

Assay Review Memo, May 13, 2010 - MenHibrix

MEMORANDUM

DATE: May 13, 2010
FROM: Stephen Feinstone HFM 448
THROUGH: Robin Levis
TO: Joseph Temenak

SUBJECT: Menhibrex assay review for ---(b)(4)---: STN 1235363

This assay that is used by GSK for measuring --(b)(4)-- was initially reviewed and accepted in 2005. That review was done by Kathleen Mihalik and Lev Sirota. The review memo dated May 6, 2005.

Based on the previous review that is appended below, I recommend the acceptance of this assay for use in the Menhibrix trials.

Previous Review:

Background:

GSK uses the -(b)(4)- test kit for antibody to -(b)(4)- called ---(b)(4)--- to test mice that have been used in immunogenicity assays for monitoring the stability of the hepatitis B vaccine, Engerix and the hepatitis B components of Pediarix and Twinrix. (b)(4) will discontinue this test kit in 2005 and GSK has developed an in house test to replace the commercial assay. The new test will use the same principle as the -(b)(4)- in that is is a ---(b)(4)--- in which -----

------(b)(4)-----

----- The major differences with the ----(b)(4)---- is that the -(b)(4)- test is done on -----(b)(4)----- is obviously different and the labeled -----(b)(4)-----.

GSK has addressed issues of quality control for all aspects of their in house test including intra- and inter-assay variability and comparability with the (b)(4) test.

Concordance between the assays

----(b)(4)----

		Positive	Negative	Total
GSK in house	Positive	(b)(4)	(b)(4)	(b)(4)
	Negative	(b)(4)	(b)(4)	(b)(4)
	Total	(b)(4)	(b)(4)	(b)(4)

95% C.I.

Global agreement (concordance)

(b)(4)

----(b)(4)----

Positive agreement (sensitivity)

(b)(4)

----(b)(4)----

Negative agreement (specificity)

(b)(4)

----(b)(4)----

Positive percentage (GSK)

(b)(4)

----(b)(4)----

Positive percentage (b)(4)

(b)(4)

----(b)(4)----

Difference (GSK-(b)(4))

(b)(4)

----(b)(4)----

Intra and inter assay variability was assessed by testing (b)(4) positive controls on (b)(4) different -----(b)(4)----- different experiments. The estimated the intra assay variability to be (b)(4).

Comments:

The sponsor compares a ---(b)(4)--- assay with the -----(b)(4)----- to confirm that both assays recognize the --(b)(4)-- antibodies and those results are comparable.

The sponsor also tests the -----(b)(4)----- using both -----(b)(4)----- and a -----(b)(4)----- . The Inter – and Intra - assay variability’s are acceptable as per the agency’s statistical branch. The details of the linearity test and justification of the X2 critical value of (b)(4) were not provided by the sponsor to date. While the concordance of new in house assay with the -----(b)(4)---- is not as high as I would like to see, the new assay results in higher (b)(4) values relative to the ---(b)(4)--- . Therefore, the new assay would fail more lots than the old assay. In addition, stability is monitored by a battery of tests which include the ---(b)(4)-potency assay but also an -(b)(4)-potency test based on an -----(b)(4)----- . This test is more accurate and much less variable than the -----(b)(4)----- potency test. Therefore, stability problems would most likely be seen with the ---(b)(4) potency assay well before they would become apparent using the --- ---(b)(4)--- potency assay. While this test is an acceptable substitute for the present assay, I also feel that the sponsor should have been more diligent in its validation of the new test. I would recommend that in the future, this sponsor should consult the ICH guidelines and submit data to support these types of submissions that conforms to those guidelines and include data directly related to the qualities of the new assay which include; accuracy, precision, repeatability, intermediate precision, specificity, detection limit, quantitation limit, linearity and range.

Committee Recommendations:

It is recommended that the supplement for the use of the in house test for ---(b)(4)--- instead of the -----(b)(4)----- for testing of the antibody responses in the the -----(b)(4)----- be approved.