

POST DONATION INFORMATION ALGORITHM

Committee Update

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65th Meeting
March 16, 2000
Holiday Inn, Silver Spring
8777 Georgia Avenue
Silver Spring, MD

Update on the Post-Donation Information Algorithm

Presentation by Edward Tabor, M.D.

Blood Products Advisory Committee,
March 2000

As you know, we have been discussing at BPAC since 1997, the topic previously called "Inadvertent Contamination," now called "Post-Donation Information." Let me remind you that, so far, these discussions have involved only those viruses for which serologic tests exist and which can be inactivated or removed by procedures applied during the manufacturing process for plasma derivatives, namely, HBV, HCV, and HIV. In summary, BPAC voted in March 1999 in favor of the "Test Positive" algorithm; in May 1999 BPAC voted in favor of the "Risk Factor" algorithm, with the proviso that Footnote "i" be shortened because the number of risk factors that could activate the algorithm was so large that post-donation information would affect every lot of every plasma derivative. At the September 1999 BPAC, a revised algorithm was presented, based on the fact that, by that time, all units entering plasma pools would have been found to be negative for HCV and HIV by NAT in minipool testing prior to pooling. The revised algorithm presented at September BPAC showed that if post-donation information were received that a donor was in a listed risk group, the pool itself would be tested, as an added precaution, for HCV and HIV by NAT test under an IND, and for HBV DNA by a NAT method validated under an IND. If all of these tests were negative, the pool or products would be releasable. A positive test would trigger a further GMP assessment.

We have made further modifications to the algorithm to reflect the BPAC discussion at its September meeting and to address issues related to prior donations by a donor with post-donation information. A copy of the revised algorithm was distributed to BPAC in recent weeks. It has also been made available to the audience at the entrance to the meeting room.

Aside from several minor corrections to the algorithm, you will find the changes are located on the second page, titled "Risk Factor: Plasma," and in some of the footnotes. If post-donation information is discovered prior to pooling, the unit from that donor would be destroyed.

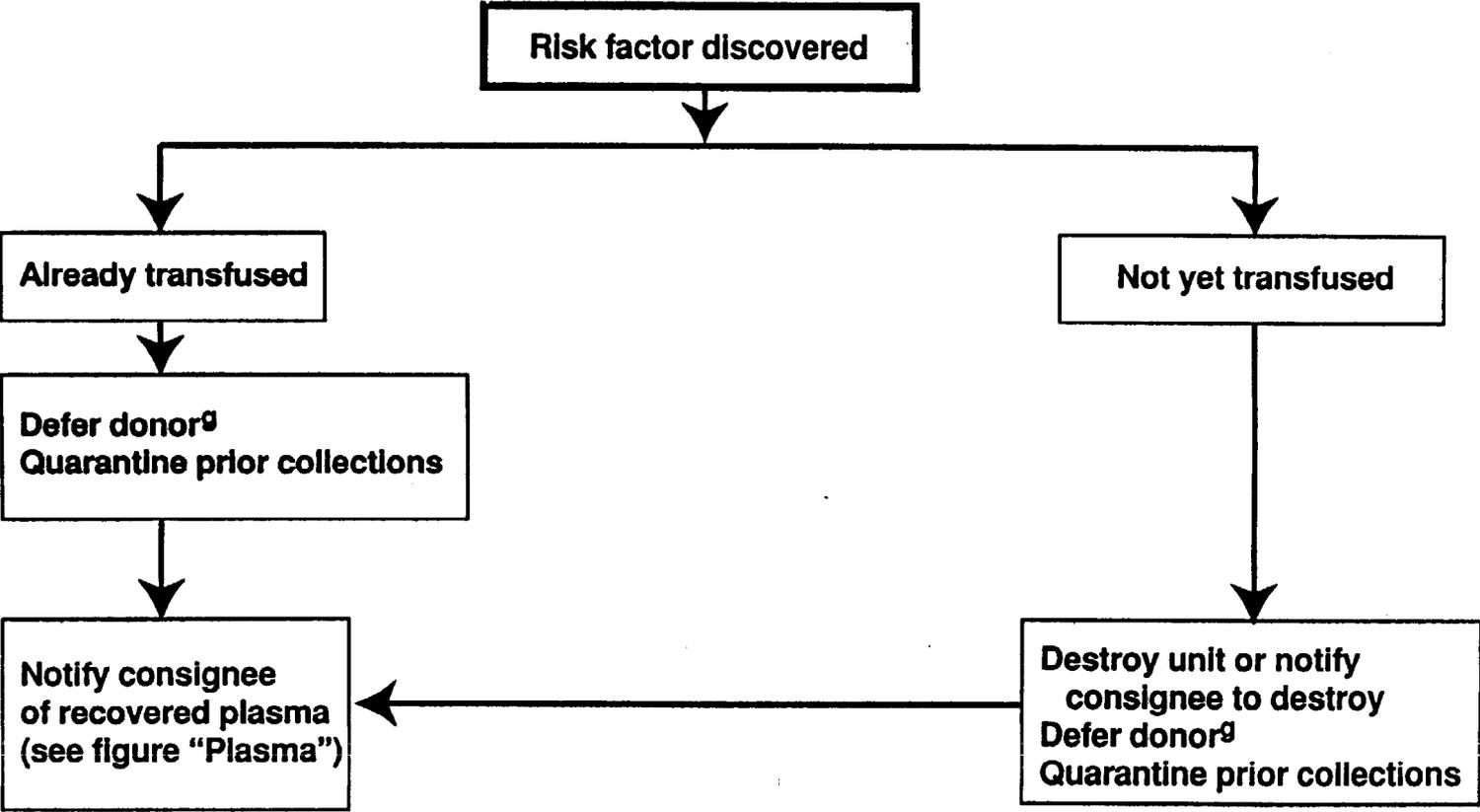
However:

