"SPECIALS" MANUFACTURE IN THE N.H.S.

WE'VE BEEN DOING IT FOR YEARS...

Sandra Millership

Summary

Over the past 30 years there has been a vast change in the manufacture of "specials" within the National Health Service. From being primitive, badly equipped units situated in the basement of nearly all hospitals, N.H.S. production units have changed to purpose built, hi-tech units licensed by the Medicines Control Agency, providing a fast, efficient and validated "specials" service. Although non-profit making organisations, N.H.S. Production units have to be self-financing. Thus staff costs, overheads and replacement of equipment must be financed by sales. Production pharmacists in the N.H.S. are now working together to rationalise the product list within their units. Certain units have taken over the roel of national supplier for items and instead of duplicating effort, other units will buy from them.

Keywords

"Specials", N.H.S., Medicines Control Agency.

Introduction

In the mid to late 60's, virtually every hospital pharmacy department had its own small production unit. These were usually situated in the basement of the hospital, in close proximity to the pharmacy and conditions were often primitive. All types of sterile and non-sterile products were manufactured, often using very old machinery, and much of the tablet pre-packing was done by hand, using dispensing triangles. Sterile production units in those days generally produced little more that Normal Saline and Dextrose infusions in 500 ml glass bottles together with a few ampoules and eye drops.

There was no proper costing carried out on these exercises so nobody knew if the products could have been bought more cheaply from industry. Controls and testing procedures were often rudimentary. Production was just another facet of pharmacy and every hospital that did not have a production unit, however primitive, was thought to be missing a vital area of post-registration training. Professional expertise alone was considered to provide sufficient safeguards for what was literally dispensing on a large scale and no outside regulatory body was concerned.

In 1968 the government produced a piece of legislation which was designated : "An act to make new provisions with respect to medicinal products and related matters, and for purposes connected therewith."[1] This legislation was called The Medicines Act 1968 and its publication has had a profound effect on the Pharmaceutical profession in the United Kingdom ever since. The purpose of the act is : "To control, by a licensing system, the safety, quality and efficacy of medicinal products."[1]

At this point manufacture of pharmaceuticals in hospital units was covered by what is known as "crown immunity" and did not require official licensing, however, as there could be no justification for lower standards applying in hospital units than in commercial undertakings the spirit of the act was applied to hospital units and they were expected to conform to the new standards.

The desirability of this course was emphasised by the Medicines Commission in their report on the preparation of infusion fluids following what is known as the "Devenport Incident" in 1972. This was an incident when 5 people died in a Plymouth hospital following the infusion of a contaminated batch of Dextrose 5%. This was actually a commercially prepared infusion but the hospital was not absolved of all responsibility as it was felt they should have examined the infusions before issuing them to the wards.

The Commission stated : ".....too many people believe that sterilisation of fluids is easily achieved with simple plant operated by men of little skill under the minimum of supervision, a view which is wrong in every respect."[2]

An interim report by Lord Rosenheim in 1972 concerned with the same incident recommended, in particular, that: "Control of hospital manufacture should be no less rigorous than that which applies to pharmaceutical firms who are required to be licensed under the Medicines Act."[3]

Accordingly, a system of inspection of hospital manufacturing units was implemented. At first this was on an informal basis, licenses not being required. But it had profound implications for the hospital service. Many units were closed down as being unsuitable and those which remained open, after extensive modification, went in one of two ways. Firstly, in the late 1970's the large scale hospital production unit appeared. These units were able to manufacture sterile fluids on a near commercial scale and were, in essence, in competition with industry. There were not too many of this type of unit but Parkfields in the West Midlands and Clatterbridge in the Wirral were two such. But the main type of unit to appear was what we call the "Specials" unit.

What is a special?

As a general rule, the Medicines Act 1968 requires all dealings in medicinal products to be in accordance with product licences and all manufacturers of medicinal products to hold a manufacturer's licence.

They do, however, recognise that practitioners may need to prescribe medicines that are not available as licensed products. Under such circumstances the product can be prepared in a pharmacy registered with the Pharmaceutical Society or in a hospital pharmacy under the supervision of a Pharmacist.

This is under what is called a section 10 exemption from the regulations and enables a small amount of preparation, for immediate use. There are strict guidelines on the amount of preparation permitted under this exemption, for example :

20 packs of a non-sterile liquid, antiseptic or cream, 100 capsules or suppositories,

10 packs of terminally sterilised products, this includes eye drops, injections, infusions and sterile creams;

25 packs of repackaged tablets, capsules or liquids.[4]

Such items are said to be extemporaneously dispensed.

It is generally not permitted to prepare "aseptically" manipulated products for stock at all. Unless made in a licensed unit, these should be for immediate use only.

For all items covered by a section 10 exemption there is a limit of one batch per month prepared for stock. An acceptable level of quality assurance is still required and products should be made in conditions which comply with good manufacturing and dispensing practices and should be regularly audited by quality control staff. In addition, unless substantiated by stability data, the maximum permitted shelf life for these preparations is 28 days. Alternatively, the pharmacist or practitioner may order the product from the appropriately licensed manufacturer.

