CHAPTER 2: LITERATURE AND HISTORICAL REVIEW

Although blood transfusions are intrinsically intended to be life-saving medical interventions, the procedure also carries a number of risks, some of which can even threaten the life of the patient. In 1981 acquired immuno-deficiency syndrome (AIDS) was identified in previously healthy male homosexuals based on the unusual prevalence of *Pneumocystis carinii* pneumonia (PCP) and Kaposi's sarcoma. Both of these conditions were very rare in otherwise healthy persons (Collier and Oxford, 1993). Since December 1982 the transmission of the unidentified agent associated with certain risk behaviours such as male homosexual intercourse and intra-venous drug abuse by the donors, causing AIDS, has been added to the list of risks to which blood transfusion recipients could be exposed. By 1983 the agent suspected to cause AIDS had been identified as a retrovirus, initially called the Human T-lymphocyte Virus III (HTLV III) in the United States of America or Lymphadenopathy-associated Virus (LAV) in France until 1986. After it was shown that the two viruses were the same, they were renamed the Human Immuno-deficiency Virus (HIV) in 1986 by the International Committee for the Taxonomy of Viruses (Swanevelder, 1994). In 1990, HIV was further subdivided into two identified species of virus in the family of *Retroviridae* and sub-family of *Lentivirinae*, namely HIV-1 and HIV-2 as defined in the National Library of Medicine – Medical Subject Headings (2007).

As summarised by Lachman (1995), HIV infection leads to functional abnormalities and depletion of a group of cells associated with a person's normal immune response, known as the CD4+ T-lymphocytes. These T-lymphocytes play a cardinal role in the immune surveillance of the body for infectious agents by the processing of the "foreign" antigens of the infectious agents for presentation to the B-lymphocytes which effect the antigen-specific immunoglobulin production. The CD4+ T-lymphocytes also control the auto-immune tendencies of the immune system in conjunction with the CD8 T-lymphocytes. Increasing functional abnormalities and depletion of the CD4+ T-lymphocytes lead to opportunistic infection by a variety of pathogens, ultimately leading to the death of the infected person. According to Lachman (1995) approximately 2.5% of cases of AIDS reported to the Centre for Disease Control (CDC) in the USA, were associated with blood transfusions. Furthermore Lachman (1995) reported that approximately 95% of recipients of HIV-infected blood became seropositive, and approximately 50% of these patients developed AIDS symptoms within 7 years of the implicated transfusion.

2.1. The early years of HIV risk management in the SABTS

It should be noted that, of the practices discussed in this section, little documentation has survived. Thus pertinent references are not possible. The information given in this section is primarily based on the recollection of the author and other staff members of the SABTS at the time, as well as deductions from surviving donor records and the few surviving circulars of the relevant period to which references are made.

In keeping with the observed epidemiology in the USA and Europe up to 1993, the development of AIDS could be associated with intravenous drug use, or male-to-male sexual intercourse (Collier and Oxford, 1993). Once the risk posed by overtly healthy persons engaging in male-to-male sexual intercourse or intravenous drug abuse was recognized in 1982, the blood transfusion services in South Africa initiated pre-donation screening of all its donors at every donation. Initially this screening consisted of the deferral of prospective donors at the discretion of donor clinic staff based on visible indicators of the possible high-risk activities stated above. This deferral followed a similar ban on the acceptance of donations from males who had recently engaged in homosexual intercourse, as was enforced in Europe and North America. The visible signs most commonly sought included needle-prick lesions in the case of intravenous drug users and, depending on the opinion of the staff-member dealing with the donor, the wearing of ear-rings and certain mannerisms considered effeminate, in the case of homosexual and bi-sexual men. This method of screening for practicing homosexual and bi-sexual men was highly subjective and depended largely on the preconceptions of the staff-member dealing with the donor at the time.

By October 1988 this method of screening was replaced by the first version of a questionnaire aimed at educating potential new donors. Life-style risk factors, as known at the time, which could place the

potential donor at risk of being exposed to the causative agent, as prescribed in the Bloemfontein Branch circular A10/88 (1988), were highlighted. It was envisaged that potential new donors who recognised elements of their own life-styles in the questionnaire, would exclude themselves voluntarily from donating blood. By September 1991 a questionnaire aimed at regular donors, asked for confirmation that the donor deemed his / her blood was safe for transfusion. This new questionnaire was implemented as prescribed in a protocol issued by the SABTS head office and numbered at the Bloemfontein Branch for reference purposes as S18/91 (1991). The various versions of the questionnaire successively in use from 1991 also attempted to achieve a more objective evaluation by requesting new donors to record answers to a number of specific questions with regard to known high-risk activities.

