Volume 1 No. 1

Plasma Perspectives

July 1981

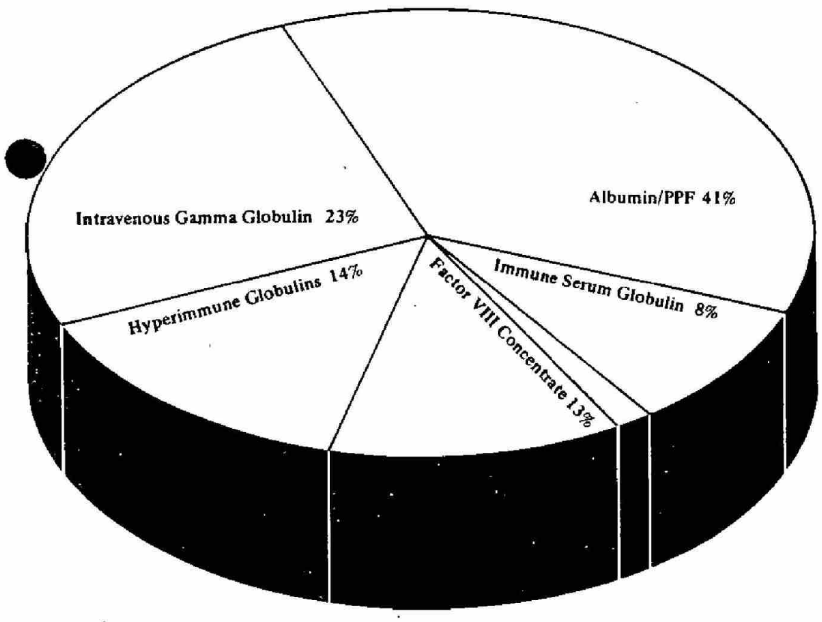
A NEW INTERFACE

It is clearly outside the scope of standard product literature to examine current and controversial issues relating to the supply and use of blood products. However, it is important that the views of both manufacturers and medical profession should have the opportunity of being voiced. Indeed, one of the recommendations contained in the International Federation of Pharmaceutical Manufacturers Association's (I.F.P.M.A.) 1980 report on blood products[1] was that although "care should be taken to avoid over-promotion of the various products made from human blood, full information on such products should continue to be made fully available".

It is the intention of Plasma Perspectives to be the vehicle of these views and to form an interface where the opinions of both producers and users can be seen. Clearly for such a publication to be of real value it has to be seen to take an objective and impartial view. Much of this objectivity will be dependent on the contributions, correspondence and reports which are received from those with a special interest in the administration of blood products. The newsletter will be published by the Plasma Division of the Armour Pharmaceutical Company and it is hoped to include an abstract and bibliography service on items of mutual interest. It will be distributed on request free of charge to members of the medical and allied professions.

The first issue of Plasma Perspectives is, for the most part, based on a report by Dr. Peter Jones, Director of the Haemophilia Centre at Newcastle, following an invitation to visit some of Armour's plasmapheresis centres and their Fractionation Plant in the U.S.A. We believe that this impartial report will go a long way to correct many of the misapprehensions and misunderstandings which have arisen in relation to the collection and distribution of plasma from commercial sources within the U.S.A.

BLOOD PRODUCTS DEMAND EXCEEDS SUPPLY



World-wide Demand for Plasma Fractions (in monetary value)[1]

Each year there is an increasing requirement in the U.K. for blood and its derivatives. This demand far outstrips its provision from National Health Service sources. For example in 1979 it was estimated that the supply of A.H.F. from the Blood Transfusion Service provided only half the 60 million units of A.H.F. which was used during the year. Worldwide more than 70% of human plasma used for fractionating is derived from commercial sources. The shortfall which would follow any supply problems in the commercial sector would be of enormous proportions.

Allegations about the incidence of hepatitis B and non-A and non-B, alcoholism and drug addiction amongst paid donors have done much to harm the commercial supply of blood products. It is therefore imperative that all the companies involved, as well as Armour, in the collection, fractionation, purification and distribution of blood derivatives comply with the appropriate regulations and requirements. This in itself will help to guarantee the quality of the product but not its continuing supply. The companies involved need to not only operate within well defined highly regulated guidelines – they have to be seen to do so.

In the U.K., Armour Plasma Division is a major supplier of blood products, particularly Human Anti-Haemophilic Factor (A.H.F.) which is available as Factorate. The most recent development in this area has been the introduction of Factorate H.P. (High Purity and Potency) which has the highest specific activity (i.u./mg protein) of all concentrates currently available in this country and could, therefore, be of particular value in the treatment of intensively infused patients, especially those with inhibitors or undergoing surgery where volume relative to potency and purity could be especially important.

ARMOUR-PLASMA COLLECTION AND CONTROL

Quality Source Plasma to F.D.A. Standards Protects Recipient

Plasma collected for the production of **Armour's** Factorate both, Standard and High Purity, is **SOURCE PLASMA** which is a Federally defined and regulated product in the U.S.A. It has a statutorily defined quality which is as follows:

"That fluid portion of human blood which has been stabilised against clotting, collected by **plasmapheresis** from humans who have not been hyperimmunised to produce specific antibodies, and intended for source material for manufacture of Anti-haemophilic Factor (Human), Immune Serum Globulin (Human), Plasma Protein Fraction (Human) and Normal Serum Albumin (Human). It is manufactured according to and conforms to all sections of Title 21 of the Code of Federal Regulations, Sub-chapter F, parts 600, 601, 606, 607, 610 and Sub-part G, 640.60 to 640.76 of Sub-chapter F, and is **"flash frozen"** as individual units at -70°C, or colder, **within one hour after** separation from red blood cells and **within two hours of withdrawal from the donor.**"

The practice of collecting plasma from Third World countries where blood products are already in short supply and where, in some cases, hepatitis B is endogenous has been severely criticised.

All of Armour's SOURCE PLASMA is collected from Federally regulated plasmapheresis centres on the **U.S.A. mainland**. In 1975, in order to help achieve self-sufficiency and total control of its operations, Armour purchased Blood Plasma Services which maintained 12 centres in 11 cities. Since that date, other plasmapheresis centres have been acquired and Armour has rationalised the network into one highly organised subsidiary, Plasma Alliance Incorporated, which now coordinates the activities in 22 centres all of which are located in North America.

Plasma Alliance's 22 centres are responsible for collecting from approximately 22,000 donors registered at any one time, records for whom are centrally controlled by computer at the Company's principal plasmapheresis laboratories in Knoxville Tennessee which are among the largest of their kind and which process over 9,000 donors per month.

Donor Protection is also Essential

In the same way that all possible steps must be taken to ensure the welfare of the recipient so does the same apply to Armour's registered donors.

Donations of plasma are restricted to two per week separated by at least 48 hours and usually comprise 0.5 to 0.7 litres per donation; there is also an annual maximum of 60 litres per donor. This is a significant amount but is a maximum and not typical of what is collected from each donor annually (usually less than 20 litres). Plasma proteins and volume are rapidly replaced in healthy individuals and to allay any concern about the long term welfare of donors it should be emphasized that the safety of the above regimes has been verified by work from the Nobel Laureate George Whipple. More recently, a collaborative study on the effects of long term plasmapheresis on donor health has been initiated by Armour and other major fractionaters. This study has the full collaboration of the F.D.A. and the final results are due later this year; if these indicate any required changes in current practices the joint group will liaise with the F.D.A. to ensure they are effected promptly.

Computer Control of Donors offers an Extra Safeguard to Donor and Recipient

The histories of all donors are recorded on microfiche and updated on a weekly basis. The data base is cross-checked for each new donor, by central control at Knoxville, and disseminated via the computer terminals at each of the 22 centres.

So that careful scrutiny is made of each new donor with computer control between centres (to avoid a potential donor who has been rejected at one centre turning up at another, etc.), the record of every new donor or donor of more than six months duration is rechecked.

All donors are identified by name, date of birth and social security number. The day following the donations each person on the centre list is checked out by the Centre's Quality Assurance Unit. Each centre then sends its updated audited list into the central Knoxville Laboratory where the central Quality Assurance Unit performs another complete audit, before distributing them to all the centres.

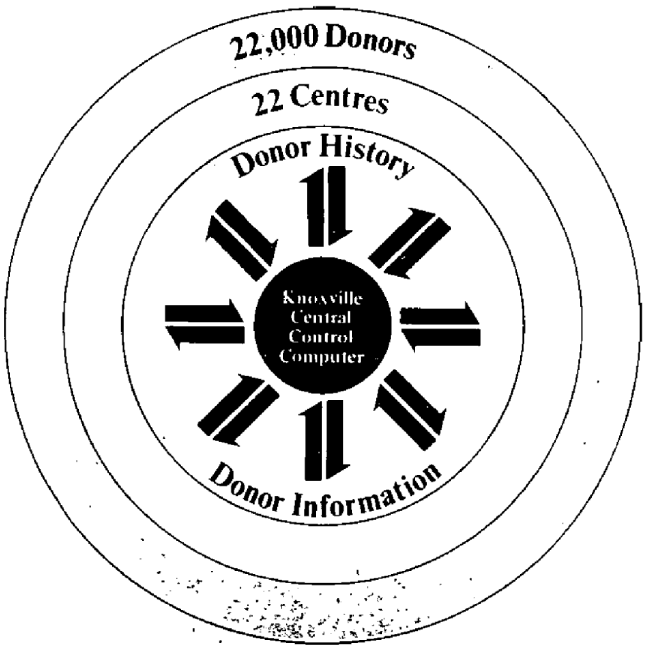
Also, at least every six months **all** the files of active donors are checked against the microfiche records. All individual donors are checked by physical examination by the Centre physician and by examination of previous medical history in terms of hepatitis infection or drug habit. No donor with an unsatisfactory history is admitted to the donor register.

Armour In-House Standard Operating Procedures Conform to F.D.A. Regulations

Embodied in the above is a rigid and sophisticated record control which, for example, covers the following critical areas:-

A. Processing of Source Plasma Donors

1. Records
2. General criteria
   Identity, Age, Weight, Appearance.
3. Health criteria .
   i) Questionnaire on medical history especially transmittable diseases,
   ii) Frequency and volume criteria. addictions, previous donation history. Heart, lung, liver, kidney performance.



Computer Control of Donor History and Information

iii) Haematological (Hb and total protein) and medical (pulse, B.P., temperature) examination.

B. **Medical Control**

i) General medical criteria: Federal Regulations, Operating Procedures, Policy.

ii) Specific medical criteria. Consent, frequency of examinations, donation history, clinical biochemistry data and review, immunisation procedures.

C. **Source Plasma Collection**

Donor preparation, equipment set-up, venipuncture and collection, centrifugation, reinfusion.

D. **Section on Adverse Reactions**

This is a section strictly concerned with the actions to be taken in the event of adverse reactions of donors resulting from problems with donation, plasmapheresis, immunisation and symptomatic reactions of temporarily lowered blood volume.

E. **Ancillary Procedures**

Including equipment calibration and maintenance, sterilisation, storage and shipping.

F. **Laboratory Testing**

Sample handling, daily quality control, blood group testing, STS testing, SPE, HB_sAg.

G. **Records and Exhibits**

Examples of forms, reports, labels, formats covering donor identification, medical examination, consent forms, laboratory results forms, processing records, FDA documents.

Rigorous Testing Ensures Consistency and Safety of Product

SOURCE PLASMA should be substantially free from red blood cells, contain not more than a permitted maximum of haemoglobin, have a total protein content of 5.5%, be free from bacterial and pyrogenic contamination and free from HB_sAg, as tested on individual units of plasma, by radioimmune assay or other assay meeting the appropriate Federal regulation (Title 21 CFR 610.40).

The Major Concern is Testing for Hepatitis B Surface Antigen

There is still no completely reliable laboratory test available to detect all potentially infectious plasma donations. However, the availability of hepatitis B serological markers that can be detected by sensitive laboratory techniques has proved extremely useful not only in considerably reducing the incidence of hepatitis B but in contributing to the advances in the knowledge of the pathogenesis of hepatitis B and the associated chronic liver disorders.

Armour uses a radioimmune assay and specifically the Electronucleonics Riausure II technique, regarded as one of the most reliable of generation 3 kits. The Knoxville Laboratories perform over 5,000 tests per day being well equipped and adapted to do so. The test is carried out on each donation and pool as well as the finished product.

Absolute Traceability to the Individual Donor is Achieved

If a donation, when first tested, gives a positive result the test is repeated and if a further sample from the donation is positive and this is confirmed by a neutralisation test, then the donor is classified as positive and excluded permanently from donating.

No unit is shipped if a positive result is obtained even if the positive is shown to be false. Once a unit has been shown to be positive, Knoxville will inform the relevant centre by telex and the unit is quarantined and tagged with the bottom half of a red tag.

The tagged material is resampled and once a unit is confirmed as positive it is destroyed and the centre is given the other half of the red tag and a reconciliation of the red tags between the central laboratories and the collecting centres is made. If a donor gives a sequence of donations of which one is found to be positive then it and all the units after it are destroyed even if the donations subsequent to the positive unit are negative.

Small Factorate Batch Sizes Facilitate Control

All batches of pooled plasma from which Factorate (A.H.F.) is produced comprise donations from only approximately 2,000 donors. Should the need ever arise, under the foregoing system and control, location of the finished product and traceability back to donor is quick, simple and efficient.

