Pathogen data sheet - HIV

Data sheet to support the development of the ECDC technical guidelines on the prevention of HIV transmission through substances of human origin

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Abbreviations

Ag	Antigen
AIDS	Acquired immunodeficiency syndrome
ART	Antiretroviral therapy
CLIA	Chemiluminescence immunoassay
CMIA	Chemiluminescence microparticle immunoassay
ECDC	European Centre for Disease Prevention and Control
ECLIA	Electrochemiluminescence immunoassay
EDQM	European Directorate for the Quality of Medicines and Healthcare
EEA	European Economic Area
EIA	Enzyme immunoassay
ELISA	Enzyme-linked immunosorbent assay
EU	European Union
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
ID	Individual test
IU	International units
MP	Mini pool
NA	Not applicable
NAT	Nucleic acid test
NR	Not reported
p24Ag	p24 antigen
PDMP	Plasma-derived medicinal product
PWID	People who inject drugs
SoHO	Substances of human origin (excluding solid organs)[1]
UV	Ultraviolet
WHO	World health organization

[1] As per the Proposal for a REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL on standards of quality and safety for substances of human origin intended for human application and repealing Directives 2002/98/EC and 2004/23/EC.

Foreword

This document is intended to support the discussions of the ad hoc scientific expert panel convened for the development of the ECDC Guidelines on the prevention of HIV transmission through substances of human origin (SoHO). These technical guidelines have been prepared in the context of the Proposal for a Regulation of the European Parliament and of The Council on standards of quality and safety for substances of human origin intended for human application and repealing Directives 2002/98/EC and 2004/23/EC. Solid organs are excluded from the definition of SoHOs in the scope of the Regulation as well as from the scope of this document. This document was finalised in March 2024 prior to the publication of the SoHO regulation and the document reflects the information that was available to the expert panel at the time the meetings were held to discuss the requirements and recommendations for HIV.

1. Description of the pathogen

Classification and relevant features

Based on the genetic characteristics and differences in the viral antigens the human immunodeficiency virus (HIV) is subdivided into the two major types, HIV type 1 (HIV-1) and HIV type 2 (HIV-2). Both types are further divided into the groups and several subtypes within each group.

Table 1. HIV-1 and HIV-2

Feature	Value
Realm	Riboviria
Kingdom	Pararnavirae
Phylum	Artverviricota
Class	Revtraviricetes
Order	Ortervirales
Family	Retroviridae
Genus	Lentivirus
Characteristics	Single-stranded positive-sense enveloped RNA virus
Cell tropism	Immune cells, e.g., – T lymphocytes (CD4 cells) – Monocytes – Dendritic cells – Macrophages – Microglial cells – Astrocytes
Receptors on host cell	On CD4 cells, macrophages, dendritic cells: – CD4 – C-C chemokine receptor type 5 (CCR5) – C-X-C chemokine receptor type 4 (CXCR4) (astrocytes only) – DC-SIGN (dendritic cells only)

From: [1-4]

2. Description of the infection and the disease

Routes of transmission

The primary mode of transmission for HIV is through contact with bodily fluids, particularly blood, semen, pre-seminal fluid, rectal secretions, cervico-vaginal secretions, and breast milk, during unprotected sexual contact, sharing of contaminated needles or injection equipment, and vertical transmission during pregnancy, childbirth, or breastfeeding. HIV can also be transmitted through transfusion of infectious blood or blood components and plasma-derived medicinal products, transplantation of different tissue types, as well as non-reproductive and reproductive cells, (see 'Transmission through SoHO'). Transmission of HIV can also occur through the transplantation of human organs (these substances of human origin are not in scope of this document).

Natural history of HIV-1 infections

Without treatment, HIV infection advances in stages, getting worse over time. Untreated HIV infection is marked by active viral replication, progressive immunodeficiency, and significant clinical consequences. Infection can manifest with a wide range of symptoms and oral, cutaneous, renal, ocular, pulmonary, gastrointestinal, neurological, metabolic, endocrine and cardiac diseases. HIV infection can usually be classified in three distinct stages [2,5-7]:

Acute HIV infection

This is the earliest stage of HIV infection. It is an acute viral illness characterised by high viral load and an intense host immune response. Symptoms in this stage may include flu-like symptoms, such as fever, headache, and rash. For a significant proportion of individuals with a recent HIV infection, the initial manifestation of HIV infection is an illness resembling mononucleosis, known as an acute retroviral syndrome. The clinical features of this syndrome are nonspecific and can vary. The onset of symptoms occurs between one and six weeks after virus exposure, peaking at around three weeks. The symptoms are often mild, and HIV infection is not recognised at this stage. During the acute infection stage, the viral load in the blood is very high, which greatly increases the risk of HIV transmission. Untreated HIV infection will usually advance to chronic infection.

Chronic HIV infection

During the second stage of HIV infection, individuals are often asymptomatic for an extended period of time which can last months to years. At this stage, indolent lymph node swelling may occur as well as nonspecific constitutional symptoms in the months or years after primary infection. Even when in an asymptomatic disease course, HIV is typically not virologically latent, and chronic viremia, inflammation, and progressive immunodeficiency will eventually lead to substantial impairment and mortality. Chronic infection may present symptoms of the skin and mucous membranes, gastrointestinal symptoms, and occasionally neurological symptoms, although the duration of the asymptomatic stage will vary based on factors such as individual immune response or viral load. Additional symptoms may include lymphadenopathy, thrombocytopenia, and neurological complications resulting in HIV-related dementia, or persistent inflammation including cardiovascular disease, dyslipidaemia, hypercoagulability, cancers, and other metabolic disorders. Without appropriate treatment, HIV infection progresses to acquired immunodeficiency syndrome (AIDS).

Acquired immunodeficiency syndrome (AIDS)

The late stage of an HIV infection, AIDS, is defined by severe immunodeficiency and increased susceptibility to life-threatening conditions. Sequelae may include neurological complications, cardiovascular disease, renal impairment, liver disease, malignancies, and opportunistic infections and neoplastic diseases arising from impaired host responses due to damage or depletion of the cellular immune system. Without appropriate treatments, the late-stage HIV infection is fatal.

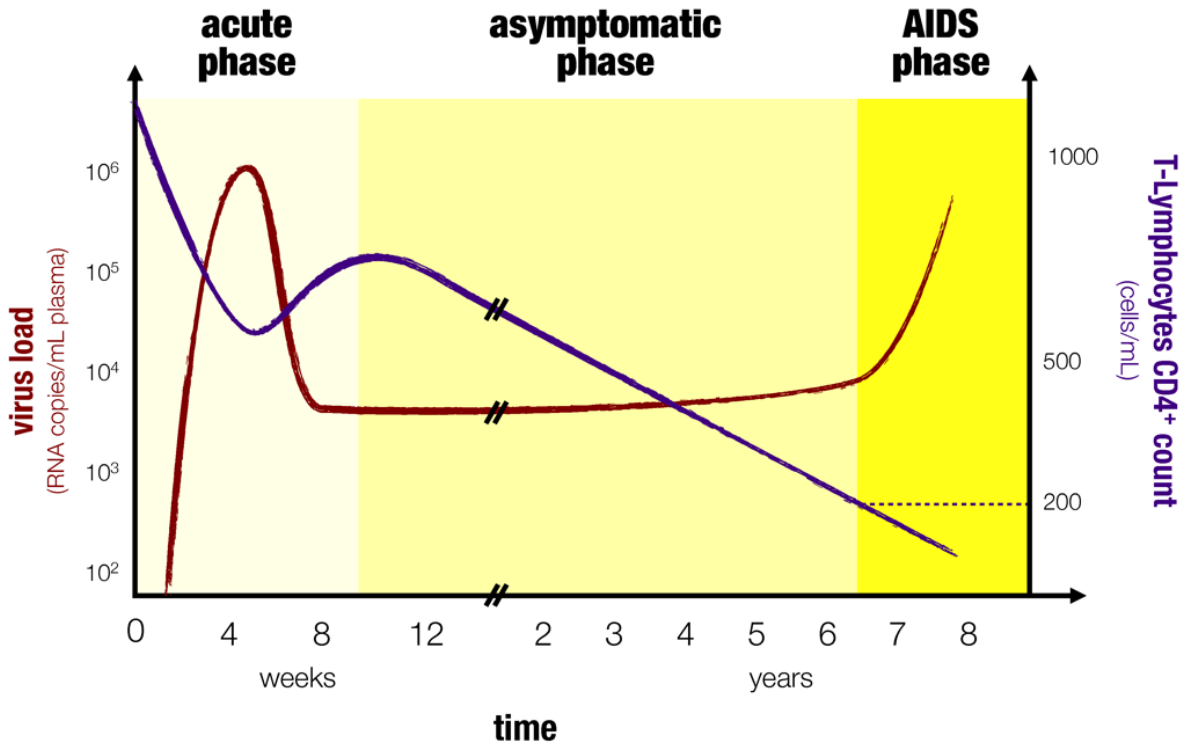
These stages are typical for infections with HIV-1. There is evidence of a second subtype of HIV (HIV-2), mainly circulating in West Africa. Though epidemiological information is lacking, it is considered to represent less than 1% of all HIV infections in Europe (see HIV-2 epidemiology), however dual infection with HIV-1 can occur where both viruses circulate. HIV-2 infections presents with a longer asymptomatic stage and slower decline of CD4-positive T-cell counts, though progression to AIDS and death will also occur in the majority of individuals affected by this subtype [8]. Screening and diagnostic tests validated for HIV-2 are required to detect this HIV subtype.

Available 4th generation antigen-antibody tests cover both HIV-1 and HIV-2 and a few nucleic acid tests can detect both infections, though assays able to detect HIV-2 RNA are limited in number and availability in Europe [9,10] (see Laboratory testing approaches).

Evolution of the viral load for HIV-1 infections

The evolution of the viral load for HIV and T lymphocyte CD4-positive counts throughout the course of an HIV infection is summarised in Figure 1, from Alizon et al [11].

Figure 1. Natural history of an HIV-1 infection



From Alizon et al. [11]

Acute HIV infection

The initial stage of primary HIV-1 infection involves the infection of target cells (see Table 1) by the virus in mucosal tissues and subsequently spreading through the lymphoid system. HIV-RNA levels in blood increase rapidly to be detectable approximately 10 days after infection and these levels increase exponentially reaching a peak a few weeks later. At this point, the adaptive immune system responds, resulting in partial control of the virus and a set level of viraemia is then established [12]. A prior period of low-level viraemia may occur in a significant proportion of individuals with an HIV infection. Whether the blood during this low-level viraemia period is infectious is unknown [13]. The time from infection to detection by available test methods for HIV-1 is described in Table 2. A detailed overview of available test methods for HIV is presented in 'Laboratory testing approaches'.

Table 2. Time from infection to positive results by test methods in the HIV-1 acute stage

Test method	Target	Approximate time to positive result
Enzyme Immunoassays – 3rd generation (antibodies only)	IgM and IgG antibody	20 days
Enzyme Immunoassays – 4th generation	IgM and IgG antibody p24 antigen	15-16 days [14]
NAT	HIV RNA	MP-NAT: 10±2 days [15] 95%LOD 100-300 IU/mL: 10 days [9,16] 95%LOD 875 IU/mL: 14 days [17]
NAT >5 copies/mL	HIV RNA	5 days

NAT: nucleic acid test. MP: mini-pool. LOD: limit of detection.
Adapted from Sax [9]

Chronic HIV-1 infection (asymptomatic stage)

Chronic HIV-1 infection is characterised by the stability of the viral level and a progressive decline in the CD4-positive cell count. When left untreated, the time from HIV infection to CD4-positive cell count < 200 cells/µL is approximately 8 to 10 years. When left untreated, viraemia will remain high throughout the disease course [7]. Effectively treated HIV infection can lead to undetectable viral levels from 3 to 12 months after treatment initiation depending on individual characteristics [7,18].

Acquired immunodeficiency syndrome (AIDS)

AIDS is the outcome of chronic HIV infection and the depletion of CD4-positive cells. Without effective treatment, the median survival for patients with advanced HIV infection (CD4-positive cell count <50 cells/µL) is 18 months [9].

Treatment options

Since the first combination therapies were approved in the 1990s, significant advances in highly effective antiretroviral therapy (ART) have been made. Treatments available today significantly prolong the median survival of treated patients with manageable side effects [19]. There are seven classes of ART, including nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), fusion inhibitors, CCR5 antagonists, post-attachment inhibitors, and integrase strand transfer inhibitors (INSTIs). They all reduce the capacity of HIV to replicate. However, though therapy lowers and even suppresses blood viral load it does not eliminate the virus and treatment is lifelong. Commonly reported side effects of ART are nausea and vomiting, diarrhoea, difficulty sleeping, dry mouth, headache, rash, dizziness, fatigue, and pain. Long-term consequences can include drug resistance, cardiovascular disease, metabolic complications, and bone mineral density changes. New ART were developed in recent years and these treatments achieve high effectiveness with fewer and less severe side effects supporting sustained treatment adherence [19-21].

Infectious dose

HIV-1 replicates with an average doubling time of 20 hours, with a peak viraemia of up to 10^7 HIV RNA copies per mL [12]. Viral load is a measure of the density of viral particles in peripheral blood. It is an imperfect but relevant measure of the severity of HIV-1 infection. Although its relationship to viral density in other body compartments and to viral replicative capacity is unclear, HIV-1 viral load has been shown to correlate with prognosis as well as with the probability of transmission between serodiscordant couples [22-24].

The infectious dose for HIV-1 is considered low. It is considered that people living with HIV-1 with a viral load of 1 000 copies per mL are at risk of transmitting the infection through sexual transmission [25]. For SoHO, and in particular for blood and blood component, the risk of transmission is higher and depends on the volume of plasma transfused and the stage of the infection [26,27]. A review of 15 reported cases showed HIV-1 positive blood components in the early window phase are not always infectious: plasma units containing 600 to 3 000 virions (1 200 to 6 000 copies) were infectious but red blood cell concentrates containing 500 to 5 000 virions (1 000 to 10 000 copies) were not infectious. Using probit analysis of reported cases, the authors propose a 50% minimum infectious dose (dose that will infect 50% of recipients) of approximately 400 virions or 800 HIV-1 RNA copies. It should be noted that using experimental animal models lead to a much lower 50% infectious dose of 10 virions or 20 HIV-1 RNA copies [27]. A recent analysis estimated a 50% infectious dose of 918 HIV-1 RNA copies in humans and 26 in animals [28].

Survival outside the human body

While HIV concentration can drop rapidly outside the human body in drying environments, the virus can remain viable in syringes for 21 days at room temperature and more than one week suspended in serum [29,30]. The half-life ($t_{1/2}$) of HIV in plasma at body temperature is approximately two days [31], and one month at 4 °C. HIV is relatively stable when exposed to UV-light, radiation or ultrasound [32,33].