"Specials" are defined as Medicinal products in respect of which a Product Licence is not in existence but which may have been made by the holder of a special manufacturer's licence, to the order of a practitioner, for administration to a particular patient.[4]

Until this year commercial manufacture, even in licensed units, had to be by, or under the supervision of a pharmacist but since the introduction of European licensing requirements this is no longer the case.[5] Manufacture under the section 10 exemption however remains under the auspices of a pharmacist.

It is licences issued under these 1994 regulations and those which these regulations superseded that are commonly referred to as "specials" licenses and the products made under there authority are termed "specials".

A "special" can be :

- An unusual formulation of a product that is only available in certain licensed forms.
- An unusual strength.
- An unusual combination of products.
- A preservative-free version of an eye-drop A discontinued product.
- An item available overseas but not marketed in Britain.
- Products made to order due to the temporary unavailability of the licensed form.

The Present Situation

Things changed again in 1990 in Great Britain and 1992 in Northern Ireland when crown exemption was removed and all units, including those situated in hospital pharmacies, were required to apply for manufacturers licences or to cease manufacture. Again more units closed leaving a nucleus of specially built, high quality units within the National Health Service.

These units were formally inspected by the Medicines Inspectors and, if the standards were met, were issued with official licences. Henceforth there would be absolutely no difference between Health Service units and commercial concerns.

It would be difficult to compare the modern day units with those of the late 60's. Most are purpose built, designed to the highest standards, and fitted with expensive, high quality air handling plants providing clean or sterile air to the working environment. The operators more resemble spacemen than pharmacists or the technicians in their one piece all encompassing suits, headgear, masks and gloves.

There are currently 212 holders of specials licenses issued by the Medicines Control Agency. Of these licenses, 123 are held by National Health Service hospitals and 99 by industrial concerns. About a dozen of these industrial concerns supply a commercial specials service.

It must be borne in mind that the onus is on the purchasing pharmacist, rather then the manufacturer, to ensure that any unlicensed medicines purchased are up to standard. Due to the increased significance of product liability over the last few years, the Quality Controllers are increasingly being asked to re-test purchased specials on receipt, unless they can be furnished with a Certificate of Analysis. This can greatly add to the cost of purchased specials. The Quality Controllers have, however, agreed between themselves to accept the testing procedures of other N.H.S. specials units without the need to re-test. We can, and do, however, provide Certificates of Analysis if required.

Some specials manufacturers offer a comprehensive service, others specialise in a particular type of product. The N.H.S. licensed units, by and large offer a very comprehensive service, many of them being licensed to provide an aseptic service. Aseptic filling is a high cost operation, very labour intensive and involving extensive validation and broth trials. Many commercial specials manufacturers do not offer this service for these reasons.

Industry is offering a commercial, profit making service, it is out to make money. The N.H.S. specials units are there to provide a service. They are able to respond rapidly to changing situations and are often in the forefront of developing new delivery systems and admixtures. Many units also undertake Total Parenteral Nutrition, Central Intravenous Additive Services or C.I.V.A.S. and Patient Controlled Analgesia services. Although these are not strictly manufacturing procedures the expertise developed in manufacturing, together with the high standards in the units make them the ideal place from which to conduct these essential services.

National Health Service units have recently introduced a comprehensive service for the relief of post-operative pain. Where Total Parenteral Nutrition was the in vogue treatment of the 70's and the Central Intra Venous Additive Service that of the 80's, Patient Controlled Analgesia is now one of the fastest growing fields in modern medicine. The ability to let a patient control their own post-operative pain allows a patient the unique opportunity to contribute to their own recovery and has been proven to increase recovery rates and the patient's feeling of well being.

P.C.A. is administered either by pre-filled syringe, which requires a syringe pump, a mini-bag, requiring an infusion pump, or, for ambulatory patients, an infusor device with a switch, worn on a wrist strap, powered by a small battery. The syringes, mini-bags, and infusors are all filled using an automatic dosing machine which acts like a mechanical thumb. This device is used for all repetitive filling in our unit. As most of the analgesics used by this method are narcotics, either morphine or fentanyl, either alone or in combination with other substances, it is important to realize that these devices are pre-set. It is not possible for the patient to exceed the required dose either by increasing the volume of the metered dose or by decreasing the interval between doses. The patients however, can control their own pain when they need it and not when the nurse or doctor has the time to give them relief.

Also, over the past 10 years the N.H.S. specials units have been working together to rationalize the product list within their units and thus reduce

duplication of effort. In the early 1980's the Regional Pharmaceutical Officers set up several sub-committees dealing with Drug Information, Quality Control, Radiopharmacy, Education and Production and asked for representatives from each region in each discipline. The Pharmaceutical Production Committee has been instrumental in rationalizing production, especially of sterile products, within the N.H.S. It is due to the work of this committee that several units have taken over the roll of national supplier for certain items.

