EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Directorate D - Health systems and products

D4 – Substances of Human Origin and Tobacco Control

Brussels,
SANCO D4/IH/ ARES (2013)

Meeting of the Competent Authorities on Blood and Blood Components

17 and 18 April 2013

Summary Report

Participants:

All Member States (MS), except Lithuania were present at the meeting. Croatia, former Yugoslav Republic of Macedonia, Norway (NO) and Turkey (TK), as well as the European Centre for Disease Prevention and Control (ECDC), WHO, Council of Europe (CoE), and the European Medicines Agency (EMA) attended the meeting. A representative of the European Blood Alliance (EBA) was also present.

European Commission – SANCO D4 and SANCO B2.

Chairman: Dr Stefaan Van der Spiegel

1. ADOPTION OF THE AGENDA

Three additional points to be covered under AOB were suggested: World Blood Donor day (FR), blood component labelling (UK), and sharing of surplus blood collection between MS.

2. SURVEILLANCE AND VIGILANCE: UPDATE ON INFECTIOUS DISEASES

2.1. variant Creutzfeldt-Jakob disease (vCJD)

The Commission outlined that there is no deferral for neurosurgery at EU level, as the final version of the EMA position paper on plasma derived medicines does not contain any reference to neurological deferrals. The Commission also presented data from IE showing that exclusion of all neurosurgery is not expected to significantly affect blood supply volumes.

It was concluded that applying deferral for neurosurgery is a national decision, but one which would not significantly affect blood supply. MS and EMA supported the Commission position.

2.2. Malaria 2012

ECDC presented the outcomes of the ECDC malaria satellite meeting on malaria, including preventive measures for avoiding malaria transmission through blood transfusion in endemic and affected regions in Europe. EL gave an update of the situation in 2012, when there were 71 cases of locally acquired *Plasmodium vivax* infections.

FR presented a case of transfusion transmitted malaria from an immuno-silent donor with chronic parasitemia. FR has had three cases of transmission to patients in the last 10 years, and has therefore introduced more stringent measures regarding malaria.

ECDC will convene a second meeting of experts on malaria to look at: (1) the definition of affected/endemic areas, (2) how to define the geographical limits of affected areas (using lessons from experiences in EL) and the possible development of EU maps, and (3) what level of local transmission is required to declare an area affected. ECDC also highlighted that there is an open question of how to deal with visitors who have only been briefly visited affected areas.

2.3. Other

MS were asked whether they had any additional information on infectious diseases to report.

2.3.1. Dengue

FR gave an overview of dengue in Saint Martin, Saint Barthelemy, French Guyana, Guadeloupe, Martinique, French Polynesia, Reunion, Mayotte and New Caledonia, as well as their deferral criteria for the disease.

ECDC commented that experiences from tropical countries are very useful when evaluating strategies for dengue. Although there has not been a dengue epidemic in continental Europe since the 1920s, ECDC also explained that, one of the two dengue vectors, *Aedes albopictus*, is present in southern Europe, raising concerns about the re-appearance of dengue in Europe.

PT gave an overview of dengue in Madeira. The situation is now under control, but is still under surveillance. There have been no new cases since the beginning of February 2013. ECDC explained that there have been 71 symptomatic cases imported to Europe from Madeira. As around 40% of dengue cases are symptomatic, an estimated 165 cases were imported in total.

2.3.2. HIV

AT presented a case of transfusion related HIV transmission, from a donation of blood during the NAT testing window period. AT explained that they had looked at a number of improvements to prevent a recurrence. This included: (1) lowering the threshold for HIV-testing, (2) introducing ‘catch’-questions in the questionnaire, (3) requiring qualified donors, and (4) defining HIV test sensitivity. AT also requested that ECDC give a scientific evaluation and recommendation for HIV.

DE supported the AT suggestion to define sensitivity/specificity of HIV tests. DE would like, however, to focus on sexual behaviour, and are conducting a trial of questions on this. The Italian government plans to propose legislation that all donors are qualified before giving blood, i.e. are tested and then donate after 45 days. CZ raised the issue that infection may occur during the time period between testing and donation. IT supported an evaluation by ECDC on donor qualification.

Member States also discussed "test seekers", who are mainly first time donors. Since the 1990s, FR has centres providing free and anonymous HIV testing, which has reduced the number of individuals donating blood to obtain an HIV test.

