Superior Health Council

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Sexual risk behaviour and blood donation
Part I: Blood donations by MSM

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This advisory report is only partially available in English for the time being.

Until the translation of the remaining parts of the document is available, please view the full advisory report in French https://www.health.belgium.be/fr/avis-9291-don-de-sang-par-les-hsh
or Dutch https://www.health.belgium.be/nl/advies-9291-bloeddonatie-door-msm.
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[1] The Council reserves the right to make minor typographical amendments to this document at any time. On the other hand, amendments that alter its content are automatically included in an erratum. In this case, a new version of the advisory report is issued.

Avenues for further reflection about methods to safeguard the blood supply

2.2.12. Proportionality of methods to safeguard the blood supply

Based on the scientific data in this report as well as the regulatory framework mentioned above, the SHC can provide decision-makers with the following avenues for further reflection that guarantee and preserve maximum safety for all recipients of blood donations and try to address the sense of stigmatisation experienced by some MSM.

2.2.12.1. The terms for lifting the ban

The proposals in support of full ban-lifting highlight the benefit in terms of social consensus and harmony, and are grounded in the currently extremely low level of residual risk for the identified viral agents. It follows that this approach relies on the accuracy of screening techniques and on ensuring the safety of the most efficient blood components.

Another argument that is often raised in support of lifting this ban is the public health benefit (a few percent more donations), especially in countries facing a structural blood component shortage. Donor selection procedures are then focused on specifying more individualised criteria as regards sexual behaviour, which is looked upon as an appropriate risk indicator.

However, this approach involves ignoring the crucial role played by the precautionary principle and current eligibility criteria in obtaining very low levels of residual risk, such as those that currently prevail in Belgium. This approach attaches a much greater deal of importance to the potential sense of discrimination felt by donors than it does to the recipients' need for safe donations.

Another important element in this debate is that the dramatic improvement in surgical techniques, organ transplantation or the treatment of severe bleeding (SHC, 2015b) has significantly reduced the need for blood transfusions, which has resulted in the fact that there is no structural shortage in the Belgian blood supply (SHC, 2013).

The SHC has assessed the information that is available on HIV in three countries that have lifted the MSM ineligibility criteria for blood donation, viz. Italy, Spain and South Africa. In these three countries, only Spain displays a difference in incidence rates in the population (CNEDGSPCI, 2015) that is comparable to the difference observed in Belgium (see Figure 4). Conversely, in Italy and South Africa, the ineligibility criterion was lifted once heterosexuals were those predominantly infected.

Spain has seen a clear rise in the HIV-test positivity rate among blood donors, with currently nine out of ten donations infected with HIV coming from an MSM-donor (Oyonarte, 2012). This goes hand in hand with an increasing number of recent HIV-infections which are diagnosed on the basis of positive NAT-results whilst immuno-enzymatic testing does not yield any positive results (Benjamin et al., 2011).

The data from Italy are less clear (cf. section 2.2.7.1.). Nonetheless, the percentage of seroconverted MSM among regular donors has gone up by 19 % since the MSM ineligibility criterion was lifted in that country, whereas it has gone down among heterosexual donors (EDQM, 2012; Piccinini et al., 2014). Finally, Raimondo et al. (2016) emphasise the need for more understandable educational material, a clearer pre-donation questionnaire and effective information campaigns to improve awareness among Italian blood donors of sexual behaviour associated with a risk of acquiring HIV.

In South Africa, the infection rate among the general population is so high that additional measures have been implemented to enhance the safety of the transfusion chain, viz. by quarantining plasma (cf. 2.2.11.8). Given the preliminary data, it is not possible to assert that there has been any change in the percentage of seroconverted MSM among regular (red cell or platelet concentrate) donors since the MSM ineligibility criterion was lifted in that country.

As noted in the SHC's analysis, there is currently a lack of strong evidence in support of a full ban-lifting strategy, even in countries where the prevalence and incidence of HIV among MSM are similar to those in the heterosexual population. Seeking to transfer this provision without careful consideration to the Belgian blood donation system, *i.e.*, in a country in which there is no doubt that the prevalence and incidence of HIV among MSM exceeds the corresponding epidemiological parameters among heterosexuals, is not an option for the time being. Indeed, the incidence rate among Belgian MSM is currently almost 450 times higher than that among heterosexual blood donors.

