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Harmonizing Race: Competing Regulatory Paradigms of Racial Categorization in International Drug Development

Jonathan Kahn, J.D., Ph.D.*

I. Introduction

Two powerful dynamics are at the forefront of contemporary pharmaceutical development: global outsourcing of clinical trials and pharmacogenomics. These two dynamics come together in the regulatory arena through the development of international guidelines to harmonize the production and use of clinical data involving diverse ethnic and racial groups. Such guidelines both produce and are produced by the drive to develop individually tailored medicines in a world market. While promulgated to promote more efficient pharmaceutical development, such mandates may also have the unintended consequence of reshaping cultural and ultimately legal understandings of race and ethnicity as genetically distinct and bounded categories. The regulatory construction of race and ethnicity as genetic has the potential to produce both skewed science and discriminatory social policies.

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This article will examine the implications of U.S. federal and international regulatory mandates in the construction and circulation of racial categories in biomedical research and drug development. It will focus on the interface between two regulatory mandates in particular: the International Conference on Harmonization (ICH) Guideline Document E-5 on “Ethnic Factors in the Acceptability of Foreign Clinical Data,”¹ and the U.S. Food and Drug Administration (FDA) “Guidance for Industry: Collection of Race and Ethnicity Data in Clinical Trials.”² The ostensible purpose of both of these guidelines is to promote more efficient and economical development of new pharmaceutical interventions. Underlying both Guidances is a presumption that race and ethnicity are relevant variables in assessing the safety and efficacy of drugs in clinical trials. Both Guidances also implicitly cast race and ethnicity as obstacles to be managed and overcome in the course of getting new drugs to global markets as quickly and cheaply as possible.

Ultimately, however, the Guidances are driven by different regulatory considerations which place them in tension with one another. The ICH guideline’s primary concern is to “harmonize” different state regulatory regimes in the international arena. Its goal is to enable clinical data produced in one jurisdiction to be used in another jurisdiction for the purposes of drug registration.³ The FDA guideline is primarily concerned with providing a standardized bureaucratic classification for racial and ethnic categories such that clinical trial data can be collected and reported in a consistent manner within the FDA’s jurisdiction.⁴ The FDA, therefore, adopts the racial and ethnic categories promulgated by the U.S. Office of Management and Budget – used most familiarly in the U.S. Census.⁵ These categories, the FDA notes, “were developed in response to the need to enforce civil rights laws in education” and should “not be interpreted as being scientific or anthropological in nature.” The FDA categories are therefore theoretically to be understood as social not genetic in nature. The ICH E5 Guideline does not set forth particular ethnic categories per se, but rather

1. International Conference on Harmonization, *Ethnic Factors in the Acceptability of Foreign Clinical Data*, (Feb. 5, 1998), available at <http://www.ich.org/LOB/media/MEDIA481.pdf> [hereinafter ICH E5].
2. U.S. Food and Drug Administration (FDA), *Guidance for Industry: Collection of Race and Ethnicity Data in Clinical Trials* (2005), available at <http://www.fda.gov/cder/guidance/5656fnl.pdf> [hereinafter FDA Guidance].
3. ICH E5, *supra* note 1, at 1.
4. FDA Guidance, *supra* note 2, at 1.
5. *Id.* at 3.

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elaborates a series of “ethnic factors” which include social/cultural practices, physiological processes, and genetics which are posited as potential variants across ethnic groups.

The ICH process is transforming global drug development and marketing, and, in particular, is opening up the large Japanese market to pharmaceuticals tested in the West. The FDA Guidance similarly promises to transform the production and organization of racial and ethnic data in clinical trials for the U.S. market. As pharmaceutical development goes global, however, the social classifications of the FDA Guidance also promise to collide with the mixture of social, physiological and genetic “factors” elaborated in the ICH guideline. These diverse classificatory schemes cannot be easily reconciled. This paper will explore how concepts of race and ethnicity are being produced and reproduced through this collision. It will further explore how these distinct attempts to “regulate race” in a bureaucratic context are shaping the development of global pharmaceutical markets.

Part II of the article will set forth the background to the ICH E5 regulatory mandate and its distinct concepts of race and ethnicity. Part III will explore how the ICH guidelines have already begun to affect global pharmaceutical development. Part IV will set forth the background to the FDA guidelines on the collection of racial and ethnic data for clinical trials. It will then go on to examine the debates that arose around the adoption of the FDA guidelines, specifically as they involved considerations of how the FDA guidelines might impact global pharmaceutical development under the ICH regulatory regime. Part V will conclude the article with an examination of the broader implications of this story for the production of social and regulatory understandings of the nature of race and ethnicity.

II. Background to the ICH E5 Guidelines

A. *The ICH*

The ICH, formally known as the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, was formed in 1990 at a meeting in Brussels hosted by the European Federation of Pharmaceutical Industries and Associations (EFPIA).⁶ Interested parties at the meeting included representatives of the regulatory agencies and industry

6. ICH, *History and Future of ICH*, <http://www.ich.org/cache/compo/276-254-1.html> (last visited May 16, 2006).

associations of Europe, Japan, and the USA.⁷ The formation of the ICH was born out of concerns “over rising costs of health care, escalation of the cost of R&D [Research & Development] and the need to meet the public expectation that there should be a minimum of delay in making safe and efficacious new treatments available to patients in need.”⁸ One underlying factor affecting all of these concerns was the diverse regulatory standards imposed by the governments of the major pharmaceutical markets in the US, the European Union (EU), and Japan. Founding members believed that the harmonization of standards for product development and regulatory approval would greatly increase the efficiency and economy of drug development and pave the way for the creation of a truly global pharmaceuticals market.⁹ More specifically, harmonization was seen as a means to lower drug development costs, reduce the time necessary to bring new drugs to new markets, improve regulatory efficiency, and minimize risks to research subjects.¹⁰

The ICH is structured around the US, the EU, and Japan. These regions account for approximately 80% of the global pharmaceutical market.¹¹ By region, the founding members were: US – the FDA and the Pharmaceutical Research and Manufacturers of America (PhRMA), which represents the leading research-based pharmaceutical and biotechnology companies in the United States; the EU – the European Commission (representing the twenty-five members of the EU) and the EFPIA, which is composed of twenty-five national pharmaceutical industry associations (plus six associations with liaison status) and forty-three leading pharmaceutical companies involved in the research, development and manufacturing of medicinal products in Europe for human use; Japan – the Ministry of Health, Labor and Welfare (MHLW) and the Japan Pharmaceutical Manufacturers Association (JPMA), which represents ninety member companies including all the major research-based pharmaceutical manufacturers in Japan.¹² These groups play the primary role in ICH decision making.¹³ Additionally, there

7. *Id.*

8. *Id.*

9. *Id.*

10. J. John Lee, Comment: *What is Past is Prologue: The International Conference on Harmonization and Lessons Learned from European Drug Regulations Harmonization*, 26 U. PA. J. INT’L ECON. L. 151,155 (2005).

