

BASIC INFORMATION.

The purpose of this document is to provide an overview of the pharmaceutical supply chain. It is intended to be for the benefit of people who are involved in some element of the provision of medicines but need an appreciation of upstream or downstream activities to better understand the potential impact of a flu pandemic. The role and responsibilities of some key regulatory, professional and trade bodies is outlined in the Appendix.

Introduction

The supply of hundreds of thousands of product lines to tens of thousands of outlets is inevitably complex. Added complexity comes from the fact that the major pharmaceutical companies operate on a global level, intermediaries (wholesalers) tend to have pan-European businesses and the local outlets (pharmacies) may or may not be vertically integrated with (ie in common ownership with) wholesalers.

Further complexity arises from the special nature of the product, which may mean the need for refrigeration throughout the supply chain or special security arrangements to meet controlled (opiates) drug legislation. Variations in global pricing create further complexity and lead to the existence of parallel traders (short line wholesalers) whose existence may facilitate the introduction into the supply chain of counterfeit product.

Despite the complexities, most products go through most or all of the following supply chain steps:

- Primary manufacture
- Shipment of bulk primary product
- Secondary packaging
- Pre-wholesale distribution
- Wholesaling
- Pharmacy storage

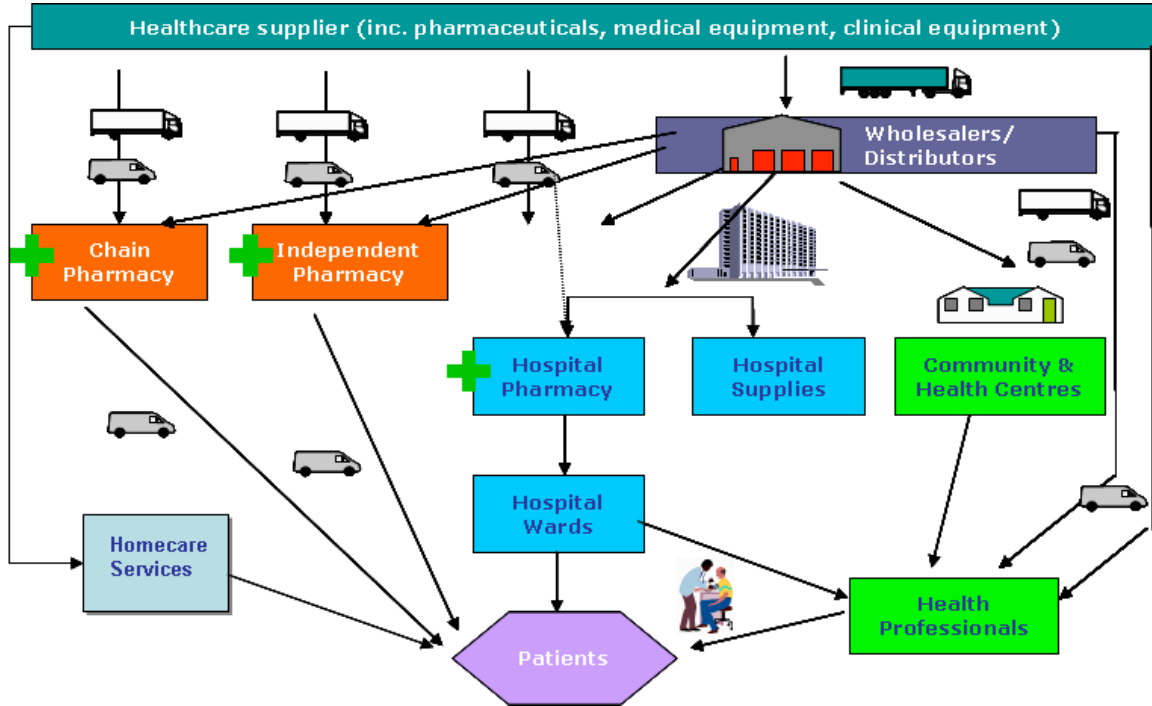


Figure 1

The primary manufacturing processes in which the active pharmaceutical ingredient is created is usually a multi-stage (typically 8-stage) activity. For some products, more complex production processes are involved – for example fermentation which may entail a “dwell time” in production vessels thus adding to lead time. Modern pharmaceuticals are tending towards increasingly complex molecules and require a multi-stage manufacturing process.