By October 1985 the SABTS instituted testing of all donations for the antibody to the HI virus, as subsequently prescribed by the National Blood Transfusion Council of South Africa (1990). This alleviated some of the risk of HIV transmission posed by donors who had been infected by HIV, through the transfusion of their donated blood. The risk posed by the transfusion of a unit of blood donated while the donor was in the window period of infectivity i.e. the period between the donor's infection by the virus and the first time that a test could provide a positive result, remained. By June 1986, management of the risk of HIV transmission was also implemented with regard to the process of

issuing blood through a directive requiring the preferential issue of blood from donors with the highest number of previous HIV tests as indicated on the blood pack label (the number of HIV tests on record prefixed by an “H”). Until 1988 fresh whole blood and fresh red cell concentrates were routinely requested for certain procedures and treatments, notably where the physicians felt the need for platelets and the labile coagulation factors. The HIV test results for these products, to be transfused less than 48 hours after collection, were generally not yet available at the time of issue, which gave the “H” number a very particular importance. This is evidenced by the Bloemfontein Branch circular B2/88 issued in January 1988, which prohibited the unauthorised issue units of blood marked “H0”, “H1” or “H2”. Only units marked “H3” or higher were considered acceptable for issue prior to the availability of the HIV test result. However, during June 1988 the Bloemfontein Branch of the SABTS discontinued the practice of routinely providing fresh whole blood and fresh red cell concentrates to patients. This decision was brought about by the identification of a probable transmission of HIV to a patient through the transfusion of a unit of fresh whole blood subsequently found to be HIV positive. Areas in the SABTS close to Johannesburg could still continue to provide these products due to the much reduced time associated with the transport of the specimens drawn during the blood collection process, to the Donor Virology Laboratory, resulting in HIV test results routinely being available within 18 to 36 hours of collection of the donation.

2.2. The broader base of HIV transmission and implementation of HIV testing in the SABTS

By the early 1990's it had been conclusively shown that HIV was infecting a substantial portion of the South African population through heterosexual transmission. Annual national surveys undertaken by the South African Department of Health in women attending antenatal clinics since 1990 have shown a steady increase in the prevalence of this sentinel group from 0.74% in 1990 to 30.2% in 2005. Estimates of HIV in the general South African population between the ages of 15 and 49 years had grown to 16.2% in 2005, as reported by Shisana *et al* (2005).

As already mentioned, it was known that a window period of infectivity existed between the time of infection with the HI virus and the development of antibodies that could be identified by means of a screening test for the first time. The poor sensitivity of these first-generation test systems resulted in an estimated window period of 45 days. As indicated by Heyns and Swanevelder (2005), donated blood or blood products collected within this period would be infective although the test used would provide a negative result. By the same token, the WHO estimated the risk of HIV infection following an HIV-infected blood transfusion to be more than 90% (Swanevelder, 1994). Since the initial test system was used in 1985 to determine the presence of the HI virus, more sensitive and specific reagents and test protocols for more viral markers have been developed, reducing the

length of the window period, but not eliminating it. This statement is supported by the Haemovigilance Annual Report: 2003 (Heyns and Nel, 2004), which indicates that in the period between 2000 and 2003, nine possible transmissions of HIV from transfused blood products prepared from eight blood donations which returned a negative test for HIV, were reported. This calculates to a risk of approximately 1:390000 transfused donations. Table 2.1 indicates the sequence of test systems used by the SABTS and SANBS since 1985, together with the estimated remaining window periods associated with these test systems.

Table 2.1: Tests for HIV used by the SABTS and SANBS between 1985 and 2005

TEST	TEST TRADE-NAME	TEST SUBSTRATE	MARKER IDENTIFIED	DATE IMPLEMENTED	SCREEN / CONFIRMATORY TEST	ESTIMATED WINDOW PERIOD
1st generation Enzyme-linked Immunosorbant-assay (12-unit pool test)	Organon Technika: HTLV-III, Uniform I, Uniform II	Viral lysate	Anti-HIV antibody	Oct 1985	Screen	45 days
2nd generation Enzyme-linked Immunosorbant-assay (individual unit test)	Dade-Behring: Enzygnost	Synthetic peptide	Anti-HIV-1+2 antibody	1991	Screen	33 days
3rd generation Enzyme-linked Immunosorbant-assay	Ortho Clinical Diagnostics: HIV-1 / HIV-2 Ab-capture ELISA test system	Recombinant antigen	Anti-HIV-1+2 antibody	Before 1996 (archived SOP effective 5/12/1997)	Screen	22 days
3rd generation Enzyme-linked Immunosorbant-assay	Ortho Clinical Diagnostics: HIV-1 p24 antigen ELISA test system	Recombinant antibody	HIV-1 p24 antigen	Jun 1996	Screen	16 days
3rd generation Enzyme-linked Immunosorbant-assay	Organon Technica: Vironostika HIV-1 antigen test	Recombinant antibody	HIV-1 p24 antigen	Dec 1999	Screen	16 days
3rd generation Enzyme-linked Immunosorbant-assay	Murex HIV-1.2.O	Recombinant antigen	Anti-HIV-1+2+O antibody	Feb 2000	Screen	16 days
3rd generation Enzyme-linked Immunosorbant-assay	Genscreen: HIV-1 / 2 version 2	Recombinant antigen	Anti-HIV-1+2+O antibody	Jun 2001	Confirmatory	16 days
3rd generation Enzyme-linked Immunosorbant-assay	Organon Technica: Vironostika HIV-1 antigen neutralization test	Recombinant antibody	HIV-1 p24 antigen	Jun 2001	Confirmatory	16 days
3rd generation Enzyme-linked Immunosorbant-assay	Innogenetics: Inotest HIV antigen mAb test	Recombinant antibody	HIV-1+2 p24 antigen	Jan 2002	Screen	16 days
3rd generation Enzyme-linked Immunosorbant-assay	Abbott: Prism	Recombinant antigen	Anti-HIV-1+ 2+O antibody	Apr 2002	Screen	16 days