Last but not least, the legislator should clearly set out the responsibilities in the event of a recipient of blood that was contaminated with HIV or HCV and was donated by MSM filing a complaint based on current legislation, which provides for a temporary (or lifelong) ban for donors whose sexual behaviour entails a (significant) risk of acquiring (serious) blood-borne infectious diseases.

It goes without saying if the HIV-seropositivity incidence rate among the MSM population were to drop to levels on a par with those among the general population, the fraction of the residual risk that can be attributed to MSM would no longer be a decisive part of the overall residual risk, which in turn would mean that the eligibility criteria could be adjusted to the latter's epidemiological situation. Reducing the risk of transfusion-borne transmission also requires prevention efforts to eradicate the HIV epidemic in the Belgian population and especially among MSM.

Until there is no longer any difference in the incidence rate of HIV among MSM on the one hand, and the general population on the other, which would mean that it would no longer constitute an eligibility criteria for blood donation, whole blood or blood components prepared with blood donated by MSM could be used for scientific research purposes only (SHC, 2013; CBS, 2014; Waller et al., 2016).

2.2.12.2. Upholding a lifelong ban

Upholding the ineligibility criterion for MSM gives priority to the objective and legal responsibilities of transfusion professionals (see 2.2.11.1.), who aim at enhancing the safety of blood components in accordance with the principles for keeping the risk as low as reasonably possible. Indeed, providing compelling evidence of the extremely low risk (Hrudey & Leiss, 2003) requires that a significant amount of resources be allocated towards producing convincing knowledge.

Managing such risks then includes taking balanced decisions in relation to the other risks that need to be considered (for example, in the event of a blood shortage) and also takes into account the shifting of the risk (to the transfusion recipients), fairness issues (giving priority to the managing of high risks), the relative risks (e.g. giving preference to low-risk donors), etc. Donor selection procedures are focused on certain individuals who belong to highly interconnected sexual contact networks and pose a significantly increased risk of transmitting serious blood-borne infectious diseases.

The SHC's analysis indicates that achieving a very low residual risk be largely attributed to the combined implementation of the precautionary principle, the current eligibility criteria and techniques for screening and ensuring the safety of blood components, which, though effective, are not, however, infallible. The donor-selection-criteria strategy is otherwise consistent with the prevention campaigns for HIV and sexually transmitted infections.

Risks may be assessed very differently, depending on whether this is done from an individual or collective perspective. The way in which an individual perceives the risks of sexual intercourse and takes precautions to reduce them, is fundamentally different from the approach taken by those in charge of blood transfusion, whose task it is to ensure that all efforts are made to prevent transfusion-transmitted infections in patients. HIV is an insidious virus that initially causes little or mild symptoms. If the infection remains unnoticed and therefore untreated, it results in immunodeficiency, usually after a few years.

The SHC emphasises that the key issues are the prevalence and multiplicity of individuals' encounters within their sexual contact networks. Given the fact that the proportion of MSM among the overall population is low (estimated at 1.5 % for Belgium), but that half of all those infected with HIV are in fact MSM (see Figure 4), the risk of acquiring the infection in this sexual contact network is particularly high (see Figure 5). Those in charge of blood safety thus find themselves in a situation in which they have to decide whether it is acceptable to shift the risk associated with some donors to recipients who are not in a position to decide what will or will not be done with their own bodies (Leiss et al., 2008; Folléa, 2016).

Indeed, it may be useful to put oneself in the position of a recipient who needs to be transfused with several hundred blood components during his/her lifetime (e.g. a patient with a haemoglobinopathy; Petermann et al., 2016): this patient will be repeatedly exposed to a very small risk, yet the cumulative risk will no longer be entirely negligible. Moreover, given the fact that several blood components are usually obtained from a single donation and that several individuals are often infected through a single contaminated sample, it would be advisable to prevent such transmissions from occurring, as there is no treatment available that can cure AIDS and the impact on the quality of life of those infected inevitably affects all three aspects of health, *i.e.*, physical, mental and social health.

The SHC points out that in Belgium, the number of newly diagnosed cases of sexually transmitted HIV is not stable but has changed over time. For the last 10 years, its incidence has continued to increase sharply among MSM (Figure 5). Some other sexually transmitted infections have also been on the rise during this period (see Table 5). In addition, as regards emerging viral infections, care should be taken not to underestimate e.g. the RNA viruses' high mutation potential, which can alter the course of the outbreak any time.