Difficulties associated with tracing donors from large pools containing many thousands of donations obtained from plasma brokers and independent collection centres do not arise under the system operated by the wholly owned and controlled Armour Plasmapheresis Centres.

Non-A Non-B Hepatitis

This is now the most common form of hepatitis that follows the transfusion of blood and certain plasma derivatives. Specific laboratory tests for the identification of this most recently recognised type of hepatitis are not yet available so that diagnosis can only be made by exclusion of hepatitis A and B. However, much information is available on its epidemiology and clinical features. Studies of the histopathological sequelae of acute non-A, non-B infections indicate that chronic liver damage, which may be severe, may occur in as many as 40-50% of the patients whose infection is associated with blood transfusion or with treatment by haemodialysis.

Experimental evidence for the existence of at least two distinct non-A, non-B hepatitis viruses has been obtained from recent cross challenge transmission studies in chimpanzees, but final confirmation must await the development of specific laboratory tests for non-A, non-B hepatitis and the identification and characterization of the virus(es).[2]

When reliable serological markers for non-A, non-B hepatitis are available Armour will be ideally positioned to take the initiative. Meanwhile research and development is an ongoing activity aimed at providing increasingly safe therapeutic blood products.

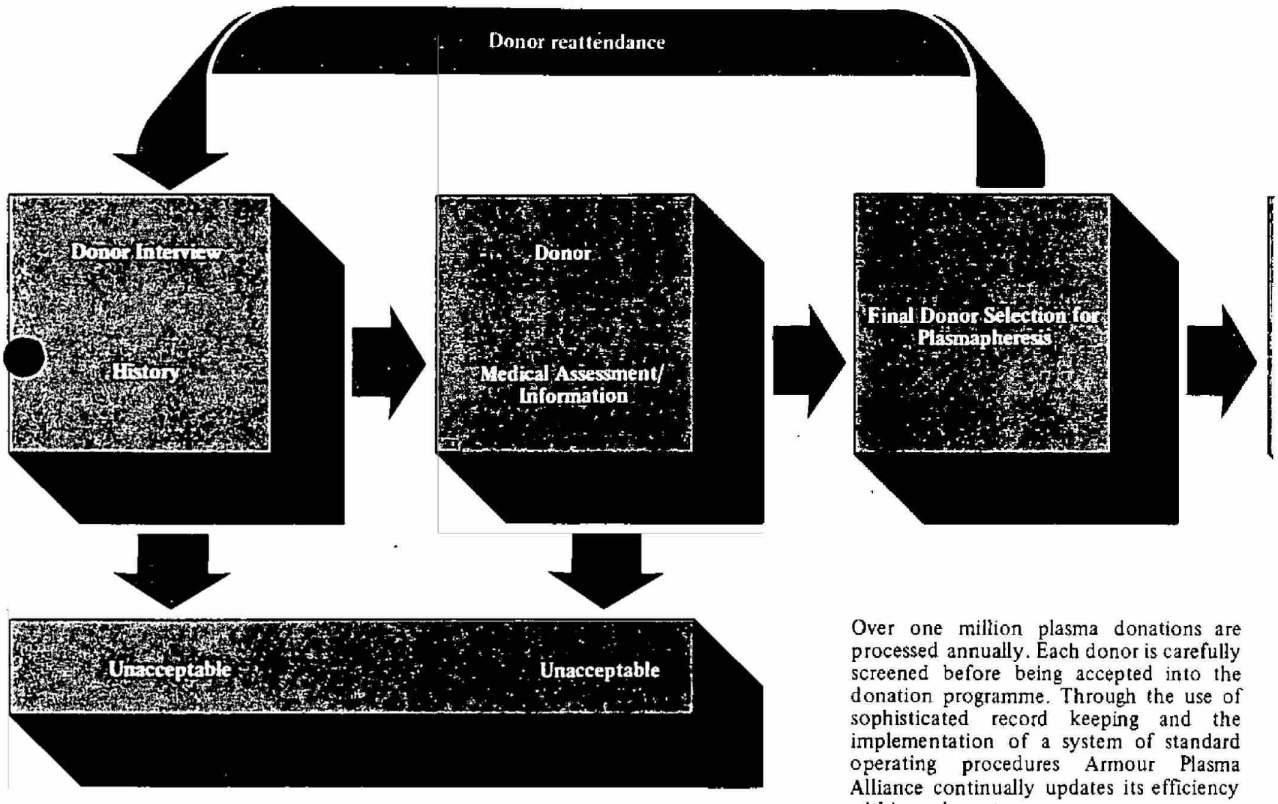
Confidence is Important

All Armour Plasmapheresis Centres are fully controlled by trained, qualified, Armour personnel as are the distribution, fractionating, processing, quality control and research facilities. This self sufficiency, control and long term commitment to the field of plasma fractionation has an important bearing upon the quality, reliability of and confidence in the products produced.

The total Armour operation from individual donor screening programmes to distribution of the final product aims at complying implicitly with the stringent standards laid down by the F.D.A. as well as the D.H.S.S. and other authoritative bodies to the benefit of both donor and recipient.

Armour – a world leader in Plasma Fractionation

ARMOUR PLASMA DIVISION (Plasma Allia



Over one million plasma donations are processed annually. Each donor is carefully screened before being accepted into the donation programme. Through the use of sophisticated record keeping and the implementation of a system of standard operating procedures Armour Plasma Alliance continually updates its efficiency within each centre.

Dr Peter Jones[3], Director of the Haemophilia Centre at Newcastle comments as follows:

"Plasma Alliance employ 888 staff (full and part-time) for the collection, testing and shipping of plasma obtained from paid donors in 22 Centres. Of these, 75 are '40 hour' employees. Total donor beds is presently 1037, with an average Centre size of 40-45 beds. Bed occupancy runs at about 60 percent. Each Centre has a Manager and an Assistant Manager, a Donor Room Supervisor, a member of staff with specific responsibility for quality control and a Physician, who is not necessarily in attendance throughout opening hours. When the Physician is not in attendance, arrangements exist with a local hospital for cover (in those Centres visited never more than 10 minutes away)."

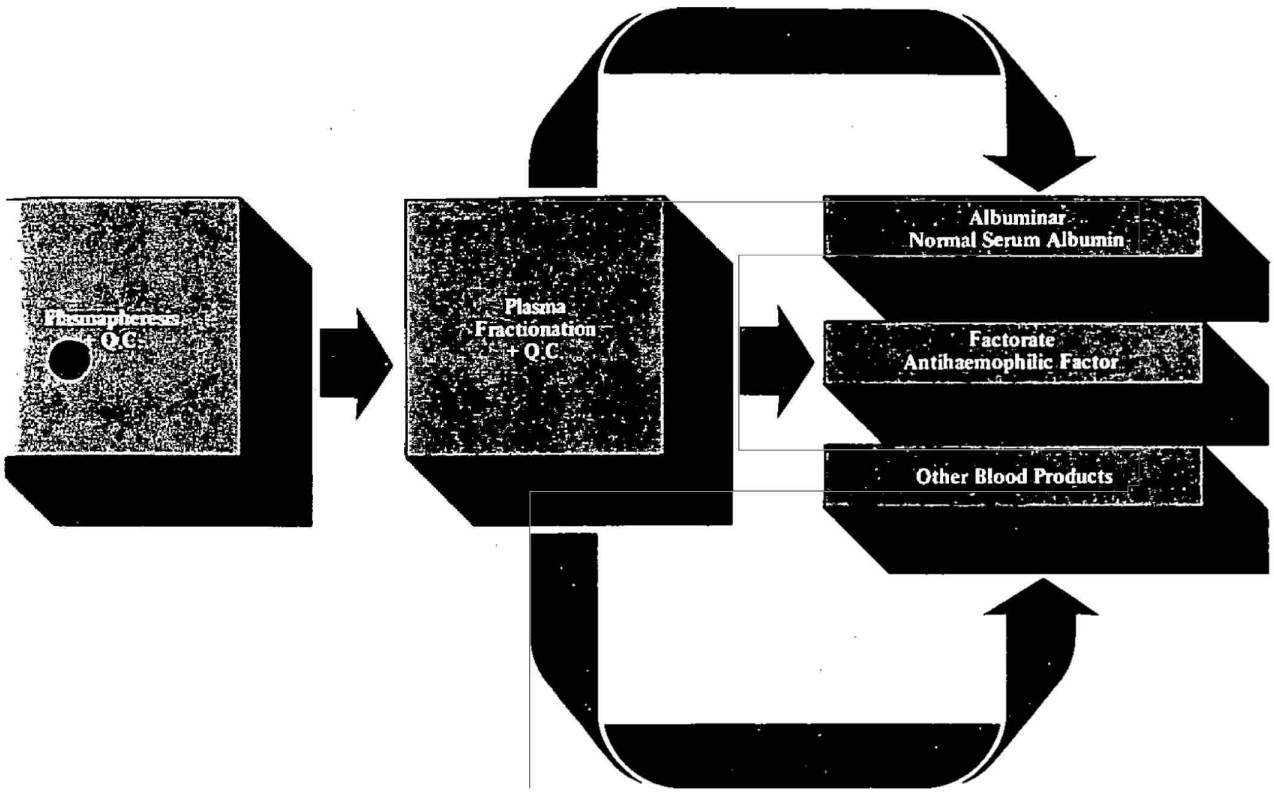
"The regulations for the acceptance, screening, medical examination and plasmapheresis of donors is laid down in the Standard Operating Manual, and was followed through in detail in Knoxville, and in a curtailed form in the other Centres visited. In all cases all operating procedures were strictly observed, and the standard of professional expertise and donor care was impressive."

"Plasma Alliance had taken special care to inform their donors about the procedures involved, and about what happened to their blood/plasma. This is good practice and is commended."

"Of special merit were firstly, the safety checks used by Plasma Alliance to guarantee donor safety and plasma/red cell identification, and the institution of the NABSAF coded system in addition to donor details and signature and bed number is applauded."

"The staff at every centre visited were clean, bright, welcoming and intelligent. Uniform varied in style but was predominantly white and always freshly laundered. Personal hygiene (hair, nails, appearance) was of a very high standard."

ice)



"Donors questioned had no complaints about the procedures and most seemed to enjoy the experience of taking a rest during plasmapheresis. This impression is not in accord with the reportedly low rate of reattendance."

"Donors are looked after by Registered or Licensed Practical Nurses or their equivalent in terms of training."

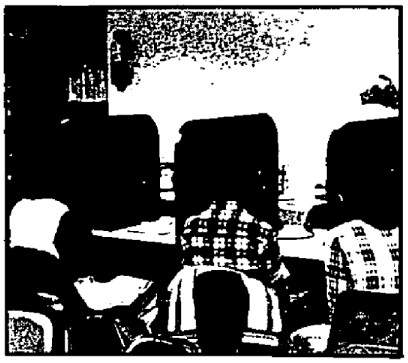
"All Centres were administered under FDA rules. An in-house Standard Operating Manual (SOM) was available in each Centre visited."

"In most Centres visited an attempt had been made to educate the new donors by wall posters and audiovisual displays. In general these were good but there is greater potential here to increase donor 'loyalty' and reattendance."

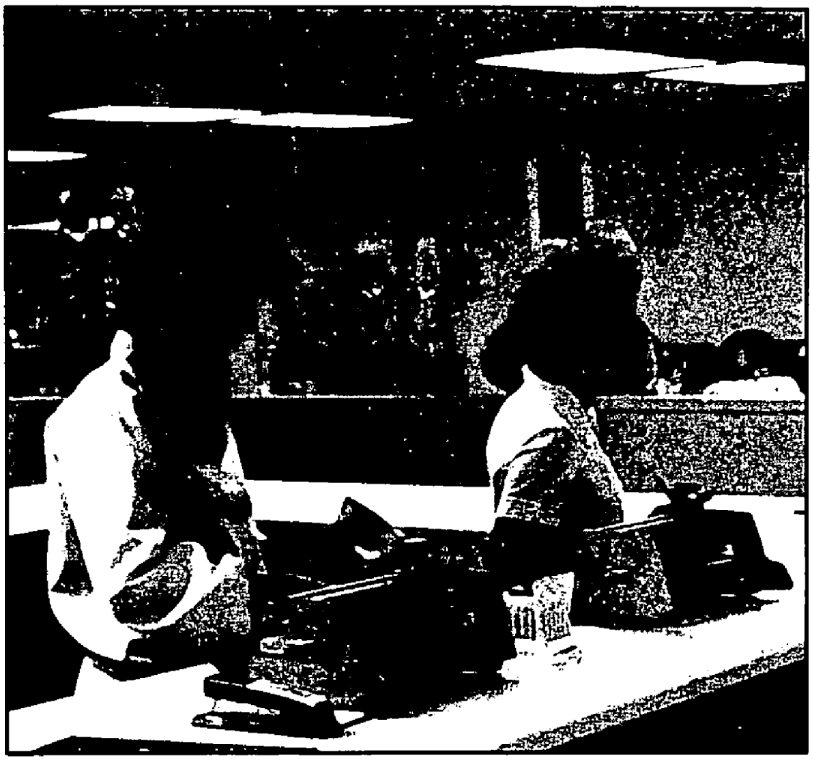
"Plasma collected by Plasma Alliance is shipped to Kankakee for processing in refrigerated lorries. Prior to shipping all plasma is stored in temperature-monitored cold rooms. "Quarantined" plasma is stored separately, and not shipped until cleared by the Company's laboratory."

