Subject Safety: The Medical view

After some considerable thought and investigation, It would be expected that the Medical group (Principal Investigators, et al) in any MRO/CRO would make the following recommendations:

1. The testing of Hepatitis “C” (HCV) antibody in all study participants become part of the standard to be performed in all studies involving the collection of body fluids.
2. All employees involved in the sampling of body fluids be tested for HCV and for the HBsAby annually. Those with low titers of HBsAby be offered the vaccine booster (or series if they are vaccine naïve).
3. The “universal precautions” be used in the sampling of body fluids (blood, urine, feces, saliva etc.) on subjects on all studies even where complete viral testing is not done.

Physicians usually understand that the responsibilities of Principal Investigators extends from before a study starts to well beyond a studies conclusion including. These responsibilities include – but are not limited to the following:

- **Clinical** responsibilities that the study meets appropriate scientific criteria and is of benefit to science.
- **Moral** responsibilities to the organization, the subjects, the IRB, the Sponsor, and to mankind in general that guarantees that, to the best of her/his knowledge, the study is reasonable and sound and that study participants are not placed at undue risk.
- **Legal** responsibilities in that no harm will come to subjects under the PI’s care and that the Protocol will be followed as written.

This matter crosses these responsibilities and has ramifications for the reputation of the MRO/CRO for which the physician is working and, as well, the health and safety of the subjects as well as the staff. This issue is a combination of the use of proper technique and the emergence of a serious worldwide problem.

Background

Physicians have long been aware of the importance of the proper handling of needle stick injuries to staff and have come to the conclusion that for maximum protection to staff (and presumably study participants as well) that the standards of care and testing presently used be reviewed. Further impetus for this reevaluation is the observation that clients are increasingly requesting that viral testing be done and that tests for Hepatitis “B” (HBV) and “C” (HCV) are being included along with the HIV test and that HCV positive Subjects are noticed to be alarmingly common.

The matter of HCV is of concern because of it’s current and emerging worldwide importance as the largest single cause of total liver failure (and subsequent need for liver transplant surgery) around the world. It is because of the seriousness of this infection and the essentially unknown modes of transmission coupled with the absence of a vaccine (in contrast to Hepatitis “A” or “B”) that has physicians taking notice.

Hepatitis “C” is singled out and placed in contrast to Hepatitis “B” and HIV for a number of reasons. Firstly, with regard to HBV, the incidence of progressive and fatal chronic hepatitis is considerably less than that with HCV infections and, importantly, there is a vaccine to protect at risk populations from HBV infections.

Most MRO/CRO's would be expected to recommend and pay for this vaccine for all at-risk employees. No vaccine is available for HCV at the present time. It is acknowledged that HCV is much less infective that HBV but there is evidence that the HCV is rather stable and will remain viable even in dried specimens. The seriousness of HCV infection cannot be overstated, a fact which seems to be noted by an increasing number of clients who request HCV along with HBV and HIV testing pre-study.

Discerning physicians working in this industry would surely notice that each time HCV is requested that there are individuals testing positive. This is of concern when a subject who has been found HCV positive has a history of having been on previous studies (where no testing was done) and who do not come from a known high risk group. If asked if this could have been acquired while in the research facility, no physician could say with certainty that exposure could not have happened in that manner. These research facilities must protect themselves as well as the subjects.

Some concern does exist for HIV infection following needle stick injuries and physicians are currently working to identify the best procedure and protocol to follow for this eventuality. There is less concern for non-needle stick transmission for a number of reasons including the relative difficulty of transmission, which is partly due to the friability of the virus. There is medical concern for the HBV but far less than with the HCV because the former only rarely becomes chronic and fulminating and, in addition, there is an excellent vaccine which all employees are encouraged to take.

Physicians clearly recommend that an important goal of study conduct was that the standard universal precautions, as to the handling of body fluids, become part of the standard. What this basically comes to is that it was stated that the changing or cleaning of gloves, by phlebotomists or others handling body fluids between sample collection from each subject become the Standard.

The medical concern was that it was possible to transmit from one subject to the next contaminants present in body fluids of previously handled subjects. Some of these contaminants could be virus particles. Of particular concern is the HCV because of it's long term morbidity and mortality even though it is the HBV that is more easily transmitted in this manner.

As a group, physicians would be expected to believe that the use of universal precautions should be used when taking blood, urine or feces samples. In addition, there was concern that the reputation of a Medical Research Organization might also be at stake if there became a perception that subjects who took part clinical studies did not receive the highest standard of care and cleanliness consistent, at least with the standards of the community within which the MRO/CRO operates.

Charles H. Pierce, M.D., Ph.D.