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REPORT FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT, THE COUNCIL, THE EUROPEAN ECONOMIC AND SOCIAL COMMITTEE AND THE COMMITTEE OF THE REGIONS

on the implementation of the Directives 2002/98/EC, 2004/33/EC, 2005/61/EC and 2005/62/EC setting standards of quality and safety for human blood and blood components

{SWD(2016) 129 final}
{SWD(2016) 130 final}

1. Introduction

Article 26 of Directive 2002/98/EC requires Member States to submit to the European Commission, before 31 December 2003 and every three years thereafter, a report on the activities carried out in relation to the provisions of the Directive, including an account of the measures taken in relation to inspection and control. The Commission is required to transmit these national reports to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions. The Commission is also required to provide them with an overview report on the implementation of the requirements of the Directive, in particular as regards inspections and control.

In addition, and in accordance with Article 20(2) of the Directive 2002/98/EC, Member States have to submit to the Commission reports on the application of the principle of voluntary and unpaid donation (VUD) every three years. On the basis of these national reports, the Commission is required to inform the European Parliament and the Council of any necessary further measures in relation to VUD it intends to take at Union level.

This overarching Report is a summary, drawing from the replies to questionnaires that the Commission sent to Member States in 2012 (verification of the completeness of transposition), 2013 (implementation survey)[1,2] and 2014 (implementation of the VUD principle) and follows up on the Report in 2006[3] and the Commission Communication in 2010[4], as well as on the two Reports on the application of the principle of VUD for blood and blood components issued in 2006[5] and 2011[6]. All Member States replied to the transposition questionnaire. The 2013 implementation survey was answered by all Member States and also by two EEA countries, Liechtenstein and Norway. All Member States, Liechtenstein and Norway also provided answers to the survey on the implementation of the principle of VUD.

The full analysis of the Member States' replies to the 2013 implementation survey and the 2014 survey on the implementation of the VUD principle is included in the two Staff Working Documents accompanying this Report[7].

Besides complying with the legal obligations, the current report sets out how Directive 2002/98/EC and its implementing Directives 2004/33/EC, 2005/61/EC and 2005/62/EC (henceforth commonly referred to as the EU blood legislation) function in practice, against a backdrop of significant scientific and organisational developments (internationalisation, commercialisation) that have taken place in the European blood and blood components sector over the past decade.

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1 Detailed Member State replies (as well as replies from Norway and Liechtenstein) can be accessed at: http://ec.europa.eu/health/blood_tissues_organs/key_documents/

2 In a number of cases clarification requests were sent to Member States for verification. It is important to note that the hyperlinks contain the original replies of Member States, whilst the report reflects the updated information provided by Member States. This can lead to certain discrepancies. In such cases this report contains the updated information.

3 http://ec.europa.eu/health/blood_tissues_organs/docs/blood_reportdonation_en.pdf

4 http://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX:52010DC0003

5 http://ec.europa.eu/health/ph_threats/human_substance/documents/blood_com_0217_en.pdf

6 http://ec.europa.eu/health/blood_tissues_organs/docs/blood_reportdonation_en.pdf

7 Links to be added once published

Where appropriate, data gathered through other channels and supporting the findings of the two surveys (e.g. exchanges with the national blood competent authorities during the bi-annual meetings with the Commission, mandatory annual reporting to the Commission of serious adverse reactions and events (SARE), alerts launched in the Rapid Alerts for Blood (RAB) platform, a study mapping the economic landscape of the sector and more recently a Eurobarometer survey[8] as well as outputs of EU-funded projects were also taken into account.

2. Transposition of EU Blood legislation

A verification of the completeness of transposition into national legislation of the EU blood legislation, carried out by the Commission, demonstrated that it is fully transposed in all but one Member State. In the latter case, an infringement proceeding pursuant to Article 258 TFEU is ongoing.

3. Implementation of the EU blood legislation

Overall, the implementation of the EU blood legislation by Member States is considered adequate and the legislation has resulted in the establishment of a network of competent authorities that oversee the field through authorisation, inspection, and vigilance. However, some difficulties in interpretation, implementation and enforcement of the legislation were identified, in some cases due to technological and scientific advances since its adoption. As the legislation in question does not provide a basis for full harmonisation and as Directives allow the Member States a certain degree of discretion as to how to ensure their implementation, there are accordingly many differences between Member States in the approaches they have taken to implementation. These differences facilitate successful integration of the requirements into national legislation but in some cases they may limit the mutual acceptance of authorisations with consequences for potential cross-border movement of blood and blood components.

