EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Directorate D - Health systems and products
D4 – Substances of Human Origin and Tobacco Control

Meeting of the Competent Authorities on Blood and Blood Components

3-4 November 2014

Summary Report

PARTICIPATION:
All Member States were present at the meeting of the competent authorities (CAs) on blood and blood components on the 3rd and 4th of November 2014. The former Yugoslav Republic of Macedonia, Norway, Serbia and Turkey, as well as the European Directorate for the Quality of Medicines and Health Care of the Council of Europe (EDQM – CoE), the European Medicines Agency (EMA) and the European Centre for Disease Prevention and Control (ECDC) also attended the meeting.

Chairman: Mr Stefaan VAN DER SPIEGEL (SANCO)

Commission: Ms I. HOLMQUIST, Ms I. SISKA, Mr R. MCGEEHAN, Mr P. CATALANI, Ms M. GHEORGHE, Ms A. HALLER (SANCO)

Day 1

1. ADOPTION OF THE AGENDA

The agenda was adopted without any changes.

2. RULES OF PROCEDURE (RoP) FOR THE CASoHO EXPERT GROUP

Pursuant to Article 12(2) of the RoP, the chair asked the representatives if they had any conflicts of interest to declare. None of the participants declared a conflict of interest. The minutes on the last CA meeting were approved.

3. REGULATORY MATTERS: POINTS FOR INFORMATION

3.1. Transposition check – state of play

The Commission informed the group that there have been no changes in the status of the transposition check since the last meeting. One infringement proceeding is on-going. One Member State still has to provide the final published version of its amended national legislation.

3.2. Survey on the implementation of the EU blood and blood components Directives (Article 26 of the Directive 2002/98/EC)

The Commission presented the key findings of the survey in nine sections, to which all Member States, Liechtenstein and Norway submitted replies. The Commission is currently analysing the replies and there may be need for further clarification of some points with Member States. Consistency with the information submitted on voluntary and unpaid donation and to the Creativ Ceutical study must also be checked.

(1.) General provisions

EDQM confirmed the observation presented by the Commission, that different Member States use different terminology. Romania reported that the use of multiple terms in the Directive, such as "authorisation, accreditation, licensing" etc. created confusion.

EDQM stated that there was a need for training and independence of staff, as one person sometimes executed various functions, including oversight over bodies in which it was involved. This was supported by several countries. Italy asked for stricter EU legislation on the independence of staff, which should define requirements for the independence of inspectors and for the level of independence. Bulgaria pointed out that CAs should be independent from the transfusion system but considered it normal if they were part of the Ministry of Health.

Italy explained that coordination was challenging if there was a multi-level structure, e. g. the Ministry of Health, technical CAs and regional authorities, instead of one central CA per country. Germany explained that its population size required a complex structure but that communication was not a problem. Coordination difficulties between regional CAs and the Ministry of Health as well as a lack of training of inspectors were also reported by Turkey, which supported independent inspections.

Romania explained that it faced a continuous decrease in the number of staff and that training was also a problem. Romania declared that it seemed not to have been clear for all Member States what professional background the "responsible person" should have.

The Commission announced that a new joint action for training and inspection, involving also tissue and cells CAs, would be launched.

(2.) Obligations on Member States

Several Member States, asked for further clarification regarding inspections on mobile and satellite centres. The Commission announced that the new joint action would reflect on this.

Sweden pointed out that obligations under the Commission Directive 2005/61/EC concerning notification of adverse events were unclear in the case of collection of plasma for fractionation from third countries because the Directive does not give any statement on to whom the blood establishments should report (there is not one given supervising competent authority). It was clarified that this is addressed in Annex 14 of GMP.

Clarification post meeting: the third country BE is to inform the EU-based plasma manufacturer of SAE's, which has to inform the pharmaceutical NCA in the EU country of fractionation. The Blood NCA can then obtain these data from its national pharmaceutical CA, for its own reporting exercises.

France stressed the point that the EU could make recommendations but that the competence for mandatory requirements lies with the Member States.

(3.) Provisions for blood establishments and (4.) quality management

EDQM announced a training course on quality management and expressed surprise that 30 countries had reported to have such system in place.