Organ systems targeted by HIV and HIV presence in different tissues

In the early stage of the infection, HIV is present in the lymphoid tissues: lymph nodes, spleen, gut-associated lymphoid tissue [2,3,5].

In the chronic stage, HIV has spread through the blood throughout the body (see Table 1 and Table 3), surviving intracellularly in the form of proviral DNA:

- Lymph nodes, spleen, and the gut continue to be primary sites for viral replication [34], even among individuals treated with ART [35];
- HIV-1 can also be detected in the bone marrow, though there are conflicting observations on whether hematopoietic progenitor cells are a reservoir among treated individuals [36,37];
- Untreated individuals have also been shown to have virus presence in the liver [38] and in lung cells of both treated and untreated individuals [34];
- Renal and tubular epithelial cells [39,40], as well as several cells of the male and female reproductive tracts have been shown to be infected by HIV, including in ART-treated individuals [34,41,42];
- Recently, adipose tissue has also been identified as a reservoir for HIV in ART-treated individuals [43]
- HIV-DNA and RNA has been detected in the brain of individuals treated with ART, including in the cerebrospinal fluid [34].

Table 3. Presence of HIV DNA and RNA in human tissues

Tissues	Presence
Lymph nodes and spleen	HIV-DNA and RNA
Bone marrow	HIV-DNA
Liver	HIV-DNA
Gut	HIV-DNA and RNA
Nervous system	HIV-DNA and RNA
Lung	HIV-DNA and RNA
Kidney	HIV-DNA and RNA
Male reproductive tract	HIV-DNA and RNA
Female reproductive tract	HIV-DNA and RNA
Breast and breast milk	HIV-DNA and RNA
Adipose tissue	HIV-DNA and RNA

Adapted from Wong et al [34]

3. Epidemiology

Incidence and prevalence of HIV in the general population in the EU/EEA

The prevalence of HIV can be approached through the total estimated number of people living with HIV which is presented in Table 4. This number is based on an empirical modelling approach or any other empirical estimate. This estimate includes diagnosed and undiagnosed people [44].

Table 4. Number of all people living with HIV per 100 000 population and proportion diagnosed with HIV, treated for HIV, and considered virally suppressed, among all people living with HIV, by country in 2021

Country	Rate all people living with HIV per 100 000 population	% diagnosed among all people living with HIV	% treated among all people living with HIV	% virally suppressed among all people living with HIV
Austria	85.7	94.2%	85.9%	63.7%
Belgium	165.2	89.5%	82.5%	80.2%
Bulgaria	53.4	83.6%	47.9%	32.5%
Croatia	42.1	84.1%	74.2%	72.3%
Cyprus	144.3	66.7%	46.2%	-
Czechia	33.4	84.2%	76.8%	74.9%
Denmark	114.7	91.0%	86.6%	85.1%
Estonia	515.4	86.6%	65.4%	-
Finland	59.0	94.0%	89.0%	83.8%
France	264.1	86.5%	82.5%	79.1%
Germany*	109.2	90.4%	87.1%	84.0%
Greece	156.8	82.4%	66.5%	-
Hungary	74.0	50.2%	-	-
Iceland	80.3	98.3%	85.1%	82.8%
Ireland	143.8	90.3%	79.2%	75.0%
Italy	231.3	92.0%	86.9%	74.5%
Latvia	-	-	-	-
Liechtenstein	-	-	-	-
Lithuania	127.3	81.8%	35.1%	27.2%
Luxembourg	207.2	85.0%	76.0%	62.4%
Malta	143.4	75.0%	75.0%	-
Netherlands	135.6	92.7%	86.4%	82.8%
Norway	82.6	92.0%	90.2%	88.4%
Poland	50.0	84.0%	70.7%	-
Portugal	406.8	95.0%	79.2%	73.6%
Romania	93.7	91.6%	70.2%	44.8%
Slovakia	19.1	80.0%	62.4%	50.0%
Slovenia	38.2	90.6%	87.8%	84.0%
Spain	319.4	87.0%	84.7%	76.6%
Sweden	86.4	90.3%	88.5%	85.9%

*Rates per 100 000 population were calculated using Eurostat 2021 population estimates published in July 2023. Estimates of people living with HIV , diagnosed, treated and virally suppressed were obtained via modelling (see methods in source). Adapted from ECDC [44]. * Data from Germany are based on [45].*

The exact incidence of HIV is not available but can be approached through the number of new diagnoses reported per year which is presented in Table 5.

The trend in reported HIV diagnoses has been declining since 2013, from 6.3 per 100 000 population for EU/EEA countries to 5.3 per 100 000 in 2019 and 5.1 in 2022. While the overall trend in EU/EEA countries indicates a decline in the last decade, trends at the national level can vary with not all countries following this decrease.

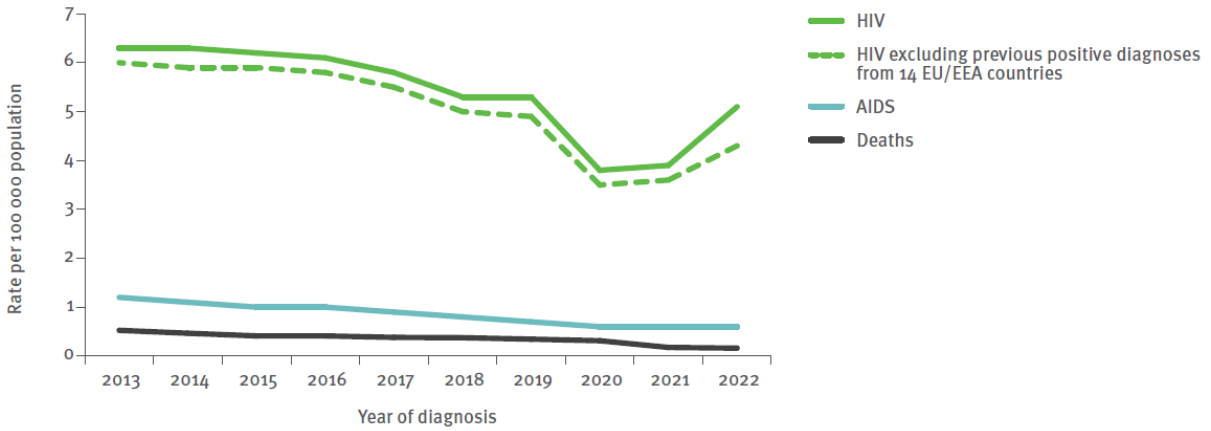
Table 5. Number of new HIV diagnoses notified and rates per 100 000 population, by country and year of diagnosis (2018–2022)

Country	2018		2019		2020		2021		2022	
	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate
Austria	222	1.3	251	1.4	173	1.0	188	0.8	189	2.1
Belgium	957	8.4	989	8.6	765	5.3	791	4.5	1 060	9.1
Bulgaria	311	4.4	258	3.7	199	2.9	237	3.4	328	4.8
Croatia	94	2.3	102	2.5	75	1.8	77	1.9	113	2.9
Cyprus	78	9.0	100	11.4	106	11.9	149	16.6	218	24.1
Czechia	208	2.0	222	2.1	251	2.3	233	2.2	870	8.3
Denmark	219	3.8	190	3.3	161	2.8	139	2.4	258	4.4
Estonia	190	14.4	178	13.4	147	11.1	125	9.4	250	18.8
Finland	153	2.8	148	2.7	134	2.4	162	2.9	273	4.9
France	5 109	7.6	5 129	7.6	3 570	5.3	3 627	5.4	4 158	6.1
Germany	2 886	3.5	3 126	3.8	2 468	3.0	2 258	2.7	3 239	3.9
Greece	725	6.7	669	6.2	623	5.8	572	5.4	565	5.4
Hungary	229	2.3	238	2.4	201	2.1	226	2.3	224	2.3
Iceland	38	10.9	28	7.8	34	9.3	20	5.4	40	10.6
Ireland	523	10.8	533	10.9	435	8.8	403	8.0	887	17.5
Italy	3 029	5.0	2 504	4.2	1 406	2.4	1 850	3.1	1 888	3.2
Latvia	333	17.2	304	15.8	257	13.5	212	11.2	229	12.2
Liechtenstein	0	0.0	0	0.0	0	0.0	1	2.6	1	2.5
Lithuania	160	5.7	151	5.4	139	5.0	121	4.3	252	9.0
Luxembourg	113	18.8	104	16.9	64	10.2	88	13.9	71	11.0
Malta	73	15.3	80	16.2	82	15.9	45	8.7	60	11.5
Netherlands	839	4.9	733	4.2	509	2.9	486	2.8	431	2.5
Norway	191	3.6	172	3.2	137	2.6	102	1.9	245	4.5
Poland	1 213	3.2	1 558	4.1	954	2.5	1 367	3.6	2 050	5.4
Portugal	1 311	12.7	1 295	12.6	967	9.4	1 072	10.4	804	7.8
Romania	768	3.9	779	4.0	522	2.7	639	3.3	670	3.5
Slovakia	102	1.9	104	1.9	103	1.9	115	2.1	197	3.6
Slovenia	38	1.8	34	1.6	29	1.4	35	1.7	42	2.0
Spain	4 015	8.6	3 879	8.2	2 843	6.0	2 981	6.3	2 937	6.2
Sweden	481	4.8	449	4.4	360	3.5	352	3.4	446	4.3
Total EU/EEA	24 608	5.3	24 307	5.3	17 714	3.8	18 673	3.9	22 995	5.1

Adapted from WHO-ECDC [46]

The crude AIDS diagnosis rate decreased from 1.2 per 100 000 in 2013 to 0.6 per 100 000 in 2022. In the 26 EU/EEA countries reporting such data, 767 people were reported to have died from AIDS-related causes in 2022, a decrease from 1 373 deaths in 2013. However, due to data collection challenges in many countries, which may have been exacerbated in 2020–2021 by the COVID-19 pandemic, this figure is affected by under-reporting. The cumulative totals of AIDS diagnoses and reported AIDS deaths from the beginning of the HIV epidemic to the end of 2022 in the EU/EEA were 346 712 and 183 383 respectively. See Figure 2.

Figure 2. People diagnosed with HIV, AIDS and deaths reported per 100 000 population, EU/EEA, 2013–2022



From WHO-ECDC [46]

Rates exclude countries not reporting consistently over the period: Germany and Sweden (AIDS and AIDS deaths), and Italy and Denmark (AIDS deaths). Previous positive diagnoses are HIV diagnoses that are newly reported a given year but represent previous HIV diagnoses done in another setting (e.g. abroad, or in another healthcare setting in the reporting country).

Reported modes of transmission of HIV in the EU/EEA

Surveillance data for HIV in the EU/EEA provides information on the transmission mode of HIV in reporting countries [46]. In 2022, for the first time, heterosexual contact was the main mode of HIV transmission in EU/EEA accounting for 33.7% of all HIV diagnoses that year and 46.3% of diagnoses with a known mode of transmission. Sex between men was the second most common mode of transmission, representing 33.3% of all HIV diagnoses in 2022, and 45.8% among diagnoses with a known mode of transmission (49.5% in 2013). Transmission associated with injecting drug use represented 4.3% of HIV diagnoses in 2022. The mode of transmission was reported as unknown for 2 418 diagnoses (26.7%), with wide variation among countries. With respect to reported modes of transmission, stigma and legal barriers may have influenced the recording.

HIV-2 epidemiology

Compared to HIV-1, HIV-2 infections are less common at around 5% of all HIV infections and are thought to affect 1–2 million individuals worldwide, mostly in West Africa. However, these figures are considered outdated, and the actual numbers may be lower as available country data indicates a decreasing prevalence in the last decade [47]. Several African countries still report a prevalence of HIV-2 infections of more than 1% in the general population: Cabo Verde, Côte d'Ivoire, Guinea-Bissau, Senegal, Sierra Leone, and the Gambia [8]. HIV-2 is also present at a lower prevalence in Brazil, India, Mozambique, Angola, and the United-States [8].

A recent meta-analysis estimated a prevalence of 3% of HIV-2 among all HIV-positive individuals in eight countries (Cabo Verde, Burkina Faso, Cote d'Ivoire, Guinea-Bissau, Mali, Gabon, Cameroon, France) and a prevalence of 10% of co-infections of HIV-1 and -2 in six countries (Guinea-Bissau, Burkina Faso, Cote d'Ivoire, Mali, Gabon, South Africa) [48]. However, these data are limited and should be considered with caution as HIV-2 surveillance data remain lacking [8,48].

Recent data on HIV-2 is not readily available for all EU/EEA countries, for countries with publicly accessible data, the total number of individuals who are HIV-2 positive remains limited in most countries with less than 1% of HIV-2 infections among all HIV infections with the exception of France (1.2% in 2013) and Portugal (2.6% in 2021), see Table 6.

Table 6. Total number of individuals with an HIV-2 infection and proportion of HIV-2 infections among all HIV infections per country

Countries	Total number of individuals with an HIV-2 infection	Time period	Proportion of HIV-2 infections among all HIV infections	Time period
Austria	7 [49]	2000-2009	-	-
France	1 200 [50]	Up to 2020	1.2% [51]	2012
Germany	-	-	0.4% [52]	2022
Greece	-	-	0.8% [53][a]	1993-1994
Netherlands	101 [54][b]	Up to 2021	0.3% [54] [b]	Up to 2021
Portugal	2 590 [55]	Up to 2021	2.6% [55]	2021
Spain	393 [56]	Up to 2019	-	-

[a] *In blood donors*
[b] *Does not include HIV-1/HIV-2 co-infections.*

Incidence and prevalence of HIV in SoHO donors in the EU/EEA

Table 7. Prevalence and incidence of HIV per 100 000 blood donors, per country, per year (2017 – 2019)

Country	2017		2018		2019	
	Prevalence in first-time donors	Incidence in repeat donors	Prevalence in first-time donors	Incidence in repeat donors	Prevalence in first-time donors	Incidence in repeat donors
Austria	8.6	1.0	1.7	1.5	5.0	1.0
Bulgaria	-	5.5	-	3.3	-	7.5
Croatia	6.7	1.0	0	0	0	0
Cyprus	-	-	-	-	18.2	4.7
Czechia	14.7	0.4	8.2	0.8	5.1	2.7
Denmark	-	-	-	-	0	0
Estonia	0	3.8	19.6	3.8	0	3.8
Finland	0	0.9	0	1.8	0	0.9
France*	2.4	0.5	4.8	0.4	4.6	0.2
Germany	4.8	1.6	4.6	1.5	5.7	1.1
Greece	18.0	2.9	14.8	4.3	17.4	2.4
Hungary	4.3	1.9	0	0.9	0	0
Ireland	8.0	5.8	0	1.5	4.4	0
Italy*	11.3	3.1	11.0	3.3	10.8	1.8
Netherlands	6.7	0.3	3.0	0.3	-	-
Norway	0	0	0	0	0	1.0
Poland	5.2	5.2	8.6	3.9	9.5	5.3
Portugal	11.6	5.4	12.2	3.9	8.0	3.4
Romania	-	-	21.3	7.3	-	-
Slovakia	0	0.9	4.0	2.8	0	0
Slovenia	0	0	0	0	0	0
Sweden	0	0.5	3.4	0.0	3.4	0

Prevalence: positive findings in first time first-time donors; Positive findings in repeat donors.
*Adapted from the European Directorate for the Quality of Medicines and Healthcare (EDQM) [57]. * Data provided by personal communication.*

Additional data were provided by personal communication for:

- Germany, for:
  - 2020 with 3.4 per 100 000 first-time donors (including candidate donors) and 1.5 per 100 000 repeat donors.
  - 2021 with 4.3 per 100 000 first-time donors (including candidate donors) and 1.0 per 100 000 repeat donors.
  - 2022 with 5.3 per 100 000 first-time donors (including candidate donors) and 1.1 per 100 000 repeat donors.