Typical lead time between the entry of raw material into primary manufacturing and production of active pharmaceutical ingredients is around 3 months.

Because primary manufacturing requires the handling and processing of bulk chemicals, it has not been seen as an attractive industry to locate adjacent to premium residential areas. In the UK therefore, primary manufacturing tended to be sited in the North West, North East, or Scotland. Much manufacturing is also undertaken in Cork in Ireland. More recently, globalisation has led to consolidation of manufacturing in countries such as Mexico (for the US market), India and China - particularly for generic products. It is believed that some 80% of the active pharmaceutical ingredients used in the UK originate in China or India.

Most pharmaceutical active ingredients are manufactured in a “batch” process rather than a continuous process. Batches fail quality control checks from time to time due to incompleteness of the process or the presence of impurities. Batch cycles are scheduled according to forecast demand, thus many months may elapse between production of a specific product.

“Switching” production capacity from one product to another can be very difficult. The introduction of new production capacity could take at least a year.

Existing manufacturing resources are estimated to have sufficient resource to increase volume by up to 20% from current levels (although even this level of increase would take some time to achieve).

Pharmaceutical production is a global business – in times of shortage, the UK may not be the most attractive market to supply into if better prices (and thus higher profits) are available elsewhere.

Shipment of Bulk Primary Product

A significant amount of primary pharmaceutical product is shipped in bulk containers (kegs) from its country of manufacture to a secondary manufacturing/packaging facility closer to the market in which it will be used. Typical transit time is one month.

Most products destined for the UK is shipped via Felixstowe.

Because of the volumes involved, airfreight would not be a viable option except for certain critical products.

Conversion of the primary product into a final pharmaceutical product ready for sale typically involves tableting, inserting the tablets into a primary package (foil), and packaging the foils into suitable printed packs together with usage instructions. The pack size and labelling may be country specific and thus make the product suitable only for a single market.

These processes have traditionally been undertaken close to the market in which the product was ultimately to be used. This is because the packaging adds to the bulk and thus the transport costs and because “in transit” damage is more likely to the finished products. Minimising the transport distance of the product thus reduces risk and makes sense. It is also often seen as useful for the pharmaceutical country to have a manufacturing presence in the country in which it sells its products.

However, in the interests of cost savings, secondary manufacturing sites have been rationalised and may often now be sited in countries with a low cost base (eg India). Pharmaceutical companies are also increasingly making use of outsourced secondary manufacturing/packaging services because they can better optimise their own in-house facilities; outsourcing thus provides a cost-effective alternative. Research-based companies are less likely to use outsourcing than generic suppliers as they prefer to retain total control of the product.

A stock of “a few months” of packaging components is maintained. Foil is the longest lead time item (3 months).