3.1. Designation of competent authority or authorities

All Member States have appointed competent authorities for blood. In half of the countries one authority is responsible for the entire oversight of the blood sector, whereas in others the tasks are divided amongst two or three authorities (based on duties, e.g. accreditation/authorisation versus inspections/vigilance, or based on the allocation of tasks between federal and regional levels). Several Member States mentioned the limited role of authorities at federal/national level and pointed to the important tasks attributed to/carried out by regional competent authorities. In the vast majority of Member States, the authorities for blood are also responsible for the oversight of other sectors (e.g. organs, tissues, cells and/or medicinal products), which can be beneficial for achieving greater efficiency and coherence.

[8] http://ec.europa.eu/health/blood_tissues_organs/docs/20150408_cc_report_en.pdf;
http://ec.europa.eu/health/blood_tissues_organs/docs/20150408_key_findings_cc_en.pdf
http://ec.europa.eu/health/blood_tissues_organs/eurobarometers/eb822_en.htm

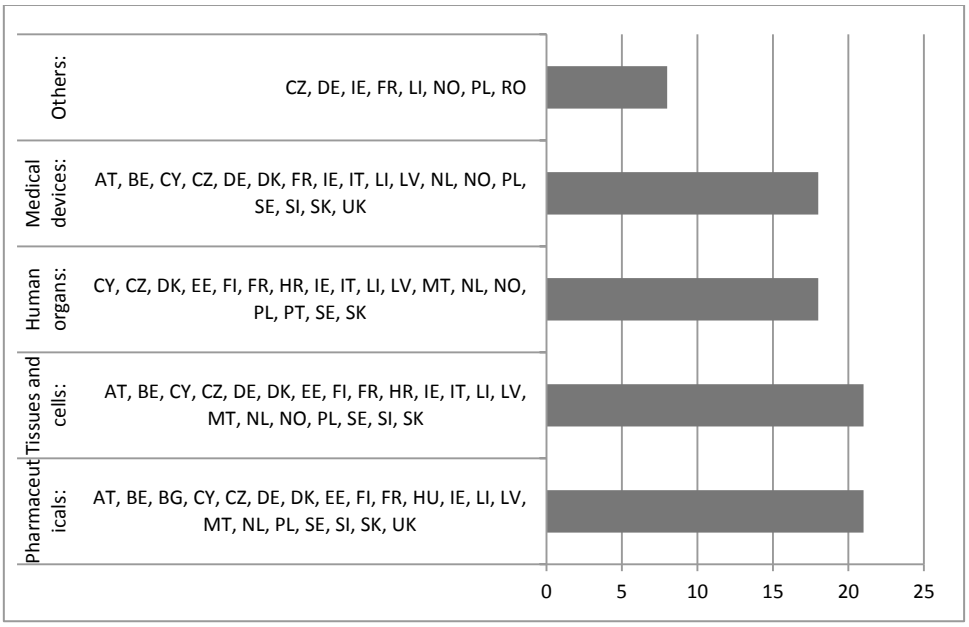

Fig. 1: Additional fields of competence for national blood competent authorities

Wherever different oversight activities (authorisation, inspection, haemovigilance) are undertaken by different authorities, good communication and coordination between respective authorities needs to be ensured. To facilitate good regulatory communication between Member States, as well as to comply with the annual reporting requirements to the Commission, a well-informed national coordinating contact point is essential, even where competent authority responsibilities are shared among multiple organisations or regions. Irrespective of the organisational set-up, it is important that authorities have appropriate resources at their disposal to enable them to carry out the required duties, as well as to ensure their independence from economic operators in the sector and from other influences.

3.2 Obligations of blood competent authorities

Accreditation, designation, authorisation or licensing of blood establishments. The implementation survey confirmed that this core responsibility of national competent authorities is well developed across the Union. At the end of 2011, 1363 blood establishments were authorised in the EU. These authorisations also cover 731 mobile sites, 534 satellite sites and 253 plasma collection centres.

There are differences between Member States in relation to the duration and terms of renewal of the individual authorisations. Some Member States called for more common procedures for authorisation across the Union.

Inspections and control measures. In 2012, 22 countries reported having performed 760 on-site inspections. In addition, thematic/focused inspections, inspections following SARE and desk-based assessments are organised. In almost all countries, the inspections of blood establishments overlap with inspections in other areas.

