Paul-Ehrlich-Institut · Postfach · D-63207 Langen

To:

All pharmaceutical manufacturers of cellular blood components, fresh frozen plasma, stem cell preparations from bone marrow, peripheral blood and cord blood, as well as tissue preparations
using ARCHITECT Anti-HCV as part of donor screening

To:

The German Federal Ministry of Health and Federal State Authorities
for information

Ihr Zeichen/Ihre Nachricht	AZ	Telefon-Durchwahl	Telefax-Durchwahl	Datum
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Prevention of risk of adverse drug reactions

Concerning conditions imposed in connection with the marketing authorisation of cellular blood components, fresh frozen plasma, stem cell preparations from bone marrow, peripheral blood, cord blood, and cell tissue preparations

ARCHITECT Anti-HCV Reagents LN 6C37.
Manufacturer: Abbott GmbH und Co. KG Diagnostika, 65205 Wiesbaden, Germany

Dear Sir or Madam,

After the written hearings of 31 March and 1 April 2010, the following

Decision

is issued:

1. The ARCHITECT Anti-HCV LN 6C37 Test may be used for testing a burden of hepatitis C virus (HCV) in the manufacture of cellular blood components, fresh frozen plasma, stem cell preparations from bone marrow, peripheral blood and cord blood as well as tissue preparations with immediate effect only if the recommendations on corrective action from the manufacturer with letter dated 22 March 2010 (see enclosure) have been followed.

2. For cryopreserved stem cells from bone marrow, peripheral blood and cord blood, as well as for red blood cell concentrates manufactured using the above mentioned test before implementing the corrective action, but not marketed yet, a follow-up

examination using ARCHITECT Anti-HCV LN 6C27 Test conforming to the above mentioned corrective recommendations from the manufacturer on a subsequent donation or blood sample of the same donor or on back-up plasma samples shall be performed if the test with the uncorrected ARCHITECT anti-HCV Test has resulted in a value in a range of > 0.6 - < 1.0 S/CO units.

3. A confirmation for the implementation of the action to be taken in 1) and 2) shall be communicated to the PEI in writing by 1 May 2010.

4. Fees shall be charged separately.

Reasons:

The condition is required pursuant to Section 28 paragraph 3c No 1 of the German Medicines Act (Arzneimittelgesetz, AMG) for risk prevention purposes since it cannot be ruled out that anti HCV positive donations are not recognised using ARCHITECT Anti-HCV LN 6C37 Test.

The Paul-Ehrlich-Institut was informed by Abbot on 22 March 2010 that S/CO testing obtained using the ARCHITECT Anti-HCV LN 6C37 test could yield a false low result if the remaining volume of the test specific assay dilution agent was ≤ 25% of the starting volume. This would lead to values of the positive control below the range required, causing diminished test results or false negative results in rare cases.

Internal assays performed by the manufacturer have demonstrated a signal reduction of 40% maximum with the positive control. Current results have revealed that decreasing S/CO values are the result of a lack of homogeneity of the assay dilution agent. The cause of the problem is currently being examined.

According to the manufacturer, a batch was tested 24, 36, and 72 hours without repeated mixing of the assay dilution agent. This batch showed a time-dependent gradient formation with a signal reduction after 48 and 72 hours. Further experiments revealed that the solution is stable at least 24 hours after mixing. Thus, sufficient data are available showing that mixing the assay dilution agent is efficient and stable if performed up to 24 h prior to testing.

For immediate corrective action, the manufacturer has transmitted the urgent safety information attached with this letter to all customers. After checking the action indicated and evaluating the data/test results submitted by the manufacturer, the Paul-Ehrlich-Institut has

considered the action suggested as sufficient and required, in order to avoid possible false negative testing results.

Follow-up testing for released but not yet marketed products is required only if the initial test result was within the critical range of > 0.6 - < 1.0 S/CO units. Since fresh frozen plasma is not released before a second testing procedure of the donor blood after quarantine storage of at least 4 months, and additional NAT testing is performed for each sample, follow-up testing is not required in this case. No follow-up test is required for platelet concentrates and allogeneic stem cells from peripheral blood and bone marrow either, since due to the short shelf life (5 days for platelet concentrates and 72 h for allogeneic stem cell products), only those products can be marketed which have already been tested conforming to the corrective action recommended by the manufacturer with letter of 22 March 2010. This does not apply to cryopreserved stem cells which do require follow-up testing.

Instructions on your right to legal remedies:
You may file an objection to this notification within one month following its announcement. The objection should be submitted to the Paul-Ehrlich-Institut, Federal Institute for Vaccines and Biomedicines, Paul-Ehrlich-Strasse 51-59, 63225 Langen, Germany, in writing or for record.

Yours sincerely

Dr. M. Funk

(Unit S2 Pharmacovigilance II)