1. General Information

Name and address of sponsor: Alba Bioscience Inc.
801 Capitola Drive, Suite 9
Durham, NC 27713

Date of Submission: 30 June 2005

Submission Tracking Numbers (STN)	Name of Biological Product	Cell Line(s)	Proprietary Name
BL 125129/0	Blood Grouping Reagent, Anti-A (Murine Monoclonal)	LA2	Alba Clone Anti-A
BL 125130/0	Blood Grouping Reagent, Anti-B (Murine Monoclonal)	LB3	Alba Clone Anti-B
BL 125131/0	Blood Grouping Reagent, Anti-A,B (Murine Monoclonal)	LA2/LB3/ES15	Alba Clone Anti-A,B
BL 125132/0	Blood Grouping Reagent, Anti-D (Monoclonal) (IgM)	LDM1	Anti D Alpha
BL 125132/0	Blood Grouping Reagent, Anti-D (Monoclonal) (IgM)	LDM3	Anti D Beta
BL 125133/0	Blood Grouping Reagent, Anti-E (Monoclonal)	DEM1	Alba Clone Anti-E
BL 125134/0	Blood Grouping Reagent, Anti-c (Monoclonal)	H48	Alba Clone Anti-c
BL 125135/0	Blood Grouping Reagent, Anti-k (Murine Monoclonal)	LKL1	Alba Clone Anti-k
BL 125136/0	Blood Grouping Reagent, Anti-M (Murine Monoclonal)	LM1	Alba Clone Anti-M
BL 125137/0	Blood Grouping Reagent, Anti-N (Murine Monoclonal)	LN3	Alba Clone Anti-N
BL 125138/0	Blood Grouping Reagent, Anti-Le^a (Murine Monoclonal)	LEA2	Alba Clone Anti-Le^a
BL 25139/0	Blood Grouping Reagent, Anti-Le^b (Murine Monoclonal)	LEB2	Alba Clone Anti-Le^b
BL 125140/0	Blood Grouping Reagent, Anti-Lu^b (Murine Monoclonal)	LU2	Alba Clone Anti-Lu^b
BL 125143/0	Blood Grouping Reagent, Anti-D (Monoclonal) (IgM Blend)	LDM1/ESD1-M	Anti-D Delta
BL 125144/0	Blood Grouping Reagent, Anti-D (Monoclonal Blend)	LDM3/ESD1	Anti-D Blend

2. Intended Use

The Blood Grouping Reagents that are the subject to this submission are monoclonal antibodies used in an *in vitro* test for detection of the presence of specific antigens on human red blood cells. See table below for specificities of each reagent.

Monoclonal Reagent	**Intended Use**
Anti-A	The detection and identification of human group A antigen on red blood cells by direct agglutination. The reagent will detect most significant subgroups of A including A_1, A_2, A_3 etc) using appropriate methods.
Anti-B	The detection and identification of human group B antigen on red blood cells by direct agglutination. The reagent does not detect acquired B antigen.
Anti-A, B	The detection and identification of human group A and B antigens on red blood cells by direct agglutination. The inclusion of the ES15 component enables the detection of weak subgroups, especially A_x.
Anti-D alpha	This IgM anti-D reagent is for the detection and identification of human D antigen on red blood cells by direct agglutination. The reagent will detect most examples of weak D (D^U) and partial D red cells by direct agglutination, but will not detect D_{VI}.
Anti-D beta	This anti-D reagent is for the detection and identification of human D antigen on red blood cells by direct agglutination. The reagent has the same D epitope specificity as Anti-D alpha (Z031) and will detect most examples of weak D (D^U) and partial D red cells by direct agglutination, but will not detect D_{VI}. It is, therefore, an ideal partner to Z031. Both Z031 and Z036 are formulated to the same specification and will further minimize typing discrepancies.
Anti-D delta	This anti-D is a blend of two monoclonal IgM antibodies and is for the detection and identification of human group D antigen on red blood cells and does detect D_{VI} by direct agglutination.
Anti-D blend	This anti-D reagent is a blend of an IgM monoclonal anti-D and an IgG monoclonal anti-D for the detection of human group D antigen on red blood cells. Designed for both patient and donor testing, the reagent will detect most weak D (D^U) and partial D red cells by direct agglutination, but will only detect D_{VI} by indirect methods (e.g. IAGT).
Anti-E	The detection and identification of human E blood group antigen on red blood cells by direct agglutination.
Anti-c	The detection and identification of human c blood group antigen on red blood cells by direct agglutination.
Anti-k	The detection and identification of human k (cellano) blood group antigen on red blood cells by direct agglutination.
Anti-M	The detection and identification of human M blood group antigen on red blood cells by direct agglutination.
Anti-N	The detection and identification of human N blood group antigen on red blood cells by direct agglutination.
Anti-Le^a	The detection and identification of human Le^a blood group antigen on red blood cells by direct agglutination.
Anti-Le^b	The detection and identification of human Le^b blood group antigen on red blood cells by direct agglutination.
Anti-Lu^b	The detection and identification of human Lu^b blood group antigen on red blood cells by direct agglutination.