11. Carly Anderson et al., *Bridging Studies in Asia and the Impact of the ICH E5 Guideline*, 37 DRUG INFORMATION J. 107S (2003).

12. *Id.*

13. *Id.*

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are three observer organizations, the World Health Organization (WHO), Health Canada, and the European Free Trade Association (EFTA) who nominate non-voting participants to attend the ICH Steering Committee Meetings.¹⁴

B. ICH E5

Since its inception, the ICH has promulgated a series of “Guidelines” grouped into three broad categories: Quality, Safety, and Efficacy. Additionally, the ICH has adopted a “Common Technical Document” (CTD)¹⁵ which serves as a standard form for drug licensing approval across all three ICH regions.¹⁶ A key consideration for global drug development and registration involves the acceptability of data in different regions. To address this issue, the ICH adopted Guideline E5, “Ethnic Factors in the Acceptability of Foreign Clinical Data,” in 1998.¹⁷ ICH E5 is intended to facilitate drug registration in the different ICH regions by recommending a framework for evaluating the impact of ethnic factors on a drug’s safety and efficacy in a manner that will enable appropriate evaluation of ethnic factors. The Guideline is premised on the “desirability of utilizing foreign clinical data that meet the regulatory standards and clinical trial practices acceptable to the region considering the application for registration.”¹⁸

In recent decades, ethnicity has become perceived as a barrier to the globalization of pharmaceutical development and marketing. Japan, in particular, has resisted the licensing of many drugs already licensed in the US and the EU on the grounds that clinical data based on studies of safety and efficacy conducted in “Caucasian” populations cannot be directly extrapolated to apply to the “Japanese” population.¹⁹ As one senior Japanese hospital official put it:

Ethnic factors in a broad sense have been regarded as one of the unavoidable reasons to have some barriers to the acceptance of foreign clinical data. Therefore, the problem of “Ethnic Factors in the Acceptability of Foreign Clinical Data” has been regarded as a difficult, but the most important, subject in the harmonization of the clinical field of ICH.²⁰

14. *Id.*

15. ICH, *Common Technical Document*, <http://www.ich.org/cache/compo/276-254-1.html> (last visited May 18, 2006).

16. Lee, *supra* note 10, at 180.

17. ICH E5, *supra* note 1, at 1.

18. *Id.*

19. Anderson, *supra* note 11.

20. Chikayuki Naito, *Ethnic Factors in the Acceptability of Foreign Clinical Data*, 32 DRUG INFORMATION J. 1283S (1998), available at <http://diahome.org/content/abstract/1998/dijs1227.pdf>.

A driving concern behind the development of ICH E5, therefore, was to allow data from clinical trials conducted in the “predominantly Caucasian” patient population of the West to be extrapolated to the population of Japan.²¹ Japan has the second largest national drug market in the world²² but it has been historically difficult for Western pharmaceutical companies to gain entry to the Japanese market for drugs tested in the West.²³ Japanese regulatory authorities have resisted approving such drugs on grounds that they may work differently in Japanese populations.²⁴ Thus, for example, of the 149 drugs approved by the US FDA between 1992 and 1996 (before ICH E5 was adopted in 1998), 51% were not available to patients in Japan by 2000.²⁵

A major objective of ICH E5 is to allow for the extrapolation of data produced in one ICH region to a different region.²⁶ It is hoped that providing a regulated framework for such extrapolation will minimize the duplication of clinical data and facilitate the acceptance of foreign clinical data in new regions.²⁷ ICH E5 also describes a mechanism known as “bridging studies” which allows for the use of smaller, cheaper studies in a host region’s population as a basis for extrapolating data from larger full-scale clinical studies about which the host region otherwise has reservations.²⁸ Bridging studies thus supplement existing data as basis for extrapolation, in effect leveraging existing data into new regulatory regimes.

It is in relation to bridging studies that so-called “Ethnic Factors” become most salient. ICH E5 is premised on the idea that it should not be necessary to repeat an entire clinical drug development program in a new region.²⁹ It provides for the development of a “clinical data package” that would fulfill the regulatory requirements of a new region based on data produced in the originating region.³⁰ At this point, the only remaining barrier to acceptance would be the concerns of

21. Anderson, *supra* note 11.

22. Stanford Jhee and Edyta Frackiewicz, *Bridging Strategies May Help Put Western Drugs on the Japanese Market*, APPLIED CLINICAL TRIALS, Sept. 1, 2003, <http://www.actmagazine.com/appliedclinicaltrials/article/articleDetail.jsp?id=79907>.

23. Carly Anderson and Faiz Kermani, *Global Acceptability of Clinical Data – Fact or Fiction?* <http://www.samedanltd.com/members/archives/EPC/Autumn2002/CarlyAnderson.htm>, (last visited Apr. 16, 2006).

24. *Id.* See also Jhee and Frackiewicz, *supra* note 22.

25. Anderson and Kermani, *supra* note 23.

26. ICH E5, *supra* note 1, at 2.

27. *Id.*

28. *Id.* at 2, 5.

29. *Id.* at 2.

30. *Id.* at 3.

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the relevant regulatory authority that “ethnic factors” might impede the extrapolation of clinical data produced in one region to apply to the new region. The concern here would be that populations from one region might have significantly different responses to particular drug, either in terms of safety or efficacy, than populations from another region. ICH E5 therefore both defines the parameters of the ethnic factors to be considered in evaluating drug response, and provides for conducting smaller “bridging studies” where necessary, to confirm relevant safety and efficacy information in the new regions population.³¹

Regulatory authorities from the three ICH regions, however, are concerned about population-based averages of drug response and the degree to which any overall variation might be attributable to ethnic factors. Responses to any drug may vary from individual to individual. Indeed, for every drug, there are some individuals who will respond better or worse or not at all, depending in part on their genes. Some genes also play a substantial role in regulating how the body metabolizes as drug. Finding an optimal dosage for a particular drug may be aided by determining whether a particular individual’s genetic profile would lead her to metabolize a drug more quickly or slowly than another.³² One irony in the promulgation of ICH E5 as a means to overcome regulatory barriers to the adoption of new drugs in different regions, especially Japan, are studies showing that that *intra*-ethnic variability in drug response is generally no greater than *inter*-ethnic variability.³³ Thus, as one study found,

Even when there may be a statistically significant difference between two or more ethnic groups in a given pharmacokinetic parameter of a drug, it is unclear how such difference relates to the total population variance in that parameter. In fact, previous surveys of potential ethnic differences in pharmacokinetics relevant to drug development and registration have suggested that in some cases, interethnic differences appear no larger or smaller than intraethnic variations.³⁴

Another study conducted by the Japanese Ministry of Health and Welfare and the Japanese Pharmaceutical Association examining eighty New Chemical Entities approved both in Japan and in the West similarly found intraethnic differences were greater than interethnic differences.³⁵ Nonetheless, the concept of *interethnic*

31. *Id.* at 3, 5-7.