1. If the unit has already been pooled, NAT would be done on the manufacturing pool; if NAT were negative on the pool (as well, of course, as prior NAT on the minipool) for HCV and HIV, and if a validated NAT were negative for HBV on the manufacturing pool, the pool and/or product could be released.
2. All pools or products containing prior donations could be released as well, provided that a recent donor sample were negative for a) all recommended serologic screening tests, b) NAT for HBV, HCV, and HIV, and c) serologic tests for anti-HBc and anti-HBs.
3. If any NAT on the manufacturing pool done after receipt of post-donation information were positive, or if a paper audit by the fractionator revealed that the minipool NAT prior to

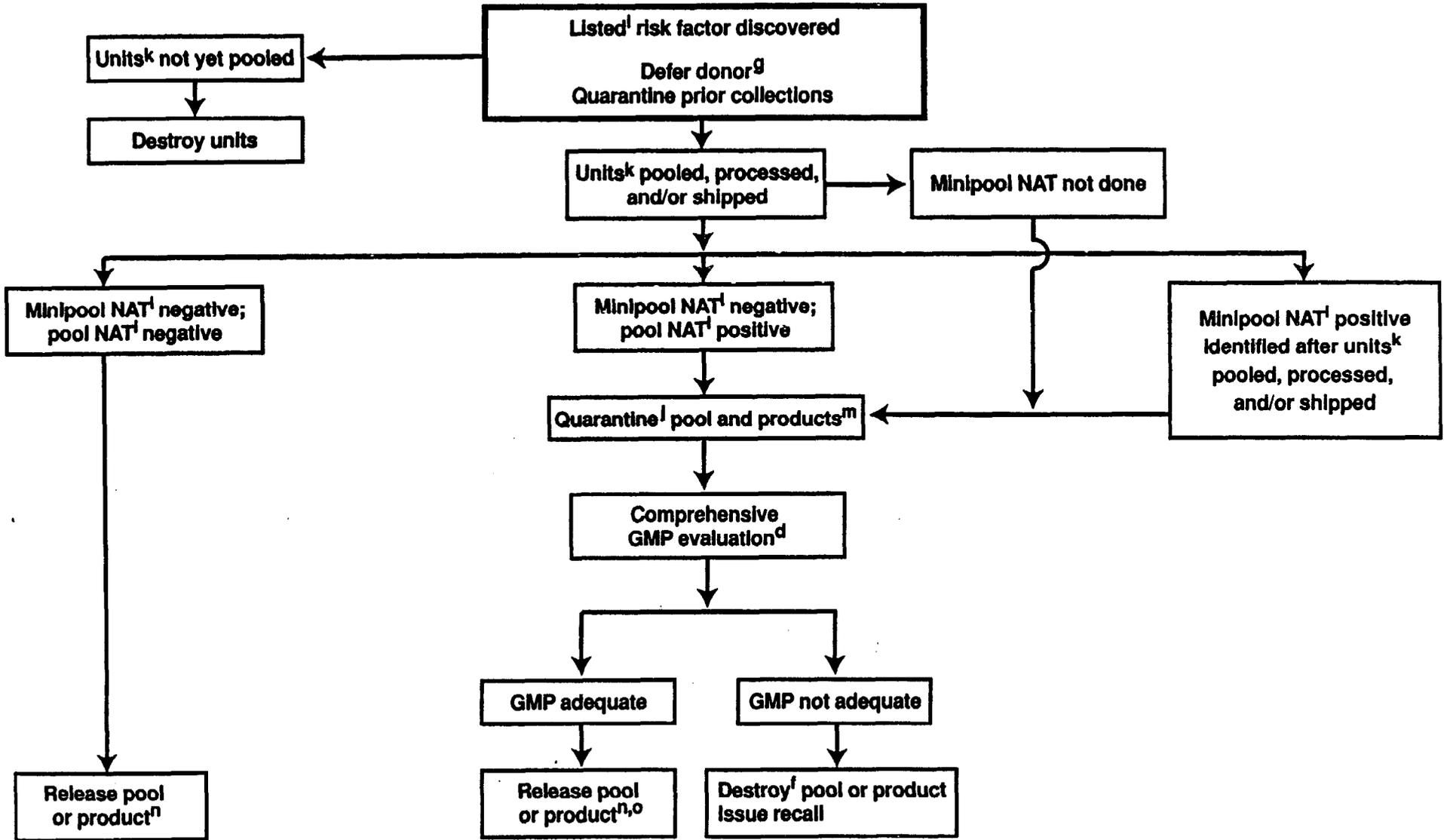
pooling had in fact been positive (had been incorrectly reported as negative), or if NAT had not been done on the minipool, then the pool and products would be quarantined and a GMP evaluation would be done. The GMP evaluation would be the same type of evaluation endorsed by BPAC at a prior meeting, as shown in footnote "d."

