Lentiviral Reference Material Working Group Meeting

March 8th, 2016

Location: ISBioTech 6th Annual Spring Meeting in Washington

Attendees: Attached signup sheet

Keith Introduction:

- Use the model Ad05 reference material
- ISBioTech is the facilitator but not the leader of the initiative

Otto Merten; Mercedes Segura and Boro Drupolic (driving parties from Lentigen, bluebird bio and Genethon) had a conference call and agreed on a proposal to be presented to other interested parties in the LVV field during the ISBioTech meeting

- Otto: We agreed that,
  1. A Lentiviral vector reference standard would be useful for the field
  2. A 3rd generation HIV-1-based VSV-G pseudotyped LVV coding for a gene that is easily detected by FACS (GFP or equivalent) should serve as an LVV reference standard material
  3. The method of manufacture of such a Lentiviral vector would determine its reference characteristics, so parties would need to agree on this method.
  4. The minimal tests that would be performed on the reference material would be p24 and titer (by PCR and GFP/equivalent expression)
- Need to decide who is doing what.
- What testing, fix SOPs
- Who is part of testing network to establish the value; AAV8 and AAV2 publication on how this was done and follow that
- Who will pool data: Martin Lock who authored AAV2 reference standard work?
- *Keith: Ad5 protocol; established steps, got CBER comments, and then went to participants with and RFP to who will manufacture.*
  - *Need a well characterized cell back, but do not want to get tied into proprietary material so we can use material and make more in the future*
- Lentigen IP a concern?
- *Keith: Anyone that could purchase the vector, would they have to get a license from Lentigen? What is the blanket immunity?*
- Otto: should be free of license if Lentigen is involved. Only use for standardization of in house assays
- Boro offer to manufacture the reference standard as long they could obtain cost recovery for provision of the reference standard through their web site. Not optimal and should go into ATCC or some other repository business and non-commercial.
- *Keith: How much material would be needed; Otto- 5000 to 10,000 vials higher concentration the better; 24 cell factories 200 mL Genethon process.*
- Question from group: Can it be one batch or can it be pooled? Could make drug substance and pool into the final drug product?

- Mercedes: What test would be done and the value would be to standardize quantitative assays (p24, titer) and not purity assays
    - Follow same path as they did for AAV standard
    - No one can do this by themselves, need a team to sponsor and who to be contacted
- *Keith: could illicit the raw materials from the vendors. Who will make the material will be cost and space.*
    - *Should be able to bring in most of the materials: Need to sequence and have as overall data package.*
- Otto: Formulation and what buffer system to use. That it is critical.
  Mercedes: High protein content media (X-Vivo 20 or other) with up to 4 year stability already
- Keith question to Jerry Ann Boose: Give some guidance on vials and concentration
- *Jerry Ann:* what tests and work backwards from there
- High titer may not be required since we have to dilute these batches anyway.
- Hanna Lesch: Would there be a need for people using reference material for other assays that may require higher titers?
    - JerryAnn: Make a core list of assays for characterization and then others can take to what is needed
- Han van der Loo: role of reference material be used to qualify their own reference material otherwise it get used up too fast. Reiterated that fill/finish is critical with semi-automated system.
- Filling will be an issue and fill can be done separately.
- ATCC may do aliquoting directly; cost and distribution
- Manufacturing one location and fill finish at another.
- Han: Does reference vector have to be purified and what is the goal for purity? What are the steps that we need to include. UF, membrane, IEX etc. so we can choose what method is adequate
- Need high quality material to start and make as pure as possible.
- Transfection suspension material instead of adherent? A typical reported adherent transfection-based manufacturing process is proposed.
- Keith: Depends on who is trying to make it and what system will be used.
    - How many companies would be interested in making it?
    - LentiGen or bluebird would be interested in making
- Mercedes: Goal is to identify a group that would like to participate and what sort of interest there is to join.
- <u>Set up a survey; web based and ask questions of who would like to be involved.</u>
- Concentration something like 2E8 TU/mL?
- NIST contacts and if they would like to be involved from pre-competitive market
- Testing considered on a regular basis: p24 and titer.
- Jerry Ann will put together preliminary list of assays (Lancaster)
- SOPs for the test should be developed and circulated for comment
- Keith: will have full support from CBER and keep involved in the process, Dr Lo, Dr. Gavin, etc.
- ACTION: Mercedes to start developing questioners for survey and circulate

Survey is intended to identify players in the field who may be able to contribute to the following:

- Who will manufacture the LVV reference material?
- Who will conduct the safety testing of the material?
- Which laboratories will perform the analytical testing?
- Who will help write the SOPs for testing the reference material?
- Who will compile and analyze the data coming from different labs?
- Who will write a publication?
- Who will coordinate to have the reference material stored and distributed?