

**CONFIDENTIAL**

Rollout of Recombinant Products to Adult Haemophilia Patients Registered at English Centres

**2004-5 Audit**  
**Interim Report 3**

**Prepared June 13<sup>th</sup> 2005**

**Quarters 1-3: April–December 2004**

**Summary**

- Audit data requested for eligible patients, but only those with a rollout allocation (plasma usage in base year)
- 528 in 2003-4, 568 in 2004-5
- By the end of the 2003-4 audit period 72% of cohort had started recombinant treatment.
- 2004-5 audit has now been carried out for Quarters 1, 2 and 3 covering the period April–December 2004.
- Centres were asked for start dates and monthly product usage.
- So far, complete response from 540 (95%) of cohort
- 474 patients (83% of cohort) are known to have started recombinant treatment
- PASA provided us with information on volumes committed to and purchased from companies under national contract
- Considerable shortfall between volumes purchased and committed. This may be due to
  - Centres failing to quote the National Contract reference number
  - Slow transfer of patients onto recombinant treatment
  - Patients using up plasma products
  - Rollover stock purchased end of 2003-2004 for use 2004-2005

### **Background to Interim Report 3**

In the first year of the rollout (April 2003-March 2004), 528 patients distributed between 40 centres were allocated funding. For each patient, centres were asked to provide the date on which the patient started recombinant treatment. By July 7th, all 40 centres had submitted complete audit data. Three hundred and eighty patients (72%) were reported as having been issued with recombinant factor products, with most start dates (70%) between February and April. A final report of the 2003-4 audit data was prepared on July 8<sup>th</sup> 2004.

In the second year of the rollout, April 2004-March 2005, funding allocations were assigned to 568 patients distributed in 45 centres and these patients comprised the cohort covered by this report. No information has yet been collected for eligible patients who did not receive a funding allocation because they used no plasma derived product in the base year.

At the end of the first quarter (April-June 2004) centres were asked to provide information on the date each of the 568 cohort patients started recombinant treatment, monthly product usage, and rollout implementation problems. Interim reports 1 and 2 describing data collected for quarter 1 were prepared in September and January respectively.

Information on the date each patient started recombinant treatment and monthly product usage for quarters 2 and 3 (July-December 2004) is now collected. In addition, PASA has supplied us with data describing purchases from pharmaceutical companies purchase volumes committed under the recombinant rollout national contract.

### **Aim of Interim Report 3**

The aim of this report is to summarise the current situation with respect to completeness of data, start dates, product volumes used by centres and purchases from companies, incorporating data previously received for Quarter 1 in addition to the newly collected data.

### **Methodology for data collection for Quarters 2 and 3 (July-December 2005)**

Centre Directors were sent by email a spreadsheet listing all patients at the centre with a rollout allocation for 2004-5. They were asked to complete the spreadsheet with the date each patient started recombinant treatment, and the product and volume issued to each patient for the months July-December 2004, and return it electronically. Two centres are currently acting as pilot sites in the development of an automated export of audit data.

PASA provided a spreadsheet of recombinant rollout product volumes committed to and purchased from each company by each centre for each month of the rollout.

## **Findings**

### **Completeness of data**

Most of the audit data for April-December 2004 has now been received, as illustrated in figure 1. Five hundred and sixty-eight patients in 45 centres received a recombinant rollout funding allocation in 2004-5. Complete information (quarters 1,2 and 3) has been received for 540 patients (95%). For a further 10 (2%) of patients, information has been received for quarter 1 only.

### **Start dates**

As shown in figure 2, it has been reported in either the 2003-4 or 2004-5 audit that 474 (83%) of patients have started recombinant treatment. A further 85 (15%) are reported not yet started. It is not known whether or not any of the remaining 9 (2%) of patients has started.

A possible indicator of the severity of the condition in a patient is the usage reported in the base year April 2002-March 2003. As shown in table 1, those not yet started are generally the lower users, with mean base year usage 36,189 IU compared to 127,114 IU base year usage for those patients with a start date reported.

The rollout programme eventually officially began in January 2004. The percent and cumulative percent of the cohort starting recombinant treatment in each calendar month are illustrated in figure 3 (based on the frequencies in Appendix 1). Although a small number of patients started recombinant treatment in the autumn of 2003, the majority (approximately two thirds of the cohort) began their recombinant treatment sometime between January and April 2004.

### **Product volumes used by centres in quarters 1, 2 and 3, 2004-5**

The five products included in the recombinant rollout are Helixate, Benefix, Recombinate or Advate, Kogenate and Refacto. Appendix 2 shows the predicted usage by quarter for both reported patients and the whole cohort, and the number of international units (IU) of each product used (issued to patients) in each calendar month by the reporting centres.