32. B. Evans et al., *Creating Incentives for Genomic Research to Improve Targeting of Therapies*, 10 NATURE MED. 1298 (2004).

33. T. Bjornsson et. al., *A Review and Assessment of Potential Sources of Ethnic Differences in Drug Responsiveness*, 43 J. OF CLINICAL PHARMACOLOGY 943, 944 (2003).

34. *Id.*

35. Helen Dumitriu, *Impact of the ICH Guideline on Ethnic Differences*, 32 DRUG INFORMATION J. 141, 142 (1998).

variation lies at the heart of ICH E5 and of the subsequent development of a new industry in bridging studies that has emerged in order to facilitate the entry of Western drugs into the Japanese market.³⁶

ICH E5 defines “ethnic factors” as “factors relating to races or large populations grouped according to common traits and customs.”³⁷ It makes a further key distinction between what it characterizes as “intrinsic” versus “extrinsic” ethnic factors.³⁸ It defines “intrinsic ethnic factors” as “factors that help define and identify a subpopulation and may influence the ability to extrapolate clinical data between regions. Examples of intrinsic factors include genetic polymorphism, age, gender, height, weight, lean body mass, body composition, and organ dysfunction.”³⁹ In contrast, it defines “extrinsic ethnic factors” as “factors associated with the environment and culture in which a person resides. Extrinsic factors tend to be less genetically and more culturally and behaviorally determined.”⁴⁰ At first blush, this distinction seems straightforward and relatively unproblematic. However, ICH E5 elaborates upon these definitions in a chart presented in its appendix in a manner that is far more troubling.

Specifically, the chart locates race as an intrinsic *genetic* characteristic. That is, it constructs race as some sort of genetic component of a larger category of ethnicity. Intrinsic ethnicity, in this scheme is presented as encompassing both genetic and other broader and more variable biological components, such as age, disease and cardiovascular function – each of which can affect the absorption, distribution, metabolism and excretion (ADME) of drugs. Extrinsic ethnicity here refers to social, environmental and cultural factors – factors “extrinsic” to the physical human organism. The chart is highly problematic for a number of reasons.

First is the basic definition of what counts as an ethnic and/or racial group. Race and ethnicity are not static objective categories. Rather they have changed dramatically over time and across space. The U.S. Census is a prime example. Since the first census in 1790, racial categories have changed over time to reflect the social and political concerns of the day. The first census had four categories: Free White Males, Free White Females, Other Free Persons, and Slaves.⁴¹ During

36. Jhee and Frackiewicz, *supra* note 22.

37. ICH E5, *supra* note 1, at 9.

38. *Id.* at 9-10.

39. *Id.* at 10.

40. *Id.* at 9.

41. MELISSA NOBLES, *SHADES OF CITIZENSHIP: RACE AND THE CENSUS IN MODERN POLITICS*

the nineteenth century, additional categories that fell in and out of use included Free Colored Persons, Black, Mulatto, Quadroon, Octoroon, Indian, Chinese, and Japanese.⁴² The twentieth century saw a new proliferation of categories including Hindu, Korean, and Negro.⁴³

Second, whatever they are, race and ethnicity are not genetic. Scientists may and do disagree on the utility of using particular racial or ethnic categories as *surrogates* for genetic groupings, arguing about different frequencies of particular genetic variations. But race and ethnicity themselves are not genetically coherent concepts.⁴⁴ Rather, they are best understood as complex and dynamic social constructs.⁴⁵ Indeed, since the 1970s, scientists have understood that race will statistically explain only a small portion of human variation.⁴⁶ As a recent editorial in *Nature Biotechnology* asserted, “[r]ace is simply a poor proxy for the environmental and genetic causes of disease or drug response. . . . Pooling people in race silos is akin to zoologists grouping raccoons, tigers and okapis on the basis that they are all stripey.”⁴⁷

Third, as noted above,⁴⁸ studies conducted largely in response to concerns raised by ICH E5 have shown that variation in drug response is often greater *within* ethnic groups, however defined, than *across* ethnic groups. This comports naturally with the observation made in a 2001 editorial in the journal *Nature Genetics* that, “scientists have long been saying that at the genetic level there is more variation between two individuals in the same population than between populations and that there is no biological basis for ‘race.’”⁴⁹

Fourth, with respect to the specific application of the ICH E5 criteria, one study

28 (2000).

42. *Id.* at 28, 44.

43. *Id.* at 44. See also generally MARGO ANDERSON, *THE AMERICAN CENSUS: A SOCIAL HISTORY* (Yale University Press 1988); Sandra Soo-Jin Lee et al., *The Meaning of ‘Race’ in the New Genomics: Implications for Health Disparities Research*, 1 *YALE J. HEALTH POL’Y L. & ETHICS* 33 (2001).

44. Francis Collins, *What We Do and Don’t Know About ‘Race,’ ‘Ethnicity,’ ‘Genetics and Health at the Dawn of the Genome Era*, 36 *NAT. GEN.*, S13-15 (2004).

45. See, e.g., American Anthropological Association, *Response to OMB Directive 15: Race and Ethnic Standards for Federal Statistics and Administrative Reporting*, Sept. 1997, available at <http://www.aaanet.org/gvt/ombdraft>; American Anthropological Association, *Statement on Race* (1998), available at <http://www.aaanet.org/stmts/racepp.htm> [hereinafter AAA, *Statement*].

46. Richard Lewontin, *The Apportionment of Human Diversity*, 6 *EVOL. BIOL.* 381, 381-84 (1972).

47. Editorial, *Illuminating BiDiL*, 23 *NAT. BIOTECH.* 903, 903 (2005).

48. See *supra* text accompanying notes 32-35.

49. Editorial, *Genes, Drugs and Race*, 29 *NAT. GEN.* 239, 239 (2001), available at <http://www.nature.com/ng/journal/v29/n3/full/ng1101-239.html>.

noted that “considering the general nature of these guidelines, there is clearly the potential for different regions or countries to apply different interpretations, thus potentially defeating some of the goals of the guidelines.”⁵⁰ This is in part because the different ethnic groups are not always well characterized, and also because even when clearly characterized the definitions often presume more homogeneity within the group than is warranted.⁵¹

Finally, in a world rife with historical examples of stigma and discrimination based on false constructions of particular groups as biologically different (and/or inferior) the geneticization of race is fraught with peril.⁵² One need not identify specific, immediate consequences that might flow directly from the ICH guidelines to caution that the formal, regulatory adoption of genetic conceptions of race could contribute to unintended and unforeseen negative consequences.

