



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service  
Food and Drug Administration  
10903 New Hampshire Ave.  
Silver Spring MD 20993

**To:** STN 125644

**From:** Karen A. Smith, LACBRP, DBSQC, OCBQ

**Through:** Kori Francis, Team Leader, LACBRP, DBSQC, OCBQ  
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**Sponsor:** Bio Products Laboratory Limited (BPL)

**Product:** Human Albumin Solution (HAS) 5% and 25%

**Subject:** Final Review Memo for Biological License Application for the Drug Product Human Albumin Solution (HAS) 5% and 25%

**CC:** Wayne Hicks

**Recommendation:** Approvable

**Summary of Review:**

A new BLA, STN 125644, for Human Albumin Solution (HAS) 5% and 25% drug product has been submitted by Bio Products Laboratory Limited. This review will focus on the Nucleic Acid Test (NAT) methods, performed by outside testing laboratories, for detecting the absence of viral markers, (b) (4), HBV-DNA, HCV-RNA, HIV-1 RNA and Parvovirus B19-DNA (limit not greater than 10,000 IU/mL) in source material (human plasma) (b) (4). Based on the review of submission, NAT assay is found to be approvable for its intended purposes.

**Background:**

The drug product HAS is indicated for use in treating hypovolemia, ascites, burns, nephrotic syndrome, acute respiratory distress syndrome and cardiopulmonary bypass. The manufacturer of the Drug Substance starts with the creation of the Start Pool which must be shown to be free of viral contamination. Testing for viral markers is carried out on all plasma donations. (b) (4) are tested for the full-range of the five relevant viruses using the (b) (4) methodology. NAT testing for (b) (4) was contracted out to the following outside testing centers: (b) (4). The collection

centers are licensed and inspected by the FDA. All three sites hold active Biological Licenses from US Food and Drug Administration for screening of source plasma for viral contamination.

**Submitted Information Reviewed:**

This is an electronic submission. Information submitted and reviewed includes:

- 125644/0 – 3.2.S.2.2 – Description of Manufacturing Process and Process Controls
- 125644/0 - 3.2.S.2.3 – Control of Materials
- 125644/0 - 3.2.S.4.1 - Specification
- 125644/0 - 3.2.S.4.2 – Analytical Procedures
- 125644/0 - 3.2.S.4.3 – Validation of Analytical Procedures
- 125644/0 - 3.2.S.4.4 – Batch Analysis
- 125644/0.24 (Amendment)
  - 1.2 Cover Letters
    - BL125644\_HAS\_Response Document Additional IR Mid Cycle Review-1-14\_10 July 2017\_1814#
    - Testing\_NAT\_(b) (4)
    - Testing\_NAT\_(b) (4)
- 125644/0.34 (Amendment)
  - 1.2 Cover Letters
    - Response Document
    - Testing NAT (b) (4)
    - Testing NAT (b) (4)
    - Testing NAT (b) (4)

**Review Narrative:**

The original submission did not have information on NAT procedures utilized by testing centers to screen (b) (4) for manufacturer of drug substance. FDA submitted information requests to Bio Products Laboratory Limited (BPL) requesting information on the NAT procedures utilized by each testing center and the validations that were performed by each center.

**First Information Request (sent on 01/17/2017)**

We are reviewing your submission for Human Albumin Solution (HAS) 5% and 25%. In section 3.2.S.4.2 Analytical Procedures, 1.2 - NAT tests for (b) (4), HBV, HCV, HIV-1 and B19, it states the NAT tests were performed by (b) (4). In order for us to continue to our review please submit detailed description of the method that was utilized for NAT tests.

The sponsor responded that the methods are the same as those submitted with (b) (4) both of which have been licensed.

**Second Information Request (sent on 02/24/2017)**

1) In your response to our request for detailed description of the test method for NAT testing, you indicated "... is it sufficient to cross refer back to the BLA for (b) (4) where information resides specific to these NAT tests for (b) (4), HBV, HCV HIV-1 and B19, performed by (b) (4)?" However, you have not provided the necessary specific details/references for locating the information including, Document name, Document number

and Module number in the BLA submission package for (b) (4). Please provide detailed reference as necessary for us to locate the information or please submit the requested information for the NAT test in our previous IR (dated 01/17/2017) to permit us to review your BLA submission.

2) In module 3.2.S.2.3 – Control of Materials, you stated the validation data of the viral screening tests is in 3.2.S.4.3 – Validation of Analytical Procedures. We did not find the data in your submission. Rather you stated in section 1.3 of 3.2.S.4.3 that NAT tests were performed by outside contractors, (b) (4) and provided no other information. Please submit the necessary validation data of the NAT tests from each of the companies.

Since there were no response from BPL, a follow up email was sent to BPL on 05/12/2017 inquiring about the previous IR.

**Third Information Request (sent on 03/28/2018)**

Previous IR was re-submitted verbatim.

BPL provided validation summaries for the the NAT testing from the outside contractors, (b) (4), the as Sequence # 34.

The submitted information are reviewed below.

**Test Methods**

(b) (4)  
[Redacted text block]

(b) (4)  
[Redacted text block]

(b) (4)  
[Redacted text block]



(b) (4)

[REDACTED]

(b) (4)

[REDACTED]

[REDACTED]

(b) (4)

[REDACTED]

[REDACTED]

Conclusion: (b) (4) and (b) (4), are approved assays which utilized outside test laboratories to screen (b) (4). We confirmed (b) (4) uses the same testing facilities ((b) (4)) to test manufacturer (b) (4) as well as use the same test kits. Prior use of testing sites and (b) (4) assays in previous submissions has shown the assays are safe and effective in the detection of infectious viral markers in (b) (4). Assay kits are approvable for use.