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Memorandum

To: Trialists

Fr: Curtis Meinert

Re: More on Joe DiMaggio?

Where have you gone, Joe DiMaggio?
Our nation turns its lonely eyes to you
Wu wu wu
What's that you say, Mrs. Robinson
'Joltin Joe' has left and gone away
Hey, hey, hey,
Hey, hey, hey
(Last verse in Simon & Garfunkel's "Mrs Robinson")

The verse above was what came to mind in my note of 14 February when expressing concerns about the future of investigator-initiated trials.

In my note I cited a phase in *Toward a new era of trust and transparency in clinical trials* (Kathy L Hudson, Michael S Lauer, Francis S Collins; JAMA; published online Sept 16 2016) that "henceforth the NIH will require all applications for clinical trials to be submitted in response to clinical trial-specific Funding Opportunity Announcements (FOA)".

Nancy Geller wrote that "you misunderstood the phrase 'clinical trial-specific Funding Opportunity Announcement' which does not mean specific clinical trial funding opportunity announcement! It is meant to be a general call for clinical trials. CIRT, PROMISE and ISCHEMIA were all investigator-initiated trials which were submitted to a dedicated FOA (the NHLBI multi-center trial RFA). It is an administrative convenience to have these reviewed by a knowledgeable study section (or more than one study section if needed)."

As a literalist farmer from Sleepy Eye it is difficult to understand how something proposed de novo by researchers can be covered in "clinical trial-specific funding opportunity announcements".

Reading between the lines of Nancy Geller's note leads one to surmise that there are two kinds of funding opportunities. Opportunities open to all and "dedicated" FOAs (gimmicks to get applicants to fellow the Yellow Brick Road for submissions?).

Obviously, I need lessons in government speak!

What is required of applicants to qualify for review varies by institute, but if you are an

investigator wanting to initiate a multicenter trial funded by the Heart, Lung, and Blood Institute involving a direct per year cost of $500,000 (virtually all will) you have a formidable task ahead of you (see https://www.nhlbi.nih.gov/research/funding/500K-cost for details). Unless you are driven, the better strategy is to wait for a request for application (RFA) or request for proposal (RFP) for the trial you want to do and then apply, rather than trying to initiate the trial de novo.

So are investigator-initiated trials endangered? Hard to say because trials are not classified as to originators. In fact, many multicenter trials funded under cooperative agreements (U01s or U10s) are the result of joint NIH - investigator efforts.

The counts below are for "clinical studies" – studies typically registered in ClinicalTrials.gov – as generated from NIH RePorter (a database of NIH-funded applications). The counts are of studies funded by fiscal year, meaning studies are counted in multiple years over the period of funding. Traditionally, R01 grants are investigator-initiated and are for small single center trials. U01 and U10 awards are for cooperative agreements between study investigators and the NIH. They are usually for studies involving multiple sites and for studies with larger sample sizes than is the case for R01 awards.

FY	R01	U01/U10
2001	1,033	2,533
2002	1,162	2,741
2003	1,385	2,997
2004	1,574	3,042
2005	1,596	3,102
2006	1,704	3,258
2007	1,801	3,247
2008	1,807	3,177
2009	1,950	3,122
2010	2,021	3,125
2011	1,910	3,027
2012	1,937	3,039
2013	1,814	2,939
2014	1,709	1,670
2015	1,529	1,505

The change in counts for FY 2015 compared to FY 2001 show an increase in R01 awards, 1,529/1,033 = 1.48 and a decrease in U01/U10 awards, 1,505/2,533 = 0.59.