

DoD Reply

1. Page 2 –Add definition for Individual Donor Testing (IDT). The definition needs to include that IDT is not a breakdown from a master pool.
2. Page 11 (IV.ii.(b)) Chiron's package insert considers an IDT that was multiplex reactive, discriminatory non-reactive to be Non-Discriminated. If the specimen is further tested and is non-reactive for multiplex testing then the specimen is considered non-reactive.

The FDA guidelines is proposing that blood units from these specimens be Quarantined and destroyed and the donor deferred. Chiron considers these test results as non-reactive, therefore proposed guidelines for testing product disposition, donor management should be changed to reflect Chiron's package insert as already approved by FDA. Why should the unit be destroyed and the donor deferred as proposed in the guidelines? Changes to Table 1 and Figure 1 must reflect this.

3. Request complete algorithms: one for facilities that start with IDT and one for donor centers that start with pooled testing. Do not combine the IDT tables for original IDT and pooled breakdown to IDT.

4. Waiting Period for Reentry Testing

IV.7.a.i.(2) NOTE and IV.8.a.i.(2) NOTE: For purposes of donor notification and counseling, the deferred donor may be tested prior to the 8 week (HIV) or 6 month (HCV) waiting period, but if the NAT results are reactive, or serologic results are repeatedly reactive, the donor is not eligible for reentry and must be permanently deferred.

COMMENT – We disagree with this provision and note that it is inconsistent with IV.7.a.ii.3 and IV.8.a.ii.3, which allow for a second cycle of reentry testing following a reactive result on the first attempt at reentry. This is further defined in Figures 7 and 8 which specify a second round of “reentry” testing when the EIA is repeat reactive (Western Blot Negative or Indeterminate with a blot pattern that is not progressing or the RIBA is negative). Consistent with this provision, we believe that when testing is performed during the 8 week (or 6 month) waiting period for purposes of donor counseling and is again reactive, a second waiting period for purposes of donor reentry should be allowed. We believe that persistent EIA reactivity detected for purposes of donor counseling should not disqualify the donor from the opportunity for reentry as it is possible that the same reagent lot numbers that generated the donor’s first reactive donation result may still be in use to test the donor counseling follow-up specimen.

5. HIV Reentry

IV.7. FDA has approved a method or process for reentry of deferred donors in the following classes:

Donors who were *NAT-Non-Reactive* (or NAT was not performed) and who were *Repeatedly Reactive* on a screening test for HIV-1 antibody, with an HIV-1 Western blot or IFA that was *Negative* (or was *not performed*), or an HIV-1 Western blot result that was *Indeterminate* (viral

bands may be present). This includes donors previously deferred because of Repeatedly Reactive HIV serologic test results prior to the initiation of testing by NAT.

These donors may be eligible for reentry only if the HIV-1 p24 antigen EIA (if done) was Negative and if a second, different, licensed HIV-2 EIA was Negative, or, if the second HIV-2 EIA was Repeatedly Reactive, an investigational HIV-2 supplemental test was not Positive. Currently, we have not approved a supplemental (additional, more specific) test for HIV-2.

Donors who were *NAT Non-Reactive* and who were *Negative* on a screening test for HIV-1 antibody, but who were *Repeatedly Reactive* on an HIV-1 p24 *antigen* EIA with a *Positive* or an *Indeterminate* (that is, an Invalid or a Non-Neutralized) result on the Neutralization test

CLARIFICATION REQUEST - It appears that donors previously deferred for HIV-2 reactivity can be offered reentry if their specimen is tested by an investigational HIV-2 supplemental test and gives a negative result. Please clarify if there are any existing investigational supplemental HIV-2 assays that can be used for reentry testing. If not, please clarify that this provision is being offered in the event such a test becomes available.

6. IV.7.a. To reenter a donor who meets FDA eligibility criteria (i.e., the donor is otherwise eligible to donate again), we recommend that you do the following (See Figure 7 and Table 7):
 - i. At least 8 weeks after the original donation obtain a new *sample* from the donor (no donation is made at this time) and perform follow-up testing using:
 - (1) a licensed HIV-1 NAT that is the same as the NAT (i.e., the Discriminatory NAT for HIV-1) that was run on the original donor sample or a licensed HIV-1 NAT that is labeled as sensitive for HIV-1 group O and HIV-1 group M variants; **This equates to Note 7 on Table 7 and Figure 7**

CLARIFICATION REQUEST – It is our understanding that there currently are no NAT tests licensed for HIV Group O claims. Information may be included in the package insert that mentions Group O antigens or indicates that the test is designed to be group O sensitive, but this does not constitute a labeling claim for Group O. We believe that this statement is included to indicate requirements in the event such a test is available. This intent should be stated more clearly.