Virtually all cases of transfusion-transmitted HIV could have been avoided if the donors had strictly abided by the current exclusion criteria and reported their sexual activity in the anamnesis or used the self-exclusion option. Between 2007 and 2014, four cases of HIV-infection were diagnosed in Belgium based on a positive NAT result, whereas the enzyme immunoassay (*i.e.*, recent infections) had yielded no positive results. Three infections were detected among the eight regular "indeterminate" male donors (see Figure 6), viz. 37.5 %, which suggests that the risk of transmission is higher for these donors. Given the fact that this concerns recent infections, these regular donors should be able to recall any "high risk" sexual behaviour (Morris et al., 2005).

The assessment is based on epidemiological data as well as the principle that no additional risk for transfusion-transmission can be tolerated; it is not grounded on sexual prejudices. From this point of view, the lifelong ban for MSM does not amount to any improper unequal treatment, despite the fact that this practice may be perceived as stigmatising by donor candidates. Moreover, the aim is not to deny any access to goods, services or personal rights. Rather, this is an act, the sole purpose of which is to benefit others, in this case the patient receiving a blood component.

2.2.12.3. Terms for donations by men who have no longer had any sexual intercourse with men for several months

This proposal arises from the observation that the risk of infections associated with a given type of behaviour disappears along with the behaviour in question and that, after a variable time interval, that individual may be tested for HIV and other communicable diseases.

Just as for other practices, some professionals believe that high-risk sexual behaviour for serious, potentially blood-borne infectious diseases can be managed by means of a temporary deferral from blood donation. Indeed, the screening tests are effective enough for the prevalent infections to be recognised reliably. It is believed that a sufficiently lengthy deferral period would be a reliable means of preventing the transmission of a newly acquired infection through the donated blood during the window period of the tests (see Figure 3). It is often claimed that such an amendment to the risk management strategy would make it possible to align the deferral period for MSM-donors with the criteria used for other situations that may entail a similar risk of transfusion-transmitted infections. Finally, the hypothesis that MSM-donor compliance with the eligibility criteria improves upon implementing such a reform has been confirmed by results published in Australia (Seed et al., 2010).

It is not possible to predict what the outcome will be of reviewing these criteria. Still, mathematical models yield a small increase in the residual risk in countries with a fairly low rate of non-compliance with the eligibility criteria. Nonetheless, prior to implementing such a change, these countries — especially Australia, Canada, France, the United Kingdom and Japan — had improved the detection capability of their NAT-screening test for HIV (Wilson et al. , 2014), some going so far as implementing individual NAT-screening first (see Figure 1).

The SHC has assessed the impact of adopting the temporary deferral criterion in several countries. This assessment reveals that the residual HIV risk for recipients, monitored through the number of HIV-positive donations screened, has remained virtually undetectable. Comparing the forecasted numbers of infectious donations with the actual numbers shows that they seem to have been overly pessimistic for Australia, Canada and the UK (Germain, 2016). Moreover, the impact on the number of additional donations has been minimal. For Japan, the data pertaining to the number of donations are not yet available as a publication. Still, the number of HIV-positive donations screened did not go up but continued to fall once the temporary deferral period had been shortened from 12 to 6 months upon reaching a low rate of non-compliance with the eligibility criteria (see Figure 9).

Outside Japan, compliance has not improved and it is possible that MSM-donors who had already failed to abide by a lifelong exclusion criterion have continued to give blood in spite of a temporary deferral. For example, in the UK, 87 of the 251 MSM (34.7 %) mentioned by Davison et al. (Davison et al., 2015b) do not comply with the eligibility criterion for men who have no longer had sexual intercourse with men for at least 12 months. This proportion is indeed in line with the statements collected during surveys among MSM, in which 31.3 to 52 % declared that they do not intend to comply with a temporary deferral criterion (Grenfell et al., 2011; Custer et al., 2015b). During the first five years after of a one-year deferral period was implemented in Australia, 5 MSM donors who screened HIV positive could be interviewed: all of them had failed to report having had a sexual relationship with a man during the last 12 months (Seed et al., 2010).

Two pieces of evidence have generally been put forward to set the deferral period at 12 months: the lack of solid data in support of shorter periods and the results of the study by Sanchez et al. (2005), which show a rise in HIV-infections among MSM-donors who had sexual intercourse during the last 12 months. The SHC has been able to gain access to the results obtained in Japan after shortening the temporary deferral period from 12 to 6 months in April 2011 — however compliance with criteria might be particularly high in that country — and comes to a different conclusion than the one drawn by Sanchez et al. (2005) (see 2.2.7.1.).

