Ref. Ares(2016)5657210 - 29/09/2016

EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

**Directorate B - Health systems, medical products and innovation**
**B4 – Medical Products: quality, safety, innovation**

# Competent Authorities on Substances of Human Origin Expert Group (CASoHO E01718)

# Meeting of the Competent Authorities for Blood and Blood Components

# 26-27 May 2016

# Summary Minutes

PARTICIPATION:

Competent Authorities from 26 Member States and Norway were present at the meeting of the national competent authorities (NCA) for blood and blood components on 26-27 of May 2016. The Former Yugoslav Republic of Macedonia, Montenegro, Serbia, and Turkey, as well as European Centre for Disease Prevention and Control (ECDC) and the European Medicines Agency (EMA) attended the meeting as observers, along with a representative of the drafting group of the Council of Europe (EDQM) Guide on Quality and Safety of Blood Components,

European Commission (DG SANTE): Mr D. SCHNICHELS (chairman), Mr S. VAN DER SPIEGEL, Ms D. FEHILY, Ms I. PUCINSKAITE-KUBIK, Mr R. MCGEEHAN, Mr P. CATALANI, Ms H. LE BORGNE and Ms A. CORNEA.
European Commission (CHAFEA): Ms A MANCHO.

## 1 WELCOME AND INTRODUCTORY REMARKS

The chairman welcomed the participants and thanked them for their efforts to change their agendas when, following the terrorist attacks in Brussels in March 2016, the meeting had been rescheduled. Apologies had been received from 2 Member States that had not been able to reschedule pre-existing engagements.

## 2 ADOPTION OF THE AGENDA

The agenda was adopted without any changes.

## 3 REGULATORY MATTERS: POINTS FOR INFORMATION

### 3.1 Infringement proceedings (court cases), parliamentary questions and complaints

The Commission informed participants regarding the results of transposition checks, which are completed satisfactorily in all MS except for one, where an outstanding infringement proceeding is ongoing. The deadline for transposition of Directive 2014/110/EU amending deferral criteria related to West Nile Virus (WNV) has expired and the Commission informed the group that the Commission had begun infringement proceedings against six Member States for non-notification of transposition of this Directive. Three of these proceedings have since been successfully closed, one MS published the new legislation and the notification was pending and for the remaining two MS the infringement process is ongoing.

The Commission also reported having responded to a number of parliamentary questions such as on Zika virus and on HIV infections in UK, FR, and other MS in previous decades. Written complaints in relation to plasma for manufacturing/fractionation have also been addressed by the Commission.

### 3.2 Mapping of More Stringent National Testing Requirements

The Commission informed participants regarding the final results of the exercise to map more stringent national testing requirements for blood donors (MSR) across 29 countries, i.e. 28 MS and Norway. The results, presented in an overview sheet for all countries combined and individual country factsheets, were published on the Public Health section of the Commission's Europa website. They reveal the more stringent requirements introduced in more than 16 MS for nucleic acid testing (NAT) for HIV, HBV and HCV, antibody testing for HBc and *Treponema pallidum*, as well as other markers for blood group testing (Kell etc.). Less common MSR (7-11 MS) include testing for HIV 1p24, antibody testing for HTLV-1, HTLV-2, CMV, *Plasmodium sp.* and NAT testing for WNV.

The Commission thanked NCAs for their participation in the survey. Participants expressed the appreciation for the work done and saw several possibilities for use of the results.

NCAs agreed that an update of this mapping exercise would be organised every 2 years.

### 3.3 Revision of Directive 2005/62/EC to include reference to GPG

The Commission explained the context for amending Article 2 of Directive 2005/62/EC that will include a dynamic reference to the Good Practice Guidelines published in the Council of Europe's Guide on the quality and safety of blood.

The Commission explained that the scrutiny period, by European Parliament and Council, would proceed into July 2016, and that the adoption and the entry into force takes place during the summer. The transposition period will last 18 months ending early 2018[1].

[1] COMMISSION DIRECTIVE (EU) 2016/1214 of 25 July 2016 amending Directive 2005/62/EC as regards quality system standards and specifications for blood establishments has since been adopted.]

## 4 IMPLEMENTATION OF THE BLOOD LEGISLATION

The Commission presented the report on the implementation of the EU Blood legislation, published on 21 April 2016[2]. The report revealed that overall there is significant progress in many areas and MS have taken measures to implement the legislation. However, there are some gaps and difficulties in applying and enforcing the rules, partly due to the lack of common definitions and interpretations for some aspects.

