Guidelines and Recommendations for Researchers Using Animal Cancer Models

General Approvals:

- Required Pathogen Screening of Biological Materials
    - All biological products (including cell lines, tissues, and PDXs) administered to animals must be reviewed by the DAR Quality Assurance and Diagnostic Laboratory [https://cores.emory.edu/dar/_includes/documents/BiologicalTestingPolicy_rev012022.pdf]. The purpose of this policy is to ensure that animals are not infected with adventitious pathogens through the administration of biological materials.
    - To get started, complete the Biological Submission Form located under the Lab-Related Services tab here: https://redcap.emory.edu/surveys/?s=DKA4EW4EH7W3JKMK.
    - When complete, attach the letter of approval to the Supporting Documents section at the end of your protocol.
- Required Review(s) by the Environmental Health and Safety Office
    - Biosafety Approval – such as for the use of viral vectors
    - Chemical Safety Approval – such as for the use of chemotherapeutic agents
    - Radiation Safety Approval – such as for the use of an irradiator
    - When complete, attach the letter(s) of approval to the Supporting Documents section at the end of your protocol.

eIACUC Protocol:

- Protocol Procedure Type: Substance Administration vs. Survival Surgery
    - Administration of cells percutaneously via injection with a needle should be considered a Substance Administration procedure in the eIACUC system.
    - Any procedure involving an incision in the skin should be considered a Survival Surgery in the eIACUC system. This includes subcutaneous implantation of tissue (such as for PDX models). Lab members who perform this procedure should be considered Surgeons, and the corresponding Aseptic Survival Surgery training and assessment should be completed. The analgesic recommendation for this procedure is one perioperative dose of systemic analgesic (such as meloxicam or buprenorphine).
        - To schedule training, email the DAR Training Group at dartrn@emory.edu.
- Unrelieved Pain and Distress
    - It is of the general opinion, including that of the IACUC, that cancer studies involve some aspect of unrelieved pain and distress. Therefore, the response to this question in eIACUC should be “yes.” Then, answer the questions (4i and 4ii) that follow.
    - Note that allowing animals to proceed to the default Humane Endpoints (IACUC Policy 357) +/- Tumor Burden Scoring endpoints (IACUC Policy 304) often involve some period of unrelieved pain and distress. Therefore, please specify how these endpoints will be applied, such as the timing of analgesic administration or euthanasia relative to onset of clinical signs. (Usually, intervention within 24 hours is required.)

- Endpoints
    - If appropriate, it is recommended to follow the default Humane Endpoints (IACUC Policy 357) and Tumor Burden Scoring (IACUC Policy 304).
    - If known, it is highly recommended to describe expected clinical signs (e.g., weight loss, lameness, ataxia, etc.), any supportive care to be provided (e.g., moist chow on the cage floor, subcutaneous fluids, etc.), and when endpoint has been reached (e.g., when lameness has progressed to paralysis).
    - If mortality is expected to be >10% despite appropriate monitoring, please provide a rationale.

For Peripheral Inoculations (Visible Tumors):

- Ulceration of Tumors
    - The evaluation of ulcerations is part of the tumor burden score (see IACUC Policy 304).
    - Sick Case Reporting
        - By default, all ulcerated tumors are reported as sick cases by the DAR Animal Care Staff. Therefore, an email notification will be sent to the lab from the DAR Veterinary Technician with a summary of the case. Unless additional steps are needed, the technician will periodically recheck the animals until endpoint is reached. This is in addition to the monitoring performed by the lab.
    - Recommended Treatment
        - If the ulceration is open and moist (but not infected), it is recommended to apply triple antibiotic ointment to prevent infection and therefore endpoint. Ointment should be applied 2-3x per week and documented on a cage-side treatment card (provided by Vet Staff). If elected, this treatment option should be described in the protocol.
        - Treatment is not mandatory. However, please note that the animal will reach immediate endpoint if/when infection of the ulcerated tumor is observed.
- Monitoring Plan
    - It is recommended to follow the IACUC Policy 304 Tumor Burden Scoring policy:

Cumulative Score	Appropriate Action
0	Lab personnel must assess general health and tumor progression and document TBS once per week.
1	Supportive care may be required. Lab personnel must assess general health and tumor progression and document TBS 3 times per week.
2	Euthanasia may be required. Lab personnel must assess general health and tumor progression and document TBS daily.
≥ 3	Euthanasia is mandatory.

        - "For peripheral inoculations, monitoring must begin once tumors have been inoculated. Following surgical resections, monitoring should be performed daily

until the incision is healed (or at least 7 days following surgical resection) and then revert to the schedule above for monitoring peripheral inoculations."
    - If there is a more appropriate monitoring plan for a specific tumor model, please describe in the protocol.

For Non-peripheral Inoculations (Non-visible Tumors):

- Monitoring Plan
    - It is recommended to follow the Tumor Burden Scoring policy (IACUC Policy 304):
        - "For non-peripheral or hematologic cancers or when metastases are likely, the minimum monitoring requirement is 2-3 days per week and then daily at the time of lesion detection by imaging or onset of related clinical signs. Specific details about monitoring must be detailed in the IACUC protocol."
    - For lung tumors and/or metastases, it is highly recommended to use the Pulmonary Assessment of Advanced Metastasis (PAAM) technique: https://pubmed.ncbi.nlm.nih.gov/24041215/.

References:

- See appendices in Tumor Burden Scoring policy (IACUC Policy 304)
- Policy for Pathogen Screening in Biological Materials (PDF)

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