- France for:
  - 2022 with 2 per 100 000 first-time donors and 0.2 per 100 000 repeat donors.
- Italy for:
  - 2020 with 9.0 per 100 000 first-time donors and 1.9 per 100 000 repeat donors.
  - 2021 with 10.7 per 100 000 first-time donors and 2.0 per 100 000 repeat donors.
  - 2022 with 9.1 per 100 000 first-time donors and 3.1 per 100 000 repeat donors.
  - 2023 with 7.6 per 100 000 first-time donors and 2.9 per 100 000 repeat donors.

The data for Italy were added after the drafting of the ECDC guidelines on the prevention of donor-derived transmission of HIV through substances of human origin.

- Slovakia for:
  - 2021 with 7.5 per 100 000 first-time donors.
  - 2022 with 3.4 per 100 000 first-time donors.

Risk factors and specific populations more at risk of acquiring HIV

HIV infection is mainly acquired through sexual contact, exposure to blood, or perinatal transmission, with higher viral loads associated with greater risks of transmission.

Sexual encounters with mucous membrane damage and bleeding carry a greater risk of HIV infection than other sexual exposures. Unprotected anal sex leads to the highest risk of sexual transmission of HIV infection (see Table 8), for heterosexuals and men who have sex with men [58]. Additional sexual behaviours associated with an increased risk of acquiring HIV involve unprotected sex with an HIV-positive partner without effective antiretroviral treatment (ART), a new or an increase in the number of sexual partners, and sex under the influence of recreational drugs (sometimes referred to as 'chemsex') [58-60]. Sexually transmitted infections (STI) are also known to increase the risk of acquiring and transmitting HIV infection through inflammation and ulceration which increase both viral shedding and HIV susceptibility [60-62]. The likelihood of transmission through these different exposures depends on the prevalence of the infection in the respective population.

Regarding blood exposure, the risk of HIV infection is highest for blood transfusions, in particular in the absence of HIV screening, needle sharing in the context of drug use, and needlestick injuries [60]. An individual may have several behaviours associated with an increased risk of acquiring HIV, for example, people who inject drugs may also participate in sexual behaviour with an increased risk for HIV infection, e.g. having multiple sexual partners and/or condomless sex [63], each increasing the overall risk of HIV infection.

Due to the factors described above, the risk of HIV infection is disproportionately high in specific populations: men who have sex with men, people who inject drugs, and sex workers. These populations also face legal and social barriers (including stigma) which increases their vulnerability to HIV infection [44,60,61,64].

Table 8. Estimated per-act probability of acquiring HIV from someone who is HIV-positive, by exposure route

Type of exposure	Risk per 10 000 exposures
Parenteral	
Blood transfusion	9 250
Needle-sharing during injection drug use	63
Percutaneous (Needle-Stick)	23
Sexual	
Receptive anal intercourse	138
Insertive anal intercourse	11
Receptive penile-vaginal intercourse	8
Insertive penile-vaginal intercourse	4
Oral intercourse receptive or insertive	Low
Vertical transmission	2 260

From Patel et al., 2014 [59]
** Risk estimates do not account for risk reduction factors or measures such as condom use, antiretroviral therapy use, blood donor screening.*

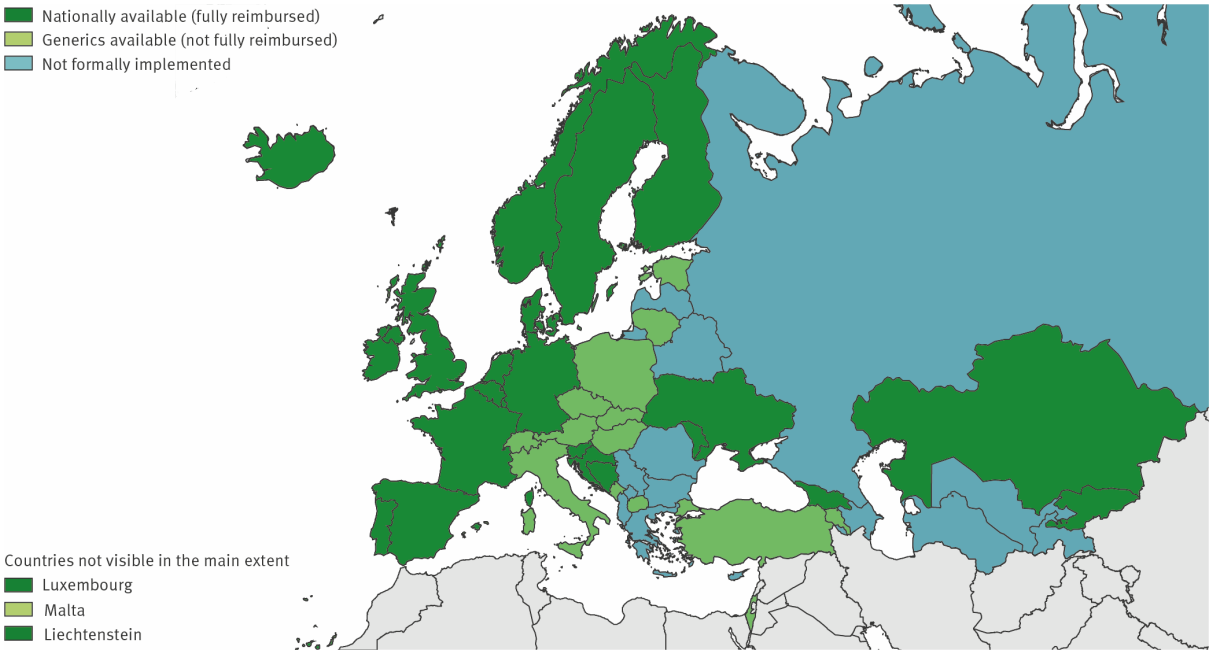
Pre- and post-exposure prophylaxis for HIV prevention

Significant advancements in HIV treatment and prevention have transformed the treatment and care of people living with HIV and individuals at risk of infection. Studies have consistently demonstrated that HIV-positive individuals on antiretrovirals pose a minimal risk of sexual transmission when their viral load remains undetectable. This finding has given rise to the 'treatment as prevention' paradigm [65]. Additionally, post-exposure prophylaxis (PEP) and pre-exposure prophylaxis (PrEP) have emerged as highly effective preventive measures, in particular when used daily and taken consistently [66,67]. An alternative 'on-demand' PrEP regimen, where the drug is administered only before anticipated sexual activity, has also been validated and found effective [66]. Long-acting PrEP regimens have recently been approved for use in the EU/EEA and may result in drug levels remaining detectable more than one year after the final injection [68].

Use of pre-exposure prophylaxis for HIV prevention in the EU/EEA

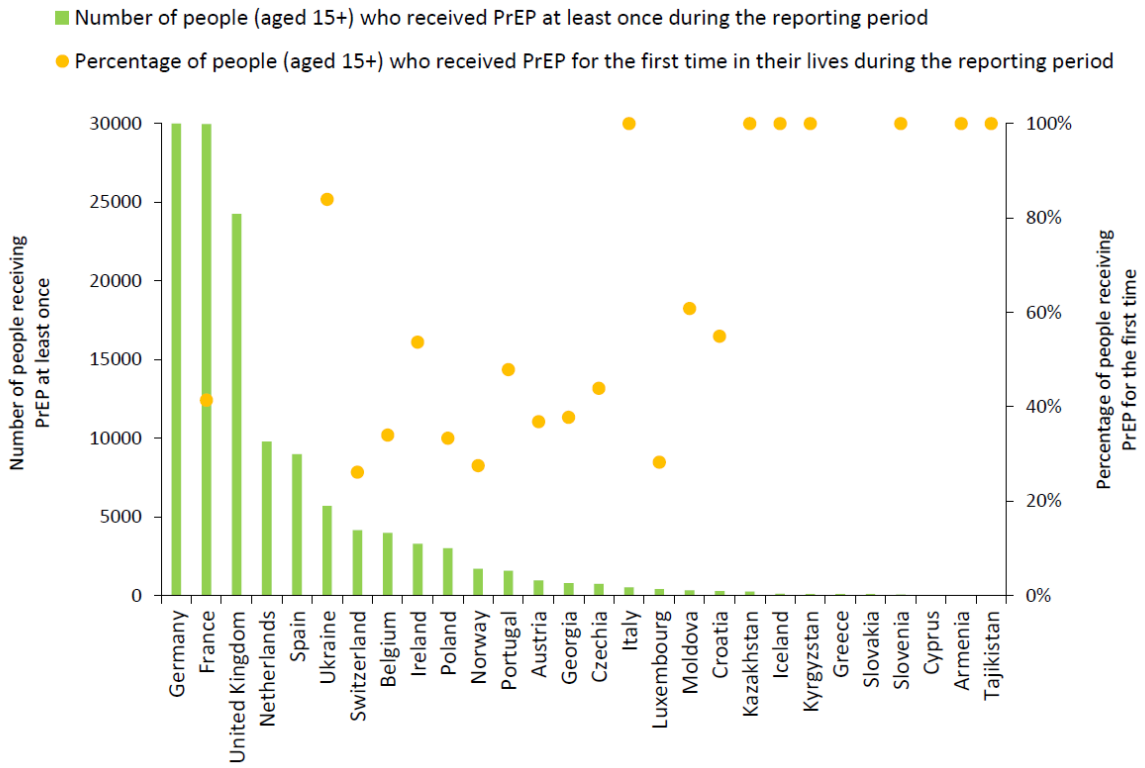
The implementation status of PrEP in Europe is described in Figure 3, and the total number of people receiving PrEP in some European countries in 2021 is described in Figure 4**.**

Figure 3. Status of implementation of pre-exposure prophylaxis (PrEP) in the WHO European Region, 2021



Note: PrEP is nationally available and fully reimbursed in Italy since 2023.
From ECDC [69]

Figure 4. Number of people receiving pre-exposure prophylaxis (PrEP) and the percentage receiving PrEP for the first time in 2021 in Europe and Central Asia (n=28)



From ECDC [69]

Impact of pre-exposure prophylaxis on donor screening

While a decline in HIV incidence in the general population due to prophylaxis use could be expected to translate to a lower risk of transfusion transmission of HIV, the use of ART can delay seroconversion or lead to seroreversion [70], and suppress viral loads. Breakthrough infections can also occur, most commonly with 'on-demand' PrEP or with suboptimal adherence [71-73]. This can result in ambiguous testing results and impact the ability to detect HIV infection through blood donation screening [74]. Through a similar mechanism of action, PEP may also interfere with testing results. The amount of evidence assessing the impact of PrEP on seroconversions and HIV detectability remains limited [75].

In a review of eight cases of 'breakthrough HIV infections' among PrEP users, detection of seroconversion ranged from 14 to 103 days, while users were still on PrEP – whether or not used optimally. One case had HIV RNA detected four days prior to seroconversion, while in another case HIV RNA was retrospectively detected in a sample collected eight weeks prior to seroconversion [75].

In a subsequent review of 10 breakthrough HIV infections among PrEP users (of which six are in common with the previous review), six individuals were identified with positive 4th generation antibody/antigen combination tests, and eight of the individuals had HIV RNA positivity, including being detected four days prior to seroconversion. Among these eight individuals, two required repeated and more sensitive testing to document HIV infection. At least one individual suggested delayed seroconversion [76].

In clinical and observational studies of the efficacy and effectiveness of PrEP in preventing HIV infections, analyses of seroconversions suggests that PrEP has an impact on the timing of Fiebig stages [77]. Fiebig stages are used to classify early HIV infection into five sequential stages based on HIV test result patterns in newly diagnosed individuals [12]. In the PARTNER trial, HIV RNA in PrEP users (as treated) was 0.74 $\log_{10}$ copies/ml (95% confidence interval: 0.36–1.11) lower than in the placebo group, and use of PrEP increased the proportion of patients with undetectable HIV-RNA during the seroconversion period [73]. In the Bangkok trial, lower HIV RNA levels were found in PrEP users prior to seroconversion compared to the placebo group [78]. Of note, in studies with low adherence, differences in viral loads between treated and untreated groups are lower or inexistent [77].

Considering worst-case assumptions for delays in Fiebig stages, the serological detection of HIV using antigen-antibody combination tests would be delayed by approximately seven days, leading to a positive test approximately 25–30 days after infection instead of 17 days [73,75,77].

In addition, while some randomised clinical trials evaluating PrEP did not indicate an association between PrEP use and an increase in risk behaviours [77], this association between PrEP use and an increase in risk behaviours – in particular condomless sex and an increase in the number of sexual partners – was found in some observational studies and a meta-analysis of open-label studies [79-82]. The use of PrEP was also found to be associated with an increased prevalence of sexually transmitted infections [83-86].

The US Food and Drug Administration recommends the deferral for a period of three months of individuals receiving oral PrEP and for two years from the most recent injection of individuals having received injectable PrEP [87].

PrEP and PEP use in blood donors

Very few studies have been published to date on the use of PrEP or PEP among blood donors. In the United States, HIV nonreactive samples from male donors aged 18-45 years from metropolitan areas with above-average access to PrEP, and high HIV prevalence, and collected between September 2018 and May 2019 were assessed for the presence of PrEP metabolites in their blood. Of 1 494 samples tested, nine (0.6%; 95% confidence interval, 0.03% to 1.1%) had detectable levels of the tested drugs [88]. At the time of this study, there was no direct question about PrEP, and instead the donor questionnaire asked if the donor was taking any medication for an infection (not to prevent an infection).

In England, a pilot study assessed samples from male donors confirmed positive for syphilis or repeat reactive for HIV antibodies but confirmed negative by reference testing and collected between June 2018 to July 2019. PrEP use was identified in three of the 46 syphilis-positive donors (6.5%) but none among the donors reactive for HIV antibodies. At the time of the study, donors were not specifically asked about PrEP usage but about the use of 'any medication' [89]. A subsequent study, focusing on male donors with *Treponema pallidum* infections in England was conducted between 2020 to 2021, a time during which the donor questionnaire specifically asked about and excluded donors with PrEP use in the previous three months. Of 177 samples tested, 10 were found positive for PrEP use (5.6%) [90]. The authors also reported that a higher proportion of male donors who were positive for syphilis and who declared a male sexual partner had evidence of PrEP use than those without a history of sex with men (7.6% vs 1.2%).

