



BIOMEDICAL ENGINEERING
THE HENRY SAMUELI SCHOOL OF ENGINEERING
UNIVERSITY OF CALIFORNIA, IRVINE
3418 ENGINEERING HALL
IRVINE, CA 92697-2715

KYRIACOS A. ATHANASIOU
DISTINGUISHED PROFESSOR
HENRY SAMUELI CHAIR
EMAIL: ATHENS@UCI.EDU

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RE: CLIN1-14764

Dear Ms. Bonneville and ICOC members:

We thank the reviewers from CIRM's Grant Working Group (GWG) for the positive review of our CLIN1 application. We would like to address two points brought up related to the budget for the animal studies:

1) *"Acquisition costs for 24 Yucatan pigs for example are billed as \$117,184 or \$4,882.66 per pig for the 2 month study. This is way out of line with other vendors that sell Yucatan minipigs for around \$1,800 each."*

We appreciate the concern. Indeed, one vendor has the listing price of young minipigs as low as \$1,800. However, in the budget we provide a higher price because 1) prices of minipigs from multiple vendors for the older animals needed in the CLIN1 studies are higher, 2) housing costs for pre-ordering pigs are included, and 3) delivery is also included. The figure we provide is indeed correct. Here is the explanation:

With regard to the listing price, we consulted Sinclair Bio-Resources and Premier BioSource. We found that both,

- 1) have sliding price scales for minipigs; older animals are more expensive. For example, although an 18-month old animal from Premier lists at \$1,800, a 24-month old animal from Sinclair is listed at twice as much (\$3,630).
- 2) indicate that older animals (18-24 months old) are limited in supply, making it unlikely that animals would be sourced from only one vendor.

Both companies advise that we coordinate with them ahead of time when ordering animals *older than 12 months*. We were dismayed to find that pre-ordering the animals can incur additional expenses. For example, Sinclair presented two scenarios for purchasing older animals: 1) purchasing 18-24 month-old animals when we need them at the prices listed for those ages *without any guarantee of availability*, or 2) pre-purchasing the animals while young, and then pay a per diem of ~\$26 a day until they are shipped. As an example, to be assured that animals of the specified age are available for timely proposal completion, the purchase of a single 12 month-old animal 6 months in advance would incur additional per diem costs of \$4,758; this is on top of the listing price of the animal.

The listing price noted in the review does not include delivery. Because pigs do not sweat and have relatively small lungs, they are sensitive to heat stress. This means that special precautions, such as air-conditioned transport, need to be taken in animal transport and delivery. There are differences in the delivery cost between the two vendors due to their location in relation to the vivarium (UC Davis). Premier, primarily located in Southern California, charges \$1,080 per delivery. Sinclair, located in Missouri and Maine, charges \$7,516 per delivery. Although we intend to batch animal deliveries so as to keep delivery costs at a minimum, the delivery cost is an unavoidable addition to the listing price. Using the dose-response 2-month study as an example, the cost for animal delivery alone would be \$30,064.

In summary, the price per animal far exceeds the minimum \$1,800 noted in the review because: 1) we anticipate purchasing from multiple vendors, and the vendors charge more for the older animals needed; 2) we have been advised of additional costs for pre-ordering the animals; and 3) the listing price of animals does not include delivery, which is significant, due to the precautions taken to ensure animal welfare.

2) *"Housing and care costs are exorbitant for the location. The vendor is charging \$51,590 for the 2 month study for 24 pigs or 35.82 per day, which is at least 33% higher than other CROs. For the 6 month study they are charging \$82,373 for 12 animals, or \$38.14 per pig per day."*

We apologize for the confusion but per diem for housing the minipigs at UC Davis is \$26.76. The dollar figures provided under "Housing and Care" include the per diem after surgery plus,

- 1) 10 additional days per animal to acclimate (required by IACUC to minimize animal stress),
- 2) carcass disposal,
- 3) additional husbandry labor for weekly weighing (to inform the proposed endpoint measurements), and

4) daily observations by the husbandry staff and additional paperwork toward GLP compliance. The UC Davis per diem (\$26.76) is on par or below that of CROs. For example, a quote from Absorption Systems in San Diego, CA, for a 24-animal study for 6 months was approximately 3-times that of UC Davis.

With CIRM's support, we are truly excited to accelerate the translation of Hyaleon to help the millions of patients afflicted by conditions of the temporomandibular joint disc complex.

On behalf of our entire CLIN1 team,



Kyriacos Athanasiou, Ph.D., P.E.
Distinguished Professor, Henry Samueli Chair
Director, DELTAi (Driving Engineering & Life-science Translational Advances @ Irvine)
National Academy of Medicine, National Academy of Inventors