At a prior BPAC meeting, we had indicated that these algorithms for "test positive" and "risk factor" post-donation information would not be developed into guidance documents until the approval of NAT testing. We are now nearer to the time when one or more PLAs will be submitted to FDA for NAT testing. Therefore, it is safe to assume that the Office of Blood Research and Review will be working on a guidance document for these algorithms during the year 2000, in anticipation of those submissions and approvals for NAT testing.

**Risk Factor:
Whole Blood (Recovered Plasma)**



Risk Factor: Plasma



Footnotes

- ^a Anytime a confirmed positive test result is belatedly found on an individual unit, the unit must be destroyed if it has not yet been pooled.**
- ^b If the positive is a result from testing a pool, the result should be repeated to verify that it is correct.**
- ^c Disposition of unit and donor status should occur as defined in each IND.**
- ^d Comprehensive GMP evaluation by fractionator to verify virus removal and inactivation. GMP inspection by FDA as needed. Fractionators will send reports to FDA listing all GMP evaluations conducted because of post-donation information.**

- e Tests for virus in question only.**
- f In some cases, pools or products can be reprocessed if under an approved protocol.**
- g Donor must be deferred. In addition, if donor can be located, all licensed tests for markers of HCV and HIV should be done on a newly obtained sample. If any tests for HCV or HIV are positive or indeterminate, lookback should be conducted.**
- h “Lookback” here indicates both product retrieval and recipient notification.**

i Risk factors for HBV, HCV, or HIV to be used for the Risk Factor Algorithm (post-donation information)

IV drug use (ever)

Male to male sex (within 12 months)*

Sex partner tests positive for current HBV infection or HIV

Exchanged sex for drugs or money (within 12 months)*

Travel to or immigration from HIV Group O area

*** Because the history accompanying this risk factor may not always be available with regard to “the last 12 months,” this risk factor will only be used as a risk factor for the algorithm if the possible exposure is known to have occurred within 12 months or if no effort has been made to ascertain this.**

- j Quarantine is not necessary if a comprehensive GMP evaluation is adequate and is completed within 72 hours of the discovery that a unit in the pool came from a donor with a listed risk factor (post-donation information)**
- k Post-donation information typically is found to apply to multiple collections from the same donor**
- l Testing of the minipool before pooling should include NAT for HCV and HIV. Testing of the pool, after the receipt of post-donation information, should include NAT for HBV, HCV, and HIV. NAT should be a validated test performed under IND or an approved test whenever available.**

- m If products have been shipped, consignees should be notified to quarantine them.**
- n All pooled and/or processed prior donations can also be released if a recent donor sample is negative for all recommended donor tests, for NAT for HBV, HCV, and HIV, and for serologic tests for anti-HBc and anti-HBs. Pooled and/or processed prior donations that are positive or indeterminate for these tests must be recalled and destroyed. Hepatitis B Immune Globulin in which the high-titer anti-HBs component (but not the diluent globulin component) had been made from prior donations can be released without this testing for anti-HBc and anti-HBs, or with a positive test for anti-HBc or anti-HBs on the recent donor sample.**

- **Even if the tests in footnote “n” are positive on a recent donor sample, pooled and/or processed prior donations can also be released if GMPs are shown to have been followed for the resulting product lot.**