Since June 1996, third generation enzyme-linked immunosorbant assay (ELISA) tests for the anti-HIV-1, -2 and -O(ther) antibodies as well as the third generation ELISA tests for the HIV-1 and -2 p24 antigen were used concurrently. The reason for this is that initially only the viral antigen occurs in sufficient quantity to provide a positive result in a test for HIV soon after infection by the virus. The amount of free virus, however, soon reduces to undetectable levels, while the anti-HIV envelope and anti-HIV core antibody levels (or antibody titres) concurrently increase to easily detectable levels. Once the viral antigen level has become undetectable, only the antibody test is effective; a period usually lasting for several years. Only in the final symptomatic stages of the disease would the viral antigen levels again become detectable. Figure 2.1 indicates this relationship graphically.

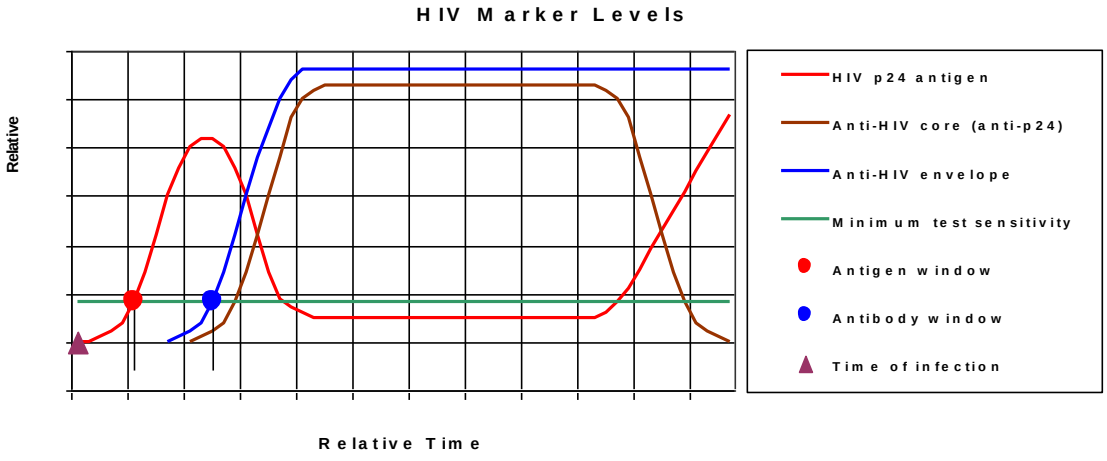

Figure 2.1: Schematic diagram of the relationship between the development of the p24 antigen and anti-HIV antibodies (after Collier and Oxford, 1993)

2.3. Risk management by donor selection in the SABTS / SANBS

The introduction of an operational computer system (Meditech, $T version) during November 1992 by the SABTS enabled the real time electronic capturing of information regarding the blood donations received, processed and tested. Prior to issuing the blood product to a patient the full set of information regarding the donor and the results of the blood group serology and virology screening tests are evaluated by the system to determine the safety and compatibility of the blood selected for that patient. The blood product issue process is completed by the capture of relevant patient and hospital data, ensuring full traceability of the donation. If the blood product was not used prior to its expiry date, the product is incinerated and those details are also captured. The electronic capture of donor data, has also allowed information on the donation history to be freely available to authorized staff in order to ensure that persons known to be at risk of being exposed to transfusion-transmissible diseases would be identifiable at all the clinics of the SABTS. In addition, blood / blood product issue rules were defined in the programme which prevented the computer-issue of untested donations and donations flagged on the system as unsuitable for transfusion.

The continued existence of the window period as seen in Figure 2.1 together with increasing prevalence of HIV (0.26% of donations confirmed HIV-1 positive in 1998) as reported by Heyns, Benjamin, *et*

al (2006), forced the SABTS to develop and adopt a structured Blood Safety Policy in 1999 (SPMED001 rev. 0, 2003). This policy as quoted by Heyns and Swanevelder (2005) encompassed a number of key principles as shown in Table 2.2.

Table 2.2: Key principles embodied in the SABTS Blood Safety Policy

1. A coordinated programme to procure sufficient safe blood from low-risk voluntary, non-remunerated blood donors.
2. A programme that aims to be nationally self-sufficient for low-risk blood products.
3. Issuing blood according to a hierarchy of risk.
4. Recognizing the right to privacy of the individual donor.
5. Protecting the health of blood donors, recipients of blood products and staff members.
6. Educating blood donors, particularly learners, on the importance of donating blood, the spread and pathogenesis of HIV / AIDS, and the effect of a safe healthy lifestyle on the quality and safety of the blood supply.

In practice this policy covered a number of aspects of the day-to-day operations of the SABTS as reported by Williamson (2006). Blood donor clinics in areas of high HIV prevalence were discontinued, a programme for targeting donors for regular repeat donations was instituted, donor education was escalated with regard to the activities leading to increased risk of exposure to HIV, and considerable improvements to the donor health / self-exclusion questionnaire coupled with the institution of the donor interview were initiated.