Manufacturing Supply Summary

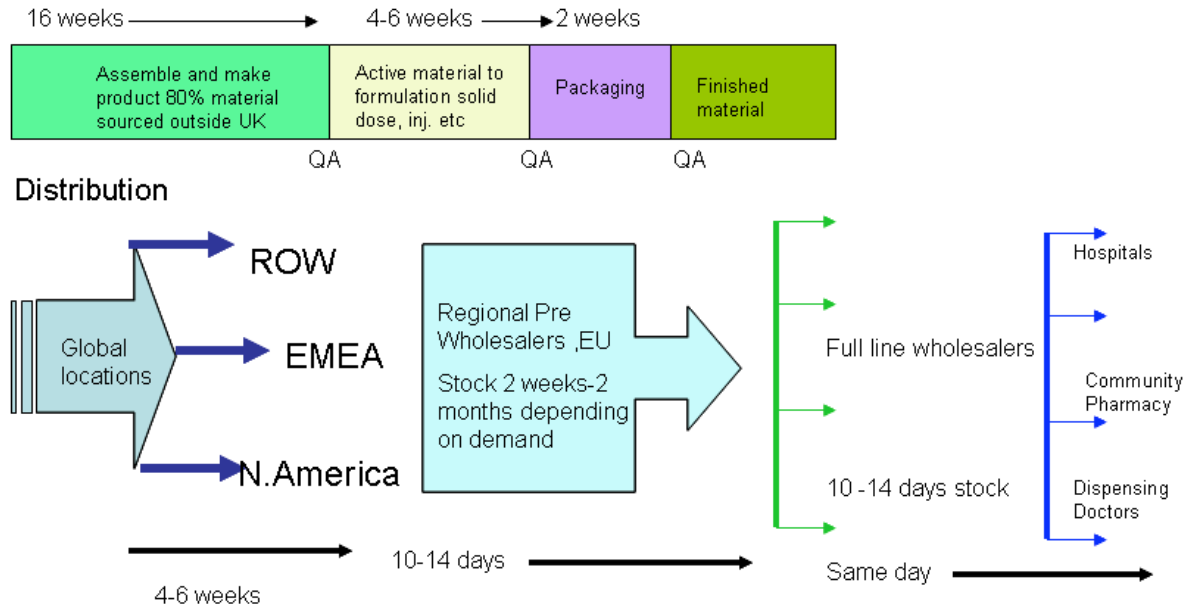


Figure 2

Pre-Wholesale Distribution

Pre-wholesale delivery is typically outsourced to companies such as DHL and Healthcare Logistics. These companies may also hold finished stocks on behalf of the manufacturers. Stock levels vary from 2 weeks to 2 months – the lower level applying to the fastest movers.

Full-line Wholesaling

Pharmaceutical wholesaling has undergone major rationalisation in recent decades. A range of regional wholesalers has been replaced by two major wholesalers (AAH and Alliance Unichem) with a handful of smaller companies (see figure 3 below). One recent merger was Boots with Alliance Unichem which has resulted in consolidation of its distribution network. The market shares of the main wholesalers for prescription medicines as at May 2007 were as follows:

Wholesaler	Volume %
Unichem	38
AAH	38
Phoenix	14
Mawdsley Brooks	3.0
Sants	2.6
Sangers NI	2.2
F Maltby	0.9
Sangers Maidstone	0.7
Norchem	0.6
Munro	0.3

Figure 3

Source OFT report

Modern pharmaceutical wholesaling relies on a high level of operational efficiency. The 25 wholesale pharmaceutical warehouses are located around the country to minimise travelling time for the twice/day deliveries that they provide to pharmacies. Each full-line wholesaler holds around 12,000 lines.

They achieve efficiency by utilising pallet storage spaces at a typical level of 90% and by investing in highly sophisticated picking equipment. This picking equipment comprises an “A frame” automated picking machine for fast moving items supported by manual “pick-by-light” systems for slower movers. Both picking areas feed into bar-coded tote boxes travelling around the warehouse on conveyors. The picking list for each tote box is generated using software which links to the “A frame” and pick-by-light system. Picking is scheduled such that the tote boxes are filled in time to be loaded onto delivery vehicles whose route is also computer calculated to ensure high operational efficiency (90-100% full, although about 30% of this is “non-essentials”).

Because of the importance of the handling equipment (“A frames” and conveyors) each warehouse will typically have an engineer and a stock of spare parts to cope with break downs.

Goods receipt usually takes place over a period of a few hours in the morning. “put-away” follows and then picking in time for the peak demand period from pharmacies at the end of the day.

Simply extending hours of operation to increase throughput would not be straightforward due to the potential for “interference” between receipt/put-away/picking to cause disruption to the flow.