AND

- (2) a licensed anti-HIV-1/2 EIA. If the original donor sample was Repeatedly Reactive on the anti-HIV-1/2 EIA, we recommend that you use that same EIA to test this follow-up sample. If the original donor sample was Negative on the anti-HIV-1/2 EIA, we recommend that you use an Alternate EIA that is labeled as sensitive for HIV-1 Group O. **This equates to note 8 on Table 7 and /Figure 7**

CLARIFICATION REQUEST – Currently, there is only one EIA test licensed for Group O claims. Is it correct that donors who enter the reentry algorithm due to NAT reactivity

arm will need to be tested by this EIA (or in the future by another EIA with an HIV Group O claim)?

Secondly, what provision has been made for those donors who enter the reentry algorithm due to EIA reactivity on an EIA assay that is no longer available? We suggest that they should be allowed to be tested by any licensed anti-HIV-1/2 EIA.

Section IV, 7 second bullet on page 20 Donors who were NAT-Non-Reactive (or NAT was not performed) and who were Repeatedly Reactive on a screening test for HIV-1 antibody, with an HIV-1 Western Blot or IFA that was Negative (or was not performed), or an HIV-1 Western blot result that was Indeterminate (viral bands may be present). This includes donors previously deferred because of Repeatedly Reactive serologic test results prior to the initiation of testing by NAT.

CLARIFICATION REQUEST – This section should clarify that this statement also applies to a Western blot that is classified as invalid or unreadable

When there is a persistent anti HIV-1/2 EIA Repeatedly Reactive result, you may wish to further test the donor's new sample using an HIV-1 Western Blot. If the Western Blot test result is *Negative*, or an *Indeterminate* blot pattern has not progressed, you may reconsider the donor for reentry by additional follow-up testing after a second waiting period of 8 weeks. If the Western blot result is *Positive*, we recommend that you defer the donor permanently. **This equates to note 9 on Table 7 and Figure 7.**

CLARIFICATION REQUEST – This section should also clarify that this reentry pathway is acceptable if the Western Blot is classified as invalid or unreadable.

HCV Reentry

IV. 8. FDA has approved a method or a process for reentry of deferred donors in the following classes:

Donors who were *NAT-Reactive* and *seronegative*. This includes donors previously deferred because of Reactive test results on an investigational HCV NAT. The HCV Discriminatory NAT may have been either Positive or Negative. If an Additional NAT for HCV (validated for use with individual donor samples) was performed, it must have been Non-Reactive.

Donors who were *NAT-Non-Reactive* (or NAT was not performed) and who were *Repeatedly Reactive* on a screening test for HCV antibody, with an HCV RIBA that was *Indeterminate* or *Negative* (or was *not performed*). This includes donors previously deferred because of Repeatedly Reactive HCV serologic test results prior to the initiation of testing by NAT.

IV. 8.a.i. At least six months after the original donation, obtain a new sample from the donor (no donation is made at this time) and perform testing using (1) a licensed HCV NAT and (2) a licensed HCV EIA.

COMMENT: The recommendation should specify that testing with a licensed HCV EIA should be performed with the most sensitive licensed assay. It is our understanding that

some facilities may be using HCV 2.0 for routine testing, but we believe reentry testing should be performed using an assay with sensitivity equivalent to HCV 3.0.

IV. 8.a.i. At least six months after the original donation, obtain a new sample from the donor (no donation is made at this time) and perform testing using (1) a licensed HCV NAT and (2) a licensed HCV EIA.

COMMENT: The recommendation should specify that testing with a licensed HCV EIA should be performed with the most sensitive licensed assay. It is our understanding that some facilities may be using HCV 2.0 for routine testing, but we believe reentry testing should be performed using an assay with sensitivity equivalent to HCV 3.0.

IV.8.a.ii. Evaluate the results of the follow-up testing on the donor's new *sample* as follows:

When there is a persistent anti-HCV EIA Repeatedly Reactive result, you may wish to further test the donor's new sample using an HCV RIBA. If the RIBA test result is *Negative*, you may reconsider the donor for reentry by additional follow-up testing after a second waiting period of 6 months. If the RIBA test result is *Positive* or *Indeterminate*, we recommend that you defer the donor permanently. **This equates to note 5 on Table / Figure 8**

CLARIFICATION REQUEST – Please explain the rationale for not allowing RIBA Indeterminate donors to be retested for reentry purposes after an additional 6 month period? This is allowed for HIV donors with an *Indeterminate* blot pattern that has not progressed.

Lookback for NAT reactive Donors that are EIA Negative

CLARIFICATION REQUEST - The draft guidance does not indicate the time period for which lookback must be performed in this circumstance. We recommend that lookback be based on the estimated duration of an antibody negative phase of infection. One year prior to the NAT reactive, antibody negative donation should provide an acceptable margin of safety.