To: University of Chicago IRB
From: [redacted]
Re: Protocol #9214 GnRH Agonist Test Gonadotropin Deficiency vs. Delayed Puberty in Teenagers

January 23, 2004

Dear Jonathan,

I met with Bob Rosenfield, MD on Friday and we discussed this protocol as well as several related protocols. The issue is whether this research is approvable without 407 review.

The study looks at puberty in healthy teenagers as well as those with delayed puberty. In addition to a physical exam, bone age (x-ray), the subjects get an IV (for blood drawing) during a sleep study and undergo a Lupron test. Lupron is a long-acting form of gonadotropin releasing hormone and is approved for sustaining puberty (although it is NOT approved for diagnostic purposes). Subjects can receive up to $200 for their participation.

Is the research minimal risk? The administration of Lupron is more problematic. In children with delayed puberty, it is clearly minimal risk. But in children who have normal puberty, or no reason to suspect delayed puberty, it requires the administration of a new drug which offers no benefit and would probably be classified as a minor increase over minimal risk.

What about the other procedures? While I am sure there is debate, the physical exam, x-ray and IV are probably minimal risk in the teenage population. However, according to Bob, some of his studies involve children as young as 6 years. I am not comfortable calling a 36 hour IV and hospital stay minimal risk in this population.

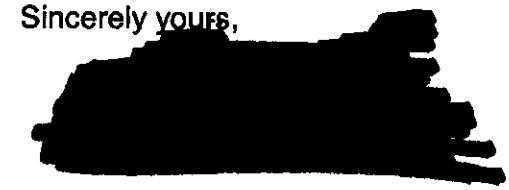
I explained to Bob several options. As I see it, since this research is on the "slow burner" due to lack of current funding, I recommended that he seek approval for now only for use in adolescents with delayed puberty. In that case, we could approve the research under 46.406. Whether 2 parents versus 1 parent provides any additional protection, the IRB committee will have to decide. I do not see that it does.

However, Bob has other protocols and other grants pending that seek to do these studies in younger children who do not have "a disease or condition" as specified by 46.406. I believe that he needs to get all of the various proposals together and that we should work with him on getting 407 review. With Bob's permission, I spoke to [redacted] who thought that several different but related proposals would be considered under a 407 panel. Without that approval, I do not see how such research can be done consistent with the current

federal regulations (with which I disagree from an ethicist's perspective, but that is for another time and place).

Thanks for asking for my input in this study. I hope this is helpful.

Sincerely yours,



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