"The open attitude of the helpful and highly motivated personnel was as apparent here as in the Centres. The impression gained in the short visit, which, for acceptable security reasons, could not include a complete breakdown of the manufacturing process, was very favourable."

Armour's participation in human plasma fractionation has grown into one of the largest fractionation facilities in the world today. An indication of the company's commitment in this area is the investment of £12 million on a new plasma fractionation and sterile filling facility at the Kankakee location. Design concepts and construction materials are the most modern available. The human plasma fractionation operation includes facilities and personnel for the receipt, testing, and storage of human plasma; large scale fractionation; process control and validation; sterile filtration and parenteral filling; packaging and quality control. In addition, a staff of developmental scientists and engineers is involved in the constant improvement and updating of processing techniques and facility design.

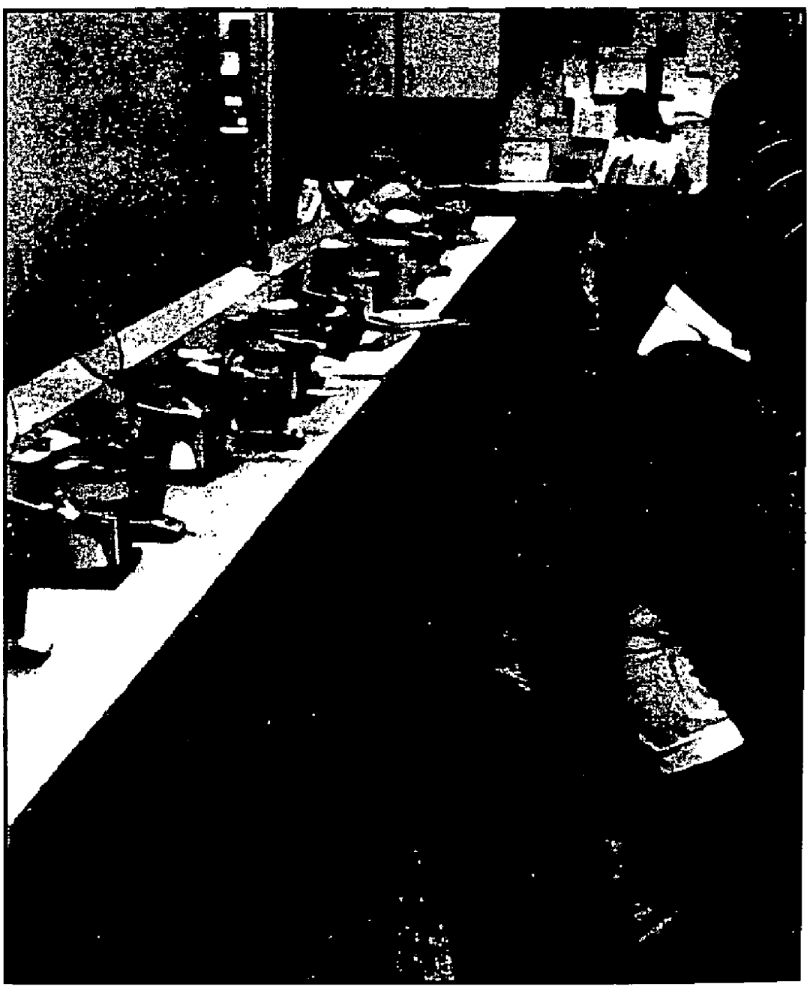


Above: "Centre lobbies were invariably bright and informal with coloured wall hangings. Records were stored within easy reach of the receptionists."



Right: "Security and cross-checking were excellent in all Centres. Here packs are being labelled and checked next to the camera which recorded donor signature as well as names and features."

Above: "The staff at every Centre visited were clean, bright, welcoming and intelligent. This girl checks the blood pressure of a potential donor."



Right: "Laboratory test areas – in this area behind the cubicles were clean and well monitored. Staff were familiar with the correct use of all equipment, and this familiarity was in part responsible for the calm, professional atmosphere evident in even the smallest, most potentially claustrophobic Centre in Atlanta."

Left: "Separation of plasma from red cells after centrifugation. Identity checks used before transfusion of red cells were stringent, quality control and handling excellent throughout in all Centres."

Above: "View of the plasmapheresis area in Knoxville. Although apparently crowded (this was a late afternoon/evening session) adequate corridors separated rows of couches. Television was provided, and this facility together with the opportunity of sitting with friends helped maintain an informal atmosphere."

Centre Left: "Sealed flasks ready for fast freezing. From this stage to factory processing plasma is kept frozen, whether in short-term storage or transit in refrigerated lorries."

Left: "Centrifuge and leaf-press section of Knoxville Centre."

In conclusion:

"General standards were excellent, and there was nothing to criticise in the caring attitude shown by staff at all levels. The complete process, from donor entry to shipment was well organised and efficiently performed within the general guidelines laid down in the FDA and in-house regulations."

ARMOUR FOLLOW 'NOTHING TO HIDE' POLICY

To allay the emotive and unsubstantiated allegations which have been made in connection with the supply of blood derivatives from commercial sources, Armour opened its doors to Dr. Peter Jones, Director of the Haemophilia Centre at Newcastle. Dr. Jones' brief was to visit a number of Armour Plasmapheresis Centres, to talk with management, staff and donors and to report his findings. It was an essential understanding within this agreement that "there was nothing to hide" and that the open nature of the visit would allow Dr. Jones to report freely on all aspects of the organisation.

In general, he found "a first class organisation with a sound commitment to quality control" and that "the recommendations made at the end of this report are made in the light of this overall judgement".[3]

The recommendations made mainly concerned the health and welfare of staff working in the centres and, of course, the donors and included:-

(i) A need for closer liaison between the Director of Medical Services and the physicians working in the centres for the purpose of standardising on medical procedures and practices.

(ii) A review and standardisation of emergency kit contents including the provision of suction apparatus.

(iii) A tightening up of donor confidentiality and continuous medical supervision.

The recommendations made by Dr. Jones have been implemented wherever possible in order to maintain the highest standards throughout the Plasma Alliance Group.

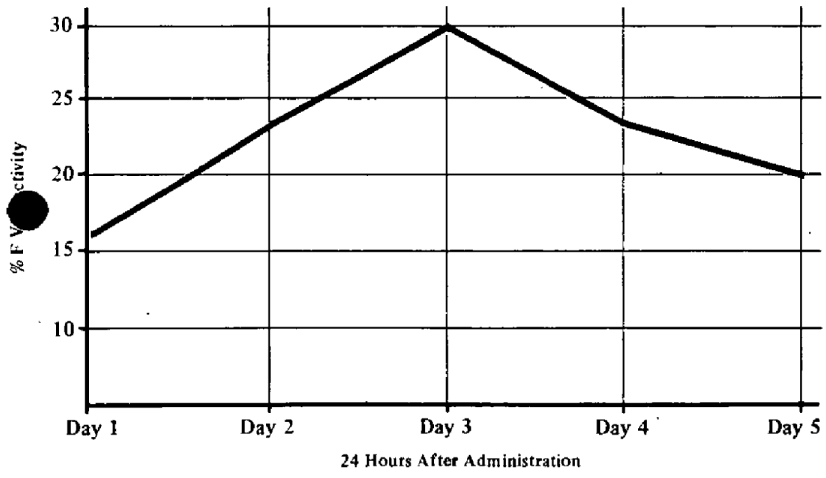
The publication of Dr. Jones' comments on what he saw follows his own recommendation, couched in the following terms: "The 'bad' image associated with procedures involving paid donors has not been helped in any way by secrecy. The organisation managed by Revlon Health Care and Plasma Alliance Inc. is, in my opinion, of so high a standard that it lends itself to a more open attitude. I strongly recommend that consideration be given to more exposure (within the bounds of necessary industrial security)."[3]

ABSTRACTS IN PERSPECTIVE

In each issue of Plasma Perspectives it is intended to include abstracts of recent publications which are of potential interest to readers. It is appropriate that in this first edition we are able to report on the experiences of Paulssen and van Pelt[1] and the oral use of Factor VIII in the management of haemophilia.

Earlier work[2] had demonstrated that oral administration of Factor VIII loaded liposomes could raise plasma F VIII procoagulant activity. Using a different technique, Paulssen and van Pelt were able to bind F VIII from four donors with chylomicra. The ability of this preparation to achieve measurable concentrations in a haemophiliac patient was subsequently demonstrated.

The patient, a 22 month old boy was admitted to hospital with a history of recurrent epistaxis and bruising. His plasma F VIII activity was 8-10% of normal and the related antigen was 0.8 μ/ml. He was diagnosed as having mild haemophilia A. The oral F VIII preparation was administered twice weekly with intervals of 3 and 4 days. Over an eight month period the F VIII emulsion was given 75 times. Subsequently the daily effects of administration were measured. It can be seen from the following chart that F VIII concentrations varied between 20 and 30% 24 hours after ingestion. No circulatory anticoagulants were measurable.



F VIII activity:- Plasma after administration of F VIII orally for four consecutive days

The authors conclude that the daily administration of this oral preparation achieved F VIII concentrations sufficient for prophylaxis and treatment of minor bleeds. They suggest that the findings are indicative of the presence of a depot from which orally administered F VIII can enter the plasma.

"This conclusion accords with that of Hemker et al[1]. We now need more experience, in adults and in patients with severe haemophilia."

References

1) Paulssen, M.M. and van Pelt, B.C. Lancet 1981, I: 1310

2) Hemker, H.C. et al, Lancet 1980 I. 70-71

References

1. "A study of commercial and non-commercial plasma procurement and plasma fractionation"

International Federation of Pharmaceutical Manufacturers Association (I.F.P.M.A.) December 1980.

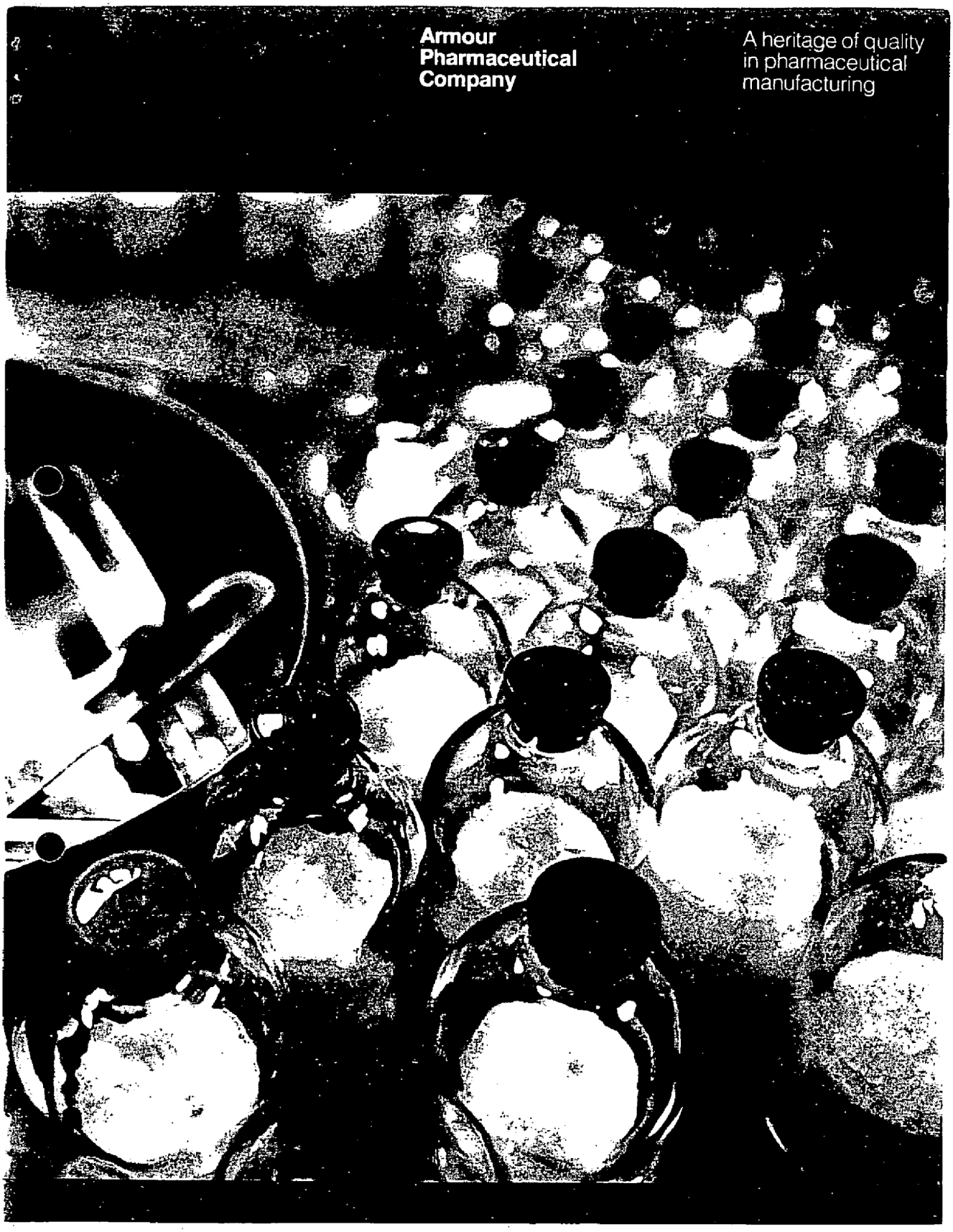
2. Acute viral hepatitis

Arie J. Zuckerman
The Practitioner, April 1981.
Vol. 225 475-486

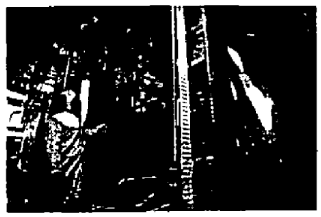
3. A Report on Plasmapheresis in the United States

Confidential Report. P. Jones. June 1980

Photographs produced from the originals by kind permission of Dr. Peter Jones.