Table 2 shows these monthly usage figures aggregated by quarter and expressed as percent of usage predicted for reported patients ahead of the rollout. These percentages vary between 72% for Refacto in quarter 1 to 117% for Benefix in quarter 2. In general, the percent used of predicted peaks in quarter 2, but the greatest value for Kogenate appears in quarter 3.

### **Purchases from company quarters 1, 2 and 3 2004-5**

For each rollout product, quarterly commitment to purchase products under the national contract is shown in Appendix 3, along with the volume purchased each month for the whole cohort of patients. Table 3 contains these monthly purchase volumes aggregated by quarter and compares them with stated commitment to purchase under the national contract. The percent of committed which has been purchased is low for all products in quarter 1, ranging from 30% for Benefix to 57% for Kogenate and Refacto. However, it increases to greater than 70% for all products in quarter 3, with Kogenate achieving 84% purchased of committed.



## **Interpretation of findings**

The rollout process and factors affecting product volumes are illustrated in Figure 4.

In the spring of 2003 centres were asked to provide information on all patients eligible for recombinant treatment under the rollout. These data included amount of product used by each patient in the base year of April 2002-March 2003, from which future volume usage for the cohort was predicted by applying an anticipated increase of 10% per year. The national contract to purchase recombinant products for rollout patients, incorporating a purchasing volume commitment, was based on an NHS Purchasing and Supply Agency (PASA) model on this cohort.

The start date for the rollout was delayed from October 2003 to January 2004. Centres were required to purchase their rollout products against a national contract reference number, and, due to the delayed start date, were advised to purchase extra stock in the final quarter of 2003-4 for subsequent use in 2004-5. Information on start date and volumes of each product issued to patients was collected as part of the 2004-5 audit and information on volumes committed to and purchased from companies was provided by PASA.

It is clear that for each product the volumes predicted, committed, purchased and used should be similar. These volumes are compared in Figure 5, although usage volumes are available only for the 95% of patients reported so far, with no usage data collected for eligible patients who did not have a rollout funding allocation.

Figure 5 shows discrepancies between these four volumes. Of particular concern is the apparent discrepancy between rollout volumes committed to the companies and volumes purchased from the companies under the national contract, since the unit price of Kogenate, Helixate and Recombinate/Advate are linked to purchase volumes.

Factors which may contribute to these discrepancies are

- i The 10% uplift allowance for anticipated annual increase in demand may have been too high, causing the predicted usage and therefore committed volumes to be higher than the volumes used and purchased by centres.
- ii The cohort on which the PASA model and therefore national contract was based has been subsequently modified by amendments received from centres. In theory this should be a random effect, with those leaving the cohort balancing those entering.
- iii Some rollout patient products may not have been ordered on the national contract reference number, causing underestimate of volumes purchased from companies. This is suggested by the differences between volumes of products used by the centres and purchased from companies in Figure 5.
- iv Rollover stock purchased in 2003-4 and used in 2004-5 may cause a discrepancy between volumes purchased and volumes reported used, particularly in the early part of 2004-5. Figure 6 shows that the proportion of committed volume purchased increases for all companies when the observation period is extended to include January-March 2004.
- v Some centres may have been slow to start patients on recombinant treatment. This may have reduced the volume of product purchased and used in the earlier part of 2004-5. This

- effect is supported by Figure 3, which shows that the process of moving patients onto recombinant treatment lasts for several months, only levelling off in June or July 2004.
- vi Since volumes used are reported only for the reporting centres, non-respondents to audit will under-estimate the true values. Any effect due to non-response will disappear when all the audit data are received.
  - vii Usage information from centres was collected only for patients who had a rollout allocation. Any usage by eligible patients with no allocation (no plasma usage in snapshot year) are not included in these figures, causing the usage volumes to be an under-estimate in comparison to the volumes predicted, committed and purchased which apply to the whole cohort.

Table 4 summarises the likely effects which each of these factors may have had on product volumes. This table does not take into account other potential sources of uncertainty which are likely to be random in nature, for example, non-typical usage for a patient in the snapshot year, data input errors and reporting errors. These random errors should have no effect on the four volumes due to a 'cancelling out' effect.

