1. BACKGROUND:

DF/HCC research activities may be subject to inspection by regulatory authorities, including the Food and Drug Administration (FDA), or European Medical Association (EMA).

2. ASSOCIATED DF/HCC POLICIES:

2.1. AUD-100

3. PROCEDURE:

3.1. **Preparation**

3.1.1. The Principal Investigator (PI) will notify the sponsor and the applicable institutional clinical trials office as per AUD-100. The responsible clinical trials office will schedule a meeting with the PI and site research team to review trial status, coordinate and plan roles for the inspection and inspection, including:

3.1.2. The clinical trials office will assist the PI with:

- Reserving appropriate space
- Requesting any required documents (i.e. medical records, off-site storage)
- Determining whether to request mock inspection or review by the ODQ.
- Ensuring all regulatory, pharmacy and subject records are accurate, complete and available for review by the inspector.
- Ensuring that the FDA inspector will have access to any electronic research records that will be needed.

3.1.3. The PI should prepare a list of all active and inactive studies where he/she is the Principal Investigator. The FDA will request to see this list when they arrive. It should include: protocol #s, protocol titles, product names, names of sponsors and study start and end dates.

3.1.4. Prior to the inspection, the research team and/or clinical trials office will verify the inspection location is prepared. Keep the room free of non-protocol materials or subject information. Lock any cabinets and drawers in the room. The location should be a comfortable place to work with ample space to organize materials.

3.1.4.1. It is recommended that all study documents be stored in a separate room from where the inspector is conducting the inspection. Only those documents that are requested by the inspector should be brought into the conference room/office.

3.2. **During the Inspection**

3.2.1. When the FDA Inspector arrives at the site, the PI (or representative) must be available to meet and greet the inspector. The PI (or representative) will ask to view the inspector's credentials, but not photocopy them.

3.2.2. The FDA inspector should be escorted by a designated member of the study team at all times while they are on location.

3.2.3. The PI will accept and sign the Form FDA 482 (Notice of Intent to Inspection).

3.2.4. Gather key study personnel for the opening meeting and introduce them to the FDA inspector. Set the proper tone. Be available, maintain a professional, cordial and cooperative demeanor at all times. **Do not** under any circumstances become defensive or argumentative.

3.2.5. The PI will designate a research team member as a liaison to facilitate the inspector. This designated liaison (or point person) will function as the inspector's escort. The designated liaison/escort will act as the coordinator for the inspection and will keep written record of all inspection related activities, including all document requests or requests for personnel interviews. Upon request, all research team members should be available to answer questions of which they have direct knowledge.

3.2.6. The PI should adjust his or her schedule and be available to address questions or requests the inspector may have during the inspection. The PI or designee should plan on checking-in at least three times during each day, once in the morning, mid-day and towards late afternoon or at the timeframes agreed upon with the inspector. If the PI tells the inspector that he or she will be available at a given time, be sure to keep the time. Do not make the inspector wait.

3.2.7. Confirm with the inspector his or her preference for handling issues and queries. Provide the appropriate pager number and paging instructions in case he or she needs to reach the PI or the designee prior to the agreed meeting time.

3.2.8. Have medical records, research charts and source documents available and provide only those specifically requested. Remember to track all requests from the inspector and make photocopies, if appropriate.

3.2.8.1. FDA inspectors may make copies of documents as necessary, but are not permitted to remove original documents from the institution grounds. If the inspector requests copies of study documents, make sure to clearly document what was copied, and keep a log of the date of the request, the name of the document and the name of the staff member providing the document.

3.2.9. During the inspection, it is likely the inspector will make "observations" relating to the conduct of the trial, documentation, etc. The designated liaison/escort should work with the research team to make every effort to address and correct these observations while the inspection is taking place.

3.2.10. Do not volunteer information; answer all questions briefly, honestly and accurately. Do not elaborate on a question unless questioned further for detail. When appropriate, limit responses to yes or no answers. Be confident that your response is accurate and factual and be prepared to supply supporting documentation.

3.2.11. Only answer questions of which you have direct knowledge. If you are not sure how to answer a question or do not feel comfortable answering a question, it is appropriate to say, "I will have to get back to you on that." Then seek advice on how to address the question. Contact the Sponsor or Contract Research Organization (CRO) with any questions or concerns, as appropriate.

3.2.12. Limit offers of hospitality to simple beverages such as water, coffee, tea or juice. It is not appropriate to provide food items.

3.2.13. A designated member of the research team or clinical trials office must communicate with all involved DF/HCC parities during the inspection, including providing daily summaries of key information, as needed, to ODQ, OHRS, appropriate IOs and site clinical trials offices.

3.3. **Exit Interview**

3.3.1. At the end of the inspection, the FDA inspector will conduct an exit interview. Interactions during the exit interview should take place primarily between the PI and the inspector. During the exit interview, tape recorders may not be used.

3.3.2. The following individuals will be invited to participate in the exit interview: PI, subinvestigators (as applicable), an ODQ representative, an OHRS representative (if it is a regulatory inspection) and a responsible clinical trials office representative. The responsible clinical trials office representative will determine if others need to be present for the findings.

3.3.3. A designated member of the research team or clinical trials office will record discussion points during the exit interview and will provide summaries of key findings to the involved research team. Any significant findings, such as the issuing of a Form FDA 483, clinical hold, suspension or other actionable finding, will be communicated the next business day to the OHRS, ODQ, appropriate IOs and the DF/HCC Associate Director of Administration.

3.3.4. If an FDA Form 483 is issued, make sure to obtain a copy before the inspector leaves.

3.4. **Response and Follow Up**

3.4.1. The PI and designated research team member will draft the preliminary response within 10 business days of the exit interview and send it to the responsible clinical trials office for review.

3.4.2. Be clear and concise, and use the observations as an outline in formulating the response to ensure each observation is responded to individually. It is critical to investigate the circumstances that may have prevented protocol compliance, summarize what occurred, and then provide both an immediate corrective action and an ongoing preventive action that will ensure the problem will not recur.

3.4.3. Any results, corrective action plans or follow-up correspondence must be communicated to the responsible clinical trials office and through them to the ODQ and other applicable offices or entities (e.g., OHRS, pharmacy, etc.). The ODQ will evaluate whether any part of the outcome of audits and inspections needs to be escalated to DF/HCC leadership or communicated with other DF/HCC institutions or the broader research community.

3.4.4. The responsible clinical trials office and other applicable offices will review and approve the preliminary response before sending it to the reviewing sponsor/agency.

3.4.5. Responses to Form FDA 483 are due at the FDA no later than 15 business days after the exit interview.

3.4.6. Follow-up for any type of inspection may involve implementation of new procedures regarding individual protocol performance or system-wide changes within DF/HCC.