## 5 EVALUATION OF THE BLOOD LEGISLATION

The Commission services mentioned an intention to carry out an Evaluation of the current legislation taking on the main conclusions of the implementation reports. The Evaluation will include the blood, tissues and cells legislation, and will consider the interaction/borderlines with pharmaceutical and medical device legislation. The Evaluation will include a number of steps such as a roadmap, a report from an external contractor, stakeholder consultation and a final report in the form of a Commission Staff Working Document with follow-up actions.

As a first step a roadmap will be prepared and published on the Commission's website. The NCAs will be invited to provide input to the roadmap and to actively participate in the stakeholder consultation. The process will likely start in the second half of 2016 and finish in Q4 2018.

## 6 PRESENTATIONS OF EU-FUNDED ACTIVITIES

### 6.1 VISTART Joint action on blood and tissues and cells (IT)

A presentation of the VISTART Joint Action was given by CNS, Co-coordinator of this action. The VISTART Joint Action consortium includes 20 collaborating partners and 16 associated partners. The action aims to promote and facilitate the harmonisation of inspection, authorisation and vigilance systems for blood, tissues and cells. It includes 10 work packages dealing with vigilance and inspection.

The Commission welcomed this cross-sectoral action that addresses a number of pertinent issues across the SoHO field, including the reporting of Serious Adverse Reactions and Events.

### 6.2 Patient Blood Management Service Contract – Final Results

The contractor – a consortium led by the Austrian Institute of Technology (AIT) – presented the PBM study and outlined the final results. The project started 3 years ago and more than 100 participants helped in the study that looked into how to support the implementation of Patient Blood Management across the EU. The concept involves treating anaemia, minimising blood loss and harnessing the natural tolerance of anaemia to reduce the need for transfusion. A pilot was implemented at 5 university hospitals: Vienna, Frankfurt, Lisbon, Copenhagen and Zagreb. Two workshops were held in 2015 in Vienna and Lisbon. The initial results included *inter alia* the reduction of complications and of length of stay in hospital.

[2] http://ec.europa.eu/health/blood_tissues_organs/key_documents/index_en.htm#anchor2

The Commission explained that one key deliverable was intended to support authorities in planning for national PBM programmes. This was addressed not only to authorities for SoHO but also for other healthcare areas such as hospital management, patient safety etc. The Commission also explained that a second deliverable was developed to support professionals in hospitals to implement PBM in a practical way. The participants were invited to send comments on the draft deliverable for authorities.

Several participating authorities welcomed this work, and looked forward to receiving the final versions of the deliverables.

The Commission also reminded the group about this year's calls in the 2016 Work Plan of the Health Programme for a JA on preparation process authorisation and a project on donor selection and protection. While the deadlines for submitting proposals have not changed, the Commission informed the group that it has a preference for delayed starts in 2017 and 2018 for any successful proposals under the 2016 Work Plan.

## 7 SURVEILLANCE AND VIGILANCE: UPDATE ON INFECTIOUS DISEASES RISKS

### 7.1 ECDC update and Zika guide on Preparedness Activities in Europe

ECDC gave an update of their activities and presented the draft guide on Zika preparedness activities in Europe.

An ECDC risk assessment on Zika was published first in February 2016 and updated several times since, and it includes a section on Substances of Human Origin.

The Commission services had coordinated the development of a guide for preparedness activities in Europe. ECDC and a group of experts from the blood, tissues & cells and organs sectors were involved in the preparation of this document that was due for publication by ECDC. The objective is to guide NCAs and Establishments for SoHO, both in Zika virus affected and non-affected areas, on how to prepare and implement measures to mitigate risk of transmitting Zika through substances of human origin. The Commission stressed that this guide is not legally binding, nor does it seek to interpret the relevant Union legislation in any way. It should be considered as a tool for authorities and establishments. The draft document was shared with the NCAs before the meeting. The Commission services asked for input and comments before the document is finalised[3].

### 7.2 Local updates on Zika – France

France reported its Zika cases in its overseas *départements* and territories (25000 cases in Martinique, 6000 in French Guyana and less in others by 19 May 2016). The French authorities mentioned as pre-existing measures (in place before the alert):

- 28-day deferral for travellers, pathogen inactivation of platelets and plasma;
- 14-day deferral in case of symptoms;

[3] The document has since been published**:**
http://ecdc.europa.eu/en/publications/_layouts/forms/Publication_DispForm.aspx?List=4f55ad51-4aed-4d32-b960-af70113dbb90&ID=1527

- quarantine for RBCs.

Further measures implemented after the outbreak were:

- delivery of surplus blood from non-affected areas to be used for pregnant women in affected areas;
- 28-day deferral after sexual contact with a traveller from affected areas in the previous 3 months;
- implementation of individual donor Zika nucleic acid testing.