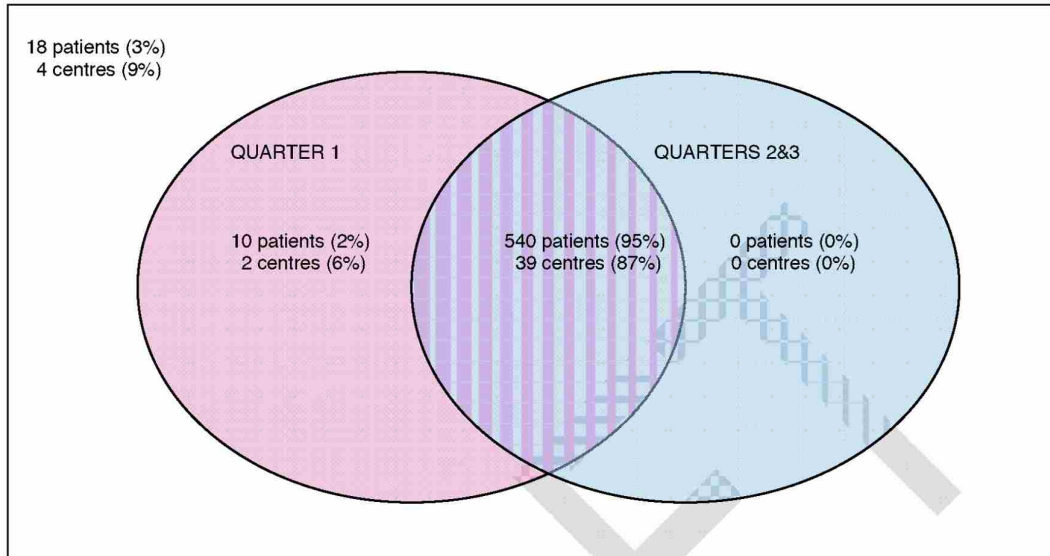
## Conclusions

- Although commitment under the national contract was based on predictions of patient usage, some slight discrepancy would be expected because the present cohort has evolved to reflect amendments and new patient registrations.
- Product volumes used by the centres are under-estimated in this report because usage volumes have been collected only for patients with a rollout financial allocation, omitting usage by those eligible patients who had no financial allocation due to no plasma usage in the base year.
- There is a considerable shortfall between volumes committed to and purchased from the pharmaceutical companies. This may be due to several factors, including centres failing to quote the national contract number when ordering stock, slow transfer of patients onto recombinant treatment, patients using up their own stocks of plasma product and rollover stock purchased at the end of the 2003-4 financial year for use in the 2004-5 financial year. This shortfall is particularly important in the case of Kogenate, Helixate and Recombinate/Advate since rollout contract prices are linked to volumes purchased.

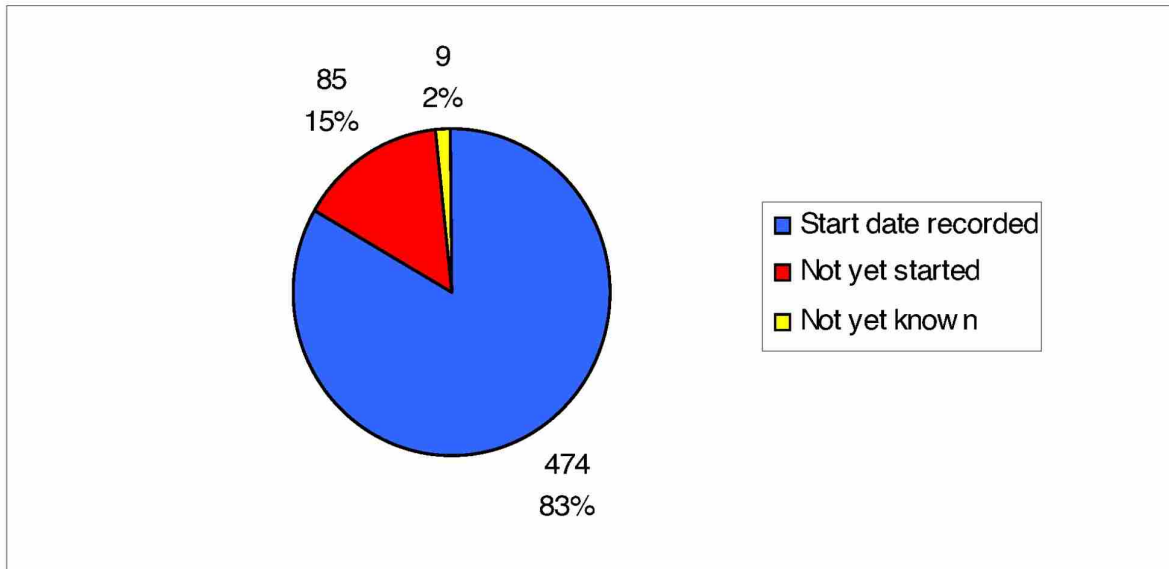
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**On behalf of:**  
**The Department of Health Forward Planning and Monitoring Group:**  
**Rollout of Recombinant Treatment for Adult Haemophilia Patients**



