



March 2, 2007

Division of Dockets Management  
HFA-305  
Food and Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, MD 20852

Re: Docket #2006D-0336 (for ASR Draft Guidance)  
Docket #2006D-0347 (for IVDMIA Draft Guidance)

To Whom It May Concern:

KS&A is the nation's oldest and largest non-profit organization serving individuals having one or more extra X and/or Y chromosomes, including 47XXY, Klinefelter syndrome, Trisomy X (47XXX) and XYY syndrome, as well as those persons with mosaicism involving these and associated karyotypes. These conditions are recognized as being among the most common – if not the single most common – chromosomal variations in live-born humans; and in the aggregate affect approximately *1 out of every 500* persons.

Although these individuals present with wide phenotypic variability, males and females born with an extra X or Y chromosome are known to be at increased risk of various diseases, including certain forms of cancer and auto-immune conditions, infertility and learning disabilities. The benefits of early and accurate diagnosis of affected individuals is well documented, both in terms of reducing the frustrating and exceedingly wasteful “diagnostic odyssey” that many families experience in going from one physician to the next looking for the source of various symptoms, as well as in assuring that affected individuals receive early interventions and timely treatment.

Notwithstanding, it is estimated that currently approximately 75% of the individuals who are affected by these conditions are never diagnosed – and of the 25% who are diagnosed at sometime in their life, that only approximately 25% of these are diagnosed before the age of puberty. This leaves a great majority of persons untreated and, in many instances, misdiagnosed and receiving maladaptive treatments, or missing windows for proper care.

KS&A, also known as Klinefelter Syndrome & Associates, is a 501(c)(3) non-profit organization whose mission is to help individuals with one or more extra X and/or Y chromosomes and their families lead fuller and more productive lives.

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Moreover, because these conditions were first discovered in the early 1940's, and received the greatest amount of research attention in the 1950's and 1960's, today's "best available treatment" modalities are out-dated and long overdue for re-examination using modern technologies and perspectives informed by the very latest genomic and diagnostic techniques. Beyond the benefit to the affected individuals and their families, this holds great promise for a much wider segment of the population through the very real possibility of discovering genotype-to-phenotype correlations associated with approximately 1200 genes located on the human X and/or Y chromosome, and thereby insights (and perhaps breakthroughs) respecting a myriad of common diseases and conditions affecting all humans.

At a time when our populations' principal needs are for more rapid and less costly access to the latest diagnostic testing, for all of the foregoing reasons, KS&A is concerned about any impediments that could potentially significantly delay access and/or increase the cost associated with the development and delivery of novel molecular tests for clinicians and patients. It is for this reason that we are writing to comment on the FDA's consideration of the ASR and IVDMA Draft Guidance documents, and to caution the FDA about the potentially adverse effects of enacting regulations that we fear may have a negative impact on the ability to fully tackle these conditions and the diagnosis and treatment of patients who suffer from them.

For example, we are concerned that the language in the IVDMA Draft Guidance could be read to suggest that all Laboratory Developed Tests (LDTs) are illegal; and the effect of the Draft Guidance on both ASR and IVDMA could stifle investment or slow down some of the most innovative research efforts into new and better diagnostic technologies.

It is ironic that at a time when, as a small non-profit organization, KS&A is investing our own scarce resources to try and encourage creativity and focus attention on the application of innovative molecular tests and personalized medicine on the conditions we serve, that the FDA is considering regulatory actions that might have the consequence of deterring and/or delaying such badly needed innovations. We strongly encourage you to be extra cautious to avoid this. We ask that you pay attention to the input you are receiving from those laboratories and research organizations which are making significant investments in new and improved testing techniques. We encourage you to find ways to create greater opportunities for these innovators to succeed, and to bring their conceptions to conditions such as the ones we serve at the earliest possible date and with the lowest possible cost, rather than burdening them with additional layers of costly and time-consuming regulations.

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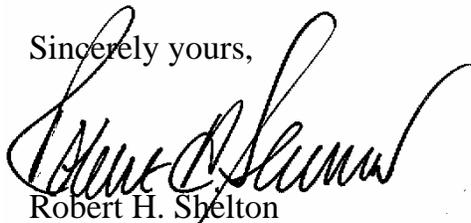
Any areas of the Draft Guidance which might tend to delay and/or undermine the value of new and innovative tests should be removed. We are concerned, should the Draft Guidances be enacted in their current form, that not only may laboratories that perform existing tests be barred from continuing those tests, but further testing and innovation will be stalled. This is a step in the wrong direction.

I previously spoke about the fact that a very small percentage of individuals affected by these conditions are ever diagnosed – and that of those who are, that most are regrettably not diagnosed until well after the time when it would be optimal for them to have begun to receive medical attention and proper educational interventions. One is left to wonder why. From our discussions, it is clear that this is *not* because the affected individuals were asymptomatic. On the contrary, many report having received much more costly and invasive therapies as a consequence of not having been properly diagnosed, and we have heard many stories from families who literally have had to beg attending physicians to order a karyotype test as the only way to conclusively diagnose these conditions.

It appears that the expense of traditional karyotype analyses in combination with the pressure providers are under to not over-use such costly diagnostic procedures is a significant cause for the lapse. One of the ways this is going to be corrected is through the development of more cost effective tests that are easier to administer and faster to read, and in turn that will lead to far less resistance to the tests being ordered. We hope you will keep in mind these needs as you consider the above-referenced Draft Guidance documents, and that you will act in a manner that is consistent with reducing hurdles, expediting breakthroughs and clearing ways for sponsors to better address rare or underserved populations such as the ones KS&A represents.

KS&A urges you to consider these important needs and wishes to thank you and your staff for your attention to the foregoing comments.

Sincerely yours,



Robert H. Shelton  
Chairman