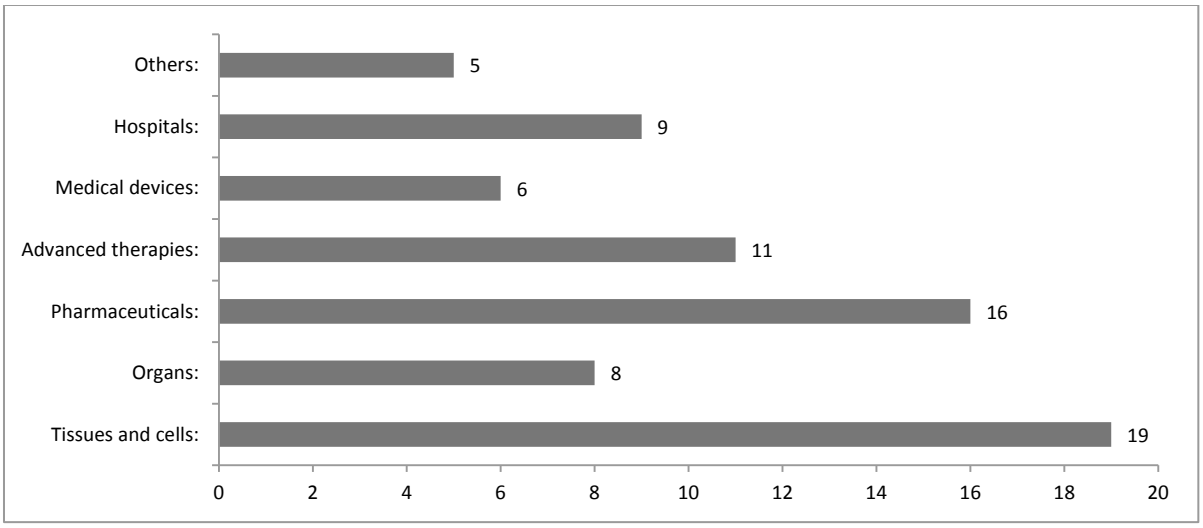

Fig. 2: Overlapping inspection schemes

Whilst overall Member States seem to correctly implement the provisions concerning inspections, a number of Member States reported difficulties related to staffing, which makes compliance with the required 2-year inspection interval challenging. Several Member States expressed interest in applying instead a risk-based prioritisation planning for inspections.

There is diversity between Member States in organisation (e.g. desk-based versus on-site), and outcome (i.e. classification and follow-up of deficiencies) of inspections. Also the inspection approaches vary significantly towards mobile and satellite sites, hospital blood banks, plasma collection centres and potential third country players.

Levels of inspector empowerment and training were regularly commented upon in the replies to the implementation survey. The value of international projects, at EU level and organised by the Council of Europe, are clearly appreciated by most of the national competent authorities as a means to help maintain an adequate level of training and know-how within the group of inspectors and to help ensure a uniform level of compliance verification throughout the EU.

Traceability. Almost all countries report that a donor identification system was implemented in their country, in the majority of countries at national level. All Member States reported that the same rules on traceability apply to blood establishments and hospital blood banks, allowing tracing of blood and blood components from donor to recipient and vice versa.

Notification of serious adverse reactions and events (SARE). All Member States except Hungary reported having a SARE notification system in place, in the majority of them based on the practical guidance developed in co-operation with the Member States for the compilation of the online annual SARE report. Twenty one Member States have dedicated vigilance officer(s) in place. However blood competent authorities in one third of the countries do not believe that all blood establishments are reporting SARE.