Armour
Pharmaceutical
Company
A heritage of quality
in pharmaceutical
manufacturing

Manufacturing excellence.
An Armour tradition.



"We've never compromised on quality. That's why we have such a rich heritage of manufacturing excellence."

[illegible]

From its beginning as a research and production laboratory of the Armour and Company meat packing facility in 1886, Armour Pharmaceutical Company has grown to a leading producer of ethical pharmaceutical and diagnostic products.

Now, a major part of the Ethical Products Division of the Revlon Health Care Group, Armour is continuing its tradition of manufacturing excellence and innovation. Today, Armour Pharmaceutical is a recognized leader in the fields of plasma fractionation, peptide synthesis, biochemical extraction, pharmaceutical formulation and glandular derivation.

At the Kankakee, Illinois, manufacturing facility, Armour people are working with the most advanced production equipment available in one of the industry's most modern physical plants. Continuing capital commitments from Revlon, ensure that the manufacturing process here will not only conform to, but actually exceed the strict guidelines established under the Food and Drug Administration's Good Manufacturing Practices.

Armour's worldwide reputation for quality is maintained through total control of the manufacturing process — from raw materials collection to final packaging. The acquisition of Plasma Alliance Inc., a nationwide system of plasma collection centers, in 1978, along with other long-term raw material supply contracts, assures steady, high-quality sources of essential ingredients. And, a totally integrated manufacturing, packaging and distribution process affords the highest degree of quality control.

Product quality through manufacturing excellence — at Armour Pharmaceutical, it is an intense commitment shared by every employee.

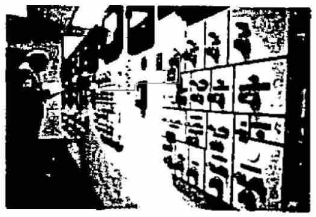
Human plasma fractionation process (top, 1).

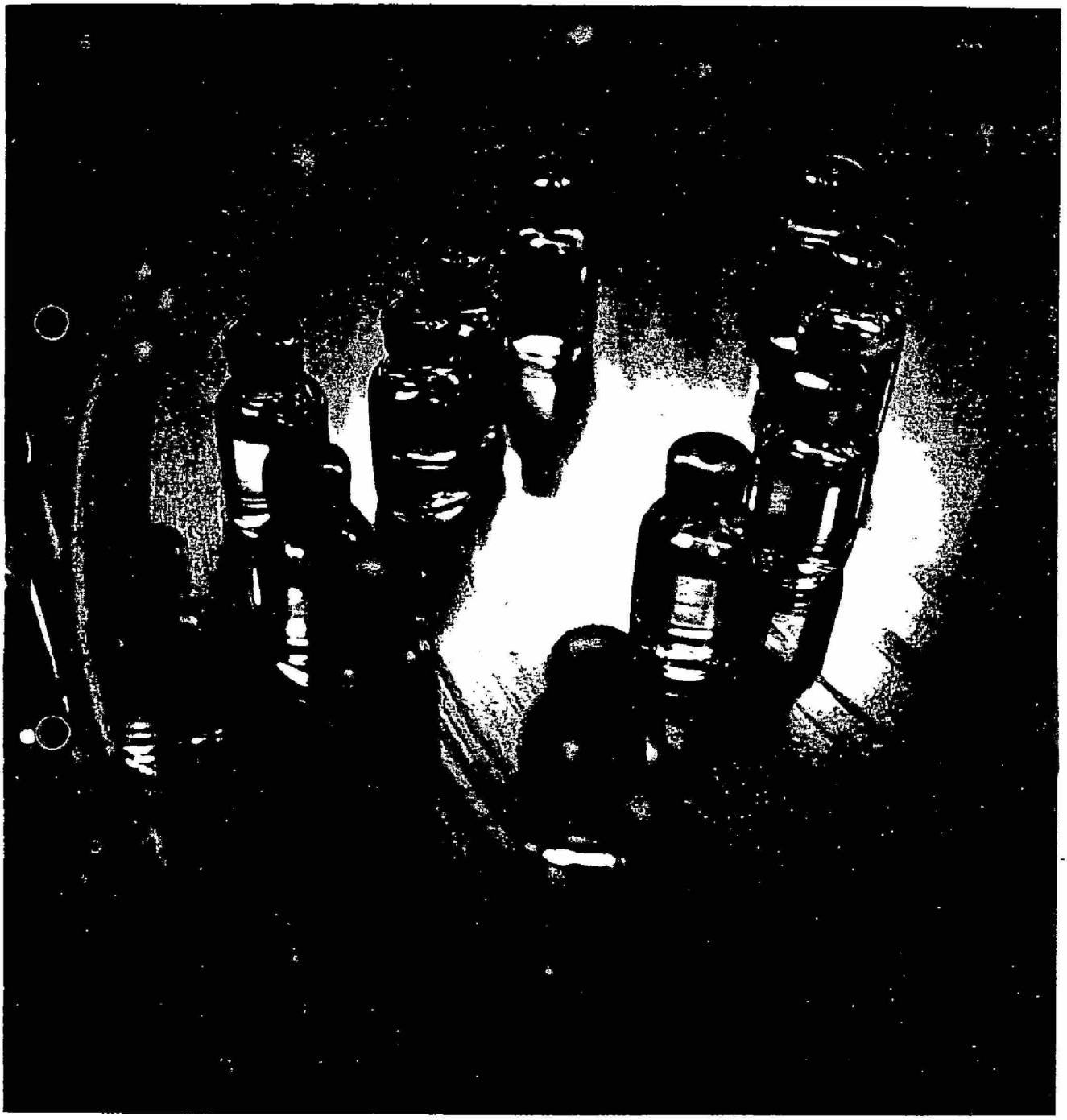
Factorate®, anti-hemophilic factor, aseptic lyophilization (top, 2).

Ultrafiltration of bovine plasma products (top, 3).

Monitoring of lyophilization process (top, 4).

Manufacture of H.P. Acthar Gel®, repository corticotropin injection (large, center).





ARMOUR001920

Kankakee.
A facility ahead of its time—engineered with the same care as Armour's products.

"We're constantly updating this facility to accommodate new products and new technologies. We think it's one of the best in the industry."

Walter Kennon
Director of Engineering

Armour's Kankakee, Illinois, manufacturing facility, originally constructed in 1953 and modernized in 1981-82, is a multi-structured complex of fifteen interconnecting buildings on a 65-acre tract. Serving as the hub for Armour's worldwide distribution system, the plant houses complete facilities for raw materials receipt and storage, biochemical extraction and purification, plasma fractionation, pharmaceutical formulation, tableting and milling, parenteral filling, peptide synthesis, pilot production, packaging and distribution.

The various departments within the plant are run as self-contained units to allow for maximum sterility and integrity of each product line. A recent multi-million-dollar expansion and modernization program has not only up-dated the facility's critical manufacturing areas, it also has provided several state-of-the-art improvements that are totally unique to the industry. Improvements such as a new double HEPA-filtered air system that changes the air in the sterile filling chambers 300 times an hour, exceeding FDA standards by as much as 10 times in some areas. Terrazzo floors and welded PVC walls — designed for ease of thorough cleaning. Automated inspection equipment to improve product monitoring. And, in the long-term, a totally computerized manufacturing planning and control system that will help coordinate inventory levels with manufacturing plans.

A separate facility near the main plant is the nucleus of Armour's national and international distribution system. Here, product inventory is maintained and matched with worldwide shipments.

From raw materials receipt to final packaging and distribution, Armour's Kankakee facility provides total control of the manufacturing process, ensuring product quality and consistency.

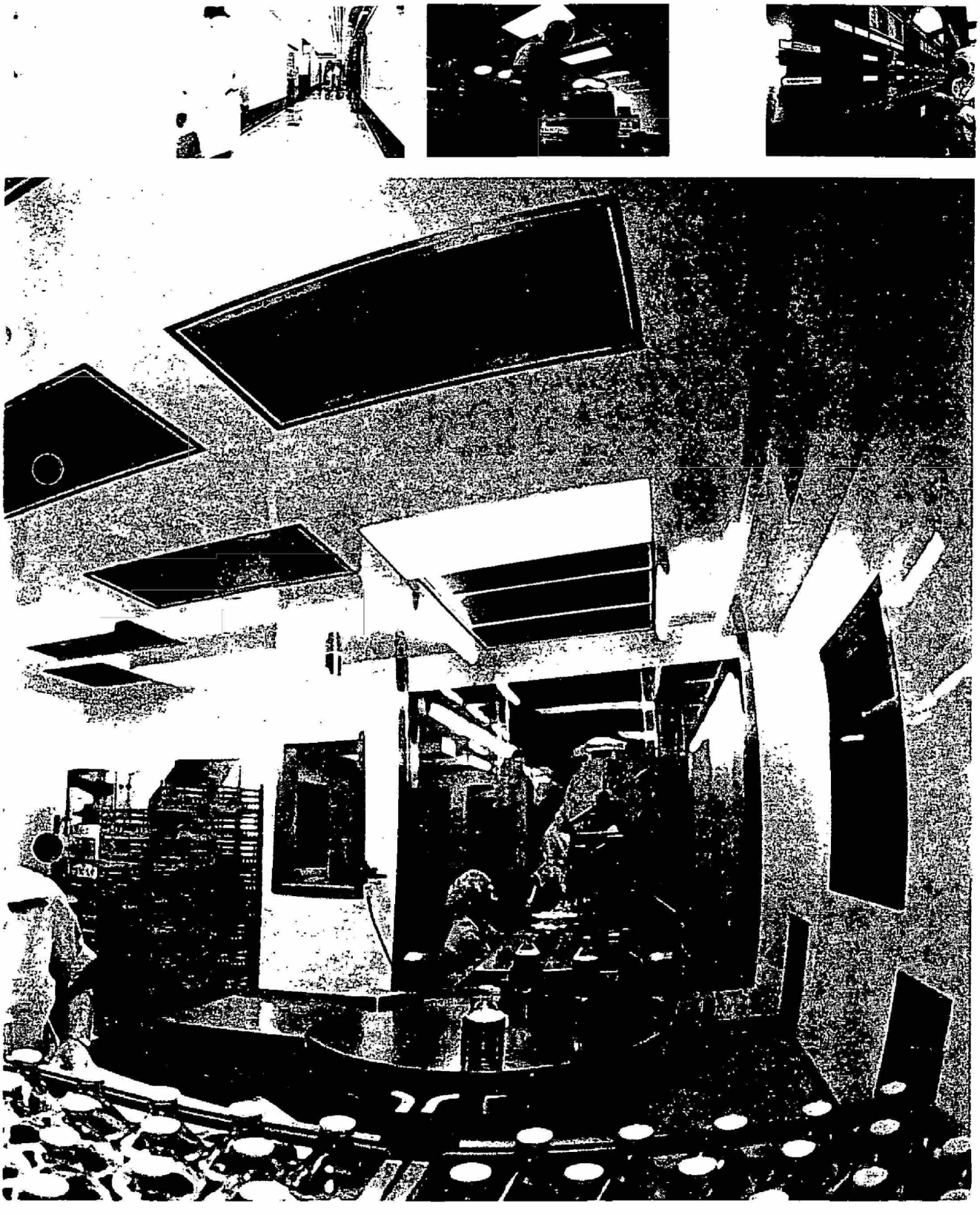
Armour Pharmaceutical's Kankakee, Illinois, manufacturing facility (top, 1).

Interior of the human plasma processing facility (top, 2).

Manufacturing area of Albuminar®, normal serum albumin (top, 3).

Microprocessor control of Factorate®, anti-hemophilic factor, process (top, 4).

Aseptic filling of Albuminar-5®, normal serum albumin (large, center).



ARMOUR001922

The Armour product.
Potent, pure and backed by intensive laboratory and clinical investigation.

"We manufacture a wide spectrum of pharmaceuticals – hospital care products, others used in diagnostic and research laboratory situations and products detailed directly to [redacted] cians."

In 1886, Armour Laboratories was established to develop medical products from the by-products of the meat-packing industry. From this early pioneering work, which led to significant findings in the usage of glandular substances, Armour Pharmaceutical Company has grown to a diversified manufacturer of over 200 products for health care and research.