Czech Republic asked for clarification what data was covered by the obligation of record keeping for 30 years. For documentation not concerning traceability, it considered a period of 15 years to be sufficient.

(5.) Haemovigilance

Turkey reported on its achievements in implementing a haemovigilance system. Serious adverse reactions and events (SARE) related to blood transfusion will be recorded as from 2015.

It was stated that reporting obligations lay not only with blood establishments, but also with hospitals. Bulgaria explained that hospitals which did not have a hospital blood bank did not reliably report SARE.

As regards root cause analysis, France stated that retrospective analysis was to be done incident by incident but that the whole system should be analysed in the case of repeated incidents. The United Kingdom pointed out that the thorough investigation could only be made by blood establishments and hospital blood banks, not by the CA. This view was supported by EDQM, which announced a 2015 training course for blood establishments on root cause analysis and work on a quality management book.

(6.) Quality and safety provisions

The possibility of immediate self-exclusion of donors was discussed. It was pointed out that this option was foreseen in Annex II.A(6),(7) of Directive 2004/33/EC.

Some countries pointed out that individual NAT testing was very restrictive and pointed out that too strict regulations might hamper innovation in the sector without bringing sufficient additional safety and quality.

(7.) – (9). Info, reports, penalties, basic data and overall comments

It was pointed out that the implementation survey, in contrast to a transposition check, was not limited to pure legislative questions.

France was invited to submit for clarification its question on what "non-transfusion purposes" meant, related to preparation of IVD for HIV positive patients, via e-mail.

3.3 Survey on promotion by the Member States of voluntary unpaid donations (Article 20(2) of Directive 2002/98/EC)

The Commission presented the draft results of the survey to which all MS, Liechtenstein and Norway had submitted replies. It was explained that the analysis was still on-going.

(1.) Provisions and policies

As regards replacement donors, it became clear that different interpretations are possible:

- Romania clarified that it had understood replacement donors to be persons who only decide to donate blood after a person close to them has needed blood. Romania explained that donors were not forced to donate and promotion of blood donation to the general supply by medical professionals was not considered as replacement donation.
- Greece explained that donors from the family or acquaintance of patients were encouraged to make donations to the general blood supply, as any other person. There is also a programme in place to convert replacement donors into regular voluntary and unpaid donors. It will circulate its report on this issue.
- Czech Republic explained that its answers on replacement donors referred to "directed donors", who give blood for patients with specific indications.

Participants asked for more information about trans-border donors, in particular as regards the structures where they donate and the social profiles of these donors.

(2.) Practices vis-à-vis donors

As regards the practice of giving donors time off work, it was explained that for those MS where time off work is granted, the same times have been reported for the public and private sectors. However several participants pointed out that information and influence on practices in the private sector practice are limited. Greece referred to a PanHellenic Study, which had shown that the public sector provided too many incentives for donors, which was not the case for the private sector.

The former Yugoslav Republic of Macedonia stated that donors were given two days off work per donation in the public sector but not in the private sector. Malta reported that, for the private sector, it promoted blood donation at the workplace with mobile collection sites. It explained that it had faced only temporary shortage of blood when it had stopped the practice of giving donors four days off work and that afterwards real altruistic, voluntary and unpaid donors came back.

Lithuania explained that under its legislation, donors were entitled to one day off work both in the public and private sector, and that they have never been informed about violation of this rule.

Regarding remuneration, Sweden explained that its plasma industry could import plasma for fractionation which was collected from remunerated donors.

(3.) Ensuring sufficient supply

There was a discussion on the observation that eight Member States (CY, IE, HR, LT, MT, PT, RO, UK) did not fractionate the plasma collected in their country.

It was explained that the plasma from Ireland and the United Kingdom was not fractionated due to risk of vCJD and that Croatia, Lithuania and Portugal had plans for fractionation in the future. Lithuania pointed out that the plasma was not destroyed but sold to Slovakia. . Romania explained that at present, it did not have a contract for plasma fractionation for epidemiological reasons, and due to the requirement of manufacturers required for NAT testing.