At our sterile unit in Belfast we produce, on a national scale, various strengths of Baclofen either as ampoules or as vials for refilling implanted reservoirs associated with a miniature pumping device to give patient controlled relief from neurological spasticity. The royal Victoria Hospital was one of the first units in the country to pioneer this treatment, and, as the shelf life of Baclofen in normal saline has been found to be only 9 months and the 12ml vials will refill a pump for the period of 2 to 3 months, the demand within any single unit is not enormous and it is more economical for other hospitals to buy from us than to manufacture their own. In fact we supply these to over 2 dozen hospitals throughout the United kingdom and Eire. We are also the national supplier for Paraldehyde injection, a particularly nasty substance to work with, used to control seizures in status epilepticus.

The Production Pharmacists sub-committee, with the collaboration of the Quality Control and Radiopharmacy sub-committees have, this year, set up, in conjunction with Leeds University an MSc in Pharmaceutical Technology and Quality assurance to ensure a constant renewal of pharmacists qualified to take over the technical jobs within pharmacy. This has become vital as, with the decrease in the number of production units and their associated quality control units, it is now not every pre-registration graduate who has more than passing contact with one of these specialties and has the chance of first hand experience.

It is also hoped that this course will lead to registration as a Qualified Person. Although this is not, at the moment, necessary for a Qualified Person to be named on the application for a "Specials" license, there is no guarantee that this will continue.

The Market Economy

In addition the Market Economy has come to the N.H.S. Although they are not producing specials primarily to make money and some units see it as a form of income generation, N.H.S. units are not allowed to make a loss. Production units are required to be self-financing. Staff costs, overheads, capital charges and repair and replacement of equipment must be financed by sales. This has led to production managers having to assume a more business like approach to their enterprises. This is made more difficult by the embargo on advertising by specials units. It is a requirement of the specials license that, although the service provided can be advertised, specific products must not be advertised and can only be supplied on receipt of an unsolicited order.

It is from the need to advertise that I get the title of my paper. Due to the need to be self-financing, we need to advertise our services. The Production Pharmacists Committee have coined the logo "We've been doing it for years...." and now use it on all their promotional literature.

At first sight the embargo on advertising specific products may seem unreasonable but if you think about it logically, if you were able to advertise an unlicensed drug, then what would be the point of applying for an expensive product license.

It is however, not illegal for a specials manufacturer to make a drug for which there is a licensed alternative. Many new products start life as specials made in N.H.S. units. From these beginnings, having proved their efficacy, they go on to licensed products. Industry jumping on the N.H.S. bandwagon. In some cases a hospital specials unit has been making a preparation for years when a licensed product becomes available. The unit will only cease to manufacture when the customer no longer requires the drug. This usually only occurs when prescribing patterns change or the licensed alternative is cheaper, definitely not always the case.

In the very odd case, an N.H.S. produced drug may be more expensive but still required. It is the prerogative of the doctor to have the drug he requires and if he has been working successfully with the N.H.S. produced drug for a number of years, he may be loathe to change. Although economic restraints are now being applied, it is generally accepted that if a doctor want something badly enough, he will get it.

Where Do We Go Next?

We are definitely seeing an increase in the requirement for injections in pre-filled syringes, especially for use in emergency situations. Also, the use of mini-bags seems to be on the increase and most new autoclaves are fitted with plastic bag cycles. Having said that, the N.H.S. is one of the few services that is now able to supply large volume infusions in glass rather than plastic and this is essential for some preparations.

On the non-sterile front, casualty and take home packs are ever increasing and in mainland hospitals, pre-packs for out-patient dispensing are always required. In Northern Ireland drugs are not given from outpatient clinics, the patient is instead furnished with a prescription. We are also seeing an increase in the use of suppositories and the need for medication to be given in a liquid form. "Specials" units are developing and manufacturing more and more of these

Conclusion

National Health Service specials units will never be able to compete with industry on a commercial scale, neither should they attempt to do so. However, they can, and do offer a high quality, comprehensive service, able to respond quickly and efficiently to the needs of the health service.

They are able to do this by harnessing their expertise to those areas which it is not commercially viable for industry to tackle and, by their increasing awareness of the commercial necessity of being self-financing, they are able to provide this service at a competitive price whilst covering their costs.

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The Authors

This represents a re-print of the paper presented at the symposium on Pharmaceutical Care in Malta in April 1994. Sandra Millership is the Principal Pharmacist in charge of production in the Eastern Health & Social Services Board in Northern Ireland where she manages both a Sterile and Non-Sterile production unit.

GLUCOCORTICOID THERAPY IN ASTHMA

Erratum

*The section **'The Authors'** at the end of this paper presented by Sonia Chetcuti and which appeared in Issue No. 2 of the journal should have read as follows:*

Sonia Chetcuti carried out this work as part of the B. Pharm (Hons.) degree dissertation, "Glucocorticoid Therapy in Asthma: Effect on T-Lymphocyte Function and Immune Responses" under the supervision of Prof. M. Cauchi MQR, AM, MD, MSc, PhD, FRCPA, FRC (Path.), Head of Department of Pathology, St. Luke's Hospital G'Mangia, Malta and Dr. C. Scerri MD, Molecular Genetics Laboratory, University of Malta, Msida, Malta. She would also like to thank Prof. A. Felice MD, PHD, Head, Department of Molecular Genetics, University of Malta for providing the research facilities used during this project.