The Commission will verify whether ECDC, along with AT, IT, SE and CoE, can look into performing an HIV risk assessment, which will, in particular, evaluate the use, including cost effectiveness, of 'qualified' donors. ECDC will also discuss with CoE on how to best conduct the risk assessment.

2.3.3. Further information

No other Member States reported information on infectious diseases.

2.4. ECDC Work plan

ECDC presented their activities on SoHO. ECDC plans to establish a program to develop a knowledge library on donor-derived infections, with the aim of preventing and controlling transmission of infections through transfusion and transplantation of SoHO. This includes scientific advice, risk assessments, and preparedness plans.

ECDC has published a call for tender for evidence and review based risk assessments for transmission of West Nile virus, dengue and malaria. CA representatives were asked for suggestions of research institutions that may be interested in the project.

3. SERIOUS ADVERSE EVENTS AND REACTIONS (SARE) AND ALERTS ON BLOOD

3.1. Annual report to the Commission 2012

The Commission presented the results of the 2012 SARE reporting exercise (2011 data). Overall the number of serious adverse reactions and events in the EU, NO and HR is low. Although reporting has consistently improved, there are still some countries that only report partial data.

The Commission and the Haemovigilance Working Group (HVWG) are continuously working to assist and facilitate MS reporting. Final reports of the 2011 and 2012 exercises are to be published on the SANCO website. These will first be circulated to the HVWG and MS for comments.

Several MS expressed congratulations to the Commission for the work undertaken and progress made in SARE reporting. EL, AT and FR highlighted the importance of thorough investigations of the causes of SAR/Es. Furthermore, all three highlighted the importance of clear definitions of SAE categories, including "human error." According to FR, an error should only be considered a "human error" when no other cause can be found. AT requested a clearer definition for "issue".

PL commented that there has been good progress on data collection and harmonisation of reporting. DE referred to a public discussion on the safety of platelets products, and asked whether states would report on these separately. The Commission explained that this was not currently the practice but it could be introduced in the future. BE stated that it would be interesting to compare EU SARE data with the scientific literature. AT expressed regret that only a few countries report recipient data. The Commission thanked the MS and the HVWG, and agreed that further improvement to SARE reporting could still be made.

3.2. Serious Adverse Events: Human error classification

Following discussions in the HVWG on root cause analysis for SAEs, the UK gave a short presentation of how they investigate SAEs and identify system failures that led to their occurrence (beyond the usual 'human error').

AT praised the work of the UK on SAEs. EL enquired about ‘system errors’, for example staff shortages. The UK explained that these errors count as ‘human errors’, as labs must manage within the system they are based. Instead of attributing mistakes to lack of staff, working methods should be reorganised.

The UK has also found that attitudes towards ‘human error’ are changing and establishments are more willing to report incidences of ‘human error.’ The UK also explained that a lot of feedback is given to blood establishments and hospital blood banks based on their investigations. The Commission will take this topic back to the Haemovigilance Working Group for further discussion.

3.3. SARE reporting exercise 2013: updates to the reporting template

The Commission introduced the 2013 data collection exercise of 2012 SARE data. The Commission explained the changes to the 2013 reporting template based on discussions with the HVWG. These are (1) a new field for reporting total number of units issued and transfused (regardless of component), (2) a new section for reporting "transfusion of more than one component" (without the possibility of reporting denominators), and (3) the removal of the A/B classification for imputability levels 2 and 3. The template will be launched in May 2013.

CZ reminded the group that changing how data is collected is laborious, and it is anyway mandated by Directive 2005/61/EC. The Commission explained that changes to the reporting template in 2013 would have a minimal effect on data collection.

3.4. RAB: Description of future RAB platform and presentation of interactions with RATC (and in future RAO)

The Commission presented the current status of the development of the RAB platform. Key changes in relation to the RATC system are changes to the types of alert allowed, the replacement of 'products' by blood components, and changes to substance categories. Member States confirmed that the HVWG was the correct forum for discussions and a subset of HVWG members would like to assist in the development of the platform. The Commission also welcomed feedback from the MS.