In Canada, an analysis of donor health questionnaires from potential donors attempting to donate in Canada between June 2019 and October 2020 identified 89 people (eight per 100,000 donations) answering 'Yes' to a question on the use of PrEP or PEP in the past four months. Two-thirds (64%) indicated PrEP use and one-third (34%) indicated PEP use; 2% did not specify. The analysis of concurrent deferral reasons showed that 56% of potential donors deferred for PrEP use, and 50% for PEP use, would not have been deferred for any other reason [91].

Anti-HIV vaccination

Several clinical trials evaluating the efficacy of anti-HIV vaccines are ongoing, or have been completed, with active sites in EU/EEA countries [92]. While participants in these clinical trials may be instructed not to donate blood, anti-HIV vaccination is likely to impact testing results [93]. These trials may also preferentially recruit participants who are at a high risk of HIV infection.

4. Laboratory testing approaches

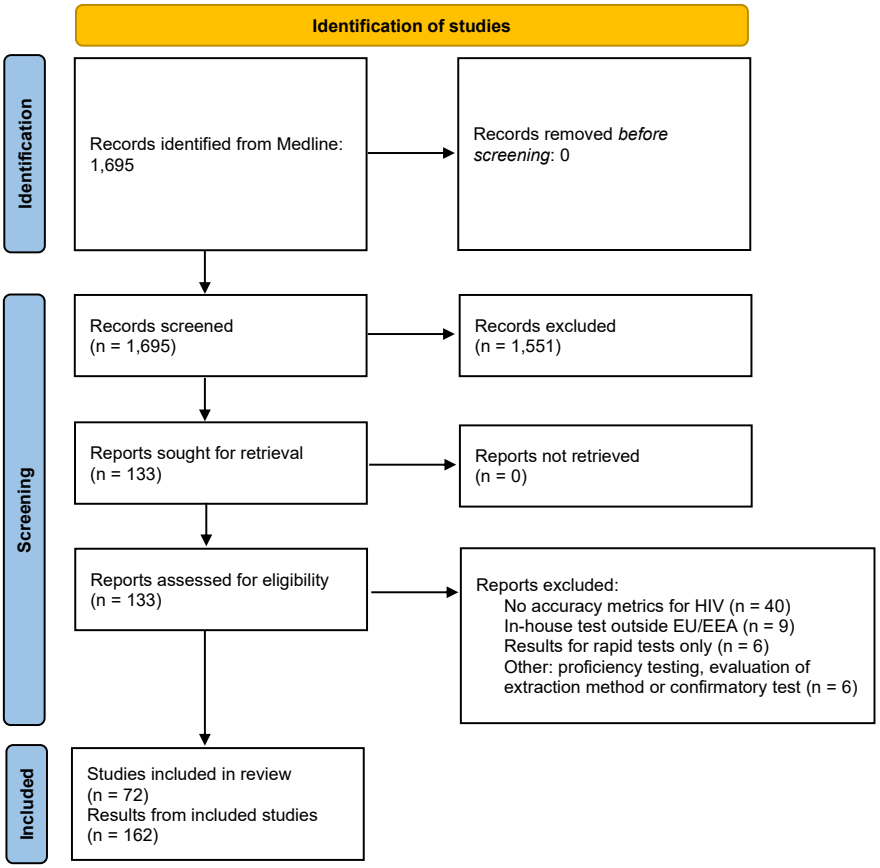
Search results

This section aims to present the performance characteristics of laboratory tests that are approved and potentially used for HIV screening in SoHO donors (living and deceased). The results summarised in this document are based on a structured but non-systematic search of Medline from January 2001 (the date from which the first 4th generation tests were considered to be in use) to March 2023. Studies were included if the test was described as being used or potentially used for the screening of SoHO donors. This included in-house (i.e. non-commercial) tests if they were used in EU/EEA countries. In-house tests used outside the EU/EEA were excluded. Studies that only included results for rapid diagnostic tests were excluded, and accuracy metrics for rapid diagnostic tests were not extracted from included studies that reported on such tests. No other exclusion criteria were applied, and results are summarised by test method and by target: antibody only, antigen only, antibody-antigen combinations, HIV-1 and HIV-2 RNA. For categories with two or fewer results, medians are not reported. No data are presented for categories with only one result.

The search methods are described in detail in Annex 1.

Four studies were identified that reported results on samples from deceased donors. These results are described separately from those conducted on living donor samples.

Figure 5. Number of records identified, screened, and included for laboratory test methods for HIV



EU/EEA: European Union and European Economic Area. A single study may include results for several different tests.

Summary of data: blood samples from living donors

Table 9. Summary of 68 studies on available methods for pathogen laboratory testing in samples from living donors [94-161]

Test method	No. results (n studies)	Range clinical sensitivity	Range analytic sensitivity	Range specificity	Median clinical sensitivity	Median analytic sensitivity	Median specificity	Window period reported
ELISA or non-specified EIA								
Overall	44 (15)	94.2% - 100.0%	0.41 - 1.18 IU/mL	84.6% - 100.0%	100.0%	0.6 IU/mL (Ag)	99.4%	
Ab HIV-1/2	11 (4)	94.2% - 100.0%	NR	84.6% - 100.0%	100.0%	NA	99.3%	
p24Ag	6 (2)	NA	0.50 – 1.18 IU/mL	NA	NA	0.6 IU/mL	NA	
Ag-Ab combination	28 (11)	97.8% - 100.0%	0.41 IU/mL (n=1)	89.0% - 100.0%	100.0%	NA	99.5%	Reduced by 11 days compared to Ab only (n=1) Increased by 1.5-2.5 days compared to HIV RNA (n=1)
CLIA								
Overall	11 (10)	98.4% - 100%	1.89 - 1.90 IU/mL 25 - 33.2 pg/mL	99.3% - 100.0%	100.0%	1.90 IU/mL 29.1 pg/mL	99.9%	
Ab HIV-1/2	1 (1)	NA	NA	NA	NA	NA	NA	
p24Ag	1 (1)	NA	NA	NA	NA	NA	NA	
Ag-Ab combination	9 (9)	98.4% - 100%	1.89 IU/mL (n=1) 25 - 33.2 pg/mL	89.0% - 100.0%	100.0%	29.1 pg/mL	99.5%	Reduced by 4 days compared to Ab only (n=1)
CMIA								
Overall	17 (12)	99.5% - 100.0%	0.87 - 1.2 IU/mL 14 - 25 pg/mL	99.1% - 100.0%	100.0%	1.09 IU/mL (Ag) 18 pg/mL (Ag)	99.8%	
p24Ag	3 (1)	NA	0.87 - 1.14 IU/mL	NA	NA	NA	NA	
Ag-Ab combination	9 (9)	99.5% - 100.0%	0.94 - 1.2 IU/mL 14 - 25 pg/mL	99.1% - 100.0%	100.0%	1.18 IU/mL (Ag) 18 pg/mL (Ag)	99.8%	Reduced by 11 days compared to antibody only (n=1) Reduced by 6 days compared to Ab only (n=1)
ECLIA								
Overall	9 (9)	83.3% - 100.0%	0.3 - 1.1 IU/mL 31 pg/mL (n=1)	99.0% - 99.9%	100.0%	1.05 IU/mL	99.80%	
p24Ag	1 (1)	NA	NA	NA	NA	NA	NA	
Ag-Ab combination	9 (9)	83.3% - 100.0%	0.3 - 1.05 IU/mL 31 pg/mL (n=1)	99.0% - 99.9%	100.0%	0.7 IU/mL	99.8%	Reduced by 1.5-5.3 days compared to Ab only (n=1)
NAT HIV-1								
Overall	54 (34)	88.0% - 100.0%	8.9 - 289 IU/mL	99.3% - 100.0%	100.0%	34 IU/mL	100.0%	
ID	39 (29)	99.9% - 100.0%	8.1 - 281 IU/mL	99.5% - 100.0%	100.0%	32 IU/mL	100.0%	Reduced by 2 days relative to MP6, 4 days relative to MP24 (n=2) 14 days compared to Antibody and 2-14 days compared to Antigen (n=2)
MP (6 - 16)	14 (10)	88.0% - 100.0%	18.9 - 289 IU/mL	99.7% - 100.0%	99.0%	50 IU/mL	99.9%	
Pool (>16)	1 (1)	NA	NA	NA	NA	NA	NA	
NAT HIV-1/2								
Overall	22 (7)	93.0% - 100.0%	4 - 187.5 IU/mL	97.7% - 100.0%	100.0%	43 IU/mL	100.0%	
ID	11 (6)	97.8% - 100.0%	4 - 100 IU/mL	97.7% - 100.0%	100.00%	28 IU/mL	100.0%	Reduced by 2 days relative to MP6, 4 days relative to MP24
MP (6 - 16)	9 (4)	93.0% - 100.0%	7.9 - 187.5 IU/mL	98.1% - 100.0%	100.0%	50 IU/mL	100.00%	
Pool (>16)	2 (2)	99.8% - 100.0%	15 - 27 IU/mL	99.4% - 100%	NA	NA	NA	

Note: One IU of HIV RNA is considered to correspond to 2 copies of HIV RNA [162]. For example, a 50 IU/mL sensitivity would correspond to 100 copies/mL.
ELISA: enzyme-linked immunosorbent assay. CLIA: chemiluminescence immunoassay. CMIA: chemiluminescence microparticle immunoassay. ECLIA: electrochemiluminescence immunoassay. EIA: enzyme immunoassay. NAT: nucleic acid test. IU/mL: international units per millilitre. pg/mL: picograms per millilitre. Ag-Ab: antigen-antibody. p24Ag: p24 antigen. ID: individual test. MP: mini pool. NR: Not reported. NA: not applicable.
For categories with 2 reports or less, median values are not provided. For categories with only 1 report, no results are provided.
See "Annex 1. Annex 1. Search strategies" for corresponding search methods.
See "Annex 2. Annex 2. Laboratory testing approaches: data extraction table" for the data extraction table (available in the embedded document).

Summary of data: blood samples from deceased donors

Four studies were identified reporting test performance metrics for seven tests for HIV in deceased donor samples recovered within 24 hours post-mortem [163-166].

Results for CLIA or CMIA were reported for three tests (three studies), all targeting anti-HIV 1 and 2 and antigen combined. These results show that sensitivity could be considered similar between samples from living or deceased donors. Where reported, the sensitivity was 100% (n=1) and the specificity was 97.6%–100.0% (n=2).

Results for NAT were reported for three tests (two studies), all on HIV-1 RNA, with the conclusion that sensitivity could be considered similar between samples from living or deceased donors. Where reported, the sensitivity was 100% (n=4).

The following text was added in the data sheet after the drafting of the ECDC guidelines on the prevention of donor-derived transmission of HIV through substances of human origin: It should be noted that the post-mortem samples used for NAT in these studies were diluted prior to testing. Dilution of post-mortem samples may be needed to achieve valid NAT results due to the potential presence of inhibitory substances.

Residual risk of HIV

The residual risk of HIV infection in SoHO donation is defined as the probability of collecting a donation from an asymptomatic viraemic donor not being detected by the screening assays. The undetected infected donation may transmit the infection to a recipient if the blood components are not pathogen inactivated or the inactivation is insufficient to render the donation non-infectious. The non-detection of HIV may be caused by test failures or by donors being in the diagnostic window period. For current modern test methods, the contribution of assay failures to the residual risk is considered negligible and is usually not considered into the residual risk. Table 10 presents the RR per million blood donations according to different incidence rates and for different test methods.

Residual risks calculated in various studies conducted in EU countries are presented in Table 11. These residual risks are provided as illustrations for different test methods. The calculation methods differ across studies and comparisons of residual risks between countries should be interpreted with caution. Overall, residual risks for 4th generation tests methods (antigen-antibody combination tests) and NAT are generally reported between 0.5 to two undetected infections per million donations.

Table 10. Residual risks (RR) of HIV per million blood donations, by test method and incidence rate in repeat donors and first-time donors

Incidence rate per 100 000	ID-NAT WP: 8	MP-16 NAT WP: 11	Ag-Ab combination EIA WP: 16	Ag EIA WP: 14	Ab EIA WP: 21
1	0.22	0.30	0.44	0.38	0.57
	0.66	*0.90*	*1.31*	*1.15*	*1.72*
2	0.44	0.60	0.88	0.77	1.15
	1.31	*1.81*	*2.63*	*2.30*	*3.45*
3	0.66	0.90	1.31	1.15	1.72
	1.97	*2.71*	*3.94*	*3.45*	*5.17*
4	0.88	1.20	1.75	1.53	2.30
	2.63	*3.61*	*5.26*	*4.60*	*6.90*
5	1.10	1.51	2.19	1.92	2.87
	3.29	*4.52*	*6.57*	*5.75*	*8.62*
6	1.31	1.81	2.63	2.30	3.45
	3.94	*5.42*	*7.89*	*6.90*	*10.35*
7	1.53	2.11	3.07	2.68	4.02
	4.60	*6.32*	*9.20*	*8.05*	*12.07*
8	1.75	2.41	3.50	3.07	4.60
	5.26	*7.23*	*10.51*	*9.20*	*13.80*
9	1.97	2.71	3.94	3.45	5.17
	5.91	*8.13*	*11.83*	*10.35*	*15.52*
10	2.19	3.01	4.38	3.83	5.75
	6.57	*9.03*	*13.14*	*11.50*	*17.25*

WP: Window period; ID-NAT: Individual nucleic acid testing; MP-16 NAT: Pooled NAT of 16 donations; Ag: antigen; Ab: antibody; EIA: Enzyme immunoassay.

Residual risk was calculated as the product of the window period and the incidence rate. The values for window periods were taken from the WHO Guidelines on estimation of residual risk using the values for the three-fold concentration of the 95% detection probability [162].

