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14 May 1991

MEMORANDUM **CONFIDENTIAL**

TO: SNBTS BOARD MEMBERS

FROM: PROFESSOR CASH

SUBJECT: HCV DONATION TESTING

Members will be aware of the article in the Sunday Times of 11 May 1991 and will wish to be briefed on the position at this time.

Since early 1984, there has been growing concern throughout the UKBTS that microbiology donation screening kits should be appropriately evaluated before their large scale use is instituted. The primary concern, in this context, has been for the UK BTS to ensure, as much as is possible, that every effort has been made by kit manufacturers to maximise both sensitivity and specificity. In short, the task has been to validate that the kits used will (a) not miss a donation which is infective (false negative) and (b) will not declare a donation +ve when, in fact, it is negative (false positive). The outcome for patients with kits of significantly lower sensitivity is self-evident. Kits with high false positive ratings cause untold stress to blood donors, escalate unit costs (confirmatory testing/medical care/counselling) and produce expanding data handling problems. Beyond these self-evident features it has become increasingly important to assess kit systems (including data handling and reagent batch variation) for their "user friendliness", for, if this is not done - and by different groups - the opportunity for operator error is enhanced. It is possible that this feature ("user friendliness") may now be the most important safeguard against adverse events in this field, particularly with respect to well established tests (Hb_sAg and HIV).

An excellent example of the patience required in the exercise was seen in the UK BTS HIV-1 kit validation studies. The kit being widely promoted, and which had been

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hurriedly introduced in some countries, proved to be less sensitive than desirable (and possible) and its specificity was very poor. It was rejected by the UK BTS.

The standards set by the UK BTS in the HIV-1 exercise have been extended to the HCV kits. The SNBTS has contributed substantially to this exercise. The results have been interesting (and a little worrying). Two different kits have been compared on 10,633 donations. 25 donations were unequivocally positive with both kits; one kit showed unequivocal +ves in 25 other donations but these were completely missed by the other kit. Similarly, the second kit registered 19 positives which were not detected by the other kit. Thus, in all, there were 69+ve - 25 both kits, 25 one kit only and 19 the other kit only.

Confirmatory tests were done on all 69 screen positive donations. All were negative in those +ve by only one kit. Of the 25+ve with both kits, 6 were positive.

As the UK BTS validating team was in the process of advising Ministers and RTCs that both these kits could be used and that UK BTS should commence full scale screening on 1st July 1991, the kit manufacturers announced their intention to withdraw their kits and replace them with second generation kits. These new kits were claimed by the manufacturers to be an improvement over those tested by the UK BTS validation team, but no satisfactory data was available to confirm this at this time and it was noted that the FDA had not yet approved their use (given a product licence). It was concluded that an evaluation of these second generation kits should be undertaken as a matter of urgency and a scheduled start time (for full RTC screening) was estimated to be 1st September 1991.

Conclusions

1. If we extend these UK observations to Scotland then each year we can predict (without HCV donation testing) the following:-

   a) There will be approximately 170 donations which are infected with HCV and placed at issue (prevalence of 1/2000)

   b) That approximately 100 of these donations would be transfused as RCC (as some 60% of 300,000 donations are transfused) Conversely, 180,000 RCC will be used which will not be infected

2. <u>If we had commenced HCV donation testing with the kits which are being withdrawn from the market then, in the first year of testing, we would have faced the following donor management problems:</u>

a) 570 donors who were +ve with both screen tests but confirmatory tests -ve

b) 750 donors who were +ve with Kit (a) but -ve with Kit (b) and -ve confirmatory tests

c) 570 donors who were +ve with Kit (b) but -ve with Kit (a) and -ve confirmatory tests

Thus, in simple terms, we would have approximately 1,900 donors to deal with who we believed were false positives.

For those interested in money, we might suggest that the current (1st generation test) false +ve rate would cost us in unnecessary confirmation tests approximately £205,000 in the first year. Moreover, we should also note that the difference in screen +ves between Kit (a) and Kit (b) would give rise to different associated confirmatory test costs - of approximately £28,000.

3. It would seem prudent and responsible to pursue the idea of full evaluation of the second generation (HCV) test kits. This new evaluation will have an important new component which will permit a much more extensive study of confirmatory tests. Beyond this, representations are being made, in the light of the developments in Newcastle RTC, as to whether, in future, the SNBTS is bound to a UK BTS approach with regard to donation testing, agains a background of Ministerial involvement.

continued/

Follow-up to Sunday Times Article:

1. Number of donations transfused annually in UK is nearer 2.2m (not 22m)

2. Factor VIII and IX concentrates now appear 100% safe from HCV because of heat treatment

3. Statement that the Government will not fund HCV donation testing does not apply in Scotland.

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