EMA asked if the Commission had considered classifying alerts by seriousness to give an indication of urgency. The Commission explained that the type of alert can give indication of seriousness. AT and PT suggested that processes be linked to facilities. The UK and EL asked if the platform would feed back to competent authorities in related fields. The Commission explained that blood CAs will need to contact their pharmaceuticals or medical device authorities directly outside the platform, but that the medical devices and pharmaceuticals units were being consulted during development of the platform.

The Commission also outlined that local problems should not be reported. Alerts should only be sent if there is an impact on another country. SE asked how reaction to alerts will be coordinated. The Commission explained that the platform is an information tool. The platform will facilitate information sharing between authorities, but how to react to alerts is a national decision.

CoE asked if data from the platform would be shared and presented at CA meetings, as this could be used to identify gaps in legislation. The Commission explained that information on alerts would continue to be presented at CA meetings, but the primary source for haemovigilance data would be SARE reporting.

The following members of the HVWG agreed to assist SANCO in developing and testing the platform: BE, EL, FR and IE. At the next meeting, the Commission will present a proposal to prepare the transfer to the new platform.

3.5. Collection and transfusion of granulocyte concentrate

FR presented preliminary results of a survey sent to CAs regarding the use of granulocyte concentrate in Member States. Apheresis granulocyte collection requires pre-treatment of donors with corticosteroids or growth factors. Optimal collection also requires the use of a sedimenting agent. Granulocyte collection by apheresis was reported in ten countries.

FR stated that it is difficult to know the effect of collection on donors, as there is no time to detect delayed side effects. FR also explained that it is important to look at the quality and safety, efficacy and indication for this blood component at EU level because it is not a commonly used component in MS. FR suggested a study on recipients at EU level. The UK added that, in the UK, donors are friends or family and are told of the risks. The UK will circulate their position paper on granulocyte collection to the CAs.

According to BE, another source of granulocytes is whole blood, which is used for children. It may also be that buffy coat granulocytes could be used instead of apheresis granulocytes. DE stated that the scope of the blood directive is only Q&S of the components and not donor selection. IE, EL and AT disagreed with this interpretation, and felt that donors should also be considered. IE referred to recitals 20 and 21 of Directive 2002/98/EC's, and explained that the quality and safety of the product and the safety of the donor are linked.

EL requested that CoE should investigate the new component. CoE will discuss the issue, as the European Convention on Human Rights requires the protection of donors as well as the protection of recipients. FR underlined the necessity of having a common approach on granulocyte concentrate in the future, and requested that the efficacy of the component be studied. IE explained that efficacy studies are not required for blood components.

FR (chair), AT, DE, IE, and the UK (and possibly EMA and CoE) will look into donor safety, as well as safety and quality of granulocyte concentrate. The Commission mentioned the analogy to living donation in the tissue and cells sector (in vitro fertilisation and heamatopoetic stem cells).

4. REGULATORY MATTERS

4.1. Points for information

4.1.1. Transposition checks – state of play

The Commission presented the current situation regarding the transpositions checks of EU blood legislation. The main open points regard record keeping, traceability, information provided to donors, "active bacterial infections" as donor deferral criteria, eligibility of minors as donors, and import.

To date there are no issues with transposition in 20 out of 27 MS. Four pilot procedures are pending, although three will probably soon be closed without an ensuing infringement

procedure. The first steps of an infringement procedure are likely in the final case. In addition, there are two clarifications and one corrigendum. MS are reminded to ensure national follow-up to align legislation with the EU Directive.

4.1.2. Definitions of the Plasma Master File (PMF) related to inspections and inspection intervals of blood establishments

IE presented a list of proposed definitions for different types of establishments. This list is based on a working document by EMA. The underlying concern is the practical difficulty of inspecting every blood establishment every two years.

BE underlined the difficulty of distinguishing blood centres and satellite centres. The UK suggested a risk based approach and would consider premises where blood is frozen as blood centres. IE agreed with this approach, stating satellite centres only collect but do not freeze blood. AT also supported the UK's risk based approach. FR and EL questioned whether it was necessary to distinguish between blood centres and establishments.

SE said the definition of a blood establishment should be linked to its activities and inspection requirements. AT agreed that there are insufficient resources to inspect all sites at the same intervals. AT, IE and FR supported a risk based inspection model.