**Figure 1** Recombinant rollout audit 2004-5 Response rates for Quarters 1, 2 and 3  
(568 patients in 45 centres)  
540 patients were reported for quarters 1, 2 and 3  
10 patients were reported for quarter 1 only  
No patients were reported for quarter 2 only



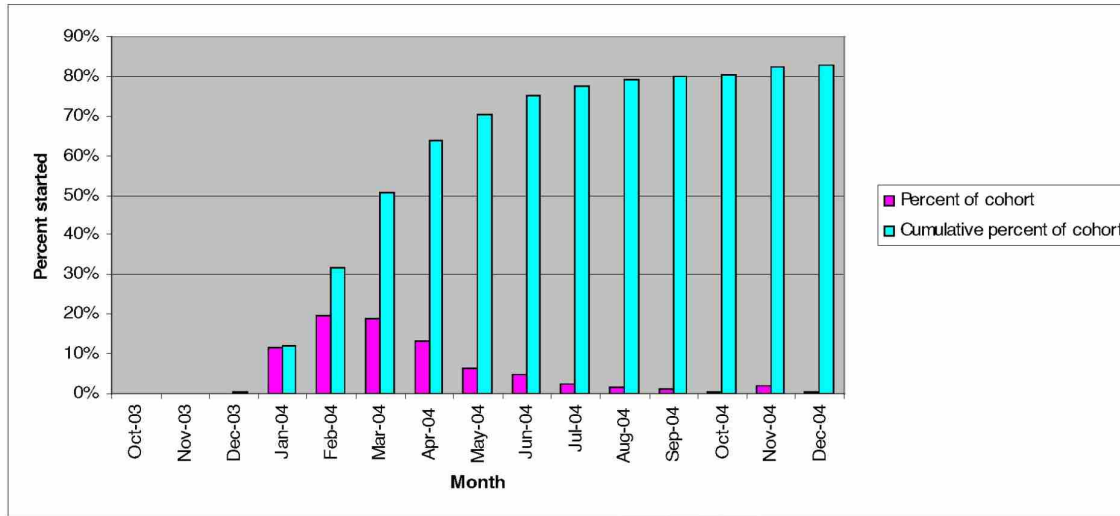
**Figure 2**      **Recombinant treatment status of audited patients (568 patients in 45 centres)**

*Start date is either from 2003-4 audit or 2004-5 audit*

| Recombinant treatment status | Number [percent] of patients | Mean [min:max] usage (IU) April 2002-March 2003 |
|------------------------------|------------------------------|---|
| Start date recorded          | 474 [83%]                    | 127,114 [100: 1,825,000]                        |
| Not yet started              | 85 [15%]                     | 36,289 [500: 307,400]                           |
| Not yet known                | 9 [2%]                       | 49,144 [500: 173,000]                           |
| Total                        | 568 [100%]                   |   |

**Table 1**      **Recombinant treatment status and mean usage in base year of whole cohort (568 patients in 45 centres)**





**Figure 3** Percent and cumulative percent of cohort starting treatment in each calendar month October 2003-December 2004