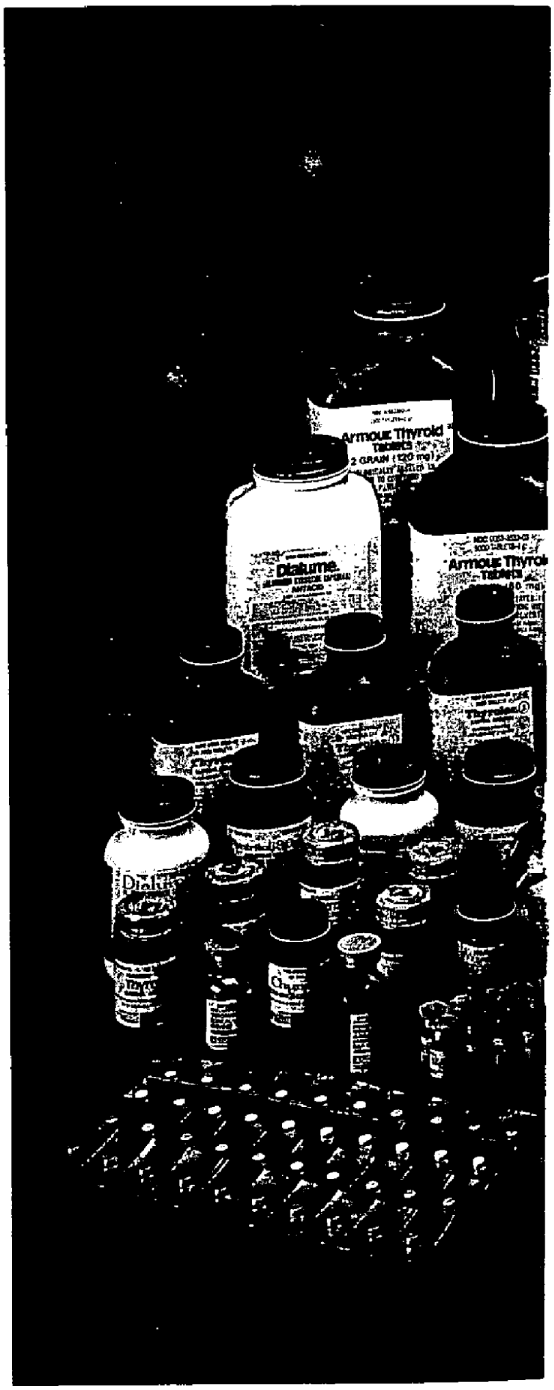
The current product line consists of *plasma derivatives* for treatment of shock, coagulation disorders and infection; *clinical pharmaceuticals* for treatment of thyroid disorders and bone diseases; *biochemical products* for use as pharmaceutical and diagnostic ingredients and growth medias used in research laboratories; and *vitamin products*.

Armour's developmental work in the standardization of natural thyroid products has made it the world's leading supplier of desiccated thyroid tablets. And, Armour's *Calcimar*® a calcium regulating hormone, is the largest synthetic molecule manufactured commercially.

In the area of plasma derivatives, Armour has, in its Kankakee plant, one of the world's largest plasma fractionation facilities. Products such as *Factorate*® — a coagulation factor concentrate for treatment of hemophilia, *Albuminar*® — a normal serum albumin used in burn and shock therapy and *Gammar*® — an immune serum globulin used to provide passive immunity against a variety of diseases, have all earned widespread professional acceptance for their exceptional high quality and potency.

Armour's line of fine biochemicals is manufactured under stringent quality assurance conditions. *Rehatuin*® — a sterile fetal bovine serum used in cancer research, *Bovine Serum Albumin* — a necessary ingredient of serologic and diagnostic reagents, and *Purified Hormone Preparations* — widely used in research laboratories, are among the standards in the industry.

Through substantial documentation, Armour products are known for their high quality, potency and consistency.



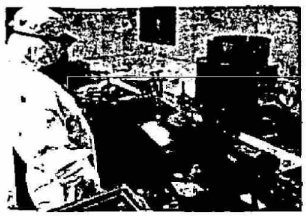
Manufacturing Development's role (top, 1).

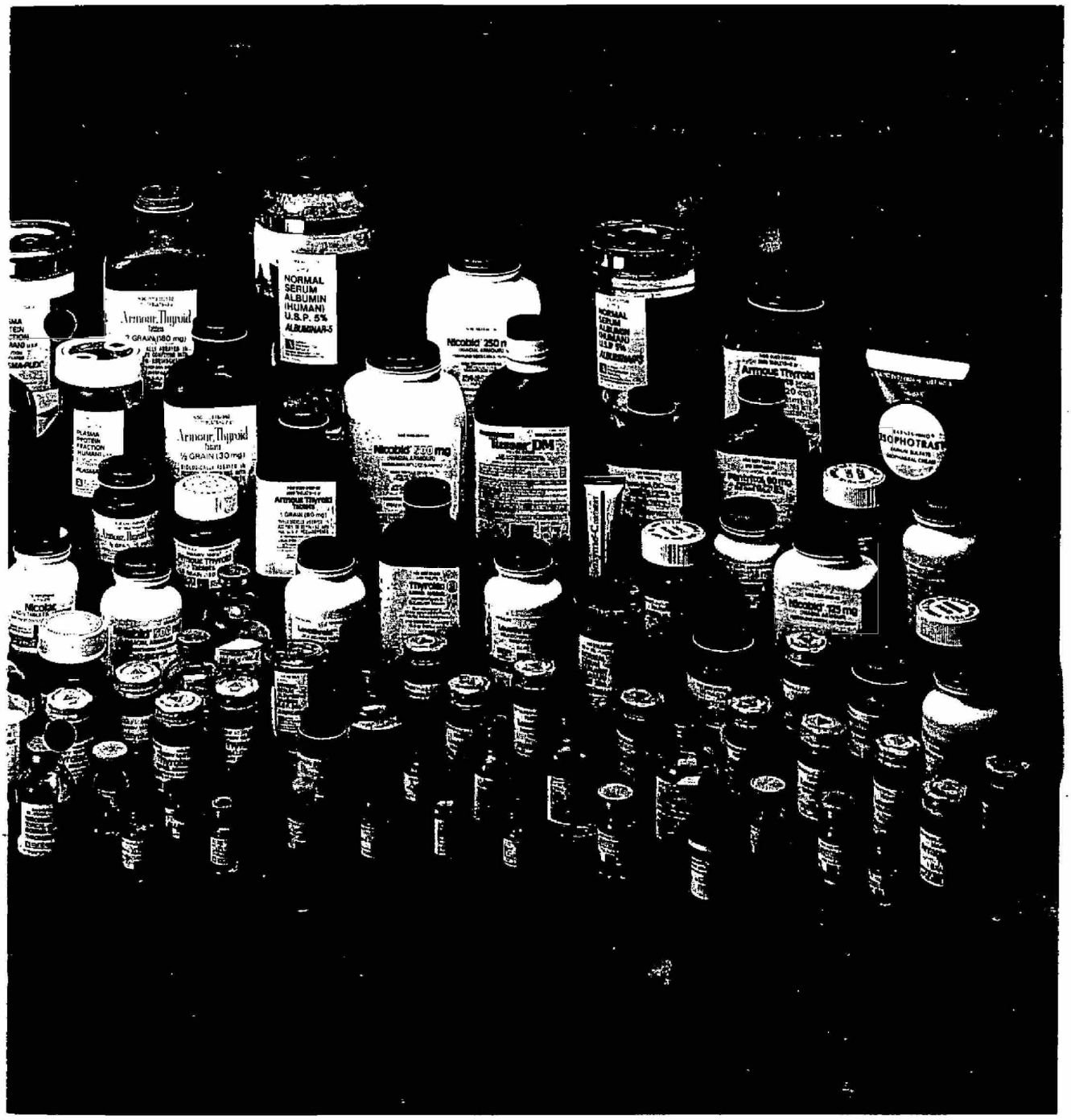
Aseptic fabrication of injectable drugs (top, 2).

Biochemical manufacturing area (top, 3).

Synthetic peptide manufacturing (top, 4).

Some of the wide variety of products manufactured by the Armour Pharmaceutical Company (large center).





ARMOUR001924

Armour Quality.
Built in at every step of the manufacturing process.

"When we say Armour Quality – we mean it. We take a tremendous amount of pride in the quality of our products."

Barry Hal
Director of Quality Control

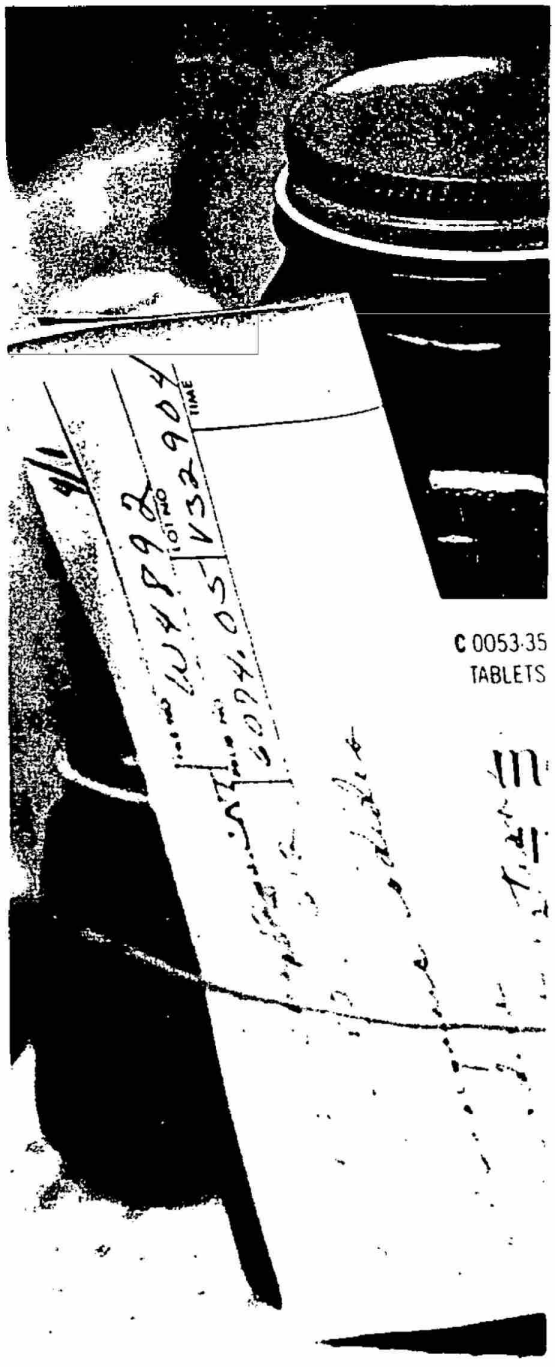
Armour Pharmaceutical Company has been meeting and exceeding the industry's stringent demands for high quality for nearly a century. Through its entire line of over 200 time-tested products, Armour builds in quality at every critical step of the manufacturing process.

Quality assurance begins with the collection and receipt of raw materials. Armour not only tests these essential ingredients, but also controls the actual collection of human source plasma through its affiliate, Plasma Alliance. With its nationwide system of collection centers, Plasma Alliance has earned a worldwide reputation of its own for product quality and dependability.

Product quality is further maintained through rigorous testing throughout the production process by the Quality Control Department. Representing almost one-seventh of Kankakee's entire work force, this department monitors each manufacturing area to ensure correct procedures are followed, samples every product at critical stages of production and tests the finished product against an exhaustive set of specifications before its final release.

Because they are making products which often have crucial impact on people's lives, Armour people are instilled with an on-going quality consciousness. From the beginning, each manufacturing employee is required to participate in the Armour Quality Assurance program under the supervision of the highly trained Quality Assurance Staff. Additionally, seminars and meetings on various aspects of The Food & Drug Administration's Good Manufacturing Practices, are held on a regular basis for operators and supervisors.

Throughout the Kankakee facility, Armour people have set their own standard for quality. It's called *Armour Quality*, because it exceeds what is required — and it is built in at every step.



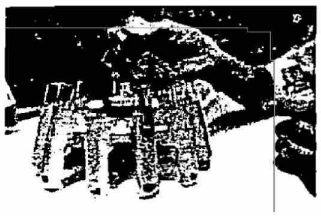
Quality control testing (top, 1).

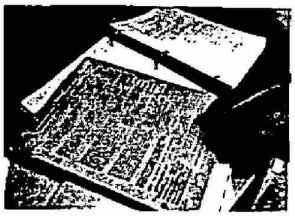
Factorate®, anti-hemophilic factor, testing (top, 2).

