

Automated dispensing of parenteral nutrition formulations

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This article describes the preparation of artificial feeds for paediatric patients and looks at the use of a microprocessor-controlled compounding device that has recently been installed at Great Ormond Street Hospital for Children



A compounder being used to prepare paediatric parenteral nutrition within the pharmacy aseptic unit at Great Ormond Street Hospital

Parenteral nutrition solutions are designed to provide patients with their nutritional requirements, and are composed of amino acids, glucose, lipid, electrolytes (eg, calcium, sodium, potassium, phosphate, magnesium), trace elements and vitamins. Paediatric licensed formulations are only available for children aged one year or above and they frequently provide an insufficient calorie content. As a consequence of this, the majority of paediatric hospitals within the United Kingdom now provide tailor-made parenteral nutrition for their patients.

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The manufacture of formulations for parenteral nutrition has improved and changed vastly over the past 20 years, moving from a "burette and syringe" system to automation and use of computer software. Nevertheless, the use of new technologies is coupled with risks, such as system failure, and sufficient validation¹ and personnel training are imperative to reduce these risks.

The Medicines Act 1968 states that aseptic dispensing is exempt from licensing requirements provided it is performed under the supervision of a pharmacist and carried out in a closed and controlled environment. Products manufactured must also have an expiry date of less than a week.

PRESCRIBING

At Great Ormond Street Hospital, a multidisciplinary team advises clinicians in prescribing parenteral nutrition. Validated AsCcribe computer software is used to formulate regimens by amending the appropriate standard trust regimen. There is a product database at Great Ormond Street Hospital that contains a list of all the ingredients required to manufacture parenteral nutrition. Worksheets, labels and details of a regimen are printed by an authorised pharmacy technician and are checked by a pharmacist. The regimen provides information on the administration process for nurses. The computer system's inherent safety checking program is used to minimise the risk of errors occurring; for example, it can check

that the glucose concentration of a parenteral nutrition regimen is satisfactory.

At Great Ormond Street Hospital, we use the Baxa Micro/Macro MM23 compounder to manufacture parenteral nutrition bags that do not contain lipids (see later). An automix (a machine that uses specific gravity to mix the large volumes of ingredients for parenteral nutrition formulations) is used to manufacture bags containing lipids, and vitamins are added manually to these bags. A giving set connects the lipid and non-lipid bags together, and a filter is incorporated into the giving set on the non-lipid side.

The British Parenteral Nutrition Group Filter Working Party² recommends filtering parenteral nutrition during both administration and aseptic dispensing.

An expiry of five days (in-house validation) is assigned to parenteral nutrition products. Prepared bags are labelled, checked and released to the wards by the pharmacist.

Any errors made in aseptic dispensing can lead to formulations being produced that are potentially hazardous. Following the death in 1994 of two children who had received parenteral nutrition found to be contaminated with microbial growth,³ the Department of Health set standards for aseptic dispensing in the National Health Service^{4,5}

The NHS standards are aimed at minimising the following:

- Microbial contamination of parenteral nutrition solutions
- Incompatibilities between ingredients, eg, between calcium phosphate complexes
- Incorrect concentration of ingredients
- Particle generation during manufacturing

RISK MANAGEMENT

The risk management strategies stated below^{6,7} are fundamental in reducing the possible problems mentioned above:

- Supervising and regularly performing aseptic validations of unit staff
- Monitoring for microbial contamination, with action taken when results do not meet the required specifications
- Supervising unit audits that highlight problem areas necessitating a change in practice
- Providing standard operating procedures for staff
- Providing portfolios for unit staff that contain evidence of competency and authorisation documents
- Enforcing a trust agreed capacity plan (matching needs to abilities), if necessary

The most important risk management policy is to encourage pharmacy staff to report any incident (eg, incorrect ingredient being used) that occurred during aseptic dispensing, and to adopt a no-blame policy.

IMPROVING THE SERVICE

The incident in Manchester increased the need for a higher level of quality assurance within aseptic dispensing. The increased provision of quality assurance that was introduced subsequently lengthened the compounding process considerably.

The pharmacy at Great Ormond Street considered ways of improving the dispensing and supply of parenteral nutrition to wards.

Pharmacy staff were faced with two options, and these were to:

- Provide a seven-day aseptic dispensing service, or
- Make greater use of automation through installation of a compounder

The provision of a seven-day service was perceived to be costly, with no expected

improvement in delivery time of products to wards. The use of automation was, therefore, the preferred choice.

USE OF A COMPOUNDER

The feasibility of installing a compounder with microprocessor control for aseptic dispensing was considered because the benefits of such automation have been reported at many hospitals within Europe and the United States.

Compounders have been associated with a fast, efficient and reliable aseptic dispensing service. They have helped rationalise the use of staff and have increased product output. However, approval for installation and use needs to be obtained from the Medicines Control Agency (MCA). Installation is also costly.

Cost comparisons between the conventional and automated methods have shown the compounder to be cheaper when large quantities of parenteral nutrition bags are being produced. This is because the amount of consumables used remains the same, regardless of the number of bags produced.

A validation master plan was designed to determine whether a compounder could manufacture bags as precisely and accurately as people using conventional methods, and also whether it would comply with the MCA's "Orange Guide"⁸ and the guide for "Good automated manufacturing practice".⁹

Also under consideration was whether or not the compounder could produce parenteral nutrition products that were:

- Free from both chemical and physical impurities
- Free from microbial contamination
- Compliant with the prescription requirements

STEP-WISE APPROACH

A step-wise approach to the use of a Baxa compounder is outlined below, and the potential problems are highlighted.