Table 11. Examples of residual risks of HIV calculated in various studies conducted in EU countries, by periods and test methods

Author, year	Country	Period	Test method	Window period (days)	Blood product	Incidence rate per 100 000 donations (95% CI)	Residual risk per million donations (95% CI)
Alvarez do Barrio, 2005 [167]	Spain	1997 - 1999	Ab EIA	22	Whole blood	4.13 (2.31-6.81)	2.49 (0.38-7.09)[a]
Alvarez do Barrio, 2005	Spain	2000 - 2002	Ab EIA	22	Whole blood	4.11 (2.40-6.58)	2.48 (0.39-6.85)[a]
Pillonel, 2005 [168]	France	1998 - 2000	Ab EIA	22	Whole blood	1.21 (0.7 - 2.0)	0.73 (0.1 - 2.1)
Pillonel, 2005	France	2001 - 2003	MP-NAT	12	Whole blood	0.97 (0.6 - 1.5)	0.32 (0.0 - 1.1)
Gonzalez, 2005 [169]	Italy	1999 - 2001	Ab EIA	22	Whole blood	3.17 (3.15-3.19)	1.91 (0.52-3.32)[a]
Offergeld, 2005 [170]	Germany	2000 - 2001	Ab EIA	22	Whole blood	0.72	0.43
Offergeld, 2005	Germany	2000 - 2001	Ab EIA + NAT	11	Whole blood	0.72	0.22
Offergeld, 2005	Germany	2000 - 2001	Ab EIA	22	Whole blood	0.60	0.36
Offergeld, 2005	Germany	2000 - 2001	Ab EIA + NAT	11	Whole blood	0.60	0.18
López-Menchero, 2019 [171]	Spain	2003	Ab EIA	21	Whole blood	14.48	7.46
López-Menchero, 2019	Spain	2004 - 2006	MP-NAT	7	Whole blood	3.00 - 7.72	0.52 - 1.34
López-Menchero, 2019	Spain	2007 - 2017	ID-NAT	4	Whole blood	7.02 - 26.29	0.71 - 2.63
Grubyte, 2021[b] [172]	Lithuania	2004 - 2007	Ab EIA	21	Whole blood	91.06 - 235.43	52.39 - 135.45
Grubyte, 2021[b]	Lithuania	2008 - 2018	Ag-Ab combination EIA	16	Whole blood	7.20 - 38.91	1.01 - 15.49
Grubyte, 2021[b]	Lithuania	2012 - 2018	ID-NAT[c]	4	Whole blood	6.08 - 38.91	0.67 - 4.26
Bruhn, 2013 [173]	Europe[d]	2005 - 2011	Ab EIA	18	Whole blood	2.7 - 7.8	0.91 - 2.50
Bruhn, 2013	Europe[d]	2005 - 2011	Ag-Ab combination EIA	13	Whole blood	2.7 - 7.8	0.65 - 1.78
Bruhn, 2013	Europe[d]	2005 - 2011	MP-NAT + Ab EIA	5.5 – 6.3	Whole blood	2.7 - 7.8	0.28 - 0.87
Bruhn, 2013	Europe[d]	2005 - 2011	ID-NAT + Ab EIA	2.9	Whole blood	2.7 - 7.8	0.15 - 0.40
Bruhn, 2013	Europe[d]	2005 - 2011	ID-NAT	2.9	Whole blood	2.7 - 7.8	0.15 - 0.40
Sulkowska, 2020 [174]	Poland	2005 - 2018	ID NAT or MP-6 NAT	8 – 11	Whole blood	3.3 (3.04–3.59)	0.204 0.366
an der Heiden, 2015 [175]	Germany	2006 - 2012	MP-NAT	9.5	Pooled platelets[e] (PTC) and apharesis platelets (ATC)	0.99 (0.88–1.10)	PTC: 2.08 (1.98–2.18) ATC: 1.70 (1.24-2.23)
Velati 2018[f] [176]	Italy	2009 - 2015	ID-NAT or MP-NAT	7	Whole blood	4.39 (4.00-4.82)	0.02 (0.01-0.05) - 0.52 (0.25-1.25)
Unpublished	France	2020 - 2022	Ab EIA + NAT	9	Whole blood	0.28 (0,12 - 0,62)	0.07

ID: Individual; NAT: Nucleic Acid Test; MP: Mini-pool; Ab: Antibody; Ag: Antigen; EIA: Enzyme Immunoassay.
a: Credible range is presented.
b: For these reports, results are provided as the range during the period.
c: Only used for donations that tested negative for the Ag-Ab combination.
d: Two separate European regions are reported as a range for this report, Central and Northern Europe and Mediterranean Europe.
e: Consisting of 4 whole blood donations which had a residual risk of 0.52.
f: For this report, the residual risk is provided as a range across different methods.

5. Current testing requirements in EU/EEA countries

Testing requirements for blood donation

Testing practices are described for blood donation screening. Information on confirmatory algorithms is not provided in this document as it is considered out of scope for the development of the technical guidelines.

The testing practices described in Table 12 are based on a report published by the European Directorate for the Quality of Medicines and Healthcare (EDQM) [57]. An updated report on testing practices in EU/EEA countries has since been published by ECDC [177]. These data were not available at the time of the drafting of the ECDC guidelines on the prevention of donor-derived transmission of HIV through substances of human origin.

Table 12. Reported testing practices for HIV in EU/EEA by country for blood donations, 2021

Country	Anti-HIV 1/2*	HIV-Ag p24	HIV NAT	Comments
Austria	Yes	Yes	Yes	
Belgium	Yes	No	Yes	When a first sample is taken from a donor, it is preceded, accompanied or immediately followed by biological analyses including anti-HIV 1 and 2, as well as that the search for the genome of the HIV virus 1.
Bulgaria	Yes	Yes	Yes	
Croatia	Yes	Yes	Yes	
Cyprus	Yes	Yes	Yes	
Czechia	Yes	Yes	Where required	NAT is obligatory in plasma for fractionation but is often done by the fractionating company.
Denmark	Yes	Yes	Yes	"Testing + donation" of first-time donors is allowed, but only one of five regions has implemented this (The Capital Region). Four of five regions perform "testing only" of first-time donors. ID-NAT tests are performed (HIV/HCV/HBV).
Estonia	Yes	Yes	Yes	
Finland	Yes	Yes	Yes	
France	Yes	Yes	Yes	Ag p24 testing is not required but performed due to the use of a combo Ag/Ab assay. ID NAT is used since 2021.
Germany	Yes	No	Yes	
Greece	Yes	Yes	Yes	HIV-Agp24 is not required but detected due to the use of Antibody-Antigen combination assays.
Hungary	Yes	Yes	Where required	
Iceland	Yes	Yes	No	
Ireland	Yes	Yes	Yes	ID NAT
Italy	Yes	Yes	Yes	
Latvia	Yes	No	Yes	
Lithuania	Yes	Where required	Yes	
Luxembourg	Yes	Yes	Yes	NAT performed at Red Cross Baden-Württemberg - Hessen / Germany
Malta	Yes	Yes	Yes	
Netherlands	Yes	Yes	Yes	HBV-HCV-HIV NAT was routinely performed as multiplex real-time PCR testing in minipools of 6 donations. HIV-Agp24 is not required but detected due to the use of Antibody-Antigen combination assays.
Norway	Yes	Yes	No	
Poland	Yes	No	Yes	HIV-Ag p24 HIV testing is recommended.
Portugal	Yes	Yes	Yes	
Slovakia	Yes	Yes	Yes	HIV NAT is not mandatory and tested in 75% of blood donations. Testing only in blood establishments of National Transfusion Service of SR, not in hospital-based blood establishments. Confirmatory testing (Ag/Ab, WB, NAT) of reactive samples is provided centrally in for HIV/AIDS prevention.
Slovenia	Yes	Yes	Yes	Combination test is used for screening
Sweden	Yes	No	No	

** Mandatory as per directive 2002/98/EC [178].*
Ag: antigen. NAT: Nucleic Acid Test.
From EDQM [57]

Testing requirements for tissues and non-reproductive cells donors

Due to the unavailability of data on testing practices in EU/EEA countries, testing requirements from the mapping exercise conducted in 2015 by the European Commission are described in this section.

An updated report on testing practices in EU/EEA countries has since been published by ECDC [177]. These data were not available at the time of the drafting of the ECDC guidelines on the prevention of donor-derived transmission of HIV through substances of human origin.

Table 13. Testing requirements for HIV in EU/EEA by country: tissues and non-reproductive cells (2015)

Country	Testing requirement declared*	Tissue / cell type	Donor type	Comment
Austria	• Anti-HIV-1 and -2 • HIV NAT	All	Living and deceased	HIV NAT: mandatory for deceased donors
Belgium	• Anti-HIV-1 and -2 • HIV NAT	All	Living and deceased	NAT tests are mandatory unless the processing includes an inactivation step validated for the viruses concerned. For living donors, NAT tests may be replaced by serology 6 months after the collection/procurement of tissues or cells
Bulgaria	• Anti-HIV-1 and -2 • Recommended: HIV NAT	All	HIV NAT for living donors	
Croatia	• Anti-HIV-1 and -2 • HIV NAT	All	Living and deceased	If there is no possibility to provide NAT testing and tissues of allogeneic living donors are stored for a longer period, it is necessary to take samples and repeat testing after 180 days
Cyprus	• Anti-HIV-1 and -2 • HIV NAT	All	Living and deceased	NAT testing is required if tissues or cells will be issued without retesting of donors after 180 days of collection
Czechia	• Anti-HIV-1 and -2 • HIV-Ag	All	Living and deceased	
Denmark	• Anti-HIV-1 and -2 • Recommended: HIV NAT for deceased donors	All	HIV NAT for deceased donors	
Estonia	• Anti-HIV-1 and -2 • HIV NAT	All	Living and deceased	Where tissues and cells of allogeneic living donors can be stored for long periods, repeat sampling and testing are required after an interval of 180 days except if tested by HIV NAT
Finland	• Anti-HIV-1 and -2 • HIV NAT	All	Living and deceased	All deceased donors need to be tested by serological test AND viral NAT-tests (HIV, HBV, HCV). All living donors (allogeneic grafts) need to be tested by serological tests AND NAT-tests (no quarantine) or 180-day-test (quarantine)
France	• Anti-HIV-1 and -2 • HIV-1 p24Ag • HIV NAT	All	Living and deceased	HIV testing is systematically a combined test with Anti-HIV1/2 and HIV-1 p24Ag.
Germany	• Anti-HIV-1 and -2 • Recommended: HIV NAT for deceased donors	All Except for cornea and skin for HIV NAT	Living and deceased	
Greece	• Anti-HIV-1 and -2	All	Living and deceased	
Hungary	• Anti-HIV-1 and -2	All	Living and deceased	NAT testing can be done, but not compulsory
Ireland	• Anti-HIV-1 and -2	All	Living and deceased	
Italy	• Anti-HIV-1 and -2 • HIV NAT	All	HIV NAT for living donors	HIV NAT is used in living donors of tissues if serology is not repeated after 180 days
Latvia	• Anti-HIV-1 and -2	All	Living and deceased	
Lithuania	• Anti-HIV-1 and -2 • HIV-1 p24Ag	All	Living and deceased	
Luxembourg	• Anti-HIV-1 and -2	All	Living and deceased	
Malta	• Anti-HIV-1 and -2	All	Living and deceased	
Netherlands	• Anti-HIV-1 and -2	All	Living and deceased	
Norway	• Anti-HIV-1 and -2	All	Living and deceased	
Poland	• Anti-HIV-1 and -2	All	Living and deceased	HIV NAT can be used as a confirmatory test
Portugal	• Anti-HIV-1 and -2 • HIV NAT	All	Living and deceased	

Country	Testing requirement declared*	Tissue / cell type	Donor type	Comment
Romania	• Anti-HIV-1 and -2	All	Living and deceased	
Slovakia	• Anti-HIV-1 and -2 • HIV-1 p24Ag	All	Living and deceased	Confirmatory testing (Ag/Ab, WB, NAT) of reactive samples is provided centrally in for HIV/AIDS prevention.
Slovenia	• Anti-HIV-1 and -2 • HIV NAT	All	HIV NAT for deceased donors	For living donors, NAT is used if the sample is taken at the time of donation or within 7 days post donation
Spain	• Anti-HIV-1 and -2 • Recommended: HIV-1 p24Ag • Recommended: HIV NAT	All	HIV NAT recommended for living donors	HIV NAT: optional testing to avoid retesting after 180 days in case of long-term storage
Sweden	• Anti-HIV-1 and -2 • HIV-1 p24Ag • Recommended: HIV NAT	HIV NAT: bone, tendons	Living and deceased	Tissue Council promotes the use of multiplex NAT testing for HCV/HBV/HIV

** Minimum mandatory requirement for tissues and cells is anti-HIV-1 and -2 as per directive 2004/23/EC [179]. HIV NAT is required for living donors (except stem-cell donors) in case of storage for long periods, if no re-testing is performed or if there is no validated inactivation step for viruses.*
NAT: nucleic acid test. p24Ag: p24 antigen. HBV: hepatitis B virus. HCV: hepatitis C virus.
Tests are reported as legally binding unless specified otherwise.
From European Commission [180].

Testing requirements for reproductive cells donors

Due to the unavailability of data on testing practices in EU/EEA countries, testing requirements from the mapping exercise conducted in 2015 by the European Commission are described in this section.

An updated report on testing practices in EU/EEA countries has since been published by ECDC [177]. These data were not available at the time of the drafting of the ECDC guidelines on the prevention of donor-derived transmission of HIV through substances of human origin.

Table 14. Testing requirements for HIV in EU/EEA by country: reproductive cells (2015)

Country	Testing requirement declared*	Donation type	Comment
Austria	• Anti-HIV-1 and -2 • HIV NAT	HIV NAT: all non-partner donation	
Belgium	• Anti-HIV-1 and -2 • HIV NAT	HIV NAT: all non-partner donation	NAT tests are mandatory unless the processing includes an inactivation step validated for the viruses concerned
Bulgaria	• Anti-HIV-1 and -2 • Recommended: HIV NAT	HIV NAT: all non-partner donation	Oocyte donors are tested at recruitment and on the day of donation and results should be available before the transfer of embryos. Sperm is usually quarantined for 180 days and donors retested after this period
Croatia	• Anti-HIV-1 and -2	All	
Cyprus	• Anti-HIV-1 and -2 • HIV NAT	All	NAT testing is required if tissues or cells will be issued without retesting of donors after 180 days of collection
Czechia	• Anti-HIV-1 and -2 • HIV-Ag	All	
Denmark	• Anti-HIV-1 and -2 • HIV NAT	All	HIV NAT is mandatory for oocyte donors. NAT testing is required if non-partner donors are not retested after 180 days.**
Estonia	• Anti-HIV-1 and -2 • HIV NAT	All	NAT testing is required if non-partner donors are not retested after 180 days
Finland	• Anti-HIV-1 and -2 • HIV NAT	HIV NAT: sperm in non-partner donation	No testing is required in the case of partner donation of reproductive cells for direct use
France	• Anti-HIV-1 and -2 • HIV-1 p24Ag	All	In non-partner sperm donation, NAT testing for HIV, HCV and HBC at the last collection will be possible in order to avoid the 180 days of quarantine (after 2015)
Germany	• Anti-HIV-1 and -2 • HIV NAT	HIV NAT: all non-partner donation	
Greece	• Anti-HIV-1 and -2	All	180-day retesting from the time of donation for all sperm donors excluding partners
Hungary	• Anti-HIV-1 and -2	All	NAT testing can be done, but not compulsory
Ireland	• Anti-HIV-1 and -2	All	
Italy	• Anti-HIV-1 and -2 • HIV NAT	All	Gametes in non- partner donation are placed in quarantine for at least 180 days, after which tests (Anti-HIV 1-2) must be repeated. Quarantine is not necessary if NAT is performed in the blood sample taken at the time of donation.
Latvia	• Anti-HIV-1 and -2	All	

