

Comments on Draft Guidance for Industry and Reviewers on Exploratory IND Studies (<http://www.fda.gov/cder/guidance/6384dft.htm>) and its impact on the issues discussed at the RDRC Public Meeting.

These comments from the UCLA Radioactive Drug Research Committee (RDRC) (# 0041) are made in regards to the role of RDRC in human research with new radiopharmaceuticals (RDRC Public Meeting docket (Docket No. 2004N-0432)). The FDA requested additional comments from its RDRCs about the structure and work of the RDRCs because of the added consideration of the exploratory IND (eIND) (Draft Guidance for Industry and Reviewers on Exploratory IND Studies <http://www.fda.gov/cder/guidance/6384dft.htm>), which was not made public at the time the Fed Reg notice about RDRCs came out.

This RDRC believes in an expanded role of the RDRCs to cover all radiopharmaceutical research with a *decrease*, not an *increase*, in bureaucratic requirements and limitations. Without entering into any major judgment of the merits of the eIND guidance we consider the latter to be contradictory with any intent of having a strong RDRC. If implemented, the eIND will take over the use of RDRCs to approve PET probe research, removing a safe, fast, efficient, and cost-effective oversight process run by experts with a superb 30-year track record. This would be replaced with a process run directly by FDA, which has shown itself repeatedly over three decades to be slow, hugely expensive, and lacks the personal expertise shown by RDRC members. We believe the exploratory IND process would probably be an improvement for nonradioactive drugs, but it should not apply to radiopharmaceuticals because it still has inappropriate and unnecessary pharm/tox requirements after five patients, *and these shouldn't be there at all for probes that don't have pharmacological responses or toxicological effects with the initial five patients*. If all radiopharmaceutical research is left to RDRCs, these committees may request certain research data, as appropriate, on a case by case basis, if there are any potential pharmacological or toxicological considerations for a new radiopharmaceutical, which is what is done now as needed and has been going on for the 30 years that RDRCs have operated. It is also the opinion of this committee that the FDA erroneously reported what an RDRC can do in footnote 9 on p.5 of their eIND notice of April, 2005, limiting what an RDRC can do *far* more than the actual regulations and the Statements of Consideration that accompanied the Fed Reg article back in 1975 (Fed. Reg. 40(144):31298-31313, 25 July 1975).

The RDRC has been one of the few lighting rods that have helped the introduction of new radiopharmaceuticals without any demonstrable risks to human subjects. It is a very valuable, safe tool, most particularly for academia, where resources for unnecessary and convoluted pharmacology and toxicology studies (e.g., NIH grants) exist only on very limited basis. This Committee very strongly suggests to the FDA to strengthen the role of the RDRC to facilitate the introduction of new radiopharmaceuticals, eliminate the current pharm/tox requirements and be in harmony with the needs of modern medicine

and patient health. There is no scientific evidence that would justify full blown pharmacology/toxicology studies for approval of radiopharmaceuticals that are used in nanomol quantities in human subjects. Due to the inherent safety of radiopharmaceuticals we need to continue to use the RDRC's, and expand their use, by allowing all radiopharmaceutical research to go through these committees, and avoid the bureaucratic clogging of the IND process, as has been timidly done for over 15 years for PET molecular imaging probes following Carl Peck's special determination in the late 1980's.