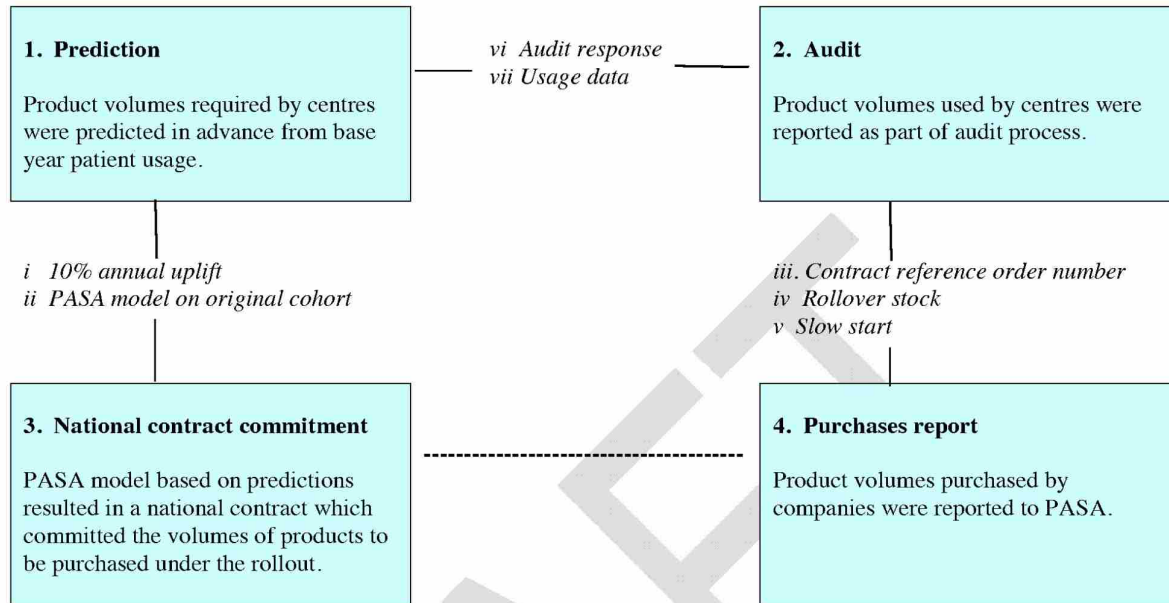
| Product                            | 2004-5 Q1<br>predicted<br>usage (IU)* | 2004-5 Q1<br>reported<br>usage (IU) | 2004-5<br>Q1 usage<br>as % of<br>predicted | 2004-5 Q2<br>predicted<br>usage (IU)* | 2004-5 Q2<br>reported<br>usage (IU) | 2004-5<br>Q2<br>usage<br>as % of<br>predicted | 2004-5 Q3<br>predicted<br>usage (IU)* | 2004-5 Q3<br>reported<br>usage (IU) | 2004-5<br>Q3<br>usage<br>as % of<br>predicted |
|------------------------------------|---------------------------------------|-------------------------------------|--|---------------------------------------|-------------------------------------|---|---------------------------------------|-------------------------------------|---|
| Aventis –<br>Helixate              | 5,024,720                             | 4,978,020                           | 99%  | 5,024,720                             | 5,478,500                           | 109%  | 5,024,720                             | 4,718,000                           | 94%   |
| Baxter –<br>Benefix                | 2,847,155                             | 2,777,000                           | 98%  | 2,790,588                             | 3,273,520                           | 117%  | 2,790,588                             | 3,199,240                           | 115%  |
| Baxter -<br>Recombinate/<br>Advate | 2,688,702                             | 2,309,615                           | 86%  | 2,688,702                             | 2,300,235                           | 86%   | 2,688,702                             | 2,051,687                           | 76%   |
| Bayer –<br>Kogenate                | 7,207,445                             | 5,937,285                           | 82%  | 7,073,060                             | 6,204,250                           | 88%   | 7,073,060                             | 6,672,800                           | 94%   |
| Wyeth –<br>Refacto                 | 899,859                               | 645,780                             | 72%  | 840,120                               | 935,058                             | 111%  | 840,120                               | 686,900                             | 82%   |
|                                    |                                       |                                     |  |                                       |                                     |   |                                       |                                     |   |
| Total                              | 18,667,881                            | 16,647,700                          | 89%  | 18,417,189                            | 18,191,563                          | 99%   | 18,417,189                            | 17,328,627                          | 94%   |

**Table 2** Quarterly product usage compared with predicted usage for reporting centres for Quarter 1 (April-June 2004; 41centres, 550 patients) and 2&3 ), 2 (July-September 2004; 39 centres, 540 patients) and 3 (October-December 2004; 39 centres, 540 patients)

*\*Predicted usage for the 3 month period for each patient is based on the number of units in base year (2002-3) uplifted by 10% for 2003-4 and a further 10% for 2004-5 and scaled by 0.25 for quarter of a year.*