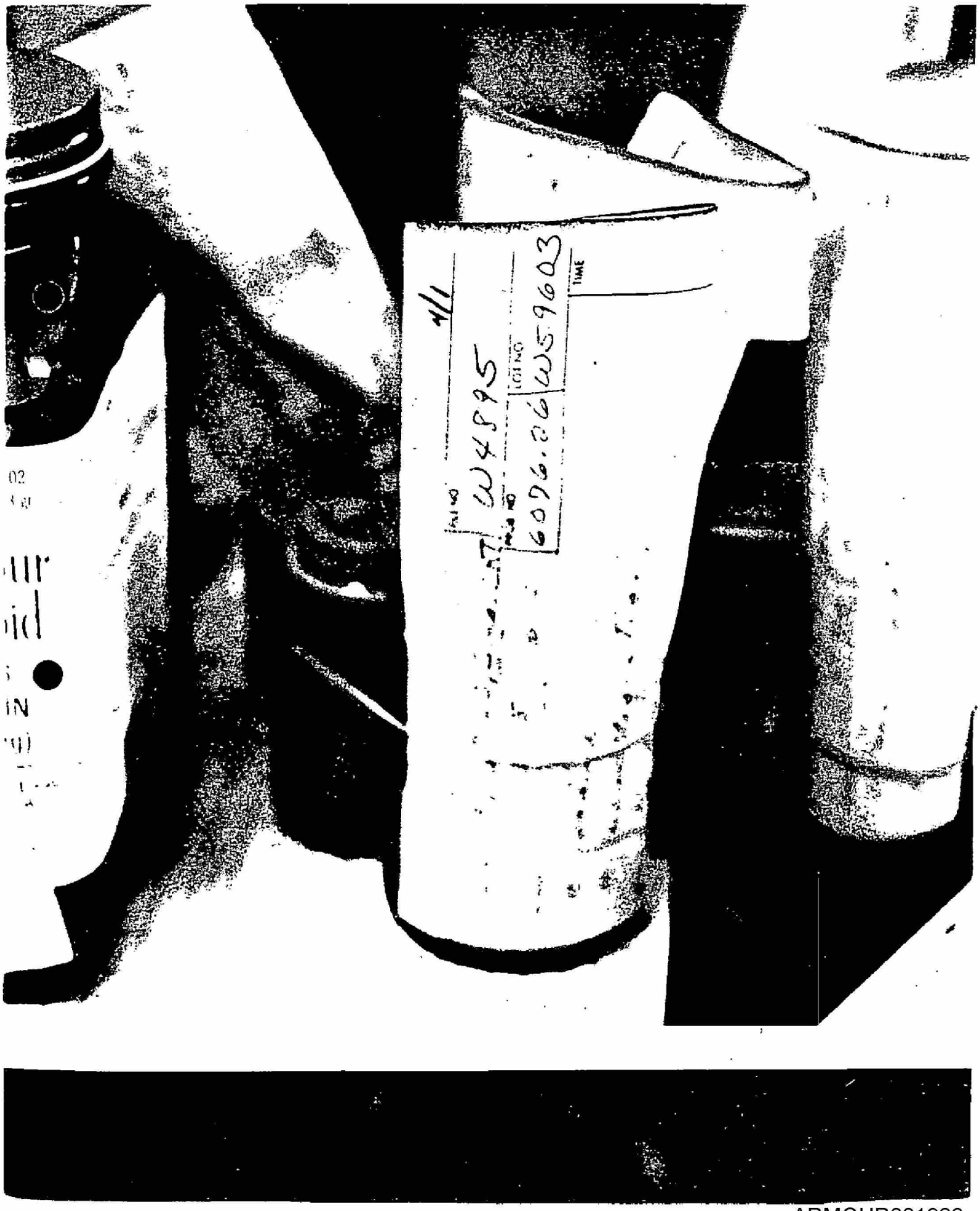
Inspection of Albuminar-25®, normal serum albumin (top, 3).

Quality assurance auditing procedure (top, 4).

Armour Thyroid® products awaiting quality control assay (large, center).







ARMOUR001926

Armour people.
Committed to excellence through teamwork and experience.

"Employees are the key. Our people take their work very seriously. When you're making products that save lives, you really care about what you're doing."

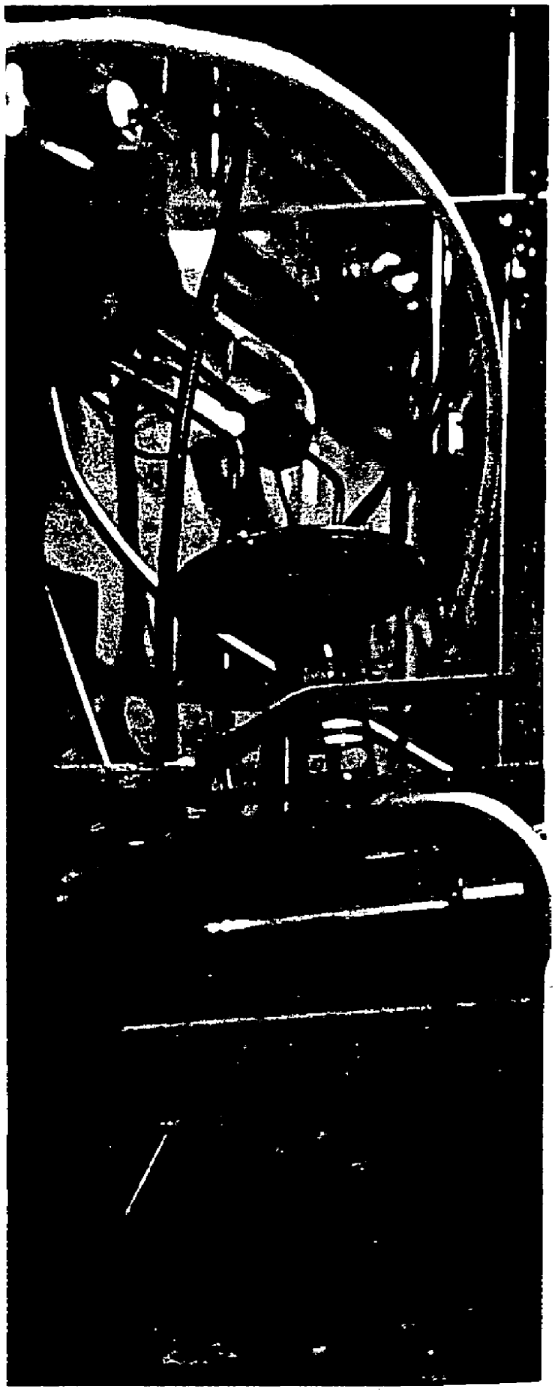
Armour's broad capability in producing quality ethical and diagnostic products for health care requires the talents and teamwork of a great many people. Scientists, engineers, managers, operators, supervisors, maintenance workers, clerical people — all uniquely blended to bring the greatest amount of expertise to bear upon product quality and performance.

Historically, Armour people have been pioneers in the development of many important pharmaceutical processes. And, today, through the efforts of the Operations Services group at Kankakee, new Armour products are being transformed from bench scale development to manufacturing reality. This team of scientists and manufacturing experts is responsible for the establishment of manufacturing standards, product line expansions, cost controls and production problem-solving. Their work has led to improved manufacturing efficiency and has established industry standards in assaying methodology.

In the manufacturing area, Armour people reflect a pride and dedication that has been built through years of experience in producing high quality products. The average length of service for the work force at Kankakee is 10 years, and many of the supervisory personnel have worked their way up through the manufacturing ranks to the management level. Frequent training and cross-training programs assure high levels of job performance and satisfaction.

The facilities management group at Kankakee works 24 hours a day, 7 days a week to ensure that the 6 acres of physical plant with its highly sophisticated equipment is properly maintained and immaculately clean. These highly-trained people perform some of the most vital tasks in the plant and are always on call.

Armour people at every level at Kankakee reflect an attitude of intense commitment to the quality of *their* product — whether it be typing a letter or filling a sterile vial. Through their efforts, Armour has earned a worldwide reputation for quality and dependability.



Left to right: Dr. Ron Orlowski, Technical Manager, Synthetic Peptides; Mr. Jay Sevcyler, Production Manager, Synthetic Peptides; Mr. Robert Colescott, Development Scientist (top, 1).

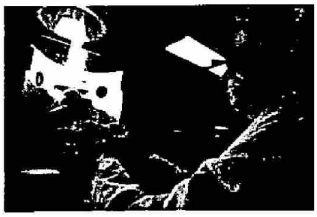
Mr. James Holcombe, Development Scientist (top, 2).

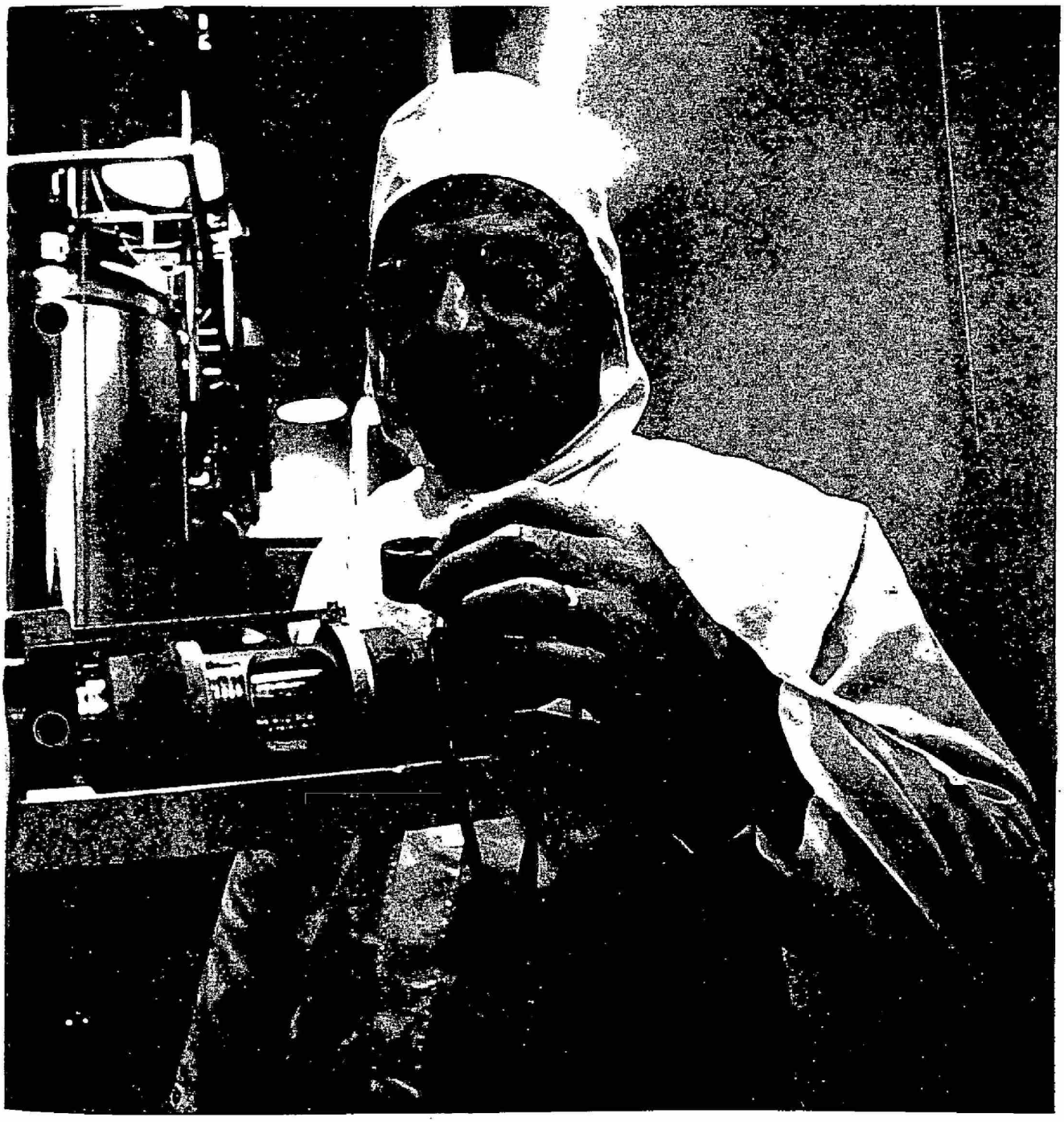
Mr. Donald Wesoloski, Senior Quality Control Analyst (top, 3).

Mrs. Bernice Fonin, Packaging Operator (top, 4).

