, Law and Ethics* 1 at 33.
9. Lisa Gannett, “Group Categories in Pharmacogenetics Research” (2005) 72:5 *Philosophy of Science* 1232 at 1233.
10. *Supra* note 6 at 236.
11. Susanne B. Haga & J. Craig Venter, “FDA Races in Wrong Direction” (2003) 301:5632 *Science* 466.
12. *Supra* note 7 at 44.
13. *Ibid.*
14. *Ibid.*
15. *Supra* note 6 at 238.
16. *Ibid.* at 225.
17. *Supra* note 7. This was suggested by Jonathan D. Kahn who held that the required trial should occur prior to approval. However Temple & Stockbridge reject it as they maintain it is unethical to withhold approval pending years of further testing in a drug which is shown to reduce mortality by 43% : See *Supra* note 5 at 59.