The Commission explained that according to Article 8(2) of Directive 2002/98/EC, there should be no distinction between different blood establishments. Instead, it suggested that the definition of inspections in Article 3(m) may also include off-site inspections. This is current practice in the tissues and cells sector based on a guidance document, although there is no similar mandate in blood legislation The Commission also explained that quality and safety cannot be jeopardized for the sake of longer inspection intervals.

AT commented that when drafting Article 8(1) of Directive 2002/98/EC only desk-based inspections were considered. The Commission questioned whether the wording of Art 8(1) was sufficiently clear to support this view.

A group of CAs (AT, DE, IE, SE, UK, EMA and the Commission) will continue to look at both the proposed definitions of establishments in the PMF and the definitions of inspections, and bring a new proposal to the next CA meeting in November 2013.

4.1.3. Octopharma: reference for a preliminary ruling – Case C-512/12

The Commission informed the participants of the views of the Commission's Legal Service regarding Octopharma. The question that has been referred to the Court is under which legal regime plasma derived from whole blood falls when it has been prepared by a method involving an industrial process. FR stated that because this was a pending court case, it should not be discussed in the meeting. The Commission clarified that this point was only for information, not discussion.

4.1.4. Classification of IVD devices used by blood establishments under the Medical Devices Directive

EBA presented their views on the Commission proposal for an in-vitro diagnostics medical devices Regulation, in particular arguing that the proposal to remove the 'in-house' derogation for Class D diagnostics test used in a single health institution like a blood establishment would create a major risk for patient safety in the EU. The Commission explained that the current in-vitro diagnostic medical devices Directive (Directive 98/79/EC) provides a derogation for devices manufactured and used within the same health institution.

This derogation was introduced to allow health institutions to manufacture and use tests for unmet medical needs. However in order to protect patient safety and ensure a high level of safety and performance for the highest risk tests, the Commission has proposed a new Article 4(5) which would submit the highest risk tests (class D) to most of the requirements of the Regulation, with the exception of CE marking, as these tests are not made available on the market place.

The derogation will be maintained for Class A, B and C tests, if the health institution manufacturing and using the tests is accredited according to ISO 15189, ensuring the quality of their practices. Furthermore, the Commission underlined that in case of unforeseen or unmet public health or patient safety needs, national competent authorities may grant single health institutions a derogation, as long as the Commission and Member States are informed.

The Commission explained that the proposal is currently being discussed in Council and Parliament under ordinary legislative procedure. Consequently it is preferable that EBA contact the Rapporteurs in the European Parliament, as well as individual national CAs responsible for medical devices, to voice their concerns that the provisions are not appropriate. Finally the Commission underlined that a similar system is already in place in Austria, and there has been no shortage of tests, nor have any specific difficulties for public health or patient safety been encountered. The Commission asked the competent authorities if they had any concerns over the proposed rules.

NO indicated that it already regulates in-house manufactured IVD tests in the same manner as the Commission proposal. Although it took NO some time to put the system in place, all blood establishments use diagnostic tests which reach this level of requirements. The UK wondered about the impact of the proposal on blood establishments and hospital blood banks. EBA reiterated their view that the rules proposed in Article 4(5) for class D IVD tests would be too burdensome.

DE presented information on their difficulties with miniaturisation of machines for the production of blood products from autologous blood, in particular whether they fall under the scope of the Medical Devices Directive. The Commission suggested that if DE requires a clarification whether the machines are medical devices, they should bring the case to the Medical Devices Expert Group on Borderline and Classification (MDEG) to collect the views of other Member States on the issue.

The Commission explained that deciding if a product is a medical device or not, remains under national competence, but that a procedure is in place to facilitate consensual decision on specific borderline cases. DE asked whether a decision in one MS is binding in all other Member States. The Commission answered that decision is not legally-binding, but if consensus is reached that a product is a medical device, MS are strongly recommended to follow this decision. The Commission further responded that unlike for pharmaceuticals, there is no formal procedure for 'mutual recognition'. Further information is available at http://ec.europa.eu/health/medical-devices/documents/borderline/index_en.htm.

4.1.5. Surveys on implementation and VUD

The Commission presented the legal obligations, timeframe and content of the questionnaires on implementation and VUD. The Implementation survey will be launched in June with a deadline of end of August 2013. The VUD survey will be launched in September, with a deadline by November 2013. Participants can send SANCO written inputs/suggestions on the VUD survey.