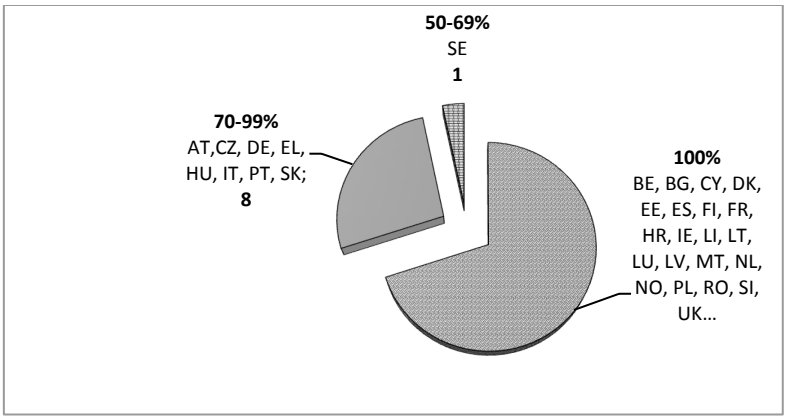

Fig. 3: Percentage of reporting blood establishments/country

While all countries report having recall procedures in place, only 14 reported recalls (1867 in total). A common reason for these recalls is information received from the donor regarding his/her health situation and made available after the donation event. While not mandatory, two-thirds of countries have put in place donor self-exclusion systems. Most countries organise root cause analyses to understand the reasons behind SARE, however there is a generally reported interest in developing this approach further, in particular to address the challenge of involving local professionals and hospitals in these analyses. There appears to be a good interconnectivity with other health-related vigilance systems, in particular on medical devices and communicable diseases. These two areas are often cause for general alerts in the blood sector, as demonstrated since the launch of the Commission managed Rapid Alert System for Blood (RAB), where a number of alerts relating to emerging disease risks with relevance to blood donor selection or testing and to medical device defects that were important in blood collection or processing were shared among the national blood competent authorities. The authorities interact effectively with the RAB system, although many mention a need to improve communication of the information from RAB to the local blood establishments, which needs to be accomplished at national level. Clarification of the operational rules on reporting SARE at EU level would be perceived as helpful by Member State haemovigilance experts.

Although the definition of serious adverse reaction (SAR) in Directive 2002/98/EC, Article 3, gives equal importance to SAR in donors and in recipients, the current requirements refer only to reporting of SAR in recipients. Nonetheless, the voluntary reporting of SAR in donors has increased, suggesting the Member States' increasing interest in the protection of living donors.

Import and export. Whole blood and blood components such as platelets and red blood cells have a limited shelf-life and are rarely exchanged between Member States, with the exception of rare emergency or humanitarian situations. Plasma and plasma derivatives can have a longer shelf-life and as fractionation plants exist only in twelve Member States, both plasma (the starting material) and plasma derivatives (the end product) are frequently exchanged across borders, within the EU and with third (non-EU) countries.

In contrast to blood components for transfusion, the demand for plasma derivatives is steadily increasing (around 6% per year) which also generates import flows from third countries into the EU.

The majority of Member States have rules to authorise and control import of blood and blood components for transfusion, while only about half have such rules for plasma for

fractionation. These include standards for verifying equivalent safety and quality standards, which in half of the Member States go beyond the requirements of the EU blood legislation, e.g. adding requirements for the use of the more sensitive nucleic acid testing (NAT) now available as a routine test for hepatitis and HIV screening.

National rules for export often limit or place conditions on export of blood and blood components, e.g. only in situations of emergency, which is seen by many countries as part of their national policy to ensure self-sufficiency (see below). Rules for export of plasma for fractionation are usually less restrictive, although practice was reported of plasma export for contract fractionation of derivatives which are subsequently to be used for patients only in the country of collection. While many countries report having data on imported volumes, it is difficult to draw conclusions in the absence of a harmonised data collection system on import and export volumes. Additionally, the distinction between import/export from/to third countries and distribution from/to other EU Member States is not consistently applied.

Data protection and confidentiality. No problems were reported regarding the implementation of the provisions related to data protection.

4. Shortages, surpluses and self-sufficiency.

The VUD survey addressed questions on the balance between supply and demand, and the measures taken to achieve sufficiency. This topic is intrinsically linked with the promotion and success of the principle of VUD, as highlighted in recital 23 of Directive 2002/98/EC. Eight countries reported regular shortages of one or more blood components in the survey. These shortages often occur in summer/holiday seasons when the number of donors is reduced and the risk of epidemiological outbreaks, such as West Nile Virus, can temporarily reduce the number of eligible donors. The ageing EU population could exacerbate supply challenges, leading both to increased demand and reduced numbers of eligible donors. Other challenges to the principle of (self-) sufficiency are outlined below.