One of the outcomes of this policy was that the SABTS and subsequently SANBS continued to refine and apply the pre-donation assessments of all prospective donors, both new and existing, to minimise the risk of a window period blood donation entering the blood supply, and through its subsequent transfusion to a patient, from transmitting HIV. The first step in the process in use at the time of this study consisted of the evaluation of the health of the prospective donor in respect of potential risks of donation to the donor as well as to the patient based on a health questionnaire (BTS53E rev. 3) completed by the donor as prescribed by SOP-DON-24 rev. 2 (2002). The health questionnaire also included the questions in Table 2.3 regarding the donor's life-style which could place him / her at risk of being exposed to the HI virus. It should be noted that this procedure is carried out every time a prospective donor presents himself / herself to donate blood, irrespective of the number of previous donations made or any other possible circumstance which may exist.

Table 2.3: HIV-risk assessment lifestyle questions (BTS53E rev. 3)

1. Do you have AIDS or are you HIV positive?
2. Is your main reason for donating blood to undergo an HIV test?
3. **In the past 6 months:**
a. Have you had more than one sex partner, had casual sex, or had sex with someone whose sexual background you don't know?
4. **In the past 12 months:**
a. Have you been a victim of sexual assault?
5. **In the past 5 years:**
a. Have you had sex with a male or female prostitute, escort or sex worker, or exchanged money, drugs, goods or favours in return for sex?
b. Have you had male to male sex?
c. Have you suffered from a sexually transmitted disease (STD) e.g. syphilis, gonorrhoea, genital herpes, genital ulcer, VD or "drop"?
6. Have you ever injected yourself, or been injected, with any drugs or any other substance (including steroids) that were not prescribed for you by a doctor?
7. To your knowledge do any of the above questions apply to your sex partner?
8. Do you consider your blood safe for transfusion to a patient?

The evaluation of the answers provided on the questionnaire was supported by a discussion between the prospective donor and one of the SANBS staff to determine whether the donor had a satisfactory understanding of the questions asked in the questionnaire and also an understanding of the implications of the window period for the HIV test as prescribed in SOP-DON-32 rev. 2 (2002). If the prospective donor was deemed to have no overt risks to himself or the patient by donating, a unit of 450ml of blood as well as two 5ml specimens of blood for virology and serology tests were collected. In the event of any

risks becoming apparent through the assessment of the questionnaire or the discussion, normal procedure dictated that the prospective donor be deferred from donating for a period of time as determined by the nature of the risk and defined in PM-MED-001 rev. 0 (2003). This procedure was also applied to the life-style questions unless the deferral could not be made without public embarrassment to the potential donor. In such cases the donation process was completed as with any other donor but the blood donation was immediately taken aside and privately marked for incineration.

2.4. Risk management by donation risk category hierarchy in the SABTS / SANBS

In 1998 the WHO issued a report which included the recommendation that populations at low risk for transfusion-transmissible infections should be identified (WHO, 1998) for recruitment of voluntary blood donations. This document, in common with other documents on the subject emanating from the WHO and its regional offices, makes little attempt to define possible low-risk populations other than the requirement that blood donations should be obtained from voluntary, non-remunerated and regular blood donors who have been educated in some way regarding life-styles and behaviours which could enhance exposure to transfusion transmissible infections such as HIV. No further attempt is made to suggest avenues of research which could possibly lead to an acceptable set of parameters defining low-risk populations of blood donors.

In the United States of America and Canada prospective blood donors from many sub-Saharan African countries are regarded as high-risk donors in respect of the potential transmission of HIV. The Food and Drug Administration (FDA) of the United States of America put a requirement in place in 1998 whereby persons who were born or lived in a number of central African states after 1977 were barred from donating blood due to the risk of HIV type O transmission as stated on the website of the American Red Cross (2005). The Canadian Blood Services have a similar bar, described as a “geographic deferral” as indicated on their website (Canadian Blood Services, 2006).

Statistical analyses published by the Department of National Health and Population Development in various issues of Epidemiological Comments during the early 1990’s (South Africa: Department of National Health and Population Development, 1993; South Africa: Department of National Health and Population Development, 1994) showed a strong race and gender association in respect of the prevalence of HIV, both in antenatal surveys as well as in data obtained from the various blood transfusion services. In addition, the data from the blood transfusion services showed a strong association with the previous donation history of the donors.

During 1998 the Natal Blood Transfusion Service started importing blood from the Netherlands to mitigate the escalating risk of HIV

transmission by the transfusion of blood donations collected from a donor base with an increasing HIV incidence in Natal as reported in the print media (Correspondent, 1999).

An important outcome of the Blood Safety Policy was therefore the development of a four-tiered HIV risk categorization hierarchy for all blood donations, described in this study as the SABTS 1999 Model (Tables 2.4, 2.5 and 2.6). The four tiers of this risk categorization hierarchy were labelled “I”, “II”, “III” and “IV” in order of increasing risk. Once the various blood products had been prepared from the blood donations, the risk categories were carried onto the blood products as issue priorities which were labelled as “A1”, “A2”, “A3” and “A4” respectively. For the purposes of this study, no distinction has been made between the HIV risk categorization hierarchy and the blood issue priority, and therefore the “A1” to “A4” labels are used throughout to describe the risk categories of the SABTS 1999 Model. In respect of the other models, the same principle has been applied and the blood issue priority labels have been used to describe the risk categories.