III. The Immediate Commercial Impact of ICH E5

In recent years an entire industry has grown up around global human subject recruitment and research for clinical trials in drug development.⁵³ Companies known as Contract Research Organizations (CROs) span the globe on behalf of Western pharmaceutical corporations looking to outsource clinical trials to more economical venues, often in developing nations.⁵⁴ These foreign sites are attractive not only because trials are cheaper, but also because human subjects are often easier to recruit, are more deferential to medical authority, and are “treatment naïve,” that is, they are not already on other pharmaceutical therapies that might mask or interfere with the effect of the drug being tested.⁵⁵ CROs have become big business as the pace of clinical outsourcing has accelerated. A recent study shows that clinical outsourcing has become a significant basis for new growth among major pharmaceutical corporations.⁵⁶

50. Bjornson, *supra* note 33, at 961.

51. *Id.* at 959-61.

52. The literature on this topic is vast and varied. *See generally* DANIEL KEVLES, IN THE NAME OF EUGENICS (1998); STEPHEN JAY GOULD, THE MISMEASURE OF MAN (1996).

53. *See generally* Adriana Petryna, *Ethical Variability: Drug Development and Globalizing Clinical Trials*, 32 AM. ETHNOLOGIST 183 (2005).

54. *Id.*; *See also* Jennifer Kahn, *A Nation of Guinea Pigs*, WIRED, Mar. 2006, available at <http://www.wired.com/wired/archive/14.03/indiadrug.html>.

55. *Id.*

56. Wai Lang Chu, *Clinical Outsourcing Drags Big Pharma Out of Doldrums*, DRUGRESEARCHER.COM, May 11, 2006, <http://www.drugresearcher.com/news/ng.asp?n=67643-tufts-outsourcing-clinical-trials>.

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In the aftermath of the adoption of ICH E5 in 1998, a new variant of this industry emerged – CROs dedicated to conducting bridging studies, largely focused on gaining entry to the Japanese pharmaceutical market. Thus, for example, Focus Clinical Drug Development (Focus), a CRO that split from SmithKline Beecham in 1992, has developed a specialized service in bridging studies which it advertises as providing “studies in healthy Japanese volunteers outside Japan.”⁵⁷ Focus notes that “[p]hase I studies involving both Japanese and White volunteers are a key element for a rapid global drug development strategy,”⁵⁸ and asserts that it “can provide pharmaceutical and biotech companies a more efficient way to conduct ICH-E5 compliant bridging studies outside Japan.”⁵⁹ Focus offers standing “panels” of “440 Healthy Japanese volunteers (male/female)”⁶⁰ most of whom are students in Europe, and “4,400 Healthy White Volunteers (male/female)”⁶¹ who it defines as “people with origin in Europe (including the western part of Russia), North Africa or Middle East.”⁶² These panels recapitulate the problematic ethnic/racial categories underlying the ICH E5 and present the same problems discussed above.⁶³ Nonetheless, Focus emphasizes that “[o]ur experience shows that Phase I bridging studies can be conducted outside Japan and based on our expertise are acceptable to the Japanese authorities.”⁶⁴ The concentration on “White” and “Japanese” panels is not incidental. ICH E5 and bridging studies are designed primarily to provide an avenue for Western pharmaceutical corporations to gain access to the lucrative Japanese market which hitherto had used concerns about ethnic variation in drug response as a non-economic barrier to trade.

Similarly, Richmond Pharmacology bills itself as the “largest provider of Japanese/Caucasian bridging studies in Europe.”⁶⁵ Clients of Richmond’s bridging studies include “US and European companies that want to launch into the Japanese

57. Focus Clinical Drug Development, Bridging Studies, <http://www.bridgingstudies.de/> (last visited Sept. 20, 2006).

58. Focus Clinical Development, Introduction: Bridging Studies, <http://www.bridgingstudies.de/html/bridgingstudies.html> (last visited Sept. 20, 2006).

59. *Id.*

60. Focus Clinical Development, Panels and Recruitment, <http://www.bridgingstudies.de/html/panel.html> (last visited Sept. 20, 2006).

61. *Id.*

62. *Id.*

63. *See supra* text accompanying notes 41-51.

64. Focus Clinical Development, Our Offer, <http://www.bridgingstudies.de/html/offer.html> (last visited Sept. 20, 2006).

65. Bridging Studies from Richmond Pharmacology, Ltd., Welcome, <http://www.bridgingstudies.com/> (last visited Sept. 20, 2006).

pharmaceutical market.”⁶⁶ Richmond boasts “a dedicated in-house Japanese recruitment department, supported by a specialized marketing strategy and the bespoke brand trials⁴Japanese. Through this innovative approach, we receive circa 250 enquiries per month from potential Japanese volunteers.”⁶⁷

These CROs construct their bridging studies around a presumption of intrinsic difference between the “Japanese” and “White” or “Caucasian” members of their human subjects panels. Such studies have provided the basis for successful drug applications to Japanese regulatory authorities. Ironically, however, Chikayuki Naito, Counselor to the Tokyo Teishin Hospital and Technical Advisor to the Japanese Organization for Pharmaceutical Safety and Research, has noted that intrinsic differences in drug response are likely nowhere near as significant as extrinsic factors such as medical practice.⁶⁸

Studies of the early effects of ICH E5 published in 2002 by CMR International, (which describes itself as “the foremost provider of R&D performance metrics to the global pharmaceutical industry”⁶⁹) found “little effect on the number of trials conducted in the EU and US,”⁷⁰ but also indicated an industry-wide belief that ICH E5 was expected to have “positive effects in terms of reducing the number of patients required for trials conducted in Japan,”⁷¹ and would “lead to a reduction in costs and development times for new drugs.”⁷² One of the CMR studies noted that until the introduction of ICH E5 “repeat clinical trials were a fact of life in drug development if a company wished to market a drug in more than one ICH region.”⁷³ ICH E5 marked a turning point in global drug development with Pfizer gaining approval of Viagra® in Japan less than a year after the guideline was finalized.⁷⁴ Between 1999 and 2003, with Viagra leading the way, twenty new drug applications were approved in Japan based on bridging studies and an

66. Bridging Studies from Richmond Pharmacology, Ltd., Who We Work With, <http://www.bridgingstudies.com/who/> (last visited Sept. 20, 2006).

67. Bridging Studies from Richmond Pharmacology, Ltd., Volunteer Panels, <http://www.bridgingstudies.com/volunteers/> (last visited Sept. 20, 2006).

68. Chikayuki Naito, *Necessity and Requirements of Bridging Studies and Their Present Status in Japan*, 38 INT’L J. CLINICAL PHARMACOL. & THER. 80, 80-81 (2000).