Stock levels average around 3 weeks. In times of shortage, the wholesalers approach alternative suppliers. If the alternative supplier is able to supply, a new stock code is allocated to the new product to differentiate it from stock from the regular supplier. The

code allocation is performed by the company's head office staff (who may be able to work from home in an emergency).

The majority of wholesalers' systems are capable of identifying when they believe customers are stockpiling – under such circumstances, stock restrictions may be put in place and “first-line” (regular) customers would be given preference over second-line customers who only use that particular wholesaler at times of shortage.

Pharmaceutical wholesaling has traditionally operated with a fixed % margin between buying price and selling cost. As a result, handling an expensive pack of drugs costs the manufacturer much more than the handling of a lower-priced similar pack. Manufacturers of research-based branded drugs (which are more expensive than generic drugs) have responded to this situation in different ways. Some deliver direct to end customers to cut out the wholesalers, others deal with the wholesalers in a different way, retaining title to the product and paying the wholesaler a handling fee based on the amount of product issued.

The “fee for service” was pioneered by GSK. Pfizer have recently adopted a similar model, dealing solely through Alliance Unichem. This model gives the manufacturers much increased control over distribution which they claim reduces the chance of counterfeit product entering the market. The recently published OFT report raises questions of overall cost to the NHS via this model.

The refrigerated area within the warehouse can generally be easily expanded because of its panel construction. The area for controlled drugs is less easy to expand but additional space can be made available by moving non-controlled, but “attractive” drugs (eg Viagra) out of the controlled drug area.

Some of the wholesalers have “overspill” warehouses which could be used in an emergency and are routinely used to store “non-essential” products such as deodorants etc.

The wholesalers' established plans in the event of an emergency include:

- Reducing deliveries from twice to once/day
- Delivering to hubs rather than individual pharmacies
- Using salespeople as drivers

Short-Line Wholesaling

Short line wholesalers carry a narrower range of stock than full-line wholesalers (typically around 2,000 lines) and may source some of them from parallel imports (PIs). The parallel import market operates by exploiting the price differences which exist between different countries. It is estimated that some 15%-18% of prescriptions are currently fulfilled by PI product in the UK (which makes it one of the largest net importers of PIs). Some products have 70-80% of their demand met by PIs.

Country	% share
Denmark	12.2
Germany	7.1
Netherlands	10.5
Norway (share of total market)	6.3
Sweden	10.2
United Kingdom	17.6

Figure 4

Source EFPIA

Retail pharmacists often operate as short line wholesalers/parallel importers, sometimes in conjunction with a group of other pharmacies. There are 1,700 wholesaler/dealer licences in the country. Pharmacies are allowed to “deal” up to 10% of their throughput. Traditionally, this has been imports from other (cheaper) countries – it could become an export trade under shortage conditions (and has been for certain products attracting higher prices overseas).

Homecare

Homecare describes the provision of medicines, medicinal supplies, or clinical services to patients in their own homes. The aims of homecare services are to cost-efficiently improve choice, convenience, and quality of life for patients, whilst addressing the service capacity constraints of NHS hospitals or facilities.

Medicines homecare can be considered as either low or high technology. Low technology describes the dispensing and supply of finished medicinal products to patients’ homes, predominantly for self administration. Such products include renal dialysis fluids, enteral feeds and anti-retroviral drugs. High technology homecare often involves the compounding, either pre-delivery or in the patient’s home, and administration of medicinal products. Such products include parenteral nutrition and intravenous antibiotics, and require skilled nursing support.

Homecare services are provided in the UK by a small number of specialists companies, under contracts specified and managed by an NHS partner. There has been significant growth in homecare provision over the last 10 years. It is estimated that about 100,000 patients are receiving some level service, and consuming some £700 million worth of medicines.

If homecare services were reduced or withdrawn, a number of strategies will need consideration and preparation.