## 8 SERIOUS ADVERSE REACTIONS AND EVENTS (SARE) AND ALERTS

### 8.1 RAB alerts and RAB Annual Report

The Commission presented the summary of SoHO alerts for 2015. For the RAB 57 alerts have been encoded since the launch of the platform. Of these, one alert is closed, 30 prepared for closure and 26 are still in progress. Ninety percent of the RAB alerts are epidemiological notices. The summaries of activities in the RAB and RATC platforms during 2015 were due for publication on the DG-SANTE website[4].

Improvements to the RAB-RATC alert platforms will be implemented during summer 2016 and presented at the next NCA meeting.

### 8.2 Information regarding a recent alert - Ireland

The Irish NCA made a presentation on a rapid alert blood (RAB) submitted in December 2015 in relation to a medical device used in blood establishments for non-invasive measurement of haemoglobin. Some incidents had been reported to the Irish National Competent Authority (NCA) from the Irish Blood Transfusion Service, where donations were accepted on the basis of incorrect haemoglobin measurements and the donors went on to become severely anaemic and had to be transfused. Upon investigation further incorrect readings were identified in the lower range of measurement which led to further failures in detecting anaemia in donors. This led the blood establishment to revert to a capillary testing method. The Irish NCA issued a rapid alert blood (RAB) and the medical device section of the HPRA liaised with the manufacturer and the relevant medical devices regulatory bodies. There has been a consequent increase of donor deferrals for low haemoglobin with concerns on sufficiency of supply during the summer. The issue is still being investigated.

### 8.3 Serious Adverse Reactions and Events (SARE) 2015 reporting exercise – final results

The preliminary results of the SARE 2015 reporting exercise had been presented during the previous meeting of the blood competent authorities. The comments and suggestions submitted by NCAs as well as by the Haemovigilance Working Group were incorporated in

[4] The Reports have since been published:
RAB: http://ec.europa.eu/health/blood_tissues_organs/docs/2015_rab_summary_en.pdf
RATC: http://ec.europa.eu/health/blood_tissues_organs/docs/2015_ratc_summary_en.pdf

the new version presented. The presentation focused on the final results including on data completeness and quality, denominators, serious adverse reactions (SAR) per components, donor reactions and serious adverse events (SAE) activity per components. The following were key findings:

- For this annual reporting exercise all countries had submitted reports. Complete data was provided by 67% of the reporting countries. This is an improvement compared to the previous years. The European Commission and Member States are continuously working to improve data collection and assist those countries which have difficulties in collecting reliable data. Considering that the data reported is partial, year on year comparisons should be interpreted with caution.
- In 2014, reporting countries notified 1410 SAR with imputability level 2-3 and 27 deaths. Anaphylaxis, immunological haemolysis and transfusion associated circulatory overload appear to be the most frequent serious adverse reactions.
- For SAE, 55% of the reports come from just three countries. Other countries reported low numbers of SAEs.

Participants were asked to send comments on the draft report by 15 July 2016.

### 8.3 Launch of SARE 2016 reporting exercise

The Commission announced the launch of the SARE 2016 reporting exercise scheduled for June or early July. The reporting template would stay the same but there will be modifications on SAE in the accompanying 'Common Approach' document. For future exercises, the inputs and recommendations of the VISTART joint action would be reflected in the 'Common Approach', in particular to provide further clarifications and ensure common implementation.

In that context, participants agreed that the VISTART consortium may obtain access to the SARE data submitted by the NCA's for its work.

### 8.4 French experience with reporting SARE

A high proportion of the SAEs reported in 2013 and 2014 were reported by FR. The French NCA explained that these cases relate largely to the collection of blood units with volumes greater than the acceptable range; these notifications are not commonly included in the reports of other Member States. Discussion followed amongst NCAs who noted that, while Directive 2002/98/EC does not require reporting of SAR in donors, Directive 2005/61/EC, Article 6(2) does put forward the need for protection of both donors and recipients. France suggested reviewing the reporting approach to the Commission in the next SARE exercise.