EDQM stated that new guidelines might help the blood establishments to ensure they can provide plasma for fractionation. Feedback might be provided on this issue from the kick-off meeting on plasma supply management under the Council of Europe.

3.4. West Nile Virus (WNV) amendment

The Commission presented the amendment of Commission Directive 2004/33/EC and informed the group of next steps towards final adoption following approval of the amendment by the Regulatory Committee on the quality and safety of blood.

Some participants expressed concern on that a requirement for individual NAT testing is too strict, however only few comments were received during the adoption process.

Member States were also asked to check the wording of the amendment in their national language(s). France, Italy and EDQM felt that the requirement for individual NAT testing was too restrictive and pooled testing should have been allowed.

3.5. Court Cases

The Commission presented the Advocate's General opinion in case C-528/13 on permanent exclusion from donation of men who have had, or have, sexual relations with other men. According to the Advocate General, sexual orientation is not the same as sexual behaviour and Member States must evaluate carefully their particular situation when deferring donors. The point will be rescheduled on the agenda once the court has made its ruling.

4. PRESENTATION OF KEY INTERPRETATION ISSUES AND DISCUSSION

4.1. Lymphocyte immunotherapy

The United Kingdom presented its evaluation whether the collection of partner immunocytes to treat women who have suffered from multiple miscarriages could be considered to fall under blood or tissues and cells legislation. According to the UK evaluation, this therapy should be regulated pragmatically, as tissues and cells or as blood, depending on the professional body that applies the related therapy.

It was highlighted that in future, lymphocytes might be used for other treatments, and it was therefore unclear which legal framework would be the most appropriate. MS will reflect on this issue and send comments to the Commission within 2 weeks.

Participants pointed to the general need for a body to decide on such borderline issues.

5. PRESENTATION OF PROJECTS, ACTIVITIES AND EU FUNDING

5.1. Patient blood management (PBM)

The Austrian Institute of Technology (AIT) presented the results of their data collection of blood issuance figures and PBM initiatives in Member States. The team also outlined their plans for the implementation of pilot PBM programmes in five European teaching hospitals.

Bulgaria and Sweden pointed out that Ministries of Health would be the appropriate point of contact for this study. The Netherlands explained that its low issuance numbers has resulted in more expensive components. Some participants consequently pointed to the need to get support from insurers for PBM. AIT explained that the risk of under-transfusion is very low and that costs from unnecessary transfusions could be avoided through PBM. Member States were asked to check their country data and send corrections to AIT.

5.2. Overview of the blood market

The Commission presented the objective, difficulties and key findings of the Creativ Ceutical study on the EU blood market. Due to difficulties with the study, the Commission will publish a separate summary paper, including the views of various stakeholders.

5.3. Eurobarometer

The Commission informed the group about the the Eurobarometer survey on blood, tissue and cell donation, which includes questions on willingness to donate, reasons to donate, attitudes towards compensation and concern about medical treatments with blood, tissues or cells.

5.4. Council of Europe – Good practice guidelines for elements of the quality system

The Commission presented the good practice guidelines developed by a joint working group of the Commission and Council of Europe, and outlined the procedure for having these formally approved.

It was agreed that competent authorities would be given the chance to send their comments on the guidelines in writing. It was also explained that a possible Commission publication of the guidelines could only take place following their approval by the Regulatory Committee on the quality and safety of blood. The Commission will continue to work closely with the Council of Europe to ensure any version of the guidelines published by the commission remains closely aligned with versions to be published by the Council of Europe.

Sweden and the United Kingdom welcomed the guidelines. Sweden stated that the different periods of record keeping were confusing. France pointed out that this was due to different periods in the Directive. The Commission explained that the guidelines would not be binding

and that there would need to be a reflection how to update the guidelines. EDQM stressed that there had already been a public consultation by CoE.

EDQM also presented the blood-proficiency testing-scheme and the blood-quality management programme for blood establishments.

5.5. WHO update

The Commission outlined the WHO initiative on 'medical products of human origin' (MPHO) which will cover all products of human origin (tissues and cells, blood and blood components, organs and SoHO-derived medicines). Common activities are suggested for (1) vigilance (a common library on alerts and of knowledge), (2) traceability and (3) common principles on ethics and safety of donors and beyond. The Commission will update the group on any developments.