69. CMR International, Home: About Us, <http://www.cmr.org/> (last visited Sept. 20, 2006).

70. Carly Anderson, Neil McAulsane & Stuart Walker, *R&D Briefing No. 36: The Impact of the ICH E5 Guideline on Global Drug Development*, 36 CMR INT’L 1, 5 (2002), available at http://www.cmr.org/pdf/r_d36.pdf.

71. Anderson and Kermani, *supra* note 23.

72. *Id.*

73. *Id.*

74. *Id.*

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additional twenty-four were approved using important foreign data as references, leading one study to conclude that “the bridging strategy is becoming a common and practical basis for the decision making of marketing approvals of new drugs in Japan.”⁷⁵ Another 2002 study of the ICH E5 noted that its “impact has been felt particularly in Japan, but as the E5 bridging strategies develop, the positive impact will be felt over a wide area in Pan-Asia and beyond to the rest of the world.”⁷⁶

IV. The FDA Guidelines

In January 2003, the FDA announced the promulgation of a Draft Guidance for Industry on the Collection of Race and Ethnicity Data for Clinical Trials for FDA Regulated Products.⁷⁷ After notice and comments, the FDA issued the final guidance September, 2005.⁷⁸ Before discussing the Guidance in detail, it is important to note that it emerged out of a longstanding concern to produce better data that would address the very real problem of health disparities in the United States. Prominent federal mandates leading up the Guidance include the NIH Revitalization Act of 1993, which directed the NIH to develop guidelines for including women and minorities in NIH-sponsored clinical research,⁷⁹ and the Food and Drug Modernization Act of 1997 (FDMA) which directed the FDA to examine issues related to the inclusion of racial and ethnic groups in clinical trials of new drugs.⁸⁰ The FDMA led to the promulgation of the FDA Guidance and the NIH has also issued detailed guidelines and guidance mandating certain procedures and practices concerning the inclusion of ethnic and racial minorities in clinical trials.⁸¹

Thus, for example, the NIH “Policy on Reporting Race and Ethnicity Data”

75. Shunsuke Ono, et al., *Utilisation of Foreign Clinical Data in Japanese New Drug Approval Review: On What Basis Did the Regulatory Agency Accept Them?*, 18 INT’L J. OF PHARM. MED. 159 (2004).
76. Frank Rockhold, *Industry Perspectives on ICH Guidelines*, 21 STAT. MED. 2949, 2955 (2002).
77. 68 FED. REG. 4788; *See also*, UNITED STATES FOOD AND DRUG ADMINISTRATION (FDA), GUIDANCE FOR INDUSTRY: COLLECTION OF RACE AND ETHNICITY DATA IN CLINICAL TRIALS (2003).
78. FDA, GUIDANCE FOR INDUSTRY: COLLECTION OF RACE AND ETHNICITY DATA IN CLINICAL TRIALS (2005), *available at* <http://www.fda.gov/cder/guidance/5656fml.pdf> [hereinafter DRAFT GUIDANCE 2005].
79. NIH Revitalization Act of 1993, PUB. L. 103-43 (1993).
80. Food and Drug Modernization Act of 1997, PUB. L. 105-115 (1997).
81. UNITED STATES NATIONAL INSTITUTES OF HEALTH, NIH GUIDELINES ON THE INCLUSION OF WOMEN AND MINORITIES AS SUBJECTS IN CLINICAL RESEARCH (2000), *available at* http://grants.nih.gov/grants/funding/women_min/guidelines_update.htm.

states, *inter alia*, that, the “NIH requires all grants, contracts, and intramural projects conducting clinical research to address the Inclusion of Women and Minorities. . . . Investigators are instructed to provide plans for the total number of subjects proposed for the study and to provide the distribution by ethnic/racial categories and sex/gender.”⁸² Similarly, the FDA recommends that individuals or corporations submitting drug approval applications use “a standardized approach for collecting and reporting race and ethnicity information in clinical trials conducted in the United States and abroad for certain FDA regulated products.”⁸³ As any federally funded researcher knows, these mandates impose significant requirements and provide incentives to identify and collect research data according to categories of race and ethnicity.

The federally mandated racial and ethnic categories, however, are not biomedical in origin; rather they derive from the Office of Management and Budget’s (OMB) 1997 “Revisions to the Standards for the Classification of Federal Data on Race and Ethnicity.”⁸⁴ These standards set forth “five minimum categories for data on race: American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, and White.”⁸⁵ There are “two categories for data on ethnicity: ‘Hispanic or Latino,’ and ‘Not Hispanic or Latino.’”⁸⁶ These categories provide the basis for the classification of all federal data on race and ethnicity, most notably, the census.

The OMB Standards, however, contain an important caveat: “The racial and ethnic categories set forth in the standards should not be interpreted as being primarily biological or genetic in reference.”⁸⁷ These categories were developed to serve social, cultural, and political purposes. When the federal government requires biomedical researchers and clinicians to import these social categories into explicitly biological and/or genetic contexts, it is creating a structural situation in which social categories of race and ethnicity may easily become confused and conflated with biological and genetic categories in day to day practice.

82. NATIONAL INSTITUTES OF HEALTH, NIH POLICY ON REPORTING RACE AND ETHNICITY DATA: SUBJECTS IN CLINICAL RESEARCH, NOTICE: NOT-OD-01-053 (2001), *available at* <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-01-053.html>.

83. DRAFT GUIDANCE 2005, *supra* note 78, at 1.

84. OFFICE OF MGMT. & BUDGET, EXECUTIVE OFFICE OF THE PRESIDENT, REVISIONS TO THE STANDARDS FOR THE CLASSIFICATION OF FEDERAL DATA ON RACE AND ETHNICITY (2003), *available at* <http://www.whitehouse.gov/omb/fedreg/ombdir15.html>.

85. *Id.*

86. *Id.*

87. *Id.*

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In a “*Talk Paper*” discussing the issuance of the Draft Guidance in 2003, the FDA elaborated upon their nature and purpose:

FDA regulations require drug sponsors to present an analysis of data according to age, gender and race. An analysis of modifications of dose or dosage intervals for specific groups is also required when manufacturers submit a new drug application for approval by FDA. To accomplish this, FDA recommends that the drug manufacturers use the OMB race and ethnicity categories during clinical trial data collection to ensure consistency in evaluating potential differences in drug response among racial and ethnic groups.⁸⁸

Consistency is a key theme throughout the Draft Guidance. It exhibits a general concern to regularize the collection and submission of data on race and ethnicity across the spectrum of clinical trials and the drug development process. The Draft Guidance specifically recommends the use of the OMB categories of race and ethnicity, first, to “help ensure consistency in demographic subset analyses across studies,” and second to help evaluate “potential differences in the safety and efficacy of pharmaceutical products among population groups.”⁸⁹ The Guidance elaborates the rationale for this concern by referencing some studies that show *on average* members of certain OMB racial groups *may* respond differently to certain drug than members of other OMB racial groups.⁹⁰ That is, the Guidelines connect race and physiology. This in itself is highly problematic, as discussed above in reference to the ICH E5 definition of race.⁹¹