This HIV risk categorization hierarchy was implemented to augment the already existing risk management procedures. The upgrading of the operational computer system to the NPR version of the Meditech programme during 1998 and the introduction of a SQL Database data repository enabled the real time analysis of the data entered. The adoption of the Blood Safety Policy in 1999 relied on the improved

functionality of the NPR version of the Meditech programme being applied to the risk management of all blood donations received, by electronically evaluating each donation according to certain predetermined criteria in order to allocate a risk category classification to each donation. The electronic issuing routine on Meditech was also modified to limit the electronic issuing of higher-risk categorized blood products under routine circumstances and by issuing a warning on which an audit trail was kept, to staff authorized to allow the electronic issue of such blood products in situations of extreme shortage.

This meant that not all donations were considered equally acceptable for the preparation of the various blood products and for freely issuing to patients. Therefore, until February 2005 the choice of blood pack into which the blood was drawn and which ultimately determined the potential usability of the blood was prescribed by SOP-DON-043 rev. 2 (2003). This choice was determined by the normally acceptable usage of the donations as applied in the SABTS 1999 Model, as can be seen in Table 2.5. In essence this meant that donations in risk category “A1” could be taken in OPTI-system triple blood packs for processing into plasma products, red cell concentrates and platelet concentrates. Donations in risk category “A2” could be taken in OPTI-system triple blood packs for processing into plasma products and red cell concentrates (except for paediatrics and immune-compromised patients). Until June 2004 donations in risk category “A3” and “A4” could only be taken into single blood packs for the use of the red cell

concentrate in situations of extreme shortage. After June 2004 the NBI was sufficiently satisfied that the disease marker incidence in donations of risk category “A3” was low enough to avoid compromising the efficacy of the virus-inactivating reagents. These donations could now also be collected into OPTI-system triple blood packs for processing into virus-inactivated plasma products while the red cell concentrates would only be used in situations of extreme shortage.

Concurrent to donation testing, initial processing of the donation was undertaken to prepare red cell concentrates, plasma and the buffy-coat concentrates (for the processing of pooled platelet concentrates). Once the virology tests had been completed, the results were sent *via* an interface from the automated test systems into the Meditech programme. These results were then accessed by the technicians in the Components Laboratory prior to the second phase processing to determine which units were suitable for the preparation of specialized products. In addition, the virology and serology test results were used to determine whether the blood or blood products could be included into the blood supply to be transfused as prescribed by the SOP-COM-71 rev. 2 (2003).

The implementation of the HIV risk categorization hierarchy made certain decisions in the components laboratories and in the cross-match laboratories considerably easier. In the components laboratories an easier choice could be made regarding the identification of low HIV

risk donations from which to prepare special products such as infant fresh frozen plasma, pooled platelet concentrates, leucocyte-depleted red cell concentrates and paediatric red cell concentrates as prescribed in SOP-COM-104 rev. 0 (2001), SOP-COM-100 rev. 2 (2003) and SOP-COM-76 rev. 0 (1999). In the cross-match laboratories the technologists and technicians selecting blood for cross-matching and issuing to patients were in a position to exercise the requirement contained in SOP-BBK-2 rev. 3 (2003) and in SOP-BBK-9 rev. 3 (2002) which stated that units of the lowest risk category available, needed to be selected for cross-matching.

During 1999 the SABTS also embarked on a plasma quarantining procedure in order to ensure a greater level of safety when transfusing fresh frozen plasma. According to SOP-COM-114 rev. 0 (2003), all fresh frozen plasma from risk category “A1” and “A2” donations returning a negative test result for the disease marker tests and intended for transfusion to patients, needed to be retained in quarantine. Only after the donor’s subsequent donation (made between 56 and 100 days later) had been tested and found negative for all the tested disease markers, could the plasma be released for patient use as “donor-retested fresh frozen plasma” as prescribed by SOP-COM-126 rev. 0 (2003). In the event of any of the donor’s subsequent donation tests for the disease markers returning a positive result, the quarantined unit of plasma (together with all the products prepared from the donation returning the positive test) would be

changed to “Contaminated” status on the Meditech programme to prevent computer issuing procedures, and all the above-mentioned physical units would be disposed of according to SOP-COM-7 rev. 1 (2003). Quarantined plasma not released after four months in quarantine, due to the donor not having been retested for the disease markers, was sent to NBI as a separate batch for production of 20% albumin. After June 2004, the same procedure applied to fresh frozen plasma from risk category “A3” donations. This procedure could only be applied to the fresh frozen plasma due to its one year shelf-life. Red cell products with a shelf-life of 35 days and platelets with a shelf-life of five days could not be held in quarantine.