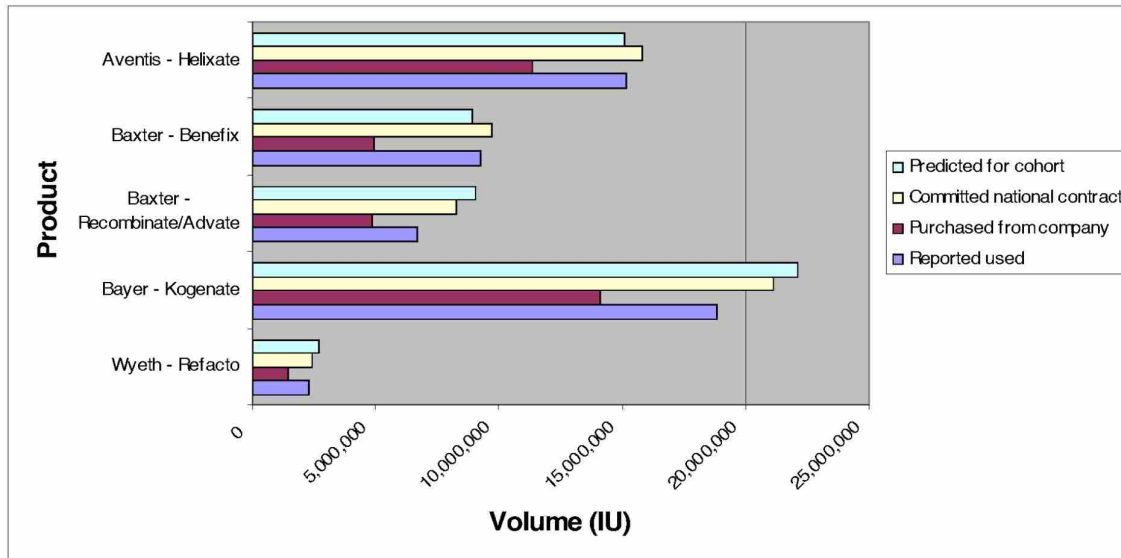
| Product                            | 2004-5<br>Q1<br>purchase<br>volume<br>committed to<br>company<br>(IU) | 2004-5<br>Q1<br>volume<br>purchased<br>from<br>company<br>(IU) | 2004-5<br>Q1<br>purchases<br>as % of<br>committed | 2004-5<br>Q2<br>purchase<br>volume<br>committed<br>to company<br>(IU) | 2004-5<br>Q2<br>volume<br>purchased<br>from<br>company<br>(IU) | 2004-5<br>Q2<br>purchases<br>as % of<br>committed | 2004-5<br>Q3<br>purchase<br>volume<br>committed<br>to company<br>(IU) | 2004-5<br>Q3<br>volume<br>purchased<br>from<br>company<br>(IU) | 2004-5 Q3<br>purchases<br>as % of<br>committed |
|------------------------------------|---|--|---|---|--|---|---|--|--|
| Aventis –<br>Helixate              | 5,272,614   | 2,526,000  | 48%   | 5,272,614   | 4,967,500  | 94%   | 5,272,614   | 3,840,000  | 73%  |
| Baxter – Benefix                   | 3,234,247   | 973,000  | 30%   | 3,234,247   | 1,684,500  | 52%   | 3,234,247   | 2,277,000  | 70%  |
| Baxter -<br>Recombinate/<br>Advate | 2,752,427   | 1,207,000  | 44%   | 2,752,427   | 1,668,000  | 61%   | 2,752,427   | 1,970,000  | 72%  |
| Bayer –<br>Kogenate                | 7,045,595   | 4,012,000  | 57%   | 7,045,595   | 4,166,000  | 59%   | 7,045,595   | 5,901,000  | 84%  |
| Wyeth – Refacto                    | 813,072   | 460,000  | 57%   | 813,072   | 430,000  | 53%   | 813,072   | 575,000  | 71%  |
|                                    |   |  |   |   |  |   |   |  |  |
| Total                              | 19,117,953  | 9,178,000  | 48%   | 19,117,953  | 12,916,000   | 68%   | 19,117,953  | 14,563,000   | 76%  |

**Table 3**      **2004-5 Quarterly purchases reported by company compared with commitment under national contract Quarters 1 (April-June 2004), 2 (July-September 2004) and 3 (October-December 2004) (45 centres, 568 patients)**



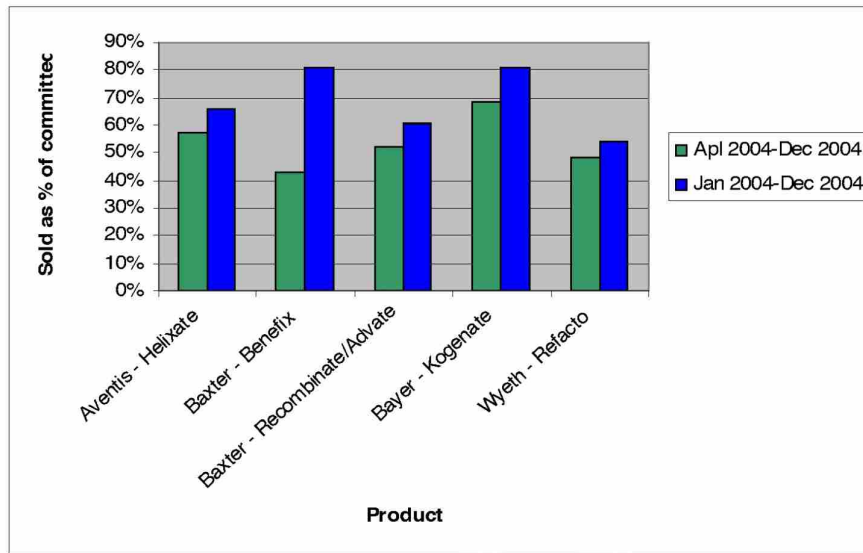
**Figure 4** Factors connecting predicted, committed, used and purchased product volumes