1. Setting up a file A validated interface between AsCrib software and Baxa (through a network link) allows parenteral nutrition regimens to be computerised and individual patient file numbers to be set up. File numbers are carefully noted and are transferred on to the relevant patient worksheet. Potential errors include an incorrect regimen being set up and incorrect transcription of a file number on to a worksheet.

2. Setting up the compounder The possibilities for the location of the compounder were a laminar flow cabinet or an isolator. The laminar flow cabinet was the preferred choice because its open front allows for manoeuvrability. The closed space of an isolator would make it difficult to clean the



An automix: uses specific gravity to ensure that large volumes of ingredients for parenteral nutrition formulations are mixed correctly

compounder thoroughly.

The compounder has interconnected 12-port primary and secondary controller valves. A configuration file identifies the position of ingredients on the ports, and this mimics the addition of ingredients by hand. Several configuration files may be stored on the Baxa compounder at any one time.

The compounder is connected to a dedicated computer terminal that is located in the aseptic unit. The compounder pumps the ingredients at a rate determined by viscosity. The setting up of ingredient files on to the compounder by quality assurance staff requires information on the viscosity of the ingredient (compared with water), the pack size, port position and the type of set used to connect the ingredient to the port.

The pumping action generates particles of an average size of greater than 2mm, and these are removed via a 1.2mm filter incorporated into the giving set.

A "set-up checklist", printed by the technician, provides the authorised pharmacist with information on ingredient positions and pack sizes and is signed subsequently by both staff. Ingredients drawn up into syringes manually must be clearly labelled and checked by the pharmacist before being attached to the ports using validated aseptic technique. Potential problems that could arise include:

- Setting up ingredients incorrectly
- Performing incomplete or inappropriate aseptic validations for staff

3. Operation of the compounder The compounder pumps the majority of the glucose solution first (universal ingredient), followed by the other ingredients and, finally, it completes the bag by flushing with the remaining glucose solution. Hence, the tubing is patent with the universal ingredient.

Before manufacturing, the system must be primed to remove air from the tubing and calibrated. The selected regimen is loaded, an empty total parenteral nutrition bag is attached and the compounder is run. The bag is labelled with the patient's name, ward, date of preparation and file number. If an ingredient runs out mid-production, the pump stops automatically and starts again once the source has been checked and changed, and the computer updated. Only authorised unit staff are permitted to update the computer.

The compounder has two password levels. The lower level password allows authorised staff to load regimens, change source ingredients and run the compounder. The higher level password allows such things as the deleting of regimens and changing of configuration files, and is held by senior aseptic and quality assurance staff. Potential problems with the compounder and its use include:

- Recalibrating because of expansion of the silicone tubing after a few hours of use
- Compounding the wrong regimen
- Deleting regimens inadvertently
- Giving the higher level password to unauthorised staff
- Operating the computer incorrectly and changing the source incorrectly
- Labelling stock syringes incorrectly
- Labelling parenteral nutrition bags incorrectly inside the aseptic unit
- Failing to remove air in parenteral nutrition bags
- The network link, compounder, or AsCrite computer software failing
- Loading too many regimens, which exceeds the memory capacity

4. Weighing and labelling parenteral nutrition bags

A confirmation sheet is printed once a bag is compounded, which is checked against the worksheet, ie, checked for the correct patient and file number and ingredients. Potential errors connected with the weighing and labelling of bags include:

- Failing to discard bags that do not meet the required specification
- Checking confirmation sheets incorrectly
- Failing to calibrate the weighing balance
- Labelling bags incorrectly
- Failing to attach a filter to a non-lipid bag

5. Deleting regimens and vial reconciliation

In theory, the total amount of each ingredient used equals the sum of volumes used for priming, calibrating and compounding the regimens. At the end of a session, an ingredient list is printed. Before printing, any regimens not compounded are deleted, and additional regimens are set up for bags that have needed to be re-made.

A vial reconciliation is performed for all amino acids, potassium, sodium, phosphate and calcium sources. Any stock bottles for these ingredients are retained throughout each production session. Potential errors at this stage include:

- Failing to perform a reconciliation
- Failing to account for regimens for bags that have been re-made

6. "Broth" bag A broth bag is compounded at the end of each production session to enable the compounding process to be tested for any microbial contamination. The bag is incubated for three days and monitored for any microbial growth by quality assurance staff. To prepare a broth bag, parenteral nutrition ingredients on the compounder are exchanged for broth bottles and syringes.

7. "Chem" bag A chemical analysis is performed on a specific nutritional regimen, which has set ranges for sodium, potassium, magnesium and calcium. Any deviations from these ranges are monitored. This

analysis will identify any ingredients not being pumped by the compounder.

PROBLEMS EXPERIENCED

Some of the potential problems associated with each step of the compounding process have been experienced. This has led to the aseptic unit incorporating in-process checks throughout the compounding session to minimise errors. With occasional network linking problems, we have had to rely on staff being able to manufacture parenteral nutrition using conventional methods and, therefore, the de-skilling of staff has not happened. In our limited experience of using a compounder, we have found that training staff in how the device works is the most important step in preventing serious mishaps.

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