**NECC\_TEMP2202: Formal Structure for the Minor Use Animal Drug Program**

Responses, Revisions and Comments to Peer Reviews

The Minor Use Animal Drug Program would like to thank all of the reviewers for their considered evaluation of our proposal NECC\_TEMP2202. Our responses, revisions, and comments are presented below and, where applicable, are incorporated into the revision.

**GK Review (Annotated)**

Comment GK: It might be repetitive below but I would suggest making reference to the number of label claims in which MUADP was involved, since the number of technical sections and Public Master Files completed and accepted by CVM represent the measurable, objective endpoint.

*Response: The following sentences were added: “During this period the Program has published 43 Public Master Files (PMF) supporting 59 new label claims and has published 211 peer-reviewed, scientific articles. Moreover, 18 stakeholder drug requests continue to represent needy potential projects.*

Comment GK: Inserted “food”

*Response: The insert was changed to “food and fiber” to reflect wool-producing sheep and angora goats.*

Comment GK: This paragraph doesn't really address what MUADP has been able to do - the next paragraph only talks about what happens if MUADP does not get this support. MUADP is an essential part of this important initiative by ensuring a safe food supply.

*Response: Response: The following sentence was inserted: “The data provided by the MUADP is an essential part of the NIFA initiative and funding of the Program is critical to performing this function”.*

Comment GK: Does the MUADP group have facilities to do marine (saltwater) studies? Offshore aquaculture appears to be getting the green light so it might be good to add this in as part of the networking effort.

*Response: The following was added: “The Cornell University College of Veterinary Medicine has an excellent facility and have conducted many therapeutic trials with marine finfish species including three AQUI-S20E (10% eugenol) target animal safety studies over the last three summers utilizing artificial seawater. In 22Q3 the Northeast Region is funded to test the margin of study for AQUAFLOR (florfenicol) medicated feed on marine finfish as well.”*

Comment GK: ...and help protect the safety/food security of the domestic food supply

*Response: The suggested wording was added.*

Comment GK: Might want to say how MUADP intends to move these forward - e.g., is the plan to look for sponsors to support these products?

*Response: This sentence was added: “The MUADP is currently working with the Minor Use Minor Species (MUMS) program of CVM to obtain sponsors for these outstanding INAD files.”*

Comment GK: This is a problem with the sponsor not MUADP. Might be helpful to say MUADP has kept the project on track.

*Response: This wording was added: “but due to delays in sponsor submissions, this program has failed to advance. Both CVM and the Program are working to maintain project momentum.”*

Comment GK: To enhance the impact of MUADP's role can you say something here about how the MUADP and Sponsor's efforts are complementary for the TAS section. They are both key to the ultimate end goal which is to get all the technical sections approved for a drug approval. MUADP has been very important in coordinating this effort.

*Response: This sentence was added: “The efforts of the MUADP and Sponsor are complementary for the TAS section. They are both key to the completion and approval of all the technical sections required for a drug approval. MUADP has been essential in coordinating this effort.”*

Comment GK: Is the funding group to whom this application is being sent aware of how much time and effort is required for each of these Technical Sections? Typically they take 1-2 years of hard work and a lot of back-and-forth'ing with FDA CVM. It might be helpful to say that somewhere in the text - you have a lot of successes listed here that shouldn’t be undersold!

*Response: Yes, from the beginning each sponsor is familiar with the time and effort required for the interactions with the FDA/CVM. Since Program eligibility requires a major species approval, the sponsors have previously been through the system.*

Comment GK: Explain the acronym (CIDR)

*Response: “Controlled Internal Drug Release (CIDR) device that releases progesterone /goats” was added*

Comment GK: Maybe also say something about continuing to work with new/interested sponsors to address some of the outstanding files?

*Response: The following was added to the final bullet point under incomplete work: “Coordinate with CVM Minor Use Minor Species program to work with new, interested sponsor to address some of the 88 outstanding files.”*

Comment GK: Should this one be listed above under "Other work completed or ongoing"

*Response: The lasalocid residue method development work is technically incomplete and “on hold” awaiting funding. What is required is a bridging, validation study from the major species.*

Comment GK: Are there publications in preparation for release in 2022 that could also be listed?