Country	Testing requirement declared*	Donation type	Comment
Lithuania	• Anti-HIV-1 and -2	All	
Luxembourg	• Anti-HIV-1 and -2	All	Non-partner oocyte donation is not allowed
Malta	• Anti-HIV-1 and -2	All	
The Netherlands	• Anti-HIV-1 and -2	All	
Norway	• Anti-HIV-1 and -2	All	
Poland	• Anti-HIV-1 and -2	All	
Portugal	• Anti-HIV-1 and -2 • HIV NAT	All	NAT testing is required if non-partner donors are not retested after 180 days
Romania	• Anti-HIV-1 and -2	All	
Slovakia	• Anti-HIV-1 and -2 • HIV-1 p24Ag	All	
Slovenia	• Anti-HIV-1 and -2	All	
Spain	• Anti-HIV-1 and -2 • HIV NAT	HIV NAT: sperm in non-partner donation	HIV NAT testing allows for the release of sperm without repeat testing after 180 days after donation
Sweden	• Anti-HIV-1 and -2 • HIV-1 p24Ag	All	Non-partner sperm donors should be quarantined for 180 days and then retested

** Minimum mandatory requirement for tissues and cells is anti-HIV-1 and -2 as per directive 2004/23/EC [179].*
*** Sperm donation may take place regularly every week or several times a week over a longer coherent period of time. In such cases, the Danish Patient Safety Authority accepts that blood sampling is performed at the time of the first donation, and subsequently at least every three months.*
NAT: nucleic acid test. p24Ag: p24 antigen. HBV: hepatitis B virus. HCV: hepatitis C virus.
Tests are reported as legally binding unless specified otherwise.
From European Commission [180]

6. Recommendations from other organisations

Recommendations for blood

Table 15. Recommendations from selected organisations for HIV testing of blood donations

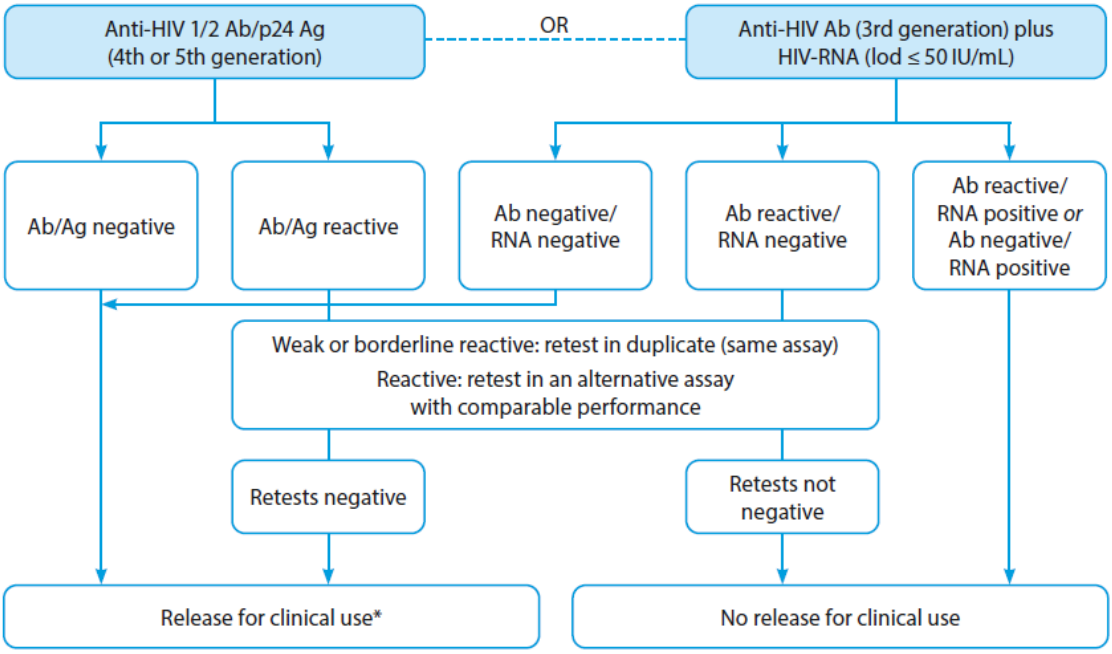
Institution	Minimum requirements and recommended tests	Risk groups	Additional information
EU Commission [178,181,182] Directive 2002/98/EC Directive 2004/33/EC, Annex III Regulation (EU) 2017/746	Minimum requirements: HIV 1/2 (Anti-HIV 1/2) Class D devices should be used for the detection of the presence of, or exposure to, a transmissible agent in blood, blood components, or in any of their derivatives, in order to assess their suitability for transfusion.	Individuals whose sexual behaviour puts them at a high risk of acquiring severe infectious diseases that can be transmitted by blood must be deferred permanently	Individuals with an HIV 1/2 infection must be deferred permanently.
European Directorate for the Quality of Medicines & HealthCare (EDQM) [183] The Guide to the preparation, use and quality assurance of blood components, 21st edition	Minimum requirements: antibody to HIV-1 (anti-HIV-1) and HIV-2 (anti-HIV-2) including outlying types (e.g., HIV-1 type O) Recommended: The application of NAT techniques shortens the window period compared with serological testing and therefore has a positive impact on blood safety.	All blood donors should be provided with information about behaviours associated with an increased risk of blood-borne infectious agents, such as HIV/AIDS and hepatitis transmission, and be given the opportunity for self-exclusion so that those persons refrain from donating.	Individuals with an HIV 1/2 infection must be deferred permanently. Where testing in NAT mini pools is performed, a risk assessment should be undertaken which takes into consideration the population prevalence of the TTI and other factors which impact residual risk. This information should be used in conjunction with the manufacturer's instructions to determine the size of the mini pool.
US Food and Drug Agency (FDA) [87,184] Nucleic Acid Testing (NAT) for Human Immunodeficiency Virus Type 1 (HIV-1) and Hepatitis C Virus (HCV): Testing, Product Disposition, and Donor Deferral and Reentry Recommendations for Evaluating Donor Eligibility Using Individual Risk-Based Questions to Reduce the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products	Minimum requirements: test of each donation intended for transfusion or for use in manufacturing a product, for evidence of infection due to HIV type 1 (HIV-1) and HIV type 2 (HIV-2). Recommended: Use of licensed HIV-1 nucleic acid donor screening tests	Individual risk-based questions that ask all donors about new or multiple sexual partners and about the use of medications to treat or prevent HIV infection (i.e., ART, PrEP and PEP).	Individuals with an HIV 1/2 infection must be deferred permanently.
Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee (JPAC) [185] Guidelines for the Blood Transfusion Services Donor Selection Guidelines	Minimum requirements: anti-HIV 1+2+O or HIV 1+2+O Ag/Ab (M) and HIV RNA (Scotland only) Screening for both HIV p24 antigen and antibody to HIV 1+2+O in a combination assay is recommended as the serological screening approach for HIV. If RNA screening, in pools of a maximum of 24 donations.	Individual risk criteria on the number of sexual partners and type of sexual contact (anal sex) and use of PrEP or PEP. Risk criteria also cover, injectable drug use.	
World Health Organization (WHO) [186]	Testing at the BE should be performed on fully automated platforms. Minimum testing should include [..] serological screening for anti-HIV.		It is strongly recommended that, where feasible, the following are considered: nucleic acid testing to further reduce the risk of transfusion-transmissible infections.

Recommendations for tissues and cells

Table 16. Recommendations from selected organisations for testing of tissues and cells donations

Institution	Minimum requirements and recommended tests	Risk groups	Additional information
EU Commission [179,182] Regulation (EU) 2017/746 Directive 2006/17/EC	Tissues and cells (except reproductive cells) Minimum requirements: anti-HIV-1/2 Reproductive cells - partner donation Minimum requirements: anti-HIV-1/2. Reproductive cells – non-partner donation Minimum requirements: anti-HIV-1/2 Class D devices should be used for the detection of the presence of, or exposure to, a transmissible agent in cells, tissues, or in any of their derivatives, in order to assess their suitability for transplantation or cell administration.		Deceased donors: General criteria for exclusion: History, clinical evidence, or laboratory evidence of […] HIV […]. Deceased child donors: Children aged less than 18 months born from mothers with […] HIV […] or at risk of such infection, and who have been breastfed by their mothers during the previous 12 months, cannot be considered as donors regardless of the results of the analytical tests. Allogenic living donors: The same exclusion criteria must be applied as for deceased donors […].
European Directorate for the Quality of Medicines & HealthCare (EDQM) [187] Guide to the Quality and Safety of Tissues and Cells for Human Application, 5th edition	Strongly recommended: Anti-HIV Ab (3rd generation) + HIV-RNA (LOD ≤ 50 IU/mL). Recommended: 4th or 5th generation assay including detection of anti-HIV-1/2 antibodies plus HIV-1 p24 antigen See algorithm in Figure 6.	• Injected drug use for non-medical reasons • Tattoos, ear piercings, body piercings and/or acupuncture in non-approved settings • New diagnosis or treatment for sexually transmitted diseases • Sexual contacts contact in exchange for money or drugs • Sexual behaviour with at risk of acquiring sexually transmitted infectious diseases	Individuals with an HIV 1/2 infection must be deferred permanently. **Sampling:** In the case of a deceased donor, blood samples must have been obtained just before cardiocirculatory arrest or, if this was not possible, the time of sampling must be as soon as possible after death, and in any case within 24 h after death. In the case of living donors, blood sampling must be obtained at the time of donation or, if this is not possible, within 7 days before or 7 days after donation. If tissues and cells of allogeneic living donors can be stored for long periods before use, repeat sampling and testing are required after 180 days, unless specific exemption criteria are met.
US Food and Drug Agency (FDA) [188] Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products	Minimum requirements: HIV 1/2 (Anti-HIV 1/2) and NAT assay for HIV-1, or combination NAT that includes HIV-1	• Men who have had sex with another man in the preceding 5 years • Persons who have injected drugs for a non-medical reason in the preceding 5 years • Persons who have engaged in sex in exchange for money or drugs in the preceding 5 years • Persons who have been in juvenile detention, lock up, jail or prison for more than 72 consecutive hours in the preceding 12 months	Individuals with an HIV 1/2 infection must be deferred permanently.
Human Tissue Authority [189] HTA Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment	Minimum requirements: HIV 1/2 (Anti-HIV 1/2)		Individuals with an HIV 1/2 infection must be deferred permanently. If the original sample is additionally tested by NAT for HIV, a repeat sample need not be taken.
Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee (JPAC) [185] Guidelines for the Blood Transfusion Services	Minimum requirements: anti-HIV 1+2+O or HIV 1+2+O Ag/Ab (M) Stem cells: anti-HIV 1+2+O or HIV 1+2+O Ag/Ab (M) and HIV RNA (Scotland only)	Individual risk criteria on the number of sexual partners and type of sexual contact (anal sex) and use of PrEP or PEP. Risk criteria also cover, injectable drug use.	If the original sample is additionally tested by NAT for HIV, a repeat sample need not be taken.
European Society of. Human Reproduction and. Embryology (ESHRE) [190]	Minimum requirements: HIV 1/2 (Anti-HIV 1/2) Recommended: Sperm sample tested with HIV PCR		Couples must be advised to […] seek active therapy to reduce viral load.

Figure 6. Algorithm for HIV testing in the EDQM's 'Guide to the quality and safety of tissues and cells for human application, 5th edition'



* Please note that when HIV NAT is done as mandatory test, it must also be negative in anti-HIV/p24Ag negative donors, to release tissues for clinical use.

Source: The Guide to the quality and safety of tissues and cells for human application, 5th edition published by the EDQM of the Council of Europe. [187]

7. Transmission through SoHO

Evidence of transmission of HIV through SoHOs

Reminder: absence of evidence is not evidence of absence.

Table 17. Evidence of transmission of HIV by type of SoHO

SoHO type	Evidence of transmission
Blood components: plasma	Yes [191]
Blood components: platelets	Yes [27]
Blood components: red blood cells	Yes [27]
Blood components: whole blood	Yes [27]
Cells: human progenitor cells	Yes [192]
Cells: oocytes	None
Cells: sperm	Yes [193]
Tissues: bone	Yes [194]
Tissues: corneas	None
Tissues: skin	Yes [194]
Tissues: tendon or ligaments	Yes [194]

Reported transmission events of HIV infections through SoHO

Table 18. Number of SoHO-transmitted HIV infections (imputability 2 or 3*) and number of units transfused or distributed in the EU/EEA (2017–2022)

Year	SoHO	Number of transmitted HIV infections	Number of transmitted unspecified viral infections	Number of units transfused or distributed**
2022	Blood	0	0	12,653,949
	Tissues and cells	0	0	610,725
	Reproductive cells	0	0	506,429
2021	Blood	0	0	NA
	Tissues and cells	0	1	NA
	Reproductive cells	0	0	NA
2020	Blood	0	0	18,881,223
	Tissues and cells	0	0	566,499
	Reproductive cells	0	0	738,282
2019	Blood	0	0	19,322,367
	Tissues and cells	0	1	523,763
	Reproductive cells	0	0	984,750
2018	Blood	0	0	19,267,785
	Tissues and cells	0	2	531,352
	Reproductive cells	0	0	746,588
2017	Blood	0	0	20,674,603
	Tissues and cells	0	0	748,757
	Reproductive cells	0	0	670,565

NA: Not available.
**2: likely, probable; 3: certain.*
*** Not reported by all countries for each year. Units are distributed for tissues and cells and reproductive cells.*
Source: SARE reporting, European Commission, 2024.