For the low technology products, alternative arrangements could be made to supply through outsourced carriers, community pharmacies, health centres or local hospitals. These alternatives may be less convenient but would ensure treatment continuity. For high technology products, where the clinical need for continuity and safety is much

greater, there could be treatment prioritisation by the service commissioners, collaboration between remaining homecare providers, or the return of the patients to direct NHS management. The latter tactic would be the most disruptive to quality of care and service capacity, such that new patients may have access to treatment deferred.

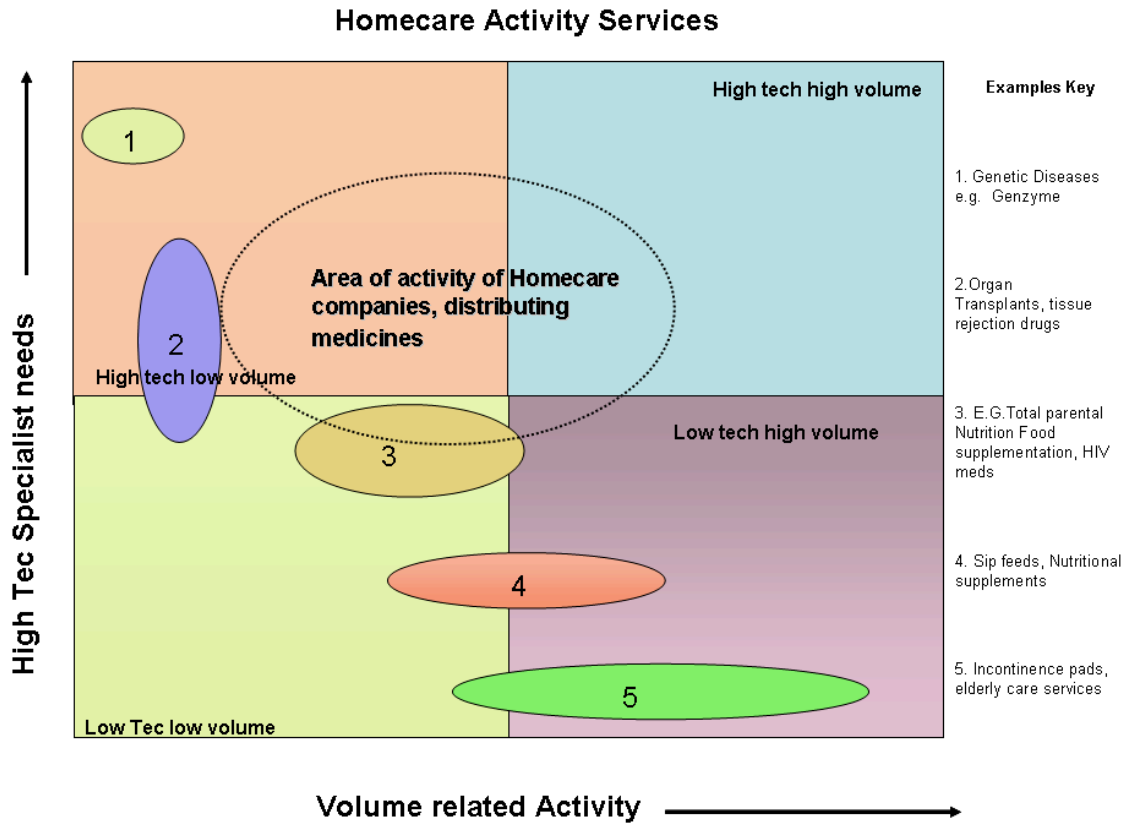


Figure 5

Figure five identifies the range of service activity provided in homecare services. Increasingly these services are commissioned by PCT's. Different companies provide specific services, some of which are very specialised.