The FDA Guidance contains the OMB caveat that its racial and ethnic categories are not to be interpreted as biological or genetic, but its recommendations, being based on physiological processes, nonetheless exist in tension with it. This tension was recognized and seized upon by many pharmaceutical companies in offering comments to the Draft Guidelines in 2003. The response of pharmaceutical companies, however, was not uniform. Large pharmaceutical companies with global marketing concerns focused in particular on inconsistencies between the FDA mandated use of the distinctively American OMB categories of race and ethnicity (e.g. “African American,” “Hispanic”) and those used internationally in other ICH regions.⁹² Their comments tended to call for a more sophisticated use of population categories that could be more easily integrated with the structure of ICH E5 and more readily translatable across

88. FDA, FDA TALK PAPER: FDA ISSUES GUIDANCE FOR COLLECTION OF RACE AND ETHNICITY DATA IN CLINICAL TRIALS FOR FDA REGULATED PRODUCTS (2003), available at www.fda.gov/bbs/topics/answers/2003/ans01193.html.

89. DRAFT GUIDANCE 2005, *supra* note 78, at 2, 3.

90. *Id.* at 3.

91. *See supra* text accompanying notes 41–51.

92. *See infra* pp. 24–26.

regions.⁹³ Smaller biotechnology companies tended to be less concerned with the international ramifications of the Guidance but rather urged the adoption of new genetic technologies to provide more precise population categories for the collection of data.⁹⁴

Generally speaking, comments submitted by pharmaceutical corporations expressed concern over (1) inconsistent definitions of race and ethnicity, (2) questionable accuracy of definitions of race and ethnicity, (3) the negative impact that using OMB categories of race and ethnicity might have on global trial recruitment, and (4) the creation of unnecessary and unscientific differences among populations through the use of inappropriate racial and ethnic categories. Underlying the concerns of large pharmaceutical corporations in particular was a perceived need to develop a globally applicable standard for the collection of racial and ethnic data – clearly more inline with the mandate of ICH E5. In short, where the ethnic categorizations of ICH E5 were perceived as opening up global markets, the OMB-based racial and ethnic classifications of the FDA Guidance were perceived as a potential barrier to globalization of drug markets.

A. Inconsistent Definitions

The Pharmaceutical Research and Manufacturers of America (PhRMA) describes itself as representing “the country’s leading pharmaceutical research and biotechnology companies, which are devoted to inventing medicines that allow patients to live longer, healthier, and more productive lives.”⁹⁵ It opened its comments to the FDA Draft Guidance with an admonition that “for these categories to be valuable globally and to permit identification of ethnic differences, there should be only one set of agreed ethnic/racial categories.”⁹⁶ It therefore recommended that the issue be brought to the ICH as a forum for the development of globally consistent categories.⁹⁷ Comments submitted by Pharmacia⁹⁸

93. *Id.*

94. *Id.*

95. PhRMA, About PhRMA, http://www.phrma.org/about_phrma/ (last visited Sept. 25, 2006)

96. PhRMA, PHRMA COMMENTS/RECOMMENDATIONS -DRAFT GUIDANCE FOR INDUSTRY ON THE COLLECTION OF RACE AND ETHNICITY DATA IN CLINICAL TRIALS FOR FDA REGULATED PRODUCTS 1 (2003), *available at* <http://www.fda.gov/ohrms/dockets/dailys/03/Apr03/040103/8005b2dc.pdf>.

97. *Id.*

98. PHARMACIA, PHARMACIA’S 5 MAR. 2003 COMMENTS RE *GUIDANCE FOR INDUSTRY - COLLECTION OF RACE AND ETHNICITY DATA IN CLINICAL TRIALS* (2003), *available at* <http://www.fda.gov/ohrms/dockets/dailys/03/Mar03/030703/02d-0018-c000001-01->

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(subsequently acquired by Pfizer) largely replicated comments submitted by PhRMA, and focused in particular on the myriad ways in which the Guidance threatened to obstruct pharmaceutical globalization. With regard to inconsistent definitions of race and ethnicity, Pharmacia observed that,

The OMB race and ethnicity categories can be used only in the US, not in the EU or in Japan; this is especially true for the ethnicity questions (Hispanic/Latino vs. Not Hispanic/Latino). A definition of the ethnicity varies among the ICH countries, as well as non-ICH countries. There will be more opportunities for the US to utilize foreign clinical data in evaluating safety and efficacy of new drugs in the future. Therefore, it is recommended that the race and ethnicity categories should be more scientific and globally accepted so that the data comparison becomes more meaningful and provides valuable information in evaluating potential differences or similarities in safety and efficacy of new drugs among population subgroups.⁹⁹

There is a clear recognition here that the OMB definitions of race and ethnicity are not static, scientifically objective categories. Pharmacia (and PhRMA) is concerned that imposing the US regulatory definitions of race on the pharmaceutical industry will inhibit the globalization of pharmaceutical markets. Its comments explicitly reference the ICH and later employ the E5's distinction between intrinsic and extrinsic factors in evaluating the significance of race and ethnicity in drug development.¹⁰⁰ Ironically, though, the comments also assume that it will be somehow possible to develop categories of race and ethnicity that are "more scientifically and globally accepted." The key focus here seems really to be on global acceptance – hence the reference to the ICH structure. Comments submitted by Abbot Laboratories expressed a similar concern that the OMB categories were "oversimplified" and "vague," and urged that the FDA "recommend a better definition of race and ethnicity that can be understood by a subject in a study and be consistent across the board."¹⁰¹ Bristol-Meyers Squibb also noted that the Guidance's "proposed ethnicity and racial categories may be understood differently in different parts of the world," and urged the development of "better defined categories."¹⁰² Thus, for example, it proposed that the OMB

vol1.pdf [hereinafter PHARMACIA COMMENTS RE GUIDANCE].

99. *Id.* at 1.

100. *Id.*

101. ABBOTT LABORATORIES, COMMENTS ON THE DRAFT GUIDANCE FOR INDUSTRY ON THE COLLECTION OF RACE AND ETHNICITY DATA IN CLINICAL TRIALS FOR FDA REGULATED PRODUCTS 3, (2003), available at <http://www.fda.gov/ohrms/dockets/dailys/03/Mar03/032703/80059c93.pdf>.

