**IACUC Training Exercise #2 – 2020 (Why are JIT notes sent to the station?)**

The following exercise may be useful in stimulating discussion regarding compliance with PHS Policy and VA Handbook 1200.07. To facilitate discussion, page 1 of the exercise may be distributed to the IACUC members prior to a meeting. After a few minutes of discussion about the exercise during the meeting, the remainder of the exercise may be distributed to provide ideas for the committee’s consideration.

Ann Marie, the Hometown VA IACUC Manager, decided to start her morning by checking on the status of her investigators’ projects in the VA Just-in-Time (JIT) Document Manager (<https://vaww.gateway.research.va.gov/jit/>). In her experience, JIT notes are usually sent by the Office of Research & Development (ORD) to let the station know that a file does not open correctly, an appendix is missing, or some other minor administrative issue has come up. However, that was not the case with Dr. Smith’s ACORP. Ann Marie was surprised by the JIT note (see below) that the ORD reviewer had uploaded to Dr. Smith’s project.

*JIT Note to Hometown station (Smith, Edward)*

*Dr. Smith’s ACORP describes novel and important work related to advanced breast cancer targeting and imaging; the protocol is complex and difficult to follow. The major concerns are outlined below:*

*Item C.2.a concerns:*

*Additional background and significance information, such as found in the MERIT application, should be summarized to help the reader understand the rationale for the proposed experiments. The revised narrative should also address the concept of click or cycloadditional chemistry, which appears to be central to this study. Terms such as theranostic agents, CD44v6, gal-3TF, G3-C12 peptide, etc. are used with little, if any explanation, please reconcile.*

*The maximum tolerated dose studies (MTD) should be explained in greater detail? What is meant by "If after 2 weeks the mice are good ..." What is the DPT site? Parameters to determine toxicity are listed but no thresholds for toxicity are indicated. Is death the endpoint for the MTD studies? If death is not the endpoint, what are the endpoints for the mice used in the MTD study?*

*Please explain why keeping mice with larger tumor burdens would be of scientific value, how is it determined that these mice are otherwise healthy?*

*All changes to the ACORP must be clearly marked, the secondary veterinary review will be completed when the requested information is provided.*

Have you received similar JIT notes for projects at your station? What do you think the purpose of this new type of JIT note is? What should the IACUC do about this?

Ann Marie is correct, routine JIT notes usually deal with relatively minor administrative matters. Nevertheless, this new type of targeted JIT note was implemented because at least some stations have not realized that the constructive criticism provided in the secondary veterinary review of an ACORP is specifically designed to progressively improve the quality of all the protocols from the station. Instead, many of the same shortcomings continue to be in evidence in successive ACORPs from the station, and they continue to be cited repeatedly. Targeted JIT notes are meant to be an educational tool to help the investigator and the IACUC identify and correct essential concerns (i.e. borderline Level 2 issues) before the ACORP is approved. Any concern about an ACORP that is brought to the attention of the IACUC in secondary review comments should be addressed in that particular ACORP, but it should also be kept in mind as potentially applicable to future ACORPs that the IACUC reviews.

The most common reason that JIT notes are provided to stations is the lack of an adequately described experimental plan (as in item C.2, and particularly item C.2.a in the ACORP). The information provided in item C.2.a should provide a brief summary of the background and significance section of the MERIT application so that the rationale for the experiments and procedures proposed is clear and the ACORP is cohesive. JIT notes are also sent when a well-described (with supporting literature citations, when applicable) justification for an invasive and/or potentially painful procedure is missing.

In order for the secondary veterinary review to be completed, the concerns raised in the JIT note must be addressed by the investigator and the local IACUC. As with the response to a Level 2 score, it is the IACUC’s responsibility to guide the investigator to understand what is needed in response to a JIT note, and to review and approve the modifications that appropriately address the concerns. You may ask how a targeted JIT note differs from a Level 2 score? The answer is that targeted JIT notes may be provided more quickly, without waiting for completion of a full review of the ACORP, so investigators have the opportunity to make the changes promptly; satisfactory modifications will likely yield a Level 1 score. Like for a Level 2 score, the IACUC must review and approve the revisions to the ACORP before it is re-submitted in JIT. If the IACUC and the investigators consistently apply the concepts presented in the JIT notes and secondary review comments, the quality of subsequent ACORP submissions will improve. Since targeted JIT notes have been introduced, ACORPs have improved and the stations that make good use of them receive relatively few targeted JIT notes or level 2 scores.