Given the uncertainty about the impact on non-compliance, the SHC emphasises the need to speed up the notification of blood-borne infectious diseases at the level of the haemovigilance monitoring system for one year after thus changing the deferral criterion. The appropriateness of setting up individual NAT-screening in this context should probably also be subjected to an economic evaluation in view of the very high cost of these tests to achieve a 37 % reduction of the corresponding window period for HIV (Byrne et al., 2011; Lieshout-Krikke et al., 2012).

Finally, there is one last aspect that needs to be addressed by decision-makers: the reaction of certain plasma fractionation companies, which could turn down Belgian plasma if the lifelong exclusion criterion is not upheld. Indeed, 90 % of the plasma collected in Belgium is currently used for industrial manufacturing (L. Muylle*, pers. comm.*; SHC, 2011).

Great care should be exercised in communicating such a change in the risk management strategy, because this reform proposal has already been represented by some as a mere diversionary tactic masking a desire to uphold the lifelong ban, which is in turn liable to result in greater rates of non-compliance with the criteria for temporary deferral. Bringing the deferral period for MSM-donors in line with the criteria used for other practices that may be associated with a similar risk of transfusion-transmitted infections would not necessarily guarantee improved compliance. Due attention should also be paid to the risk of adversely affecting the trust enjoyed by those in charge of the transfusion chain, who are still experiencing the aftermath of the transfusion-transmitted cases of HIV and hepatitis C in the early 1980s. The impact could be felt, for example, as regards the compliance with other eligibility rules. Great care must therefore be taken when disclosing the results of the evaluation to the general public and patients requiring regular transfusions. It should clearly be explained that the reliability and relevance of the data used have been verified based on the assessment of current medical, scientific and epidemiological knowledge and that individuals who may be at an increased risk of communicable infections are not eligible to donate blood.

The SHC expressly advises that any potential amendment to the eligibility criteria be combined with a concerted awareness raising campaign aimed at improving rule compliance. This includes refocusing the debate on the place and responsibility of the person who gives blood (Riquet et al., 2016) and developing an easily understandable, standardised questionnaire for the whole country to check the blood donor's history (Kort et al., 2014).

2.2.12.4. Terms for donations from MSM having shared an exclusive, closed-couple relationship for several months

There is no risk of HIV-transmission from people who state that they share an exclusive, closed-couple relationship in which both partners have had negative screening results in the 6 to 12 months prior to donating blood.

However, it is possible that, whilst a potential donor does commit to a monogamous type of relationship, his partner does not behave accordingly. Therefore, without evidence from negative HIV-tests for both partners, there is the possibility of there being unknown, occasional partners, with a correlated, average relative risk of 55 (95 % CI: 15.4 to 193.6) among MSM compared to heterosexuals with a new partner (see Figure 3).

No physician collecting the blood is able to rule out with certainty, by means of a pre-donation interview, the possibility that a person sharing an exclusive, closed-couple relationship (including a man describing himself as a monogamous MSM) has recently acquired an HIV, HBV or HCV infection.

To date, none of the questions in the pre-donation interview have allowed for the reliable identification of a subgroup of MSM (e.g., based on the stability of couples or on safer sex) who do not display any significantly higher rate of HIV-infection compared to the general population or accepted blood donors (Offergeld et al., 2014; Preuβel & Offergeld 2015). In the past 15 years, there has been a trend that shows that among MSM, most HIV-infections are due to sexual intercourse with the main partner. On the one hand, the frequency of unprotected anal sex is close to 80 % with long-term partners (see Figure 2), on the other, the proportion of sexually transmitted HIV-infections due to the male condom slipping off, tearing or being put on too late seems substantial (Remis et al., 2014)[2]. More than a third of non-compliant MSM-donors who screened positive for HIV in the Netherlands were part of a stable couple (Schippers, 2015).

In Spain — a country in which there are no eligibility criteria for MSM — collection centres not only defer donors who have had sexual intercourse with multiple partners, but also those who have had unprotected sex[3]: this has not prevented HIV rates from going up among blood donors, with nine out of ten infected donations coming from a MSM donor (see 2.2.9.2a).

There are reports of transfusion-borne HIV from a monogamous MSM-donor in whom the transmission of infection could clearly not be prevented despite consistent condom use (Kalus et al., 2009). This highlights once again the purpose of the precautionary principle.