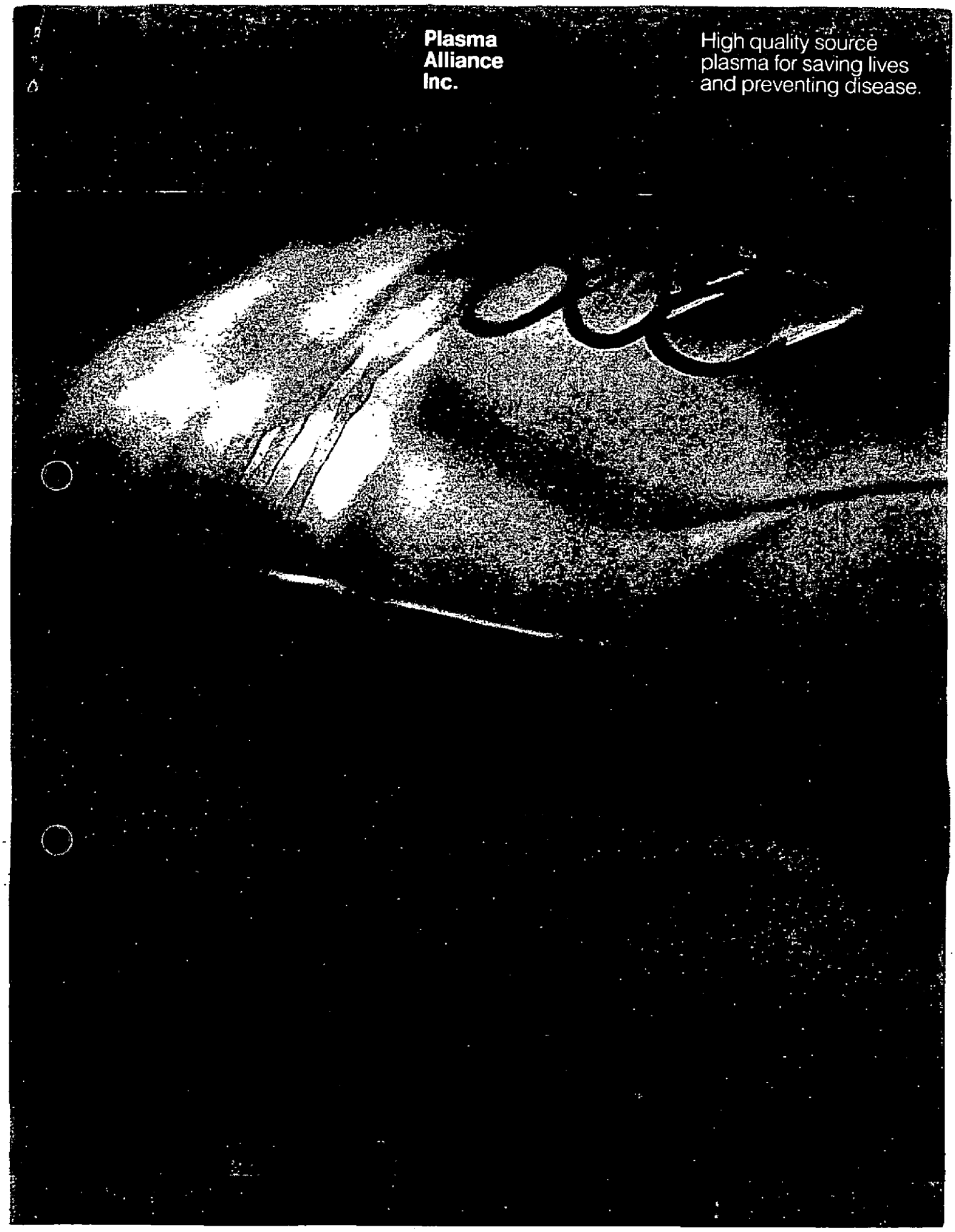
Mr. Bob Humphrey, Production Checker (large, center).

ARMOUR001927





ARMOUR001928



ARMOUR001929

ARMO0000229_0020

Plasma Alliance.
People producing vital source plasma for products that save lives and prevent disease.

"Plasma Alliance has earned the reputation of being one of the most dependable suppliers of source plasma in the world. And, we've done it because of our people."

– Ty Foster
Vice President, Operations

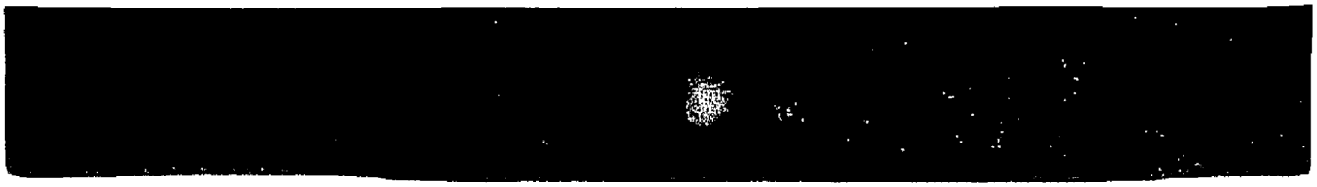
During World War II, it was discovered that portions of the blood known as plasma could be used for whole blood replacement. The first derivative to be extracted was serum albumin, initially used as a volume expander for battlefield injuries and then for other cases of severe blood loss.

Today, the products derived from plasma include Factor VIII — for treatment of classic hemophilia, immune globulins — used to provide immunities against measles, mumps, tetanus, pertussis and rubella and normal serum albumin — used in surgery and for treatment of burn victims.

At Plasma Alliance, a world leader in plasma collection and a member of the Ethical Products Division of the Revlon Health Care Group, there are many people working to provide a consistently high quality of source plasma for these products. People whose commitment to excellence has earned for us a reputation for quality and dependability that is unsurpassed by any other in its field.

Plasma Alliance. People helping people by providing a vital product that helps save lives and prevent disease.

Blood donations collected at Plasma Alliance centers (top, 1) are then centrifuged (top, 2) to separate the source plasma, used in surgery (top, 3), for manufacture of Factor VIII (top, 4) and serum albumin (large centers).



ARMOUR001930

ARMOUR001931

The Plasma Alliance donor.
A normal, healthy individual who is carefully screened, selected and monitored.

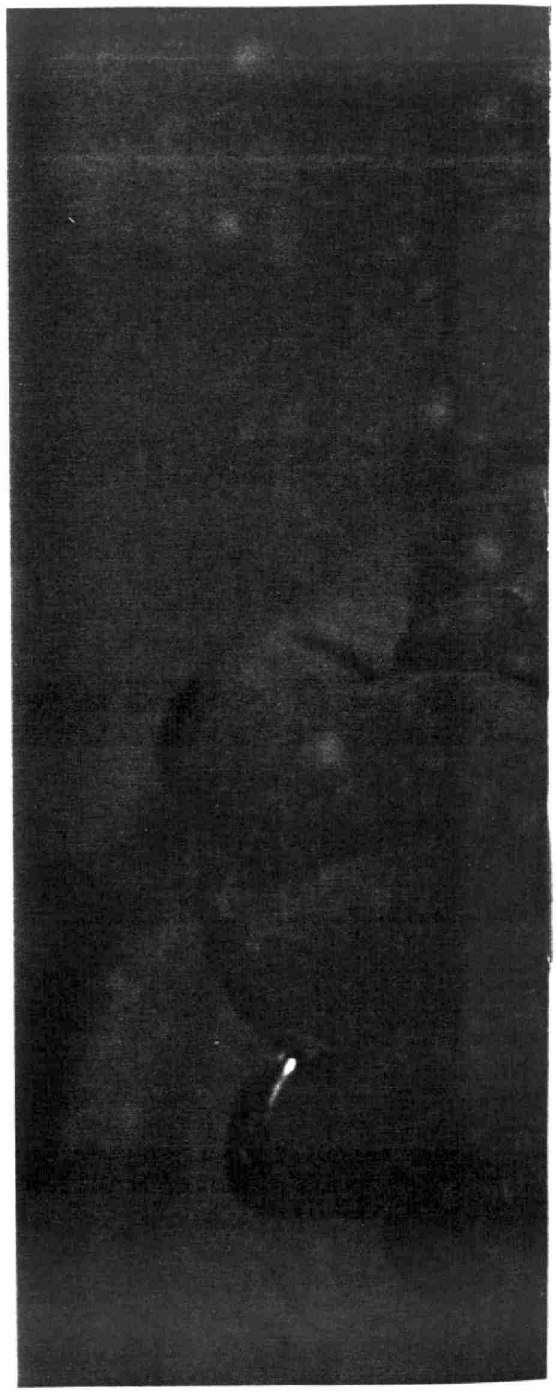
"We're looking for the kinds of donors who are healthy young people who are local, repeatable donors. We are not looking for people who are in the hard roads of life."

The quality of the Plasma Alliance product is largely due to the quality of the donor. In each of our centers nationwide, special care is given to the screening of each individual before he is allowed to join the plasmapherisis program. An initial physical examination is conducted by a Plasma Alliance physician, followed by a check-up each time he comes in to donate. In fact, a regular Plasma Alliance donor is checked and tested more often than the regular population.

To make certain the prospective donor has not been rejected for any reason in the past, current files and extensive cross-referenced microfiche records are checked daily.

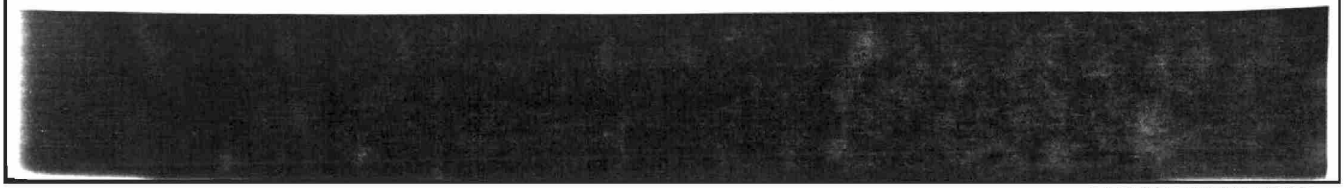
Once a donor is approved, the entire plasma collection procedure is thoroughly explained. Since plasmapherisis is unique in that a donor must be reinfused with his own red cells, the donor must be completely familiar with the process. During donation, Plasma Alliance nurses and technicians check and double-check each donor frequently to insure his safety, and thus, the safety of our product.

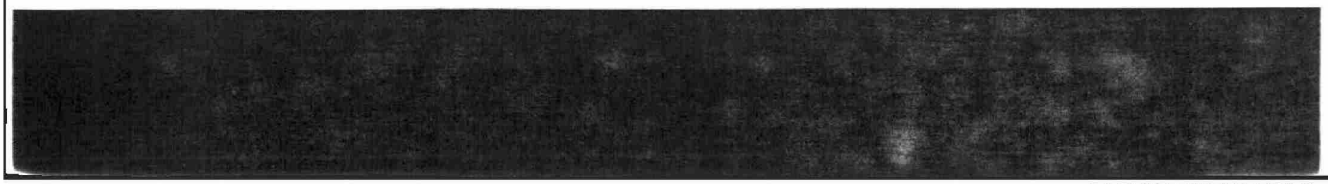
For Plasma Alliance and for the many people needing the products derived from plasma, a donor is a valuable asset to his community and to the quality of our product.



Plasma Alliance nurses and technicians monitor each donor carefully, step-by-step, and a special lock and key system stops the process that each donor will get back his or her own red cells.

The entire donation process takes approximately two hours, and donors can relax, read or watch TV during the time.





ARMOUR001933

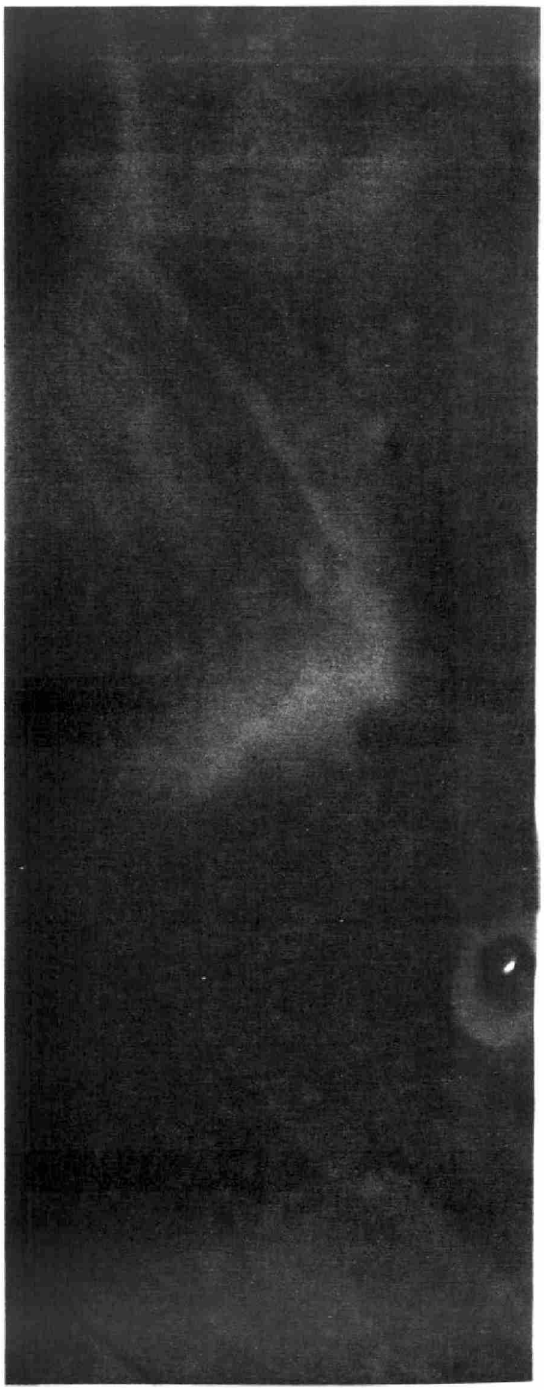
Quality and dependability. Setting a standard of excellence and professionalism that is above what is required.

"We will run 1.2 million tests a year – particularly for hepatitis. And our immunology laboratory is very specialized in the sense that they are doing fairly sophisticated tests that are unique the blood banking ustry."

Each year, Plasma Alliance processes approximately one million liters of source plasma. At the heart of our widely respected quality assurance program is one of the industry's most experienced professional staffs working with state-of-the-art instrumentation and technology. Utilizing advanced screening and testing procedures that begin with donor selection, Plasma Alliance people are dedicated to maintaining the strictest quality control in all phases of operation.

To keep everyone aware of regulatory requirements, we have implemented a "Good Center Practices, Plus" program at every center. We want to develop an attitude among our people that, at Plasma Alliance, we have the people and the technology to exceed what is required.

Since 1972, when Plasma Alliance began its plasmapherisis program, we have been working to improve our screening and testing methods. Constantly surveying the market for even better instrumentation and equipment. Finding more effective ways of attracting and screening donors. Working with the major pharmaceutical companies and universities in conducting research programs. This keeps us constantly familiar with new drug procedures and with the exacting requirements needed to maintain the integrity of data and supply.

