

COAGULATION UPDATE
28 June 1985

NON HEAT ACTION

Effective 21 June 1985 all non-heat treated KOATE® and KONYNE® were discontinued for sale in the United States. A letter was sent to all customers who purchased these products in 1984 and 1985, announcing action and recommending return of any existing product. Internationally, a telex and bulletin were sent to all distributors and all affiliates announcing similar action. We are not requesting return of existing inventories of non-heat product internationally due to difficulties in customs, licenses, etc.

No estimation of the volume of returns to Clayton available to date.

The NHF and WPH have complemented Cutter for the action. The phone calls received from Customers all have been very positive, none have been negative. Most common remark is that of appreciation and admiration for the responsibility shown by Cutter. Additional comments have been on the completeness of the announcement package as compared with Hyland's letter.

Competitively, Hyland announced similar action on 11 June 85 but did not remove non-heat treated Proplex® and Autoplex®. On 19 June 85, Hyland recalled four lots of Proplex® due to an AIDS donor in the plasma pool. Armour is reportedly not withdrawing any non-heat treated product. Alpha has reportedly sold all existing non-heat treated Profilnine to the NYBC leaving them with no existing inventory and no plans to make an announcement.

INVENTORY STATUS

Desired inventory levels are approximately 52 million i.u. of finished product. Current inventory is running around 20 million. We will complete year with 17 million i.u. This lower than desired inventory has been caused by:

- (1) increased demand for HT products
- (2) inability to acquire source plasma sufficient to meet demand
- (3) Use of 120,000 liters plasma from which no AHF may be taken.

Net effect is that we continue to experience back orders, spot shortages and will do so into 1986. Sales will equal production in 1986. Production is expected to be 289 million i.u.

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ULTRAFILTERED (NON-HEAT) INVENTORY

We currently have 28 million i.u. inventory of non-heat ultrafiltered KOATE® in three countries, US, UK, Japan. We are selling 1.5 million i.u. per month in Japan and anticipate HT sales to begin in September. Once sales of HT begin, non-heat KOATE will be unsaleable.

Rework procedures, through PMT have met with minimum success. The final container product is full of particulates. Additional testing and work is being done. Yields are reported to be about 28% of original container potency. Toxicity studies have been recommended. OOB has given indication that any application for rework of non-heat AHF would be expedited with minimal delay.

Effort will be made to sell reprocessed UF KOATE in the United States. It is felt that given favorable toxicity reports, the optimum process may result in saleable product for a reduced price to selected accounts.

JAPAN AND KOATE®-HT

The Japanese MHW has approved the license for all heat treated AHF. Final pricing and dating decision is awaited. Anticipated sales to begin in September 1985. Initial shipment of KOATE®-HT has been made and additional shipments will be made following final Chosakai approval.

It has been reported that the Green Cross may have some difficulties in supplying heat-treated AHF immediately and Immuno did not submit a license. There exists a real potential for immediate sales growth with long-term implications for CJL. Annual sales for CJL are projected at 23 million in 1986, all heat treated.

AIDS IMPACT ON MARKET

While there remains substantial anxiety in the minds of hemophiliacs, treatment has resumed the pre-AIDS level of 1982.

We are experiencing a decline in the number of new AIDS cases among hemophiliacs. According to MMWR 3 May 85, the level of new cases now stands at five cases for the first four months of the year, compared with the high of 15 cases during first quarter of 1984 and ten cases in the last quarter of 1984. The decline in the number of cases reflects steps taken by medical community and commercial manufacturers:

- elimination of high-risk plasma donors
- development of heat-treated concentrates
- selective patient education.

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CUTTER ADDRESSES AIDS AND HEMOPHILIA

Addressing the anxiety of patient and clinician in order to relieve their fears, is seen as the pivotal point for increasing Koate®-HT and Konyne®-HT sales over the next twelve months.

Cutter solidified its position with regard to the validity of viral inactivation data on the concentrates by action taken 21 June 1985.

The following activities are planned in the US for the remainder of 1985:

1. Production of an educational program directed toward the patient and clinician explaining safety and efficacy of coagulation products and the importance of early treatment.
2. Publication of McDougal, et al paper in Journal of Clinical Immunology and Levy, et al paper in the Lancet. Both discuss collaborative efforts with Cutter regarding thermal inactivation of HTLV III/LAV.
3. A direct mail campaign to hemophilia treating physicians, calling attention to the validity of the Cutter viral inactivation data and offering reprints of published papers.
4. Special issue of ECHO, devoted exclusively to the AIDS issue. This will provide reassuring data relating to AIDS and hemophilia.

Internationally, Cutter will continue the "Harmony of a Full and Productive Life for Hemophiliacs" program with the publication of two follow-up patient education pamphlets emphasizing homecare. A selling piece on KOATE®-HT and KONYNE®-HT will also be released for market in Latin America and Far East.

RESEARCH UPDATE

Among the several active projects:

- Copper Phenanthraline viral inactivation
- Wet heat KOATE®
- Inhibitor indication for KONYNE®-HT
- Pure IX Concentrate
- Activated VII

Most pressing immediate need is to complete study and submit data supporting indication for KONYNE-HT in patients with Factor VIII inhibitors.

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Dr. Levy concluded that this mouse C retrovirus was inactivated by the unique Cutter heat-treated process. It should also be noted that in Table II on page 723 of the Lance article the IP/ml figure opposite the 72 hour interval should read 10 to the 0.2 power not 10 to the 10.2 power. This typographical error should be corrected on your copy.

LAV and ARV Data

The page titled "KOATE-HT Human Virus Inactivation Data", offers a summary of independent studies done by the Center for Disease Control of the U.S.A. on the lymphadenopathy associated virus (LAV) and by Dr. J.A. Levy on the AIDS-related virus (ARV).

As noted in both studies, using the Cutter process of treating AHF concentrates, the retroviruses LAV and ARV were inactivated. CDC in an independent research study using the LAV retrovirus, first isolated by the Pasteur Institute in France, was able to demonstrate that the LAV does not survive the unique Cutter heat-treating process. Dr. Levy performed tests with the ARV which his team at the University of California, San Francisco isolated and preliminary results suggest that Cutter's heat treatment process virtually inactivated the AIDS related virus (ARV).

NHF Heat-Treat Announcement

The Medical and Scientific Advisory Council of the National Hemophilia Foundation (NHF) after the NHF Meeting in Rochester, N.Y. released the attached medical bulletin. They state in Section C of Paragraph 1 of the bulletin that those treating hemophiliacs and using concentrates should strongly consider changing to heat-treated products. Apparently this decision was based on preliminary reports of the effectiveness of heat treatment against AIDS-like viruses.

Discontinuance of Hepatitis B Core Screening

As a result of the success of our heating process against viral contaminants, the anti-hepatitis B core tests will no longer be performed.

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Based on the best information available, it was decided by Cutter management that in the future, Cutter will supply only KOATE-HT to customers. Some physicians remain skeptical of heat-treated AHF because the data are still preliminary. For those physicians Cutter will supply KOATE (non-heat-treated). Please check with your Area Marketing Manager if you have questions regarding product availability.

Best Regards,

GRO-C

Gary Mull
Product Manager

GM/cfg

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