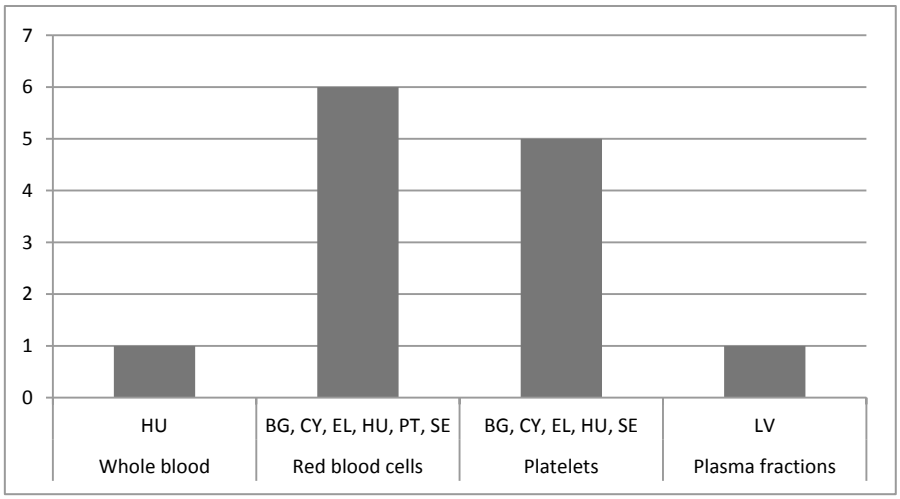

Fig. 4: Countries reporting regular shortages

A limited number of countries report surpluses for some blood components which indicates the potential for cross-border agreements. One national competent authority has taken the lead on developing such an initiative within the network of national competent authorities.

Seven countries do not recover all plasma from whole blood donations for plasma fractionation into derivatives. The UK and Ireland apply this policy as part of their risk mitigation strategy for transmission of variant Creutzfeldt Jacob disease. Other Member States reported to be negotiating agreements for fractionation, while one reported having difficulties finding a partner to carry out fractionation.

In order to address shortages, countries can put in place policies to increase supply and to optimise usage. In almost every country, donation promotion activities are the main actions taken to increase supply. Most common are awareness building campaigns for specific donor groups, such as students, or events such as the World Blood Donor Day (WHO, 14 June) or Thalassemia day (8 May in Greece and Cyprus). Many countries reported financially supporting blood establishments and local players in the organisation of such promotion activities (although the financial support in many of these countries also relates to collection, processing, storage and distribution activities). The debate on possible compensation and incentives for donors plays an important role in supply management (see below).

In order to manage demand and supply of blood and blood components, almost all countries have policies in place that combine annual forecasting with weekly monitoring. These policies involve players at multiple levels, national competent authorities as well as local clinicians. To engage these local stakeholders, countries mention the use of audits and programmes such as the implementation of patient blood management (PBM) (for which there is currently a tendered study on-going under the Union's Third Health Programme). The service contract aims to develop best practices, which could allow for a significant reduction of blood demand for many treatments.

A majority of countries report having policies to also optimise the clinical use of plasma derivatives, with a small number of countries having national prioritisation strategies to ensure supply to those patient groups who are highly dependent on treatment with these products. Some Member States would welcome an exchange of best practices in this respect.

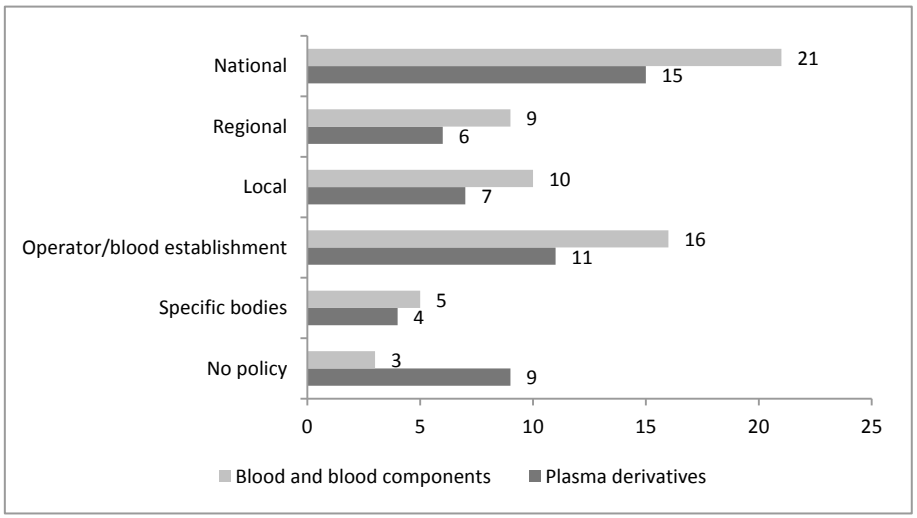

Fig. 5: Policy setting to ensure effective use of blood, blood components and plasma derivatives

The global growth of utilisation of plasma derivatives, particularly intravenous immunoglobulin (IVIG), requires a growing number of donations. Many countries are largely supplied with plasma derivatives by just one supplier, either public or private. Public, national suppliers are predominant in a minority of EU countries. There are a small number of international companies that supply the majority of countries.