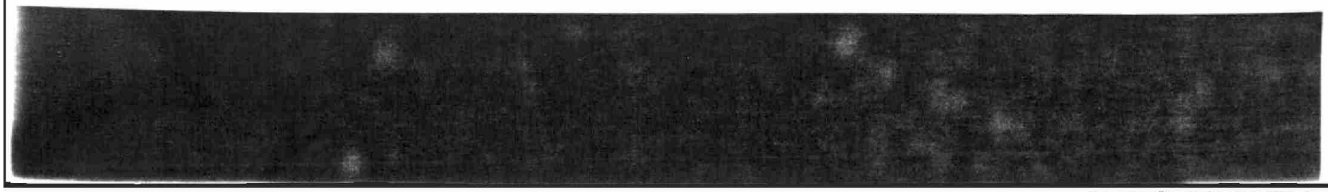


Sophisticated quality control procedures ensure donor safety and product quality. Samples drop, 1 into all protein electrophoresis and serology testing drop, 2 is for ABO blood grouping.

RIA testing drop, 3 indicates Plasma Alliance donors are among the safest of all.

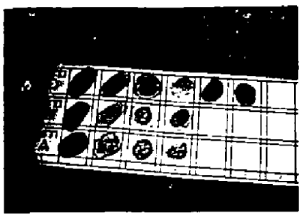
Hemoglutination titer plates for antibody testing drop, 4.

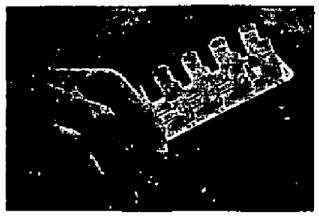
Central laboratory testing for hepatitis (large-centers) must occur before plasma can be released for shipment.

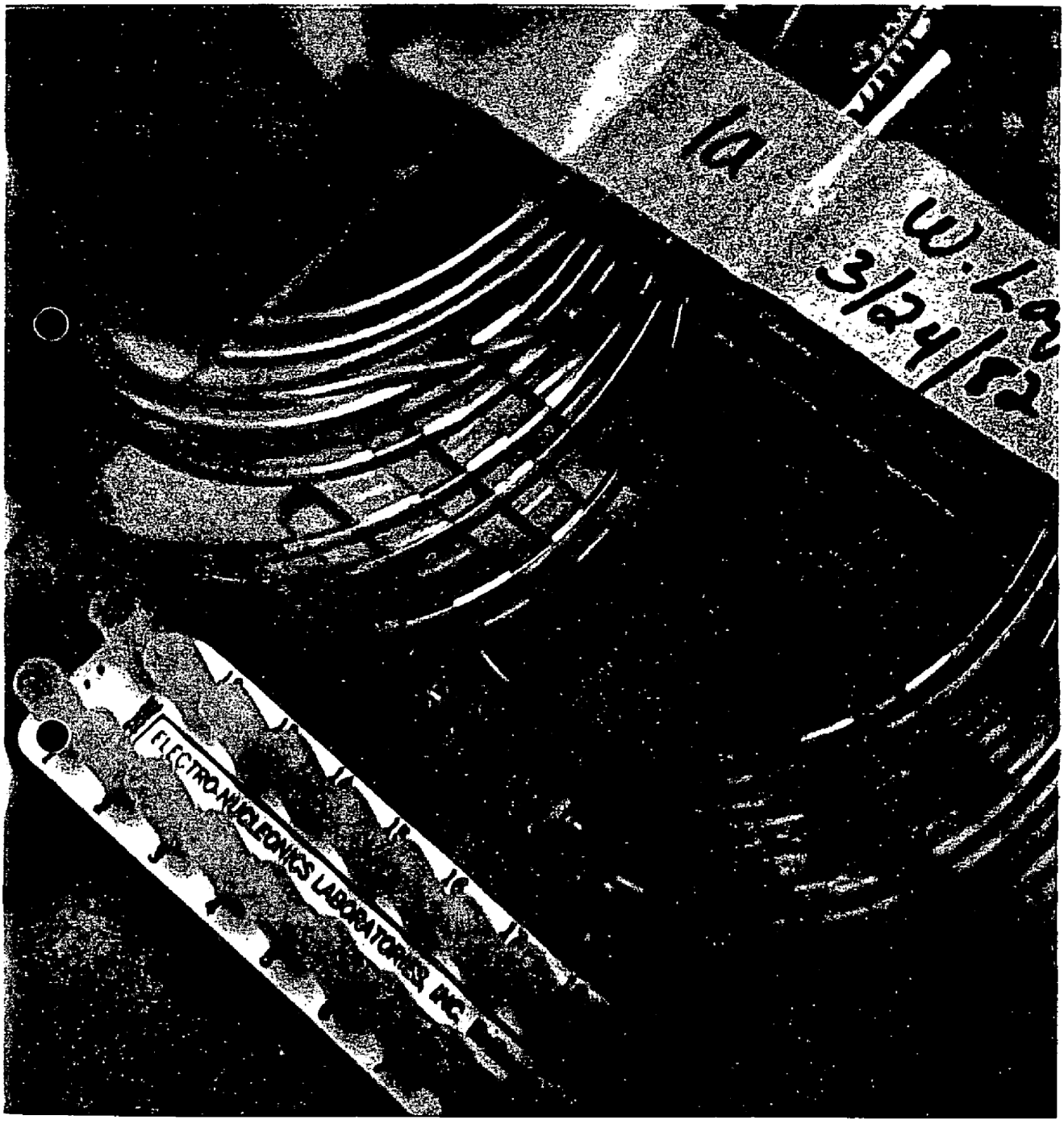


ARMOUR001934

ARMO0000229_0025







ARMOUR001935

Shipping and delivery. Making certain the high quality is maintained from collection to destination.

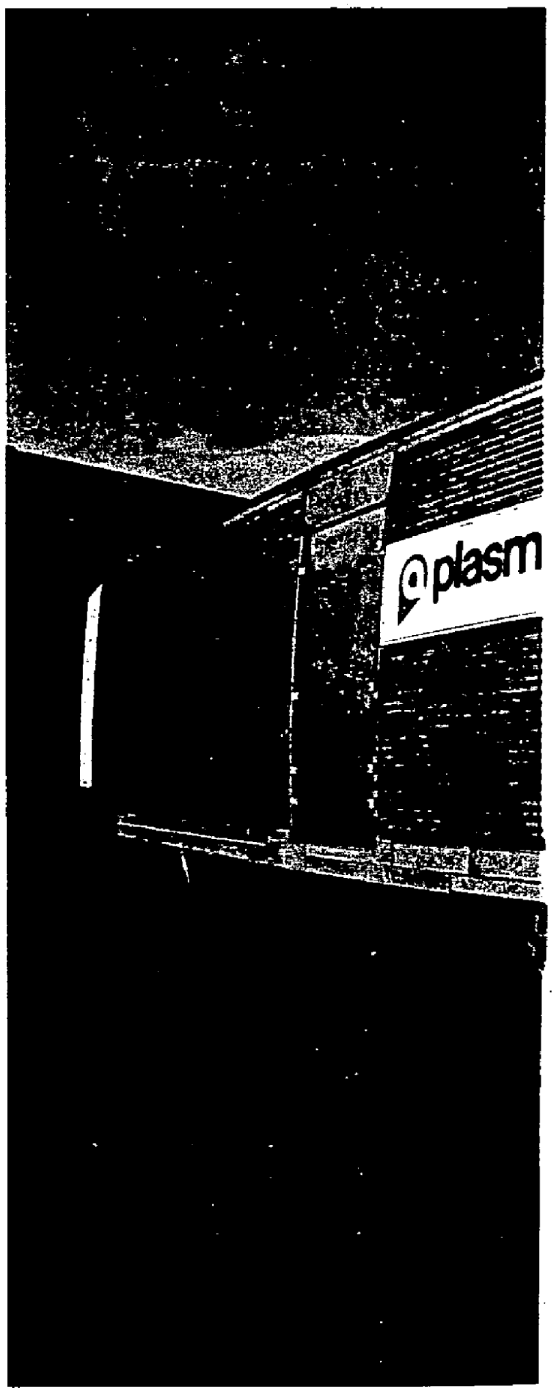
"As the centers produce plasma, it is held in quarantine in each location until it is released for shipment. Our tractor trailers will hold about 10,000 liters of plasma and we can unload it in a matter of minutes."

- Dave Gowin
Distribution Manager

Maintaining product integrity from donation to delivery merits special attention in each Plasma Alliance center. Immediately after collection, the plasma is recorded on our worksheets, permanently sealed and then flash-frozen at a -70° or colder. After this has occurred, it is removed from the liquid freezing units and placed into a quarantine freezer where it is held until all testing has been completed and the plasma is released for shipment.

Quality control is maintained all the way through a packaging and delivery system tested and perfected over many years and many miles. It is based on careful packing at the centers, close monitoring of temperatures enroute and fast, efficient transport. Each of our temperature-controlled tractor trailers can hold 10,000 liters of plasma, and we can load or unload it in a matter of minutes. Special foam-insulated shipping containers, packed with dry ice and boxed in specially-treated corrugated boxes, are used to transport our plasma units anywhere in the world within the time requirements of the order.

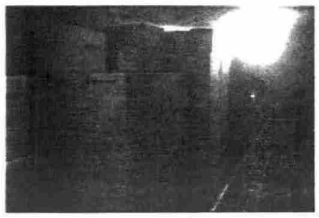
Because of these standards and the close supervision of our people, the high quality product collected and shipped from a Plasma Alliance Center is the same high quality product when it arrives at its destination.

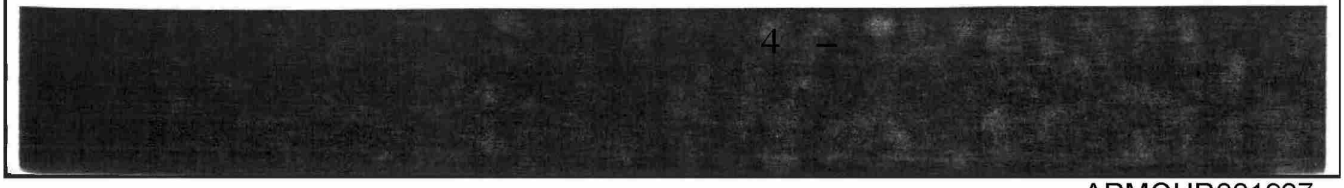


Once the collected source plasma has been aseptically transferred (top, 1) to the final shipping container, it is then flash-frozen and kept in cold-storage units (top, 2) until it is released for shipment.

Upon arrival at Armour's Kankakee manufacturing facility (top, 3), the frozen plasma is then held in additional cold-storage units until final fractionation (top, 4).

Special Plasma Alliance freezer trucks (large center) can transport up to 10,000 liters of plasma at carefully controlled temperatures.





ARMOUR001937

Plasma Alliance.
People to people.

"I think the uniqueness about Plasma Alliance is its compassion for people, both donors and patients – the fact that we care for people."
- George Barsnevext
Area Manage

It takes many people to make the life-saving products derived from plasma available to the people who need them. It takes people in the Plasma Alliance centers across the country — people in the quality control laboratory which extensively tests plasma samples from thousands of donors each month — and people at the headquarters of the Armour Pharmaceutical Company, parent company and member of the Ethical Products Division of the Revlon Health Care Group.

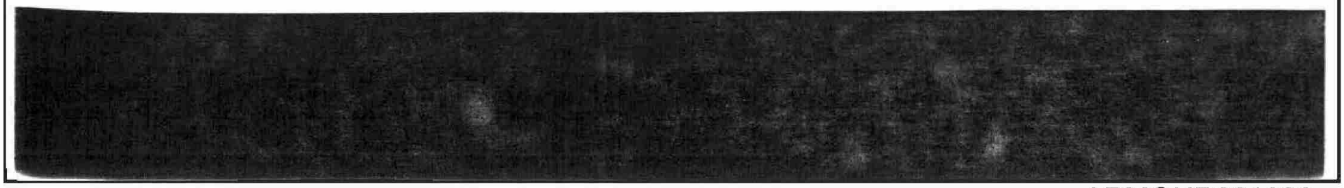
In fact, one of the most meaningful accomplishments of Plasma Alliance has been the nurture and development of our people — from staff positions to top management. Their experience and expertise has seen the company move from early pioneering in plasmapherisis into the technological mainstream. In fact, many of our key people have been with the company from its earliest days. Their insight and counsel have made significant contributions to both Plasma Alliance and the industry.

Setting and maintaining a level of excellence in donor safety and product quality above what is required, has been the special achievement of Plasma Alliance people in every center. There is a constant awareness that the technical details of our work are critical to the safety of our donors and our product, and there is an attitude that even with all the technology, it still takes people who care and will go the extra mile.

Beyond technical skill and dedication, the uniqueness about Plasma Alliance is its compassion for people — both donors and patients. For nearly a quarter of a century, the rewards of working in such a vital industry that is important to so many, have made Plasma Alliance a true people to people business.

Plasma Alliance people bring special talents and dedication to the diverse nature of plasma collection.

People such as:
Page Hamilton, Technical Director (top, 1), Rene Guida, Processing Technician (top, 2), Tonja Nord, Laboratory Technician (top, 3) and Jerry Matthews, LPN, Phlebotomist and Group Leader, are making significant contributions to the company and to the industry.



ARMOUR001939