3. Manufacturing and controls

A. Site of Manufacture and Assembly

The contract manufacture of Alba Bioscience Blood Grouping Reagents is performed at Alba Bioscience, a division of Scottish National Blood Transfusion Service, 21 Ellen's Glen Road, Liberton, Edinburgh, EH17 7QT. Contract manufacturing responsibilities include cell banking, tissue culture, fermentation, formulation, filling, labeling and packaging. This site has been inspected by the FDA.

B. Site of Final Quality Control and Release

The manufacturer of Alba Bioscience Blood Grouping Reagents is Alba Bioscience Inc., 801 Capitola Drive, Suite 9, Durham, NC 27713, USA. This site is responsible for FDA submissions, lot release, storage and distribution.

C. Manufacturing

The cell lines used in making the monoclonal antibodies for these Blood Grouping Reagents are either of murine or human origin. Fusing a single antibody forming cell from tumor cells produces a hybridoma that generates murine or human monoclonal antibodies. Alba Bioscience prepares the ---------- ---------- ----------. ---------- are optimized and characterized before being ----------. The blood grouping reagents are formulated by the ------- of specific chemicals before ---------- ---------- processes are carried out. Final packaging and labeling takes place at Alba Bioscience. Alba Bioscience Inc. performs the lot release tests for the product before final release for distribution. Testing includes the determination of product specificity and potency and microbiological and biochemical analyses. Each of these reagents must meet FDA potency standards. Three conformance lots of each specificity have been submitted to CBER for testing and have been shown to meet the requirement for potency.

4. Environmental Impact Analysis

Alba Bioscience claims Categorical Exclusion for the submission of an Environmental Impact Statement pursuant to 21 CFR 25.3(c). The manufacture of these monoclonal Blood Grouping Reagents is performed under controlled conditions and in compliance with the appropriate international, national and local environmental regulations. The disposal of waste from the use of this product is performed in compliance with the appropriate international, national and local environmental regulations. Based on the materials, concentration, volumes used in the product, and the method of product disposal, it is unlikely that the release of any of the substances in these products at the expected level of exposure will be harmful to the environment or toxic to organisms in the environment.

5. Stability Studies

The approved dating period for these monoclonal Blood Grouping Reagents when stored at 2-8 degrees centigrade (36-46 Fahrenheit) is twenty-four months. A minimum of twenty-four months real time stability data has been collected on all Blood Grouping Reagents covered in this application. The real time data indicated that the products are stable and meet performance specifications near, on, and after the expiration date.

6. Field Trial Summary

Field trials have been completed at two immunohematology laboratories in the US to generate US data in support of the application. The number of tests performed and the types of samples used reflect requirements in FDA Docket No. 91N-0467. Samples tested include clinical, neonatal and cord blood samples where available and various diseased states as they presented on a routine basis. All tests were performed, where possible, in parallel with a US licensed ---------- reagent.
Field trials were also completed on cells showing a weakened expression status. The types of samples used reflect requirements in FDA Docket No. 91N-0467. Due to the rarity of some of the specified conditions some frozen red blood cells were included from patients historically conforming to the diseased /interfering substance category. A study was also undertaken to establish the compatibility of the monoclonal Blood Grouping Reagents in this submission with a spectrum of anticoagulants that would be routinely used for collection of clinical and donor blood samples.

7. Labeling

The product labeling, including immediate container labels and package inserts, have been reviewed for compliance with 21 CFR 610.60, 610.61, 610.62 and 809.10 and were found acceptable. The product inserts clearly state their intended use; that the monoclonal Blood Grouping Reagents are for the *in vitro* detection and identification of human blood group antigens A, B, AB, D, c, E, k (cellano), Lu^b, Le^a, Le^b, M and N on red blood cells by direct agglutination.

8. Benefit Analysis

The following are a list of benefits to be realized by the USA blood supply organizations and professionals when these regents are licensed:

- Availability of Anti-Lu^b and Anti-k (cellano) monoclonal – No other monoclonal Blood Grouping Reagents are currently available in the US market for these two specificities. Laboratories have had to rely on polyclonal blood grouping sera to determine these blood types. The disadvantage in this is that these reagents are of limited supply and variable in quality.

- Availability of Anti-D – This license application includes four anti-D Blood Grouping Reagents manufactured from clones not previously available in the US, supplementing the existing reagents that can be used to differentiate the D status of a patient or donor. Additionally, these four Anti-D reagents were designed specifically for testing patients or testing donors In accordance with international recommendations which require that for patient testing two different monoclonal reagents should be used and they should not detect D_{VI}. On the other hand, the same recommendations for donor testing require that two different monoclonal reagents should be used and at least one should detect D_{VI}. The Anti-D *delta* detects D_{VI} by direct agglutination and can be used in conjunction with Anti-D *beta*, which contains antibody from a different clone. While these testing recommendations have note been universally adopted in the US, availability of these for Anti-D reagents will be beneficial to those who have voluntarily adopted these recommendations.

- Provision of clone diversity – Part of the aim of this application is to license reagents manufactured from clones, which are not currently available in the USA. This will allow more choice as well as providing the ability to use antibodies from different clones for confirmatory typing.

9. Post License Commitment – ----------

Alba Bioscience Inc.
President

Noel R Brown FIBMS