Cross-border movement of donors. Five countries reported having donations by donors from abroad, while six countries reported having citizens that travel to donate abroad. While two of these latter six countries also report regular shortages in national supply, the information provided was not sufficient to establish a causal link between these shortages and the cross-border movement of donors. The reported picture seems not to be complete, with some inconsistencies between the information provided by countries whose citizens travel to donate and those who have donors coming from another Member State to donate. While most cross-border donations seem to be individual initiatives, Hungary and Slovakia reported organised transport for their citizens to travel to Austria for plasma donation.

Views vary on whether such cross-border donations are desirable. Ten countries reported facilitating donations by donors from abroad by providing donor questionnaires in different languages. Sixteen reported discouraging such donations by requiring a local ID document or a proof or local residence.

Replacement donors, i.e. donors that are encouraged to make donations to replace those being used for a relative or friend, are reported as important for maintaining supply in five countries. Policies towards them vary, from prohibition to seeing replacement donations as an opportunity to contribute to national self-sufficiency by converting them into regular donors. From an EU perspective, the relevant question is whether blood collected from these donors might have a different safety and quality profile (see below).

5. Voluntary and unpaid donation (VUD)

The ways in which EU Member States have implemented the principle of VUD are difficult to assess in a comprehensive manner. VUD is a factor which is not only ethical in nature, but which might also contribute to higher safety standards and, therefore, be important for the protection of human health. In a system allowing donor payment, some individuals may find the monetary remuneration so important that they might not disclose relevant medical and/or behavioural information. Additional screening and testing may reduce, but cannot completely eliminate, the possibility of a transmission from donor to recipient. Therefore, information provided by the donor contributes to an accurate assessment of all risks associated to the transfusion of blood and blood components and the clinical application of plasma derivatives.

Although the large majority of the responding countries (26) reported that the principle of VUD is mandatory at national level, their legislations often refer to an "encouragement" or to a "strong recommendation".

The practical application of the VUD principle varies across the Union. Seventeen Member States reported having penalties in place, addressing different situations such as making financial gain or collection of donations without consent. According to reports from Member States, no such penalties have so far been imposed. Most countries have additional supportive measures in place, primarily focused on promoting VUD or defining compensation and

incentives (see below). The EU is significantly reliant on importation of plasma for the manufacture of plasma derived medicinal products, mainly from the United States. In this context, it is challenging for MS to apply a requirement for the exclusive importation of plasma sourced from voluntary and unpaid donors.

It is common practice to provide refreshments to donors (27 countries) and to give them small tokens such as pin badges, pens, towels, t-shirts and mugs (24 countries). In around half of the Member States, donors have their travel costs reimbursed and get time off work in the public and private sector. In some Member States, donors receive a fixed payment that is not directly related to actual costs incurred.

There is considerable heterogeneity across the EU, with certain practices perceived as compensation in one country and as incentives in another. For the purpose of the survey, "compensation" was defined as "reparation strictly limited to making good the expenses and inconveniences related to the donation" and "incentive" was defined as "inducement or stimulus for donation with a view to seeking financial gain or comparable advantage", but even with these (non-binding) definitions Member States reached divergent classifications. The difference in purchasing power between Member States might be one factor which explains the diverging views on what is or is not an incentive to donate.

The maximum reported values of compensation and incentives are around EUR 25-30 per donation while the reported values of refreshments and small tokens are between EUR 1 and EUR 10 per donation. Reimbursement of travel costs can cover the actual costs or be a standard lump sum. Time off work varies from less than half a day to up to two days. Some countries foresee compensation for loss of earnings in some circumstances, e.g. one Member State foresees this for plasma apheresis donations.

Less than half of the countries reported having national guiding principles to define what form of compensation or other practice is allowed and under which circumstances. In half of the countries, the blood establishments either determine, or are involved in determining, the value of the compensations and incentives, while in one-third of the countries the national blood competent authorities are involved.