**Figure 5 Volumes of products predicted, committed, used and purchased 2004-5 Q1,2 and 3**

*Predicted, committed and purchased volumes are based on the whole cohort, volumes used are available for reported patients only.*



**Figure 6** Cumulative product volumes purchased as a percentage of volumes committed

|   | <b>Predicted summed over whole cohort</b>                             | <b>Committed</b>     | <b>Purchased</b>   | <b>Used</b>   |
|---|---|----------------------|--|---|
| <b>i 10% annual uplift too high</b>   | Predictions too high  | Commitments too high | No effect  | No effect   |
| <b>ii Modified cohort</b>   | Predictions reported in audit summed over cohort larger than original | No effect            | Products purchased for cohort larger than original   | Usage reported in audit summed over cohort larger than original |
| <b>iii Not quoting reference no.</b>  | No effect   | No effect            | Under-reporting of rollout purchases from company  | No effect   |
| <b>iv Rollover stock</b>  | No effect   | No effect            | Purchases from company figures for Q1 artificially low due to using up rollover stock purchased spring 2004. | No effect   |
| <b>v Slow starters</b>  | No effect   | No effect            | Reduction in purchases from company until everyone started   | Reduction in usage until everyone started                       |
| <b>Vi Non-response to audit</b>   | No effect   | No effect            | No effect  | Under-estimates actual volume of products used                  |
| <b>Vii Usage data collected only for patients with a funding allocation</b> | No effect   | No effect            | No effect  | Under-estimates actual volume of products used                  |

**Table 4** Likely effects of factors on predicted, committed, used and purchased volumes reported to date for 2004-5 Quarters 1, 2 and 3.

## Appendix 1

Number, percent and cumulative percent of patient starting recombinant treatment in each calendar month April-December 2004

| Month started  | Number of patients* | Percent of cohort | Cumulative percent of cohort |
|----------------|---------------------|-------------------|------------------------------|
| October 2003   | 1                   | 0%                | 0%                           |
| December 2003  | 1                   | 0%                | 0%                           |
| January 2004   | 67                  | 12%               | 12%                          |
| February 2004  | 111                 | 20%               | 32%                          |
| March 2004     | 108                 | 19%               | 51%                          |
| April 2004     | 75                  | 13%               | 64%                          |
| May 2004       | 37                  | 7%                | 70%                          |
| June 2004      | 27                  | 5%                | 75%                          |
| July 2004      | 13                  | 2%                | 77%                          |
| August 2004    | 9                   | 2%                | 79%                          |
| September 2004 | 6                   | 1%                | 80%                          |
| October 2004   | 2                   | 0%                | 80%                          |
| November 2004  | 11                  | 2%                | 82%                          |
| December 2004  | 3                   | 1%                | 83%                          |

\* 2 patients with a start date in January and 1 with start date February are not included in this table



## Appendix 2

**Product volumes (41 centres and 550 patients for quarter 1, 39 centres and 540 patients for quarters 2&3)**

### Quarterly predicted usage for reported patients and whole cohort

| Product                     | 2004-5 Q1<br>Reported patients<br>predicted usage | 2004-5 Q2<br>Reported patients<br>predicted usage | 2004-5 Q3<br>Reported patients<br>predicted usage | 2004-5<br>Predicted usage whole<br>cohort all<br>quarters |
|-----------------------------|---|---|---|---|
|                             | 41 centres<br>550 patients                        | 39 centres<br>540 patients                        | 39 centres<br>540 patients                        | 45 centres<br>568 patients                                |
| Aventis - Helixate          | 4,605,915   | 4,605,915   | 4,605,915   | 5,024,720   |
| Baxter - Benefix            | 2,772,930   | 2,729,370   | 2,729,370   | 2,978,289   |
| Baxter - Recombinate/Advate | 2,514,459   | 2,659,662   | 2,659,662   | 3,025,899   |
| Bayer - Kogenate            | 7,014,885   | 6,990,609   | 6,990,609   | 7,364,342   |
| Wyeth - Refacto             | 899,859   | 840,120   | 840,120   | 899,859   |
|                             |   |   |   |   |
| Total                       | 17,808,048  | 17,825,675  | 17,825,675  | 19,293,108  |