*Response: The following was added: “In preparation: Getchell, Rodman G., et al.: Three AQUI-S20E (10% eugenol) target animal safety studies are in preparation for publication in 2022, and the AQUAFLOR (50% florfenicol) marine finfish safety research will be submitted for publishing in 2023-2024.”*

Comment GK: General comment - do you want to say something about standards to which the FDA-CVM studies are held? Specifically, MUADP studies have to meet GLP and GMP, which are difficult, document heavy standards, so you might want to indicate that meeting these is a real achievement. Also these studies at academic institutions need to meet IACUC standards for animal welfare so that might be worth mentioning too. Not everyone can meet both of these sets of standards.

*Response: The following was inserted: “All MUADP studies are conducted under a series of government regulations and standards. These include FDA Good Laboratory Practice for Nonclinical Laboratory Studies (GLP), Good Clinical Laboratory Practice (GCLP), and Institutional Animal Care and Use Committee (IACUC) regulations. Few academically-based programs have qualified to meet such an array of regulations successfully.”*

**Reviewer 1**

Comments: There is an impressive track record of this group of scientists, and stopping the project now would not only represent a waste of scarce financial resources previously invested in the program but also cause an immediate cessation to projects that are nearing completion. This project is vitally important to US agriculture, and additional approvals of products for use in minor species should lead to growth in those industries and concomitant decrease in reliance on food imports into the US.

*Response: Thank you for the recognition of our uniqueness and importance to US agriculture. As noted above, the Program operates under a spectrum of regulations that, in combination, are generally not found in academic institutions. Continued functioning of the Program should not only lead to growth in minor species industries and a decrease in reliance on food imports, but enhance biosecurity for the US food supply.*

**Reviewer 2**

Comments: Researchers involved with this program should be lauded for having successfully obtained USDA-NIFA grants to help fund projects but additional funding is likely to be needed and is noted in the expected outcomes and impacts. In addition, these grants have allowed for the movement from individual activity(ies) to development of collective interdependent activity with that involvement collaborators from other institutions/agencies/pharmaceutical companies. Besides the publications listed, presentations based on the data generated from this program have been used to battle the misinformation about therapeutics/drug use in minor species that is often present in social media. There has also been a modest but successful educational effort and there are plans for this to continue in the immediate future.

*Response: As the Reviewer has pointed out, our education efforts have been modest. The Program has been working with the Tactical Sciences Network to enhance our outreach and educational activities through them.*

**Reviewer 3**

It may be very helpful to consider involving the product owners (NADA Sponsors) more fully in your activities. Being responsible for providing updates to CVM for several of these projects and to maintain their MUMS designation, it would be extremely helpful to be more fully updated on the progress of these projects. It is only through information received from CVM's MUM's group that I have any idea of project progress up until I read this report. It might be helpful for sponsors to be invited during reviews of their projects. I have been included in several meeting for one project and as the owner of the NADA, i have access to a great deal of information on the approval in the major species and therefore I am able to provide information that can be helpful to the research team that could both minimize cost and help speed these projects. I believe that the NADA owner could greatly assist these projects. I also suggest clarification about CIDR. This is an intravaginal device that release progesterone. The current description seems to indicate to the contrary.

*Response: The Reviewer correctly identified a significant shortfall of the program over the last three years. Communications with shareholders have been left to Regional Coordinators and CVM liaisons. This format does little to educate shareholders about the breadth of the operations. The Program is working with the Tactical Sciences Network to establish a more formal system to enhance shareholder and public knowledge of our work. As noted above, the following was added to the description: “Controlled Internal Drug Release (CIDR) device that releases progesterone /goats.”*

**Reviewer 4**

Over the past years MUADP has clearly demonstrated the capacity to conduct regulatory research and to coordinate efforts required to meet the high standards of GLP and GMP now required for drug approvals. Peer reviewed publications have helped to educate end about safe and efficacious use of these therapeutants. This solid foundation, plus the capacity to work with diverse academic institutions, is much needed to continue to address health and welfare of minor species raised for food.

*Response: Thank you for your recognition of one of the hidden features of the Program - the MUADP operates under a spectrum of regulations that, in combination, are generally not found in academic institutions. As such we are unique and we would be difficult and expensive to replace or replicate.*