## 9 UPDATE OF THE EDQM (COUNCIL OF EUROPE) GOOD PRACTICE GUIDELINES (GPG) FOR BLOOD ESTABLISHMENTS AND HOSPITAL BLOOD BANKS

The development of GPG for blood establishments is foreseen in Article 2 of Directive 2005/62/EC. The published GPG, developed jointly by the Commission and Council of Europe (EDQM), are currently integrated in the EDQM guide ('Blood guide'). The Blood guide is revised every two years and currently the 19th edition of the guide is in preparation, including an update of the GPG. The work of updating the GPG was presented by a member of the drafting group that has been tasked by CoE's CD-P-TS Committee to carry out this work. The update will include integration of concepts developed in ICH guidelines, a major shift in combining science with risk management and quality system over the lifecycle of

products and process and alignment with new technologies. The main chapter that has been revised includes more detailed and updated guidance on qualification and validation activities in a more scientific and evidence-based way. In line with the agreement between DG-SANTE and EDQM, the draft update of the GPG had been shared with the NCAs for comment. Three NCAs had sent their comments to EDQM prior to the meeting. Any final remarks were to be sent by 5 August 2016 (as part of the general public enquiry on the full guide) to EDQM (Note: deadline subsequently extended to August 20th).

## 10 EMA UPDATE

EMA presented a document "Application of Inspection and Control Measures to facilitate risk based inspection planning of sites registered in Plasma Master Files (PMF)" for endorsement by the group. The document has been discussed at previous NCA meetings and any comments were accommodated in the latest version.

EMA proposes a categorisation of blood establishments under the definition in Directive 2002/98/EC based on the activities which such establishments undertake which would be used as a basis for assessing the necessary frequency of inspections and control measures working within the requirements on inspection and control measures laid down in Directive 2002/98/EC.

It was agreed that final remarks should be submitted to EMA in the course of the subsequent weeks. The final version of the document will be published on the EMA website and considered as endorsed by the CASoHO Expert Group.

## 11 INTERACTION WITH STAKEHOLDERS

### 11.1 Update on meetings with stakeholders.

The Commission informed the group that a number of bilateral meetings had taken place since the previous meeting of the group and presented the key points that have been brought forward in these meetings with EBA, Biotest, CSL, PPTA, IPFA and NHSBT (UK).

To ensure the transparency, the Commission services have published summary minutes of the meetings on the Public Health section of the Commission's Europa website. Summary minutes of any further meetings with stakeholders will also be published on the website. It was clarified that such meetings only address topics of EU-relevance. Topics of relevance for one Member State only are referred to the appropriate national authorities.

### 11.2 Proposal for meetings of stakeholders with NCAs and DG SANTE/B4

As discussed in the previous NCA meetings, the Commission plans to create opportunities for key EU or international stakeholders to interact with the Commission and with the NCA representatives. It was considered that, when appropriate, certain stakeholders could be invited for such meetings that would be organised separately from, but adjacent to, the meetings of this Expert Group. Stakeholders are to be selected applying certain criteria and on the basis of the agenda topics of EU relevance. The Commission services would discuss possible agenda topics upfront with the NCAs, and their participation would be voluntary.

The Commission clarified that it will circulate draft terms of reference in due course for feed-back from the NCAs. Participants raised initial ideas on the selection and participation of the stakeholders as well as on the scope of meetings. The Commission noted that such meetings

will be formalised and summary minutes will be published on the Public Health section of the Commission's Europa website. After the finalisation of the terms of reference, an open call for stakeholder interest will be launched.

## 12 ANY OTHER BUSINESS

### 12.1 Deferral of potential donors with a history of basocellular epithelioma

The Belgian NCA presented a discussion on whether donors with basocellular epithelioma should be excluded from donation as is currently the case. Basocellular epithelioma is the most frequent case of skin cancer. The Belgian CA suggested that these donors should not be excluded based on the low metastatic potential (only 0.03%) and the lack of documented cases of transmission and asked for other NCAs views on this. FR CA supported the Belgian CA suggestion. It was agreed that NCAs should send their comments to the Belgian CA who will report back in the next meeting. A potential need for change in the legislation may be discussed.

### 12.2 Medical Devices update

The Commission explained that the discussions in the Council and Parliament on medical devices should conclude during the NL presidency. The key concern for the blood transfusion sector relate to the use of in-house developed kits for diagnostics. This technical point seems to be taken into account in the proposal, and is not expected to change during the last political negotiations.

### 12.3 Transatlantic Trade and Investment Partnership (TTIP) and blood, blood components and blood products

TTIP negotiations are currently ongoing at political level with no particular developments for the blood sector at this time.

## 13 FINAL REMARKS

The Commission explained that it plans to reduce the frequency of blood NCA meetings from 2 meetings a year to 3 over the course of a 2 year period due to resource constraints. This proposal was accepted by the group. The next meeting of the blood NCAs is thus scheduled for 1-2 December 2016.



Electronically signed on 29/09/2016 11:36 (UTC+02) in accordance with article 4.2 (Validity of electronic documents) of Commission Decision 2004/563