In the Eurobarometer survey on Blood and Cell and Tissue Donation[9], only 12% of EU citizens reported that they thought compensation additional to the costs related to donation was acceptable, when donating blood or plasma. In contrast, 47-48% considered that receiving refreshments, free blood testing or a free physical check-up were acceptable.

6. Quality and safety of blood and blood components

Safety and quality of the blood supply is an important issue for EU citizens, with 56% of respondents to the Eurobarometer survey on Blood and Cell and Tissue Donation citing the risk of contracting a disease as a major concern when accepting donated substances.

Safety and quality of blood depends on the implementation of a combination of three pillars: donor screening for deferral criteria, donor testing and, where possible, pathogen inactivation techniques. Combining the implementation of all three pillars, where possible, is probably the most effective way to minimise risks.

[9] http://ec.europa.eu/health/blood_tissues_organs/eurobarometers/eb822_en.htm.

Donor screening for eligibility. The main causes leading to deferrals of candidate donors reported by Member States were low haemoglobin levels (putting at risk the health of the donor) as well as risk of transmission of infectious diseases, (sexual) risk behaviours, travel, medication and other medical reasons (putting the health of the recipient at risk).

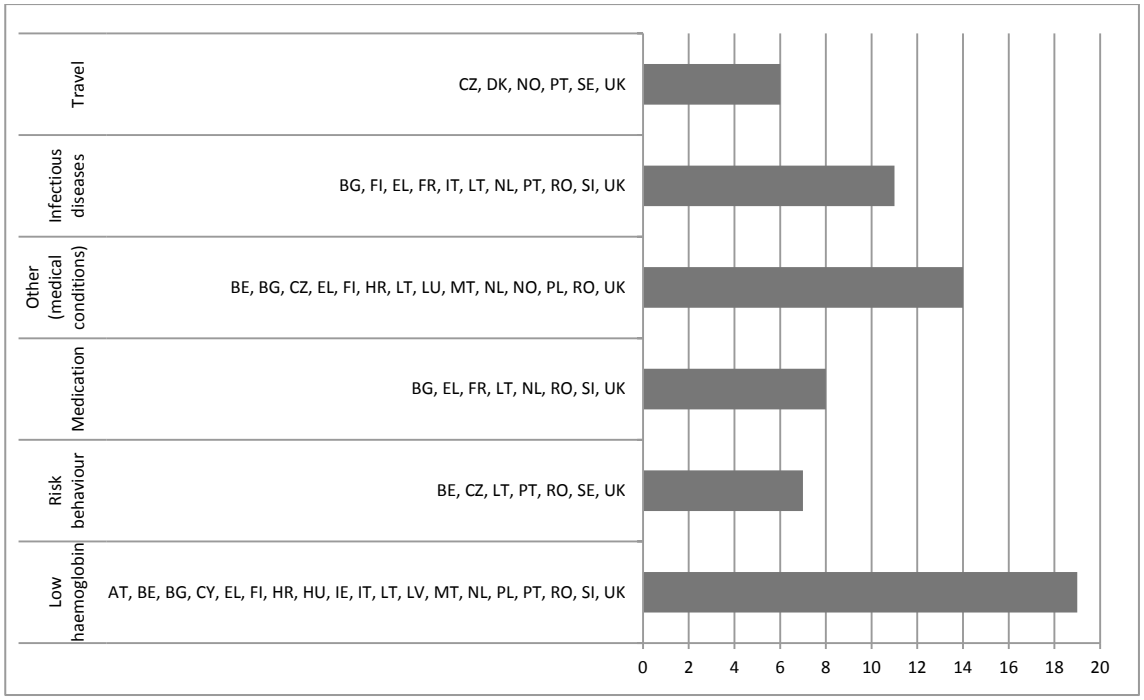

Fig. 6: Main causes leading to deferrals/country

Many countries reported in 2013 on the feasibility/appropriateness of deferring donors on the grounds of sexual risk behaviour and about two-thirds of the countries have national guidance in place. Men having sex with men (MSM) is the most commonly reported sexual risk exclusion criterion due to the higher incidence of infections such as HIV within this population. Since the survey was conducted, changes in national policies have been reported by some countries during the bi-annual meetings of Competent Authorities; the trend is to move from permanent to temporary (usually 12 months) deferral for MSM.