102. BRISTOL-MYERS SQUIBB PHARMACEUTICAL RESEARCH INSTITUTE, RE: DOCKET NO. 02D-0018, DRAFT GUIDANCE FOR INDUSTRY ON THE COLLECTION OF RACE AND ETHNICITY DATA IN CLINICAL TRIALS FOR FDA REGULATED PRODUCTS AVAILABILITY, (2003)

category of “Black or African American” be revised to “Black, of African heritage or African American.”¹⁰³ Given the OMB’s own caveat that its categories are not genetic or biological, the clear concern is such a proposal is not to present a more “scientific” definition of race but rather to produce a more globally acceptable definition. The two are not necessarily the same.

Of all the OMB categories incorporated in the Guidance’s mandate, the ethnicity category of “Hispanic or Latino” caused particular concern in terms of consistent global application. Bristol Meyers Squibb noted that, “the requirement that Hispanic or Latino versus not Hispanic or Latino ethnicity be collected even in trials that are conducted entirely outside the US seems contradictory to the spirit of the ICH guidelines. If ethnicity designations, as per the guidance, are to reflect the sociocultural construct of the society, then the proposed category is generally inappropriate outside the United States.”¹⁰⁴ Again, there is a patent concern for potential conflict with the ICH E5 guidelines and resulting barriers to the efficient globalization of markets.

B. Questionable Accuracy

The asserted inappropriateness of the Latino/Hispanic category in a global context was also used to highlight the questionable accuracy of the Guidance’s terminology. Thus, Pharmacia argued that “[t]he terms Hispanic and Latino will not have the same meaning outside the U.S. as they do within the U.S. According to the definition, Spaniards are considered Hispanic, but they are both culturally and racially more similar to French than Mexicans.”¹⁰⁵

Similarly, Bristol Meyers Squibb notes that, “terminology – like ‘Latino’ – can be confusing outside the United States, while the medical relevance of such category is not demonstrated inside the US.”¹⁰⁶ Pharmacia goes on to make similar criticisms of the accuracy of the OMB categories noting that “there is no distinction among the Asian group, which may be more genetically variable.”¹⁰⁷ In mentioning similarity and difference, medical relevance, and genetic variability, these comments go beyond the earlier stated concern for globally consistent

available at www.fda.gov/ohrms/dockets/dailys/03/Mar03/032603/02d-0018-c000006-01-vol1.pdf.

103. *Id.*

104. *Id.*

105. PHARMACIA COMMENTS RE GUIDANCE, *supra* note 98.

106. Bristol-Meyers, *supra* note 102.

107. PHARMACIA COMMENTS RE GUIDANCE, *supra* note 98.

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definitions to the basic scientific accuracy of the categories themselves. And yet, after these criticisms, the corporations do not call upon the FDA to reject such classificatory schemes as inherently lacking “medical relevance” for drug development, but rather simply suggests developing more globally applicable, uniformly adoptable ethnic and racial categories – categories, in short, whose primary purpose is to serve efficient globalization rather than accurate science.

Significantly, however, smaller biotechnology companies specializing in genetic research urged a different approach to overcoming similar problems of definitional accuracy. These companies, notably Genaissance Pharmaceuticals and DNAPrint Genomics do not have the global reach of corporations such as Pharmacia or Bristol Meyers Squibb. Genaissance, for example, describes itself as “a biotechnology company whose business is based on the discovery of human gene variation for the development of personalized medicines.”¹⁰⁸ It markets its technology to large pharmaceutical corporations rather than engaging directly in global drug development and marketing.¹⁰⁹ The focus of their criticisms of the FDA Guidance, therefore, was less on developing globally consistent categories of race and ethnicity, and more on using their own proprietary genetic technologies to provide purportedly more scientifically objective and accurate definitions of race and ethnicity.

In its comments on the OMB Categories employed by the Draft Guidance, Genaissance focused on genetic accuracy, observing that,

Although these categories may be useful for national demographics, they are substandard with regard to the state-of-the-art in genetic analysis of ancestry. In a population such as the United States that increasingly is mixed, the boundaries between these classifications are likely to be blurred further. For example, Genaissance has conducted genetic analysis of Hispanic populations from Florida and California. It is very clear that the label “Hispanic” encompasses individuals with African descent and Native American descent, as well as Caucasian descent.¹¹⁰

Genaissance here very subtly introduces the concept of genetic ancestry as a metric to assess the validity of the OMB categories of race and ethnicity. In speaking of blurring and mixing, the comment implies that there are some underlying genetically pure categories of “Caucasian,” “African,” and “Native

108. GENAISSANCE PHARMACEUTICALS, FEDERAL REGISTER DOCKET NO. 02D-0018, COMMENTARY ON THE FDA GUIDANCE FOR INDUSTRY “COLLECTION OF RACE AND ETHNICITY DATA IN CLINICAL TRIALS” (2003), *available at* <http://www.fda.gov/ohrms/dockets/dailys/03/Apr03/040103/8005b2de.pdf>.

109. *Id.*

110. *Id.*

American” – a very problematic assertion. Moreover, focusing, like many other comments, on the term “Hispanic” as mixed and blurred, it sets forth a straw man. It is precisely because of the lack of conceptual congruence between the term Hispanic/Latino and terms such as African, Caucasian, and Native American that the OMB separated out ethnic from racial categories.

Nonetheless, Genaissance recognizes the questionable accuracy of using *any* racial or ethnic categories in the context of pharmaceutical research and development. Commenting on the Draft Guidance’s discussion of the relation between race and drug metabolism, Genaissance notes that, “the link between these clinical outcomes and race is anecdotal at best and discriminatory at worst. New genetic technologies offer much more precise relationships between the genotype of an individual and the clinical management of disease.”¹¹¹ Genaissance presents a solution to this problem in the form of its proprietary technology which it asserts “would afford a high-resolution genetic identification of ancestry, consistent analysis of ethno-geographic backgrounds, and possible use directly to diagnostics for improvement of drug therapy.”¹¹² That is, it urges the FDA to replace OMB categories of race with genetic categories of ancestry, recommending “the adoption of new genetic systems for ancestry determination rather than antiquated and potentially inaccurate racial denominations.”¹¹³ Unlike the suggestions from large pharmaceutical corporations, Genaissance here is less concerned with global uniformity per se and more with the purported scientific accuracy of the categories – accuracy to be provided by its own technology. One basic problem with Genaissance’s claim to more rigorous scientifically based categories of ancestry is that its own discussion of them is premised on definitions of ancestral population that essentially replicate the OMB categories. Thus, in discussing its genetic analysis of samples from US populations, it groups the samples as “African American, Asian, Caucasian, and Hispanic/Latino.”¹¹⁴

In a similar vein, the comments from DNAPrint Genomics (which describes itself as “an applied science company focused on the development and marketing of innovative genetic testing products and services,”¹¹⁵) urge that “for the sake of science and the health of us all . . . it is time to incorporate molecular