2.5. The application of the SABTS / SANBS risk management system in use since 1999

The intention of the risk management system in a country like South Africa with a high HIV prevalence is to protect the recipients of blood transfusions from being infected by this virus. The risk categorization is therefore intended as an aid to limit the possibility of window period transmission of HIV during transfusions by defining low-risk issue parameters. The use of the risk management system as an aid in issuing the lowest risk blood was implemented in July 1999 when the Blood Safety Policy was adopted. It was also used as an aid for targeting low risk donors during recruitment efforts in order to reduce the collection of donations from populations with higher HIV prevalence levels. The categorization system needed to be based on sound

scientific analysis and objectively applicable by the staff of the service as described in SOP-MLD-002 rev. 0 (2003). As mentioned previously, statistical analyses showed a large difference in HIV prevalence between new donors and regular donors, as well as a strong race and gender association.

The risk categorization in use until 30 September 2005 (SABTS 1999 Model) was based on relatively easily identifiable indicators provided by the donors and captured on Meditech as prescribed in SOP-DON-60 rev. 2 (2003), as well as previous donation data captured on the computer as described in SOP-DON-043 rev. 2 (2003). The indicators are shown in Table 2.4.

Table 2.4: Indicators for donation risk category in the SABTS 1999 Model

INDICATOR	DEFINING ALTERNATIVES
Previous donations	New donor (no previous donations on computer record)
	Old donor (previous donations on computer record)
Interval since last donation	Regular donor (<12 months since last donation)
	Lapsed donor (>12 months since last donation)
Gender	Male
	Female
Race	White
	Asian
	Coloured
	Black

According to this risk management system the donations were categorized into issue priorities ranging from “A1” to “A4” in order of increasing HIV risk as shown in Table 2.5. The risk model from which the system is derived defines the HIV prevalence limits for the four risk categories and the normally acceptable usage of the blood after the donor screening processes proved sufficiently effective to consistently remain within the HIV prevalence limits over an extended time period.

Table 2.5: Risk category application of the SABTS 1999 Model

RISK CATEGORY	ISSUE PRIORITY	HIV PREVALENCE LIMITS	NORMALLY ACCEPTABLE USAGE	BLOOD PACK USED
I	A1	<0.0100%	All products for infant and adult immune-compromised patients	OPTI-system triple blood pack
II	A2	0.0100% – 0.0999%	All products for adult immune-competent patients	OPTI-system triple blood pack
III	A3	0.1000% – 0.9999%	Quarantined or virus-inactivated plasma	OPTI-system triple blood pack
IV	A4	1.0000% and greater	Incinerated	Single blood pack

The specific risk allocation of each individual cohort of donors, as determined by combinations of defining alternatives for the four indicators shown in Table 2.4 above, was determined by statistical analysis of the HIV test results obtained from donation testing between 1996 and 1997 (coinciding with the introduction of p24 antigen testing). In the absence of incidence estimates in first-time donors, the

incidence of HIV in the donations was assumed to have a directly proportionate relationship to the number of units anticipated to be within the window period. The parameters of the SABTS 1999 Model are summarised in Table 2.6.

Table 2.6: SABTS 1999 Model parameters

<table>
<tr><th>RISK CATEGORY</th><th>NEW DONORS (includes donors not previously recorded on Meditech)</th><th>REGULAR DONORS (<365 days since previous donation)</th><th>LAPSED DONORS (>365 days since previous donation)</th></tr>
<tr><td rowspan="4">A1</td><td rowspan="4"></td><td>Asian male</td><td rowspan="4"></td></tr>
<tr><td>Asian female</td></tr>
<tr><td>White male</td></tr>
<tr><td>White female</td></tr>
<tr><td rowspan="4">A2</td><td>Asian male</td><td rowspan="2">Coloured male</td><td>Asian male</td></tr>
<tr><td>Asian female</td><td>Asian female</td></tr>
<tr><td>White male</td><td rowspan="2">Coloured female</td><td>White male</td></tr>
<tr><td>White female</td><td>White female</td></tr>
<tr><td rowspan="2">A3</td><td rowspan="2">Coloured male</td><td>Black male</td><td>Coloured male</td></tr>
<tr><td>Black female</td><td>Coloured female</td></tr>
<tr><td rowspan="3">A4</td><td>Coloured female</td><td rowspan="3"></td><td>Black male</td></tr>
<tr><td>Black male</td><td rowspan="2">Black female</td></tr>
<tr><td>Black female</td></tr>
</table>

By selecting blood for transfusion from cohorts of donors exhibiting a very low prevalence of HIV, it was anticipated that the risk of a window period transfusion would be correspondingly low. This risk

categorization model, however, allowed very limited progression for donors' donations through the various risk categories, resulting in the situation where a considerable number of very regular black donors could only reach an "A3" risk category. This meant that their donations were only used in processes where additional safety measures entailing virus inactivation could be put in place, such as fractionated blood products (albumin and factor VIII concentrate) or dried plasma products. Only in very exceptional emergency circumstances could blood products such as red cell concentrates be used.