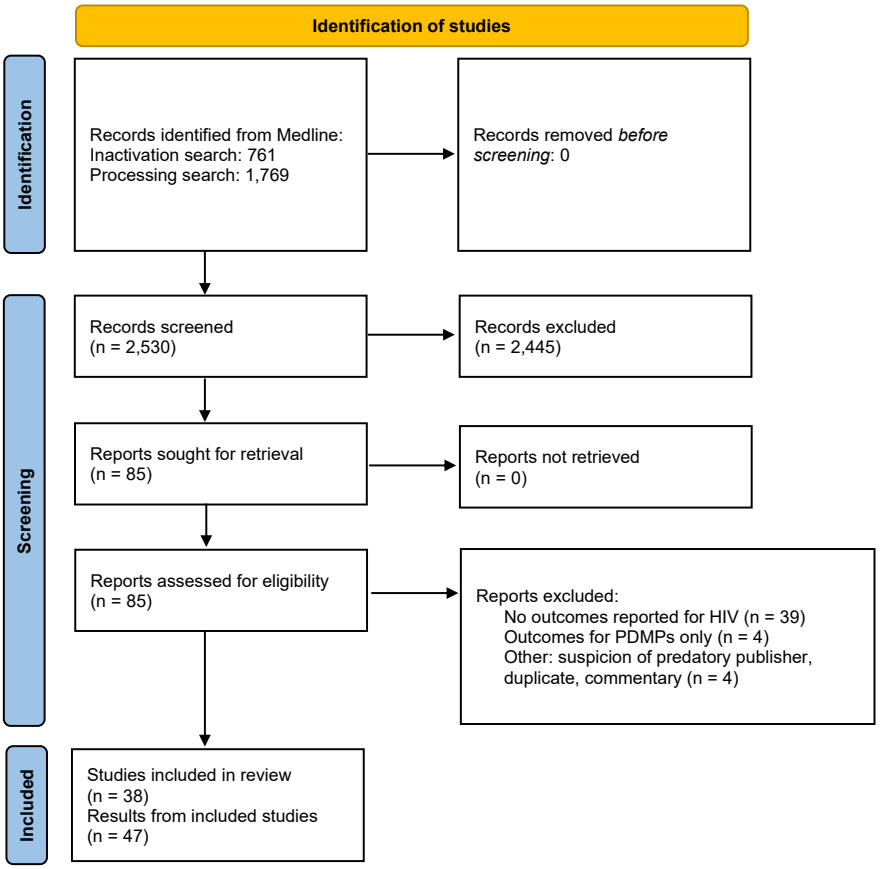
8. Pathogen reduction

Search results

This section aims to present the outcomes in terms of pathogen reduction for HIV for inactivation (and processing) methods used for different SoHOs. The results presented relied on a structured, non-systematic search in Medline from January 2001 (first 4th generation tests) to March 2023.

The search methods are detailed in Annex 1.

Figure 7. Number of records identified, screened, and included for inactivation methods for HIV



PDMP: plasma-derived medicinal product.
A single study may include results for several different tests.

Pathogen reduction outcomes of HIV for identified inactivation and processing methods

Table 19. Pathogen reduction outcomes for HIV by inactivation method and SoHO from 40 studies [195-234] *

Inactivation method	SoHO	Number of studies	Pathogen reduction range	Qualitative assessment
Psoralens + UV-A Light	Plasma	4	Log reduction cell-free: >3.4 to ≥6.6 Log reduction cell-associated: ≥6.1 to ≥6.4	Reduction below detection limit
Psoralens + UV-A Light	Platelet concentrates in plasma	6	Log reduction cell-free ≥3.3 to >6.6 Log reduction cell-associated: ≥5.4 to >6.7	Reduction below detection limit
Psoralens + UV-A Light	Red blood cells	1	Log reduction cell-free: >6.5 Log reduction cell-associated: >6.2	Reduction below detection limit
*Amustaline (S-303) + glutathione (GSH) **	*Whole blood*	*1*	*Log reduction: >6.5*	*Reduction below detection limit*
Heat treatment	Bone	1	Log reduction: >5.51	Reduction below detection limit
Irradiation (various)	Bone	2	Log reduction: >3.20 to >4.0	Reduction below detection limit
Irradiation (various)	Musculoskeletal allografts	2	Log reduction: >2.90 to 9.0	Reduction below detection limit
Methylene blue	Red blood cells (no information on product additives)	1	Log reduction: ≥6.32	Reduction below detection limit
Methylene blue	Fresh frozen plasma	1	Log reduction for HIV-1: ≥5.45	Reduction below detection limit
Nanofiltration	Plasma	2	Log reduction: ≥3.8 to ≥6.9	Reduction below detection limit
Pasteurization	Plasma	1	Log reduction: ≥5.7	Reduction below detection limit
PEN110	Red blood cells (no information on product additives)	1	Log reduction: 5.57	
Peracetic Acid-Ethanol	Bone	2	Log reduction: 2.54 - >4	Reduction below detection limit
Riboflavin + UV Light	Platelet concentrates in plasma	4	Log reduction cell-associated: 4.5 - 6.5 Log reduction cell-free: 4.2 - 5.9	Reduction below detection limit
Riboflavin + UV Light	Whole blood	1	Log reduction cell-associated: 4.5	
Solvent/ Detergent	Log reduction: ≥6.0	1	Log reduction: ≥6.0	Reduction below detection limit
Sperm washing	Sperm	4		0 infection infections out of >500 serodiscordant couples treated
*Supercritical processing **	*Bone*	*1*	*Log reduction: >14.22*	*Cumulative log reduction for 4 distinct processing steps*
Terminal ethylene oxide disinfection	Musculoskeletal allografts	1	Viral titers ≤ 10^5	Reduction below detection limit
Thiopyrylium / Dipyridamole	Red blood cells (no information on product additives)	1	Log reduction cell-associated: ≥6.2 Log reduction cell-free: ≥6.8	Reduction below detection limit
UV-A Light	Plasma	1	Log reduction: 4-5	
UV-C Light	Platelet concentrates in plasma	2	Log reduction: 1 to 1.4	
UV-C Light	Plasma	2	Log reduction: 0.6 to 1.4	
Xenon flash-pulse	Platelet concentrates in plasma	1	Log reduction: 1.8	

** Two studies were identified after the search and added to the results. These studies are presented in italics in the table.*
UV: ultraviolet.

See "Annex 3. Pathogen inactivation methods: data extraction table" for the data extraction (available on request).

9. Public health resources

ECDC

- HIV infection and AIDS
- HIV surveillance and disease data

US Centers for Disease Control

- CDC HIV resource library
- HIV Risk and Prevention Estimates | HIV Risk and Prevention | HIV/AIDS | CDC

US Food and Drug Agency

- Complete List of Donor Screening Assays for Infectious Agents and HIV Diagnostic Assays
- FDA Blood Guidances
- FDA Tissue Guidances

European Directorate for the Quality of Medicines & HealthCare

- EDQM Blood guide
- EDQM Guide to the quality and safety of tissues and cells for human application

World Health Organization

- HIV
- HIV Global health observatory
- Blood transfusion safety
- Transplantation

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Annex 1. Search strategies and methodology

Section 1: Description of the pathogen

Search questions and objectives

The objectives for this section are:

- To describe the biological characteristics of HIV-1 and HIV-2 including the following elements:
  - Classification and taxonomy;
  - Virologic characteristics;
  - Receptors on host cell.
- To describe the pathogenesis of HIV-1 and HIV-2 including the following elements:
  - Natural route of transmission;
  - Infectious dose;
  - Viremia (not present/transitory/intermittent/long lasting);
  - Duration of viremia (days);
  - Organ systems targeted;
  - Presence in the different tissues (list of all tissues);
  - Intracellular/extracellular;
  - Seroconversion (appears/day/doesn't appear).

General search strategy

- Targeted review with pre-selected sources
  - ICTV Virus Taxonomy;
  - Mandell, Douglas, and Bennett's principles and practice of infectious diseases, 9th edition (2020);
  - Shetty, Nandini, et al. Infectious Disease: Pathogenesis, Prevention and Case Studies, John Wiley & Sons, Incorporated, 2009.

Section 2: Disease description

Search questions and objectives

The objectives for this section are:

- To describe the disease in terms of:
  - Frequency of asymptomatic cases (non/rare/moderate/frequent);
  - Duration of illness;
  - Severity (mild, serious, fatal);
  - Long term or permanent sequels;
  - Diagnostic possibilities (laboratory testing/clinical);
  - Incubation period;
  - Duration of infectivity;
  - Treatment options;
  - Consequences of treatment (short-term, long-term, mild, severe).

General search strategy

- Targeted review with pre-selected sources
  - Mandell, Douglas, and Bennett's principles and practice of infectious diseases, 9th edition (2020);
  - Shetty, Nandini, et al. Infectious Disease: Pathogenesis, Prevention and Case Studies, John Wiley & Sons, Incorporated, 2009.

Section 3: Epidemiology

Search questions and objectives

The objectives for this section are:

- To describe the prevalence of HIV infections in EU/EEA countries in:
  - The general population;
  - SoHO donors.
- To describe the incidence of HIV infections in EU/EEA countries in:
  - The general population;
  - SoHO donors.
- To describe known risk factors for HIV.
- To describe any other relevant issue related to SoHO safety and HIV as identified by the expert panel.

General search strategy

- Identification of appropriate sources with ECDC internal experts on HIV and input from the scientific expert panel.
- Targeted literature search and use of grey literature from reference organizations: ECDC, EDQM, WHO, CDC.

Section 4: Laboratory testing approaches

Search questions and objectives

The search questions for this section are:

- To describe the characteristics and test accuracy properties (O) of laboratory tests that are approved or used for the screening of HIV (I) in SoHO donors (living and deceased donors) (P).
- To describe the test accuracy properties of the NAT tests approved or used for the screening of HIV in blood donations according to pooled or individual donation use.
- To describe the test accuracy properties of the tests approved or used for the screening of HIV in blood donations according to PrEP/PEP use.

P= SoHO donors
I= HIV tests used for screening in a SoHO context
T/O= HIV-1/2 test accuracy
Comparators = reference standards

Searches

Searches will be restricted from January 2001 (start of 4th generation tests) to present and will cover MEDLINE only.

Customised searches of grey literature using generic web search engines (e.g. Google) combined with searches in targeted websites will be also conducted.

Only publications available in English.

Letters and commentaries, conference abstracts, case reports, and case series will be excluded.

Types of study to be included

Randomised controlled trials, non-randomised controlled trials, prospective and retrospective cohort studies, case control studies, and cross-sectional studies. Test accuracy studies will be considered eligible for inclusion, including (random)-paired comparative studies and prospective/retrospective cross-sectional studies, systematic reviews reporting on HIV-1/2 test accuracy in the context of SoHO.

Condition or domain being studied

HIV (Human Immunodeficiency Virus) is a virus that attacks the immune system, specifically CD4+ T cells. HIV is transmitted through contact with certain body fluids, such as blood, semen, vaginal fluids, and breast milk. Symptoms of HIV can vary from person to person and may not appear immediately. The initial symptoms are often flu-like, including fever, headache, muscle aches, and fatigue. Without treatment, HIV can lead to acquired immunodeficiency syndrome (AIDS), defined as an HIV infection with a CD4+ T cell count below 200 cells per µL or the occurrence of specific associated diseases.

The risk of HIV transmission through blood donation is very low in countries where strict screening procedures and testing protocols are in place. It is important to note that there is a window period between the time of infection and the time when the pathogen (or antibodies) can be detected in the blood. During this period, a person may test negative for HIV but still be infectious. The length of the window period varies depending on the type of HIV test used, but it typically ranges from 2 weeks to 3 months.

Participants/population

SoHO donors, excluding organs.

Index tests considered

- Enzyme immunoassays (EIA);
- Enzyme-linked immunosorbent assay (ELISA);
- Indirect Fluorescent Antibody assay (IFA);
- Immunoblot (western blot);
- Chemiluminescent immunoassay (CMIA or ChLIA/CLIA);
- Nucleic acid amplification test.

Target condition

HIV-1 and HIV-2

Comparator(s)/control

No reference standard is prespecified.

Context

Screening tests for donors of SoHO approved or in use.

In-house (i.e., not commercial) tests are in scope if they are used in EU/EEA countries. In-house tests used outside EU/EEA will be excluded.

Studies reporting accuracy metrics in the context of proficiency testing will be excluded.

Main outcome(s)

- Test characteristics
  - Type (e.g. antibody, antigen, NAT…);
  - Target (e.g. p24);
  - Manufacturer.
- Test accuracy estimates (as reported)
  - Sensitivity: clinical and analytical;
  - Specificity;
  - Window period.

Measures of effect

Relative and absolute measures of effect for dichotomous and continuous outcomes.

Data extraction

- Studies will be assessed for relevance, first by title/abstract and then by full text, excluding at each step studies which do not satisfy the inclusion criteria.
- The studies will be assessed by a single reviewer.
- Data will be extracted by a single reviewer using a standardised data extraction form. Extracted data will be reviewed by a second reviewer.
- Where multiple publications of the same study are identified, data will be extracted and reported as a single study.

Risk of bias (quality) assessment

Will not be performed.

Strategy for data synthesis

The extracted data will be described in a tabular format and no meta-analyses will be conducted. The data corresponding to the protocol outcomes will be presented by the type and target of the test. Test accuracy metrics that are not reported and can be calculated from the reported information will be calculated.

Analysis of subgroups or subsets

Donor type (living, deceased) sample

Keywords for the search

PubMed

Concept	No.	Query	Results
All, >2001	**6**	**#5 AND 2001:3000 [dp]**	**1,509**
All	5	#1 AND #2 AND #3 AND #4	2,792
Accuracy metrics	4	"Sensitivity and Specificity"[Mesh:NoExp] OR "Predictive Value of Tests"[Mesh] OR "sensitiv*"[Text Word] OR "specific*"[Text Word] OR "npv"[Text Word] OR "ppv"[Text Word] OR "negative predictive value*"[Text Word] OR "positive predictive value*"[Text Word]	5,500,798
Test methods	3	"Polymerase Chain Reaction"[Mesh] OR "Enzyme-Linked Immunosorbent Assay"[Mesh] OR "Immunoblotting"[Mesh] OR "Immunoassay"[Mesh] OR "screen*"[Title/Abstract] OR "test*"[Title/Abstract] OR "serolog*"[Title/Abstract] OR "sero log*"[Title/Abstract] OR "assay*"[Title/Abstract] OR "antigen*"[Title/Abstract] OR "antibod*"[Title/Abstract] OR "PCR"[Title/Abstract] OR "nucleic*"[Title/Abstract] OR "polymerase*"[Title/Abstract] OR "ELISA"[Title/Abstract] OR "EIA"[Title/Abstract] OR "IFA"[Title/Abstract] OR "immunoblot*"[Title/Abstract] OR "immuno blot*"[Title/Abstract] OR "western blot*"[Title/Abstract] OR "immunoelectroblot*"[Title/Abstract] OR "electroimmunoblot*"[Title/Abstract] OR "CMIA"[Title/Abstract] OR "CLIA"[Title/Abstract] OR "ICT"[Title/Abstract]	7,303,130
SoHO	2	"Tissue Donors"[Mesh] OR "Tissue Transplantation"[Mesh] OR "Blood Transfusion"[Mesh] OR "donor*"[Title/Abstract] OR "donat*"[Title/Abstract] OR "transfus*"[Title/Abstract] OR "transplant*"[Title/Abstract] OR "tissue graft*"[Title/Abstract]	1,050,829
HIV	1	"HIV"[Mesh] OR "HIV Infections"[Mesh] OR "Human immune deficiency virus*"[tiab] OR "Human immunodeficiency virus*"[tiab] OR "Human immuno deficiency virus*"[tiab] OR "aids virus*"[tiab] OR "Immunologic Deficiency Syndromes"[Mesh:NoExp] OR AIDS[OT] OR "Acquired Immune Deficiency Syndrome*"[tiab] OR "Acquired Immuno-Deficiency Syndrome*"[tiab] OR "Acquired Immuno Deficiency Syndrome*"[tiab]	395,281