111. *Id.*

112. *Id.*

113. *Id.*

114. GENAISSANCE COMMENTARY, *supra* note 108.

115. DNAPrint Genomics, Home Page, available at <http://www.dnaprint.com/welcome/home/>.

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anthropological data metrics”¹¹⁶ to supplement the OMB categories in the collection of racial and ethnic data for clinical trials. It argues that its own proprietary genetic concept of “Biogeographical Ancestry”¹¹⁷ (BGA) is better suited for evaluating drug response than the OMB categories of race and ethnicity. Like Genaissance, DNAPrint emphasizes the lack of accuracy inherent in self-reporting of race and suggests “that the FDA should pay more attention to molecular characterization of population structure when evaluating and assisting with the construction of clinical trials.”¹¹⁸

Ironically, the genetic approaches taken by Genaissance and DNAPrint comport well with ICH E5’s own categorization of race as an intrinsic genetic factor. However the genetic approaches also suffer from the same dangers and inaccuracies as the ICH E5 definition as discussed above,¹¹⁹ despite the patina of scientific rigor layered upon them in the comments. In the end, where big pharmaceutical corporations simply want to regularize race and ethnic categories in whatever form they take so as to facilitate global drug development, small biotech companies want to take control of the actual process of racial and ethnic categorization and transform it into a function of genetics.

C. Negative Impact on Global Trial Recruitment

Beyond inconsistency and inaccuracy, large pharmaceutical companies also expressed a pragmatic concern that being required to collect data according to the OMB categories could have a significant detrimental impact on their ability to recruit human subjects for clinical trials in a global environment. Here again, the category of Hispanic/Latino was of particular concern. Pharmacia addressed this issue most directly, noting that

Asking subjects about their race/ethnicity may be very sensitive in many circumstances and could be viewed as a bureaucratic burden. Conducting a study in Japan, e.g., and asking a subject whether they are Hispanic may result in patients taking questionnaires less seriously and compromising other data being collected.¹²⁰

The specific reference to Japan echoes discussions surrounding the adoption of

116. DNAPrint Genomics, Inc. Docket: 02D-0018 - *Collection of Race and Ethnicity Data in Clinical Trials for FDA Regulated Products; Draft Guidance*, Comment Number: EC-2, (April 2, 2006), available at <http://www.fda.gov/ohrms/dockets/dailys/03/Feb03/020603/8004e14c.html>.

117. *Id.*

118. *Id.*

119. *See supra* text accompanying notes 121-23.

120. PHARMACIA COMMENTS RE GUIDANCE, *supra* note 98.

ICH E5 regarding the need to open up Japanese markets to Western pharmaceuticals. Companies wishing to conduct bridging studies in Japan in accordance with the ICH E5 guidelines certainly would not want their efforts complicated or even subverted by the dictates of the FDA Guidance. Recruiting human subjects for clinical trials is difficult under the best of circumstances. In a commercial environment where ever increasing numbers of clinical trials are being outsourced to countries around the world, Pharmacia here recognizes that the regulatory construction of race and ethnicity may pose as great a barrier to the globalization of markets as the medical construction of racial and ethnic difference that underlay Japanese barriers to the approval of Western pharmaceuticals.

D. The Creation of Unnecessary and Unscientific Difference

Many of the comments, as discussed above, challenge the accuracy and consistency of the OMB categories as a basis for collecting clinical data. An important subset of these concerns was a recognition by both Pharmacia¹²¹ and PhRMA¹²² that using the social categories of the OMB in the context of drug development might lead to the creation of the perception of relevant differences where in fact none existed. Such differences would present unnecessary barriers to global drug development. Pharmacia noted that:

The first paragraph [of the Draft Guidance] states that the categories are not based on scientific principles. It is understandable that the U.S. government wants to sort issues by various socio/cultural groups. However, if there is no scientific basis for examining the effects (either positive or negative) in these groups, doing so may provide an opportunity for identifying differences where none exist. Collecting the data by these definitions is one thing, using it to distinguish effects in different populations is another.¹²³

Pharmacia here recognizes that racial and ethnic data is a double edged sword. While it may be used to open up Japanese markets, it also may be misused and misinterpreted in a manner that obstructs markets. Once again, the OMB categories are criticized as barriers to globalization. And yet, in all of this, the calls for uniform globally applicable standards of race and ethnicity bring us back to the ICH E5 Guidelines which characterize race as an intrinsic genetic attribute – with all the problems and dangers that entails.

121. *Id.*

122. PhRMA, *supra* note 96.

123. PHARMACIA COMMENTS RE GUIDANCE, *supra* note 98.

V. Conclusion — Harmonizing Race

The FDA responded to the comments¹²⁴ and issued its final Guidance¹²⁵ in September, 2005. The final Guidance remained substantially the same as the Draft. Among the significant revisions was added text that allowed the omission of the characterization of Hispanic or Latino for international clinical trials, and a change in the characterization of “Black, of African Heritage,” to “Black” for studies conducted abroad.¹²⁶ The Guidance continues to recommend the use of the OMB categories when collecting data – even for studies conducted outside the United States, but recognizes that “these categories may not adequately describe racial and ethnic groups in foreign countries.”¹²⁷ The FDA, therefore, does seem to have been at least somewhat responsive to the concerns expressed by large pharmaceutical companies that the categories not impede global research, development and marketing. Nonetheless, the final Guidance makes no concession toward the suggestions to adopt purportedly more genetically based classifications of ancestry proposed by Genaisance and DNAPrint.

The story of ICH E5 and the FDA Guidelines reveals the complexity of navigating distinct regulatory regimes in the context of increasingly globalized drug markets. It points up the enduring conceptual power of race and ethnicity to shape understandings of human populations in diverse venues. Of greatest concern, perhaps, is that the drive to harmonize race also threatens to geneticize race. Throughout this story, race and ethnicity are presented largely as barriers to globalization – differences that need to be somehow overcome in order for markets to grow. Harmonization, both as an explicit concern of the ICH and as the unavoidable backdrop to the FDA Guidance, is providing the impetus to produce regular, standardized categories of race and ethnicity. In both ICH E5 and in the discussions surrounding the FDA Guidance, a prominent attribute of calls for harmonization has been an appeal to genetics – whether as an “intrinsic” aspect of race or as a component of “Biogeographical Ancestry.” These purportedly more objective or scientific understandings of race and ethnicity as a function of genetics are proposed as a means to stabilize the inconsistency of social categories and provide a basis for unifying global markets. In the drive to harmonize international drug development we must be careful to avoid adopting a harmonized conception of race as genetic.

124. 70 Fed. Reg. 54946 (Sept. 19, 2005).

125. DRAFT GUIDANCE 2005, *supra* note 78.

126. 70 Fed. Reg. 54946 (Sept. 19, 2005).

127. DRAFT GUIDANCE 2005, *supra* note 78.