### Monthly product usage for Quarters 1, 2 and 3 reported to date

| Product                     | Apr 2004<br>usage<br>(IU) | May 2004<br>usage<br>(IU) | Jun 2004<br>usage<br>(IU) | Jul 2004<br>usage<br>(IU) | Aug 2004<br>usage<br>(IU) | Sep 2004<br>usage<br>(IU) | Oct 2004<br>usage<br>(IU) | Nov 2004<br>usage<br>(IU) | Dec 2004<br>usage<br>(IU) |
|-----------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|
| Aventis – Helixate          | 1,478,020                 | 1,247,000                 | 1,785,000                 | 1,902,000                 | 1,316,500                 | 1,715,000                 | 1,330,500                 | 1,619,000                 | 1,460,500                 |
| Baxter – Benefix            | 1,042,900                 | 809,000                   | 836,300                   | 1,089,240                 | 956,860                   | 1,132,420                 | 837,780                   | 1,215,100                 | 987,360                   |
| Baxter - Recombinate/Advate | 787,960                   | 602,030                   | 772,740                   | 576,730                   | 807,845                   | 915,660                   | 547,557                   | 859,955                   | 644,175                   |
| Bayer - Kogenate            | 2,066,500                 | 1,927,000                 | 1,835,785                 | 1,960,750                 | 2,106,000                 | 2,089,500                 | 1,720,000                 | 2,622,500                 | 2,290,300                 |
| Wyeth – Refacto             | 300,280                   | 154,520                   | 190,980                   | 335,350                   | 279,128                   | 320,580                   | 214,400                   | 273,730                   | 198,770                   |
|                             |                           |                           |                           |                           |                           |                           |                           |                           |                           |
| Total                       | 5,675,660                 | 4,739,550                 | 5,420,805                 | 5,864,070                 | 5,466,333                 | 6,173,160                 | 4,650,237                 | 6,590,285                 | 5,581,105                 |

### Appendix 3 Commitments to and purchases from companies (45 centres, 568 patients)

#### Quarterly committed usage under national contract

| Product                        | 2004-5 Q1<br>Commitment<br>to company<br>(IU) | 2004-5 Q2<br>Commitment<br>to company<br>(IU) | 2004-5 Q3<br>Commitment<br>to company<br>(IU) |
|--------------------------------|---|---|---|
| Aventis - Helixate             | 5,272,614                                     | 5,272,614                                     | 5,272,614                                     |
| Baxter - Benefix               | 3,234,247                                     | 3,234,247                                     | 3,234,247                                     |
| Baxter -<br>Recombinate/Advate | 2,752,427                                     | 2,752,427                                     | 2,752,427                                     |
| Bayer - Kogenate               | 7,045,595                                     | 7,045,595                                     | 7,045,595                                     |
| Wyeth - Refacto                | 813,072                                       | 813,072                                       | 813,072                                       |
|                                |   |   |   |
| Total                          | 19,117,953                                    | 19,117,953                                    | 19,117,953                                    |

#### Monthly purchases from company under the national contract 568 patients, 45 centres

| Product       | Apr 2004<br>purchase<br>from<br>company<br>(IU) | May 2004<br>purchase<br>from<br>company<br>(IU) | Jun 2004<br>purchase<br>from<br>company<br>(IU) | Jul 2004<br>purchase<br>from<br>company<br>(IU) | Aug 2004<br>purchase<br>from<br>company<br>(IU) | Sep 2004<br>purchase<br>from<br>company<br>(IU) | Oct 2004<br>purchase<br>from<br>company<br>(IU) | Nov 2004<br>purchase<br>from<br>company (IU) | Dec 2004<br>purchase from<br>company (IU) |
|---------------|---|---|---|---|---|---|---|--|---|
| Helixate      | 457,000   | 992,000   | 1,077,000                                       | 2,673,000                                       | 1,661,500                                       | 633,000   | 1,674,000                                       | 1,008,000                                    | 1,158,000                                 |
| Benefix       | 96,000  | 65,000  | 812,000   | 667,500   | 402,000   | 615,000   | 514,000   | 712,000                                      | 1,051,000                                 |
| Recomb/Advate | 471,500   | 390,000   | 345,500   | 583,000   | 408,000   | 677,000   | 470,000   | 842,000                                      | 658,000                                   |
| Kogenate      | 931,000   | 1,478,000                                       | 1,603,000                                       | 1,083,000                                       | 1,354,000                                       | 1,729,000                                       | 1,787,000                                       | 2,012,000                                    | 2,102,000                                 |
| Refacto       | 253,000   | 0   | 207,000   | 150,000   | 140,000   | 140,000   | 125,000   | 190,000                                      | 260,000                                   |
| Total         | 2,208,500                                       | 2,925,000                                       | 4,044,500                                       | 5,156,500                                       | 3,965,500                                       | 3,794,000                                       | 4,570,000                                       | 4,764,000                                    | 5,229,000                                 |