EBA stated that there are some aspects in the current questionnaire which are unclear and added that, according to a court ruling, the reimbursement of travel costs is in line with the principle of VUD. EBA also proposed that certain definitions in the survey, such as 'shortage', should be changed.

4.2. Interpretation questions

The Commission presented interpretation questions on two issues: inspections (see above point 4.1.2) and scope. Questions on scope concerned platelet rich plasma, eye drops manufactured from whole blood, and the Orthokine® system.

The Commission stated that, based on consultation with the SANCO legal unit, these procedures could fall under the Directive, as it applies to "the collection and testing of human blood and blood components, whatever their intended use …" As the Commission is aware that it may be difficult in practice to ensure that these procedures comply with the provisions of EU blood legislation, changes could be considered during a future revision of the legislation.

5. RISK BEHAVIOURS FOR DONOR DEFERRAL

The CoE resolution was adopted in March at the CoE's Ministerial meeting (voting was restricted to members of European Pharmacopoeia) and is now available as official document. This document can be found on the CoE's website.[1] The EU statement developed at the occasion of the last CA meeting will be included in the minutes of the CoE meeting. FR expressed concerns regarding how MS were consulted leading up to the adoption of the resolution.

6. PRESENTATIONS OF PROJECTS AND ACTIVITIES

6.1. WHO model list of essential medicines: whole blood and red blood cells

AT and IT brought introductory presentations on the application by AABB, the American Red Cross and Canadian Blood services to add whole blood (WB) and red blood cells (RBCs) to the WHO model list of essential medicines (WHO EML).

AT gave an overview of the procedure, including the application, expert reviews and comments for and against an addition to the list. AT also presented EU legislation on blood and the regulation of blood in Austria. AT explained that the EU blood directive works well in EU MS, and that most EU MS are also close to reaching their goal of self-sufficiency. It was therefore concluded that mainly actors/blood establishments in developing countries should be consulted before a decision is reached.

IT presented an overview of the essential medicines list, the expert reviews, and the Italian legal framework. IT also gave a more general overview of previous work by the WHO on blood systems, including voluntary non-remunerated blood donation (VNRBD), blood safety and quality management systems. IT explained that many countries will require a step-wise approach to achieve self-sufficiency from VNRBD. This will require taking into account the complex interactions between national blood services, health-care institutions, civil societies,

[1] https://wcd.coe.int/ViewDoc.jsp?Ref=CM/Res(2013)3&Language=lanEnglish&Site=COE&BackColorInternet= C3C3C3& BackColorIntranet= EDB021&BackColorLogged=F5D383

and individuals who donate blood. It was concluded that a careful assessment of potential impacts must be made before listing whole blood and red blood cells on the WHO EML. This assessment should include a broad consultation with various stakeholders including governments, national blood services, NGOs, international organisations, blood alliances and networks. The consultation should also fully involve developing countries, which are most likely to be affected by an inclusion on the list.

Discussion:

No MS expressed support at this point for an inclusion in the list and several MS explicitly opposed to an inclusion of WB and RBCs on the EML list. DE explained that the supportive opinion expressed by the Paul Ehrlich Institute on the WHO website is not the official government position [Note: the DE Ministry of Health afterwards wrote to WHO requesting more time for assessment].

There were more detailed questions and concerns on the impact of a listing of RBC/WB on the EML on safety, on commercialisation, on the principle of voluntary unpaid donation and on legal conflicts between pharmaceutical and SoHO legislation. It was questioned whether such decision would not rather reduce than increase supply.

There were questions on the mandate of the WHO and on the skills/capacities of the members of the EML Expert Committee. None of the blood competent authorities had been involved or knew of colleagues that were involved in the decision. Some participants questioned why the WHO Global Blood Safety Network was not involved. As also other medical devices are on the EML, it was suggested to broaden the scope of EML to essential therapies. This would allow recognition of the essential nature of blood and avoid confusion.

It was also suggested to see whether the quality guidelines developed by the Council of Europe can be shared with/through the WHO as an alternative and more adequate approach to address the concerns for safety and quality of blood supplies in developing countries.

The IT and AT position, requiring more in-depth assessments of the different concerns before RBC/WB can be listed on the EML, was supported

The Commission agreed to inform the WHO secretariat on EML of the outcome of the discussion, a letter was sent to WHO Director General Margaret Chan on 29 April 2013.