Alternative search strategy for quality control (Embase and Cochrane) – Not performed due to lack of resources

Embase

Concept	No.	Query	Results
All, >2001	**6**	**#5**	
All	5	#1 AND #2 AND #3 AND #4	
Accuracy metrics	4	('sensitivity and specificity':ti,ab NOT animal/ex NOT human/ex NOT nonhuman/ex NOT vitro/ex NOT invertebrate/ex NOT plant/ex NOT bacterial/ex) OR 'predictive value of tests'/exp OR sensitiv*:ti,ab OR specific*:ti,ab OR npv:ti,ab OR ppv:ti,ab OR 'negative predictive value*':ti,ab OR 'positive predictive value*':ti,ab	
Test methods	3	('polymerase chain reaction'/exp OR 'enzyme-linked immunosorbent assay'/exp OR 'immunoblotting'/exp OR 'immunoassay'/exp OR screen*:ti,ab OR test*:ti,ab OR serolog*:ti,ab OR 'sero log*':ti,ab OR assay*:ti,ab OR antigen*:ti,ab OR antibod*:ti,ab OR PCR:ti,ab OR nucleic*:ti,ab OR polymerase*:ti,ab OR ELISA:ti,ab OR EIA:ti,ab OR IFA:ti,ab OR immunoblot*:ti,ab OR 'immuno blot*':ti,ab OR 'western blot*':ti,ab OR 'immunoelectroblot*':ti,ab OR 'electroimmunoblot*':ti,ab OR CMIA:ti,ab OR CLIA:ti,ab OR ICT:ti,ab)	
SoHO	2	('tissue donors'/exp OR 'tissue transplantation'/exp OR 'blood transfusion'/exp OR donor*:ti,ab OR donat*:ti,ab OR transfus*:ti,ab OR transplant*:ti,ab OR 'tissue graft*':ti,ab)	
HIV	1	('hiv'/exp OR 'hiv infections'/exp OR 'human immune deficiency virus*':ti,ab OR 'human immunodeficiency virus*':ti,ab OR 'human immuno deficiency virus*':ti,ab OR 'aids virus*':ti,ab OR 'immunologic deficiency syndromes'/exp NOT 'animal'/exp) OR aids:ti,ot OR ('acquired immune deficiency syndrome*':ti,ab OR 'acquired immuno-deficiency syndrome*':ti,ab OR 'acquired immuno deficiency syndrome*':ti,ab)	

Cochrane reviews

ID Search Hits

- #1 MeSH descriptor: [HIV] explode all trees = 3733
- #2 "Human immunodeficiency virus*" OR "Human immuno deficiency virus*" OR "HIV" = 32512
- #3 ("Polymerase Chain Reaction" OR "Enzyme-Linked Immunosorbent Assay" OR "Immunoblotting" OR "Immunoassay" OR "screen*" OR "test*" OR "serolog*" OR "sero log*" OR "assay*" OR "antigen*" OR "antibod*" OR "PCR" OR "nucleic*" OR "polymerase*" OR "ELISA" OR "EIA" OR "IFA" OR "immunoblot*" OR "immuno blot*" OR "western blot*" OR "immunoelectroblot*" OR "electroimmunoblot*" OR "CMIA" OR "CLIA" OR "ICT"):ti,ab,kw = 368652
- #4 MeSH descriptor: [Tissue and Organ Procurement] explode all trees = 230
- #5 (donor* OR donat* OR transfus* OR transplant*):ti,ab,kw = 68870
- #6 (#1 OR #2) = 32512
- #7 (#4 OR #5) = 68879
- #8 #3 AND #6 AND #7 = 358

Section 5: Current testing requirements in EU/EEA countries

Search questions and objectives

The objectives for this section are:

- To describe the laboratory testing procedures in use for blood donors in EU/EEA countries.
- To describe the laboratory testing procedures in use for tissue and cell donors in EU/EEA countries.

General search strategy

- Use of the data published in the collection, testing and use of blood and blood components in Europe by the EDQM.
- Use of the data published in the Mapping of More Stringent Blood Donor Testing Requirements - Mapping Exercise 2015 by the European Commission.
- Input from the scientific expert panel

Section 6: Recommendations from other organisations

Search questions and objectives

The objectives for this section are:

- To describe the recommendations for the prevention of transmission of HIV through the application of SoHO from relevant organisations.

General search strategy

- Use of the recommendations published by the following organisations:
  - European Commission;
  - European Directorate for the Quality of Medicines & HealthCare (EDQM);
  - US Food and Drug Administration (FDA);
  - Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee (JPAC);
  - World Health Organization (WHO);
  - Scientific international societies where relevant: EBA, ESHRE, EATCB.

Section 7: Transmission through SoHO

Search questions and objectives

The objectives for this section are:

- To provide evidence of demonstrated transmission of HIV through SoHO, by SoHO type.
- To describe the number of HIV transmission through SoHO in EU/EEA, by SoHO.

General search strategy

- Targeted literature review, including search on the Notify library (www.notifylibrary.org).
- Summary of Serious Adverse Reactions and Events (SARE) data provided by the European Commission for 2017 - 2021.

Section 8: Processing and pathogen inactivation approaches

Search questions and objectives

The search questions for this section are:

- To describe the effectiveness properties (O) specific to HIV of pathogen inactivation or reduction methods (I) that are approved or used in each type of relevant SoHO: blood (including all blood products), tissues, or cells (including reproductive cells) (P).

P= SoHOs
I= pathogen inactivation or reduction methods
T/O= Reduction metrics for HIV

- To describe the impact of specific SoHO processing steps on HIV levels in each type of relevant SoHO: blood (including all blood products), tissues, or cells (including reproductive cells) (P).

P= SoHOs
I= Processing steps:

- Sperm wash;
- Density gradient centrifugation;
- Filtration;
- Freezing;
- Lyophilisation;
- Glycerolization;
- Vitrification.

T/O= HIV levels and reduction metrics for HIV

Searches

Searches will be restricted from January 2001 to present and will cover MEDLINE only.

Customised searches of grey literature using generic web search engines (e.g., Google) combined with searches in targeted websites will be also conducted.

Only publications available in English.

Letters and commentaries, conference abstracts, case reports, and case series will be excluded.

Types of study to be included

Randomised controlled trials, non-randomised controlled trials, prospective and retrospective cohort studies, case control studies, and cross-sectional studies. Any study reporting efficacy/effectiveness measures of pathogen inactivation or reduction in the context of SoHO will be considered eligible for inclusion.

Condition or domain being studied

HIV (Human Immunodeficiency Virus) is a virus that attacks the immune system, specifically CD4+ T cells. HIV is transmitted through contact with certain body fluids, such as blood, semen, vaginal fluids, and breast milk. Symptoms of HIV can vary from person to person and may not appear immediately. The initial symptoms are often flu-like, including fever, headache, muscle aches, and fatigue. Without treatment, HIV can lead to acquired immunodeficiency syndrome (AIDS), defined as an HIV infection with a CD4+ T cell count below 200 cells per µL or the occurrence of specific associated diseases.

The risk of HIV transmission through blood donation is very low in countries where strict screening procedures and testing protocols are in place. It is important to note that there is a window period between the time of infection and the time when the pathogen (or antibodies) can be detected in the blood. During this period, a person may test negative for HIV but still be infectious. The length of the window period varies depending on the type of HIV test used, but it typically ranges from 2 weeks to 3 months.

Participants/population

SoHO donors, excluding organs.

Reduction/inactivation methods

- Pathogen reduction.

Processing methods

- (Sperm) wash;
- Density gradient centrifugation;
- Filtration;
- Freezing;
- Lyophilisation (lyophilised);
- Glycerolization (glycerolized);
- Vitrification.

Target condition

HIV-1 and HIV-2.

Comparator(s)/control

Not applicable. Effectiveness will be assessed based on the quantitative or qualitative presence of pathogen in the SoHO sample after application of the inactivation, reduction, or processing method.

Context

Reduction, inactivation or processing methods specifically used in the context of SoHOs for human application. Processing or inactivation methods for plasma-derived medicinal product will be excluded.

Main outcome(s)

- Reduction/inactivation methods
  - Qualitative assessment of effectiveness (e.g., pathogen no longer detectable);
  - Quantitative assessment of effectiveness (e.g., log reduction).
- Processing methods
  - Qualitative assessment of impact on pathogen reduction;
  - Quantitative assessment of impact on pathogen reduction (e.g., log reduction).

Measures of effect

Relative and absolute measures of effect for dichotomous and continuous outcomes.

Data extraction

- Studies will be assessed for relevance, first by title/abstract and then by full text, excluding at each step studies which do not satisfy the inclusion criteria.
- The studies will be assessed by a single reviewer.
- Data will be extracted by a single reviewer using a standardised data extraction form. Where multiple publications of the same study are identified, data will be extracted and reported as a single study.

Risk of bias (quality) assessment

Will not be performed.

Strategy for data synthesis

The extracted data will be described in a tabular format and no meta-analyses will be conducted. The data corresponding to the protocol outcomes will be presented by the type of reduction/inactivation or processing method.

Analysis of subgroups or subsets

SoHO type, processing method

Keywords for the search

PubMed

Search strategy – reduction or inactivation

Concept	No.	Query	Results
All, >2001	**5**	**#5 AND 2001:3000 [dp]**	**768**
All	4	#1 AND #2 AND #3	817
Virus, HIV	3	"retroviridae"[MeSH Major Topic] OR "retroviridae infections"[MeSH Major Topic] OR virus*[Title/Abstract] OR "viral"[Title/Abstract] OR "retrovir*"[Title/Abstract]	1,253,178
Pathogen reduction or inactivation	2	"pathogen"[Title/Abstract] AND ("reduction"[Title/Abstract] OR "inactivation"[Title/Abstract] OR "solvent-detergent"[Title/Abstract] OR "methylene blue"[Title/Abstract] OR "ultraviolet"[Title/Abstract] OR "amotosalen"[Title/Abstract] OR "alkylating agents"[Title/Abstract] OR "washing"[Title/Abstract] OR "riboflavin"[Title/Abstract] OR "uv light"[Title/Abstract]) AND (effect*[Text Word] OR effic*[Text Word] OR impact[Text Word])	8,377
Donors and SoHO	1	"Tissue Donors"[Mesh] OR "Tissue Transplantation"[Mesh] OR "Blood Transfusion"[Mesh] OR "donor*"[Title/Abstract] OR "donat*"[Title/Abstract] OR "transfus*"[Title/Abstract] OR "transplant*"[Title/Abstract] OR "graft*"[Title/Abstract] OR "soho*"[Title/Abstract] OR "mpho*"[Title/Abstract] OR "blood"[Title/Abstract] OR "cell*"[Title/Abstract] OR "tissue*"[Title/Abstract] OR "plasma"[Title/Abstract] OR "cornea*"[Title/Abstract] OR "bone*"[Title/Abstract] OR "tendon*"[Title/Abstract] OR "skin"[Title/Abstract] OR "islet*"[Title/Abstract] OR "valve*"[Title/Abstract] OR "rbc"[Title/Abstract] OR "platelets"[Title/Abstract] OR "sperm*"[Title/Abstract] OR "oocyte*"[Title/Abstract]	10,722,543

Search strategy – processing methods

Concept	No.	Query	Results
All, >2001 without # 3	**6**	**#1 AND #2 AND 2001:3000 [dp]**	**14,305**
All, >2001	**5**	**#4 AND 2001:3000 [dp]**	**1,438**
All	4	#1 AND #2 AND #3	1,684
Virus, HIV	3	"retroviridae"[MeSH Major Topic] OR "retroviridae infections"[MeSH Major Topic] OR virus*[Text Word] OR "viral"[Text Word] OR "retrovir*"[Text Word] OR "hiv"[Text Word]	1,547,614
Processing methods	2	(("pathogen"[Title/Abstract] OR "safety"[Title/Abstract] OR "microb*"[Title/Abstract]) AND ("processing"[Title/Abstract] OR "wash*"[Title/Abstract] OR "density gradient centrifugation"[Title/Abstract] OR "filtration"[Title/Abstract] OR "freezing"[Title/Abstract] OR "lyophilis*"[Title/Abstract] OR "glyceroli"[Title/Abstract] OR "Vitrification"[Title/Abstract]))	41,640
Donors and SoHO	1	"Tissue Donors"[Mesh] OR "Tissue Transplantation"[Mesh] OR "Blood Transfusion"[Mesh] OR "donor*"[Title/Abstract] OR "donat*"[Title/Abstract] OR "transfus*"[Title/Abstract] OR "transplant*"[Title/Abstract] OR "graft*"[Title/Abstract] OR "soho*"[Title/Abstract] OR "mpho*"[Title/Abstract] OR "blood"[Title/Abstract] OR "cell*"[Title/Abstract] OR "tissue*"[Title/Abstract] OR "plasma"[Title/Abstract] OR "cornea*"[Title/Abstract] OR "bone*"[Title/Abstract] OR "tendon*"[Title/Abstract] OR "skin"[Title/Abstract] OR "islet*"[Title/Abstract] OR "valve*"[Title/Abstract] OR "rbc"[Title/Abstract] OR "platelets"[Title/Abstract] OR "sperm*"[Title/Abstract] OR "oocyte*"[Title/Abstract]	10,730,103

Annex 2. Laboratory testing approaches: data extraction table

Data extraction table available on request.

Commercial tests available for the donor screening of HIV

This table is based on the list of licensed donor screening tests for tissues and cells[ii] and blood[iii] published by the FDA and restricted to assays with an available CE mark.

Trade name	Test type	Targets (HIV)	Use
ABBOTT PRISM HIV Ag/Ab Combo	ChLIA	p24Ag HIV-1 and HIV-2 Ab	Living donors
Access HIV Ag/Ab combo	CLIA	p24Ag HIV-1 and HIV-2 Ab	Living donors
ARCHITECT HIV Ag/Ab Combo assay	CMIA	p24Ag HIV-1 and HIV-2 Ab	Living donors
Elecsys HIV combi PT	ECLIA	p24Ag HIV-1 and HIV-2 Ab	Living and deceased donors
BioPlex 2200 HIV Ag-Ab Panel	EIA	p24Ag HIV-1 and HIV-2 Ab	Living donors
Genscreen ULTRA HIV Ag-Ab	EIA	p24Ag HIV-1 and HIV-2 Ab	Living donors
Cobas MPX	NAT	HIV-1 RNA, HIV-2 RNA	Living and deceased donors
Procleix Ultrio Elite and UltrioPlex E Assays	NAT	HIV-1 RNA, HIV-2 RNA	Living and deceased donors

[ii] https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/testing-human-cells-tissues-and-cellular-and-tissue-based-product-hctp-donors-relevant-communicable#approved

[iii] https://www.fda.gov/vaccines-blood-biologics/complete-list-donor-screening-assays-infectious-agents-and-hiv-diagnostic-assays

Annex 3. Pathogen inactivation methods: data extraction table

Data extraction table available on request.