2.6. The demerits of the SABTS / SANBS risk management system in use since 1999

Over the past years this situation has resulted in declining blood donations from the black population, primarily as a result of the discontinuation of active recruitment and reminder programmes in respect of donors whose last donation had an "A3" and "A4" risk categorization as calculated by the SABTS 1999 Model (see Table 2.6). This made the approximately 80% of the geographical area of South Africa served by SANBS almost totally dependant for its blood supply on the second largest and smallest population groups, namely the white and Asian population groups. These two population groups only constitute 20% of the population in this area. The steadily increasing number of black staff in the lower to middle management positions and in positions in the donor clinics and blood processing laboratories, where the risk categorization needed to be applied, also

placed a strain on their relationship with the higher management levels. This was highlighted in the Commission for Conciliation, Mediation and Arbitration (CCMA) case no FS5169/04 when Hospersa (the trade union which represents the majority of the staff) filed a dispute on behalf of a staff member against SANBS in November 2004 (CCMA, 2004; O'Connor, 2004; Correspondent, 2004). This dispute revolved around the withdrawal of an offer of a permanent position in the Bloemfontein Branch due to the fact that the staff member had inconclusively expressed an unwillingness to work for an institution which used race as part of its risk categorization system. Many of the staff questioned the moral ethics of continuously accepting donations from black donors in order to improve screening techniques and to obtain continually updated statistics while incurring the financial burden of the collection of the blood and knowing that it was highly unlikely that the blood would be transfused to a patient. Finally, the general public, particularly as represented by the media, had difficulty understanding and accepting a rigid risk categorization system which allows the blood of a regular donor with a considerable history of donations with a negative test for HIV, to be almost automatically incinerated based solely on the fact that the race of the donor precludes progression to risk categories "A2" or "A1", as shown in Table 2.6, which is commonly used for transfusions (Pienaar and Rossouw, 2004; Dladla, 2004). Even the medical fraternity was divided on the question as to whether a risk categorization model using the race of the donor as one of the indicators, was acceptable when

measured against the safety of blood transfusions for the patient (Bateman, 2005).

Mikkelsen (2006) subsequently in an article highlighting donor rights and expectations, states that "…the patient's right to safe blood (stemming from his right to health) competes with the right of the donor not to be discriminated against." He concedes that a patient's right to safe blood may prevail, but maintains that the donor still retains a right to a proper explanation for his / her deferral. He therefore suggests that, in order to avoid undue discrimination, all donor deferrals must be based on scientific evidence. The experience of SANBS with the public reaction to the SABTS 1999 Risk Categorization Model has also proven that scientific evidence is not always a match for public socio-political sentiments.

2.7. Alternative models for donation risk categorization

Given the issues above, there has since 2002, been a regular call from the branch managers of SANBS for the institution of a new risk categorization system, or the modification of the existing system, although no specific suggestions were made. As SANBS was the only blood transfusion service in the world using donation risk categorization beyond the distinction between new donors and regular donors, no other existing models could be investigated. During the southern area branch managers' meeting in April 2004, the Kimberley branch manager (Mr D H Brown) suggested that a risk management

model based entirely on the interval since the last donation be investigated. In this study this model is referred to as the Donation Interval Model. The suggested parameters for the model entailed that all donations from new donors and donors whose previous donation had been made more than 365 days (one year) previously, are categorized at the highest risk level of a four-tiered system. With each successive donation made by the donor within a period of 121 days (four months) the risk category of the donation drops by one level till the lowest risk category level is reached. Any donation made by the donor between 122 and 182 days (four to six months) after the previous donation, would result in the risk categorization of that donation remaining the same as that of the previous donation. Any donation made by the donor between 183 and 365 days (six months to one year) after the previous donation, would result in the risk categorization of that donation increasing by one level until the highest risk categorization level is reached. The parameters of the Donation Interval Model are summarised in Table 2.7.

Table 2.7: Donation Interval Model parameters

RISK CATEGORY / CHANGE	DONATION / TEST INTERVAL
Category DI4	>365 days
	New donors
Previous donation category +1 level	183 – 365 days
Previous donation category	122 – 182 days
Previous donation category –1 level	0 – 121 days

However, the author felt that the Donation Interval Model could place severe strains on the total low risk (“A1” and “A2”) blood supply due to the limited regularity of donations by voluntary blood donors. A second alternative model is suggested by this author. This alternative model uses the parameters of the SABTS 1999 risk categorization model as a base-line which is then augmented by the parameters of the Donation Interval Model, and is described as the Combination Model in this study. The parameters of the Combination Model are summarised in Table 2.8. The defining difference between this model and the SABTS 1999 Model is the fact that regular donations at intervals of not more that 121 days (4 months) by a donor, would result in following donations being categorized at the lowest risk level irrespective of the donor’s ethnic group or gender. On the other hand the difference between this model and the Donation Interval Model lies in the fact that donations made by a donor at extended intervals greater than 182 days (six months) would result in a progressive increase of the risk categorization level to the maximum risk category as determined by the SABTS 1999 Model for donors of the specific ethnic group and gender.