The WHO secretariat have asked to merge the Italian proposal (Rome Declaration) with the Spanish proposal on ethical and (donor) safety principles. Germany expressed its concerns regarding the strict approach towards VUD under the Rome Declaration. Italy stated that the Declaration had been significantly revised and explained that at present it considered to suggest a – potentially combined – proposal to the WHO at the end of January 2015.

5.6. EMA update

EMA briefly presented an update on inspection and control measures and the use of risk-based inspection planning for plasma.

Day 2

6. SURVEILLANCE AND VIGILANCE: UPDATE ON INFECTIOUS DISEASE RISKS

6.1. ECDC updates

ECDC presented an epidemiological update on the Ebola virus disease (EVD) and their EVD recommendation for SoHO. Preliminary risk assessments and prevention of infectious diseases transmission through substances of human origin, and a report from the second meeting of the working group on pre-qualification of newly registered blood donors were also presented. ECDC provided information on preparedness plans for dengue and Chikungunya. CAs were asked to express their interest in participating in a working group for the preparedness plans and the prioritisation of bacterial infections with SoHO relevance. ECDC will also work on the elaboration of a map overlaying disease outbreaks to determine maximum donor deferral periods. The Commission will share ECDC factsheets on SoHO-relevant diseases on CIRCA-BC.

The Netherlands objected to the two month deferral period for those returning from an Ebola area and considered a deferral of four weeks to be sufficient, stating that implementation of the two month deferral would be difficult. ECDC explained that the double incubation period was required to declare an individual EVD free. The deferral period can, in any case, be modified if new evidence on the exact incubation period becomes available. For persons

returning from currently affected countries, a malaria deferral period (at least 6 months) is in any case to be respected.

As regards the risk assessments for SoHO-transmissible diseases, ECDC explained that plasma derivatives were not yet considered to be substances of human origin and had been excluded. ECDC will reflect whether it might be useful to also cover them, which was welcomed by CAs.

6.2. Alerts

6.2.1. Hepatitis E

Germany and France reported on the impact of HEV on blood safety. There is a general increase in prevalence in Europe. It was general agreement that the risk was low, except in immunosuppressed patients. It was also mentioned that plasma inactivation techniques seem not efficient against HEV. EMA will circulate a reflection paper to CAs. France suggested extending tests to all blood components, which it already does for part of its supply. Germany reported that there was a problem of awareness among doctors regarding the risk of HEV to immunocompromised patients. Measures by food or veterinary authorities were not envisaged.

Participants are invited to share and present additional information during the next meeting.

6.2.2. Follow-up on reported cases of Chikungunya

France provided an update of the Chikungunya epidemiological situation and precautionary measures in its overseas departments.

6.2.3. Follow-up on reported cases of WNV

Greece reported that there had been 14 severe and one mild case of WNV, but no blood donor had tested positive. However, in 2014, Greece had the highest fatality rate (40 %) for WNV in Europe, opposed to 20 % in previous years. Greece pointed out that the preparedness plan should be updated.

Hungary stressed the importance of prevention and had applied the deferral period after one case was reported. Among 11 patients, only 3 were confirmed to have WNV. From 2015, Hungary will perform NAT testing for WNV.

Romania reported cases along the Danube river, and had implemented measures according to the preparedness plan, Although testing was only possible in Bucharest. One county reported a decrease of 35 % in collections. Bucharest reported a decrease of 15 % in distributed units. This decrease was covered by neighbouring counties.

Italy explained that there had been a 50% decrease in the number of WNV cases compared to last year (24 cases). From 2014, Italy had also applied a vector index strategy, which was triggered by the notification of WNV or veterinary surveillance of wild birds. The number of positive donors was low (three). Italy highlighted that the entomological surveillance helped to anticipate viral circulation by 30 days. It also allowed the detection of two positive blood donors before human cases occurred. Italy will present data on cost-effectiveness at the next meeting.

6.2.4. Follow-up on reported cases of dengue

France reported that the epidemiological situation and precautionary methods for dengue were similar to those for Chikungunya. Mainly French overseas departments are affected.