Countries identify an increase of the maximum donor age as the most promising initiative to improve the supply of blood and blood components. Other eligibility criteria that several countries would wish to reflect on relate to the history of malignancy, donor risk behaviour and haemoglobin levels. Overall, Member States expressed interest in an increased level of donor protection and in an overview of additional national eligibility criteria in order to increase transparency and mutual trust in exchanges.

Testing and inactivation technologies. EU legislation defines the minimum serological testing for human immunodeficiency virus (HIV) 1/2, hepatitis B and hepatitis C to be carried out for every whole blood and apheresis donation. In all Member States these tests are performed by authorised laboratories. Member States can add tests for specific components or epidemiological situations. They reported conducting additional tests for syphilis, malaria, hepatitis A, hepatitis E and Parvovirus B19. About two thirds of the countries mention that blood establishments also apply more sensitive nucleic acid testing (NAT), along with

serological testing, although several countries also raised questions regarding the cost-benefit ratio of this relatively costly testing technique. No additional testing was reported for plasma collection, compared with collection of whole blood donations.

Sixteen countries report having pathogen inactivation technologies in place. Inactivation techniques are mainly used for plasma although pathogen inactivation of platelets is likely to be more common going forward.

In their responses to the implementation survey, several countries suggested making syphilis testing mandatory at EU level, while some suggest making NAT testing for HIV and hepatitis mandatory, despite the reservations mentioned by other countries. Member States also highlight the need for good validation of testing technologies, and also pathogen inactivation technologies, in order to achieve an effective level of safety and quality. Countries also see value in further centralisation of laboratory test results at EU level to facilitate benchmarking against average EU rates of positivity.

Every change in deferral, testing or pathogen inactivation policy has a possible impact not only on safety and quality, but also on the economics and on the volume of donations and supply. The role of common assessments by ECDC and the Commission was recognised in this context, e.g. when developing a preparedness plan to help blood establishments address the seasonal outbreaks of West Nile Virus in some southern EU countries.

7. Support for the Implementation of the Blood Directives

The European Commission has been supporting the implementation of the legislation by the Member States by encouraging the active participation of national Competent Authorities in a series of actions, from bi-annual expert meetings to EU-funded projects.

The regular meetings of the expert sub-group on blood and blood components (which is part of the Competent Authorities on Substances of Human Origin Expert Group - CASoHO E01718) allow for sharing best practices and clarification of common difficulties encountered at national and EU level.

Since 2003, a number of projects have been funded under the multi-annual programmes for Union action in the field of health addressing the area of blood and blood components. Projects such as EUBIS, CATIE, DOMAINE, Optimal Blood Use, EU-Q-Blood-SOP and the on-going joint action VISTART provide strong support to Member States in their efforts to implement the requirements of the blood directives. These actions brought improvements in areas of common interest such as quality management and inspection and donor selection and included training courses for Member States Competent Authorities and their inspectors.

As regards the risk of transmission of communicable diseases thorough blood and blood components, the collaboration with ECDC proved extremely valuable. In addition to providing regular updates during the bi-annual meeting of the blood expert sub-group on the epidemiological situation relevant to the blood sector, the development of risk assessments (e.g. for HTLV, malaria, dengue and chikungunya) and preparedness plans (e.g. for WNV outbreaks) provide a valuable contribution to policy and decision making in this sector at both national and EU level.

Finally, the Commission developed, in close cooperation with the Member States, a Rapid Alert Platform for Blood (RAB) which facilitates web-based communications between Member States in case of alerts with relevance in two or more Member States.

8. Conclusions

In conclusion, this Report reveals an overall adequate level of application of the current quality and safety requirements of the EU blood legislation. Significant progress has been made in many areas, often through the active support of Commission funded projects and other initiatives.

However, the Report also points to some gaps and difficulties in relation to the application and enforcement of the existing provisions (e.g. definitions, provisions for donor safety, inspections framework), some due to different approaches taken by the Member States and others due to technological advances and changing risks observed since the legislation was adopted. The Commission will follow-up with Member States to address situations where the legislation might not have been fully or correctly implemented.

The VUD survey shows that Member States overall comply with Article 20 of Directive 2002/98/EC requiring them to take the necessary measures to encourage VUD. However, Member States' perceptions of what is considered compensation and incentive vary.

The gaps and difficulties identified may suggest that a further in-depth evaluation might be useful. The Commission will consider the need for an evaluation in order to assess the relevance, effectiveness, efficiency, coherence and the EU added value of Directive 2002/98/EC and its implementing Directives.