Table 2.8: Combination Model parameters

RISK CATEGORY / CHANGE	DONATION / TEST INTERVAL				
COHORT	New donors	>365 days	183 – 365 days	122 – 182 days	0 – 121 days
Asian male	Cb2	Cb2	Prev. cat. -1; max = Cb2	Prev. cat.	Prev. cat. +1; min = Cb1
Asian female	Cb2	Cb2	Prev. cat. -1; max = Cb2	Prev. cat.	Prev. cat. +1; min = Cb1
White male	Cb2	Cb2	Prev. cat. -1; max = Cb2	Prev. cat.	Prev. cat. +1; min = Cb1
White female	Cb2	Cb2	Prev. cat. -1; max = Cb2	Prev. cat.	Prev. cat. +1; min = Cb1
Coloured male	Cb3	Cb3	Prev. cat. -1; max = Cb3	Prev. cat.	Prev. cat. +1; min = Cb1
Coloured female	Cb4	Cb3	Prev. cat. -1; max = Cb3	Prev. cat.	Prev. cat. +1; min = Cb1
Black male	Cb4	Cb4	Prev. cat. -1; max = Cb4	Prev. cat.	Prev. cat. +1; min = Cb1
Black female	Cb4	Cb4	Prev. cat. -1; max = Cb4	Prev. cat.	Prev. cat. +1; min = Cb1

Before a study of the implications of the suggested alternative models could be launched, the arbitration and mediation of the labour dispute between the staff member and SANBS took place. As a result of the media coverage of the case and the risk categorization system used by SANBS, unpublished discussions were held between SANBS and the Department of Health during November and December 2004, regarding possible alternative risk categorisation models which would also be in keeping with the South African constitution. At a further

meeting in February 2005 between SANBS and the Department of Health, a model was proposed which is based on the number of donations made by a donor within the previous 24 months, officially designated as the "Donor Status Risk Management Model" by Heyns, Swanevelder, *et al* (2006) and described as the SANBS 2005 Model in this study. This proposal was implemented on 1 October 2005 together with nucleic acid amplification testing (NAT) (Hill, 2000) in place of the HIV p24 test. This model provides for the risk categories and usually appropriate usage of the donations collected in the Inland Region as indicated in Table 2.9. In the East Coast Region of SANBS, this model was implemented with modified criteria based on the specific HIV prevalence statistics of the region.

Table 2.9: Risk category application of the SANBS 2005 Model in the Inland Region of SANBS

RISK CATEGORY	NORMALLY ACCEPTABLE USAGE	CRITICAL SHORTAGE USAGE
C	Red cell products for adults and infants, platelet products and plasma products	
R	Red cell products for adults and plasma products	Platelet products
PLR1	Plasma products	Red cell products for adults
PLR2	Plasma used	Red cell products for adults if no PLR1 red cells available
PLR3	Plasma used	Red cell products for adults if no PLR2 red cells available
P	Plasma used	

An unpublished predictive statistical analysis carried out by the SANBS data analyst, which was presented at a branch managers' meeting in March 2005, indicated that this model, coupled with the implementation of NAT, appeared potentially safer than the SABTS 1999 Model. An informal predictive statistical analysis of the donation frequency of the donors on the panel, as carried out at the branch managers' meeting in March 2005, indicated that 85% to 90% of donations received would be expected to fall in the "C" and "R" risk categories, which represented a considerable decrease in routinely available blood when compared to the 94% of donations which fell in the "A1" and "A2" risk categories. The parameters of the SANBS 2005 Model are summarised in Table 2.10.

Table 2.10: SANBS 2005 Model parameters defined for the Inland Region

RISK CATEGORY	DONATIONS IN 24 MONTHS	DONOR AGE	DONOR SEX
C	4 and more	All ages	Male & female
R	2 to 3	All ages	Male & female
PLR1	1	All ages	Male & female
PLR2	New donors	16 – 25 years	Male
PLR3	New donors	16 – 25 years	Female
P	New donors	>25 years	Male & female

During a discussion between the Chief Executive Officer (CEO) of SANBS and the author at the branch managers' meeting in March 2005, the CEO made a suggestion that consideration be given to the

use of the donor age as a possible indicator for a more effective risk categorization model. The intention of the suggestion was to find a model combining the anticipated safety of the SANBS 2005 Model with an increased availability of blood categorized as low risk. However, an informal unpublished pilot study of the HIV-positive donations received at the Bloemfontein branch of SANBS since October 1997, which was undertaken prior to the start of this study, showed very little correlation with specific age groups among new donors and is therefore not reported in this study. This can probably be attributed to the fact that the HIV-positivity rate is more reflective of the HIV prevalence in the potential donor population than of the incidence of new HIV infections. A similar situation exists in respect of existing donors who have not donated for more than 24 months (lapsed donors) where the time of seroconversion is poorly defined. The finding in this pilot study did not correspond with the results of Shisana *et al* (2005) when applied to new and lapsed donors. This discrepancy may have been the result of the informality of the pilot study or the ethnic bias inherent in the donor population at the time of this study when compared to the study by Shisana *et al* (2005). In the case of "regular" donors (previous donation within 24 months) the time of seroconversion is more closely defined, resulting in rates of HIV positivity which may more closely approach the incidence of new HIV infections. Analysis of the data obtained in this informal pilot study by the author showed that in the case of "regular" donors there were noticeable differences in the prevalence of HIV-positive donations among the donors of differing ages and

therefore forms the basis of a 5th model. Data published by Shisana *et al* (2005) also shows an unequal prevalence of HIV among different age-groups, similar to the results obtained in the pilot study with regard to “regular” donors. In addition, the study by Shisana *et al* (2005) shows a marked difference in HIV prevalence between males and females within individual age-groups.

The model which is primarily based on the donor age at the time of the donation is described as the Age-based Model in this study. The determination of the final parameters for this model forms the first phase of this study.