In Madeira (Portugal) there have been 2,000 cases but no deaths. There have not been any reports of transfusion-transmitted dengue in Madeira. There was, however, an increase in detected eggs but vector control measures are being strengthened.

6.2.5. Malaria

Greece had no local malaria cases in 2014. In contrast, in 2013, there had been 42 cases, 16 locally-acquired and 26 imported (18 from endemic countries). Greece pointed out that there was a need for a systematic review of risks and raised the question if definitions were to be reviewed.

6.3. Other

ECDC explained that the 2015 preparedness plan meeting aimed to update the WNV plan and develop plans for Chikungunya and Dengue.

Greece will publish and share data on WNV and protecting factors of some blood types. Member States were invited to share publications on related issues with the group.

When asked about other alerts, Greece reported that one patient had died from serratia from apheresis platelets. Despite thorough investigation the origin had not been detected. There had been no comments from the medical devices sector.

7. SERIOUS ADVERSE REACTIONS AND EVENTS AND ALERTS

7.1. RAB alerts

The Commission presented an overview on the alerts sent through the rapid alerts platform for blood and tissues and cells. Member States were asked to check their alerts and to close them, where appropriate. For comments on the functioning and possible improvements to the system, emails can be sent to the functional mailbox.

7.2. Apheresis machine and collection procedure

France mentioned that in some cases the apheresis machine returned the entire volume of platelets collected to the donor and explained that the device was used in many blood establishments in Europe. It highlighted errors and corrective measures and stressed the point that it did not constitute a major safety concern to donors. France pointed out that the machine might not be the source of the problems. This was supported by Malta, where similar problems had occurred even after the machines had been changed.

France had informed medical device authorities but were also encouraged to upload an alert onto RAB. Greece asked how borderline cases concerning medical devices and blood should be handled in RAB. The Commission explained that national medical device authorities should be informed and if the alert was of cross-border relevance an alert should be uploaded onto RAB.

7.3. Initial SARE results

The Commission presented the SARE annual reporting 2013 data, which was much appreciated by the CAs. The Commission explained that it will contact MS for further clarifications on some points.

France and the United Kingdom pointed out that it was difficult to report SAEs, as there were often contributing factors and an insufficient number of categories. For serious adverse reactions, France referred to national guidelines of various Member States on the use of blood components and stated that the date of the transfusion should be known.

8. ANY OTHER BUSINESS

8.1. Alzheimer's and blood products

The Commission work on health technology assessments was explained and final results on an assessment to use Immunoglobulins for Alzheimer are expected to be made public early 2015. The assessment covered clinical elements, considering ethics and impacts on supply.

8.2. Surplus blood

Greece presented the work on intra-MS exchange of surplus blood. The current legislation on import-export of blood and blood components, contracts for external exchange and agreements for internal exchange were presented. As a next step, the group will prepare a proposal with the list of requirements for exchanging surplus blood.

8.3. Plasma as treatment for Ebola

The Commission presented the WHO paper on plasma from EVD recovered patients as a treatment for Ebola. Spain informed about a patient treated with plasma donated by a convalescent person. The patient (a clinical assistant) was recovered for the infection but, of course, the impact of this treatment in that recovery is unknown. Spain will circulate the document defining the acceptance requirements for blood donors convalescent of Ebola Virus that was recently created by the Scientific Committee on Transfusion Safety of the Ministry of Health. France explained that according to scientific experts the immunisation rate for European convalescent patients would mean that their plasma could not be used as a treatment for Ebola.

8.4. Service for regulatory queries on regenerative medicine

The United Kingdom presented the new 'one-stop shop' service for regulatory advice from HTA, HFEA, HRA and MHRA

8.5. SCENIHR public consultation on DEHP

Member States were invited to send comment to the public consultation, in particular as regards exposure to DEHP from PVC blood bags.

8.6. Joint action in blood and tissues and cells

The Commission outlined the joint action which will cover common approaches on inspections, training of inspectors and the implementation of the coding system for tissues and cells. More than 20 Member State authorities will participate. Italy had expressed interest to take the lead of the joint action. Member States were invited to participate as observers and asked to express their interest via e-mail to Chafea.