In the future, amended questionnaires could be useful to improve the assessment of the risk from blood donor candidates, but this cannot be asserted without proof from negative viral screening results (O'Brien et al., 2006; HHS, 2016). Moreover, there are data that show that MSM who are generally reluctant to the idea of a deferral from blood donation, also find specific questions about their sexual activities unacceptable (Go et al., 2011).

2.2.12.5. Requirements for donors with negative HIV-screening results

Some donor-candidates share a resolutely monogamous sexual partnership and can provide proof of a negative HIV-screening test carried out prior to presenting themselves for donation. They may – mistakenly – believe that there is no risk of transmitting HIV since, in Belgium, the window period for the HIV-test that is currently performed on each donation ranges from about 5.6 to 9 days (see Table 2). However, this approach requires that there be no sexual intercourse between the negative screening results and the time of donation. This period must be determined based on the evolution of epidemics of serious sexually transmitted diseases (HIV, HCV etc.). Lieshout-Krikke et al. (2015) presented a first assessment of the benefits of pre-donation screening, but only for donors who were eligible based on existing criteria. The SHC takes the view that, given the current means of detecting serious blood-borne infectious diseases, a deferral period of 12 months should be abided by.

2.2.12.6. The terms for plasma and pathogen-reduced platelet donations

Blood-borne viruses are often found in plasma. Some pathogens, such as HIV, have the ability to enter cells or form aggregates on their surface. Plasma and platelet concentrates therefore undergo pathogen reduction (see Table 3). At the level of industrial fractionation, the plasma is treated by means of the solvent-detergent method, followed by additional virus inactivation/removal steps. With HIV potentially reaching 10^7 gEq/mL plasma (Cohen et al., 2011), a combination of methods is necessary. This combination of methods has been validated for the manufacture of plasma products (Dichtelmüller et al., 2010). The Belgian blood establishments also use pathogen reduction for plasma intended for transfusion as well as for platelets.

[2] For further explanation, see Stone et al. (1999), THT (2011), Sanders et al. (2012) and Schippers (2015).
[3] see http://www.donarsangre.org/donantes-de-sangre/

Given the fact that genomic screening displays an excellent detection limit for RNA viruses, it is conceivable that pathogen reduction technology allows for the inactivation/removal of such residual amounts of infectious particles. However, this technology must be validated for each pathogen specifically under realistic conditions of use (SHC, 2015c), taking into account - among other things - the fact that HIV is known to aggregate to platelets.

Recently, several publications have reported cases in which incompletely inactivated/removed pathogens present in low amounts in platelet concentrates were transmitted through transfusion (SHC, 2011b). Álvarez et al. (2016) have only just described such a case for HIV in virus-inactivated plasma from a regular donor. It should not be forgotten that Rujirojindakul (2015) described a case in which plasma intended for transfusion was contaminated despite the fact that NAT-screening had been performed on a *minipool* of 6 donations. Apart from this preliminary description, the SHC has been unable to obtain any further information, especially as regards the possible use of pathogen reduction technology.

There is no pathogen reduction technology available yet for red blood cell concentrates.

In the future, methods that are more efficient in enhancing the safety of these blood components could allow for donations of plasma and pathogen-reduced platelets from high-risk donors to be accepted.

2.2.12.7. Accepting quarantined plasma donations

This approach seeks to ensure the safety of plasma donations by installing a retention period, at the end of which the donation is only accepted if the donor returns and if the screening results for the new donation turn out negative. This plasma is retested only for the pathogens for which screening is implemented to ensure the safety of the transfusion chain. However, given the fact that the plasma is virus-inactivated and tested a second time upon the donor's return, there can be no more transfusion-borne transmission of HIV, HCV and HBV.

In the event of MSM being accepted, the estimated number of additional donor candidates (see Table 10) suggests that some 4,000 new donors will be concerned by the plasma-quarantine approach. If the donor fails to return, the non-retested MSM-plasma could, for example, be used for scientific research purposes (SHC, 2013; CBS, 2014; Waller et al., 2016).

There is a need to set up the necessary organisation so as to avoid any erroneous release from quarantine (cf. case of HIV-transmission revealed by Sobata et al., 2014). In addition, in order to avoid having to discard and destroy other components from a sample of whole blood, fresh frozen plasma shall be collected by means of plasmaphaeresis.

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