6.2. Council of Europe

The 17th edition of the CoE "Guide to the Preparation, Use and Quality Assurance of Blood Components" will be published soon. The TS66 Working Group has been tasked with implementing elements of GMP in Appendix I of the Guide. In the coming months, the working group will collect comments and evaluate them. The final version of the appendix is expected to be adopted in October. The Commission will reflect on the legal status of the appendix, which is meant to be used for inspectors.

EL expressed their support for the work. The UK explained that the intention was for the appendix to be used by all stakeholders – blood establishments, hospital blood banks and regulatory agencies. The UK also felt that it is important that the appendix have the same legal status and be updated along with the EMA GMP guide. IE supported the UK position.

CoE stated that the Appendix 1 shall be considered a living document and that there is a procedure to allow for updates of the good practices (GP) requirements in blood

establishments. Two inspectors from TS66 will be nominated to take part in GTS drafting group.

6.3. Training programme for inspectors of establishments (CATIE)

A member of the CATIE consortium presented the current state of play and next steps of the project. Two courses have been run so far in Budapest (August 2012) and Bilbao (March 2013). The Commission encouraged those MS which have not yet sent at least three participants to the training to do so, as the stated aim of the project is to train at least three inspectors per country (population size allowing).

6.4. Overview of the Blood Market

The Commission presented an update of the project, which has been suspended, on behalf of Creativ Ceutical. Many countries expressed their disappointment with the progress and quality of the project. It was agreed that the country reports will be sent to MS to be checked before final publication. The suspension of the project will also allow additional data from the CoE and Market Research Bureau to be analysed and included. The Commission also clarified that no further questionnaires shall be sent to MS and that the data which has been already collected will be used.

6.5. WHO update

WHO gave an update of their activities on blood transfusion safety. This aims to strengthen blood systems through WHA resolutions, ethical and evidence based policy recommendations, standards setting, technical support and monitoring.

7. ANY OTHER BUSINESS

7.1. Intra MS agreements to supply surplus blood collection

The Commission explained that although exchange of surplus blood components does not fall within its mandate on quality and safety, MS may wish to share their experiences of exchanging blood components. It was mentioned that some states have reduced their blood collection activities while in other states there have been insufficient blood supply.

EL expressed interest in developing a proposal for surplus blood exchange. IE stated that, at least for emergencies, it was a good idea but would require harmonisation of blood labelling. Due to CJD in the population, UK blood establishments have agreements with AT establishments for fresh frozen plasma. The UK raised the issue whether donors should be informed that their donation could be used in another country, and whether there will be separate donor drives for blood for export.

DE mentioned that, according to German law, blood establishments must have agreements with each other in order to exchange blood, but that, in principle, this would be no barrier to export. CY, EL, IT, and NL will discuss the possibility of exchanges between MS, and will report back at the next CA meeting. SANCO suggested that the scope of discussions is limited to surplus and emergency situations. Those MS which are aware of inter-country contracts between BEs will share these with the group if possible (DE, MT, AT, and UK).

7.2. World Blood Donor Day

The 10th edition of WBDD will be held be in Paris on June 14. WHO, IFRC, IFBDO and ISBT will attend. FR will circulate the programme.

7.3. Blood component labelling: removal of the EU requirement to state the original composition of the anticoagulant on the base label of the component

The UK requested that the EU remove the requirement to state the original composition of the anticoagulant on the base label of the component. Adding the composition of the anticoagulant does not provide accurate information to the clinician and can even be misleading if they read the label as being an accurate representation of the content of the bag. FR considered it a good idea to shorten this list, and only provide essential information to physicians. As the requirement is outlined in Annex III of Directive 2002/98/EC, it can be amended by the Regulatory Committee. The Commission takes note of this request for any future revision of EU blood legislation.

7.4. EAHC cluster meeting: Transplantation & Blood Transfusion.

The meeting is about how the European Union contributes to save and improve the quality of life of citizens, through facilitating transplantation & blood transfusion. It will take place in Madrid, Spain on June 27/28 2013. Competent authorities were asked to send the contact details of journalists they think might like to attend the cluster meeting.

DOMINIK SCHNICHELS