Pharmacy Storage

There are around 9,000 pharmacy outlets in the UK which are part of national chains, plus around 3,500 independent pharmacies with one or a few outlets. The main pharmacies by market share are shown in figure 6 below:

Pharmacy	Market Share
Alliance Boots (Unichem)	20.8
Lloyds (Celesio – AAH)	13.3
Rowlands (Phoenix)	4.2
Co-operative pharmacy (Sants)	2.8
Superdrug	2.2
Sainsbury	1.5
Tesco	1.4
Asda	0.9
Morrison	0.8
Others	52.1

Figure 6

Source OFT Report

In addition to the pharmacies, there are approximately 1,800 dispensing doctor practices providing services in areas where community pharmacy is not easily accessible.

Pharmacies will tend to hold very little stock because they receive a twice/day delivery service from the wholesalers.

Prescribing and Dispensing

The procedure for prescribing and dispensing using the Electronic Prescribing System (EPS) is summarised in the diagram below (figure 7). The diagram indicates EPS at first phase. Subject to on-going development CfH (Connecting for Health) expect to see phase two in place by 2010. The expectation is a fully integrated EPS. EPS is being rolled out nationally to replace the traditional paper prescriptions (eg FP10s).

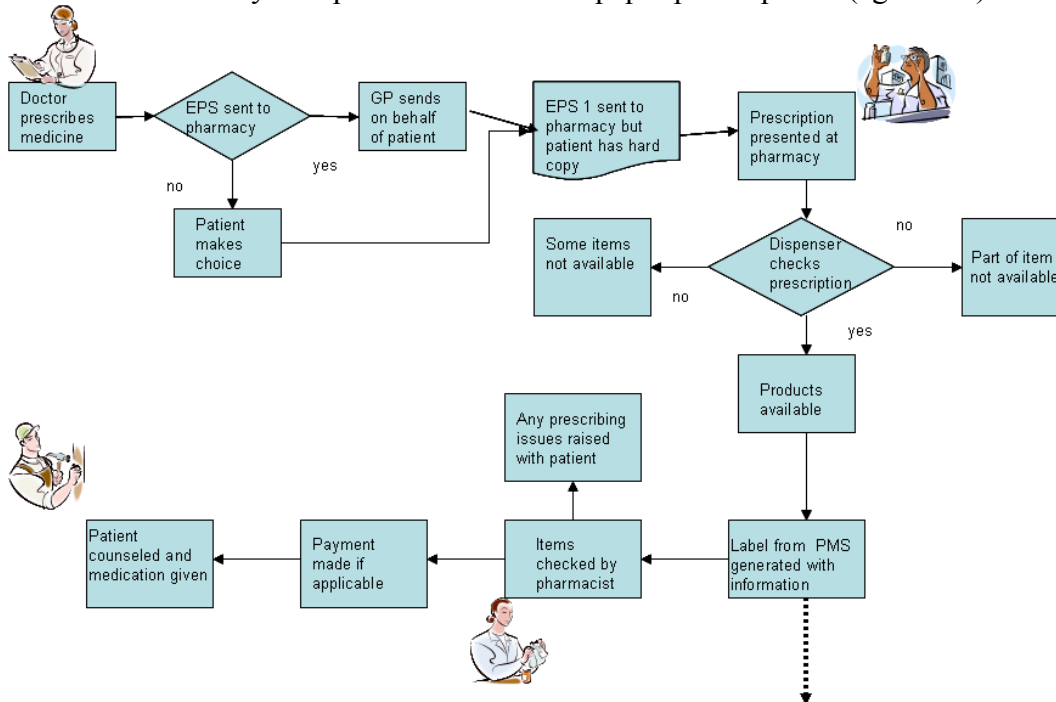


Figure 7

Replenishment By Pharmacy

Stock management and replenishment is controlled via the Pharmacy Management System (PMS). Within the system, default (first choice) and alternative sources of supply will be set. In times of shortage, orders will be placed with the first choice supplier and alternative suppliers. Whilst this may maximise the chances of prompt supply of the medicine, it also artificially magnifies the overall level of demand apparent to the wholesalers.

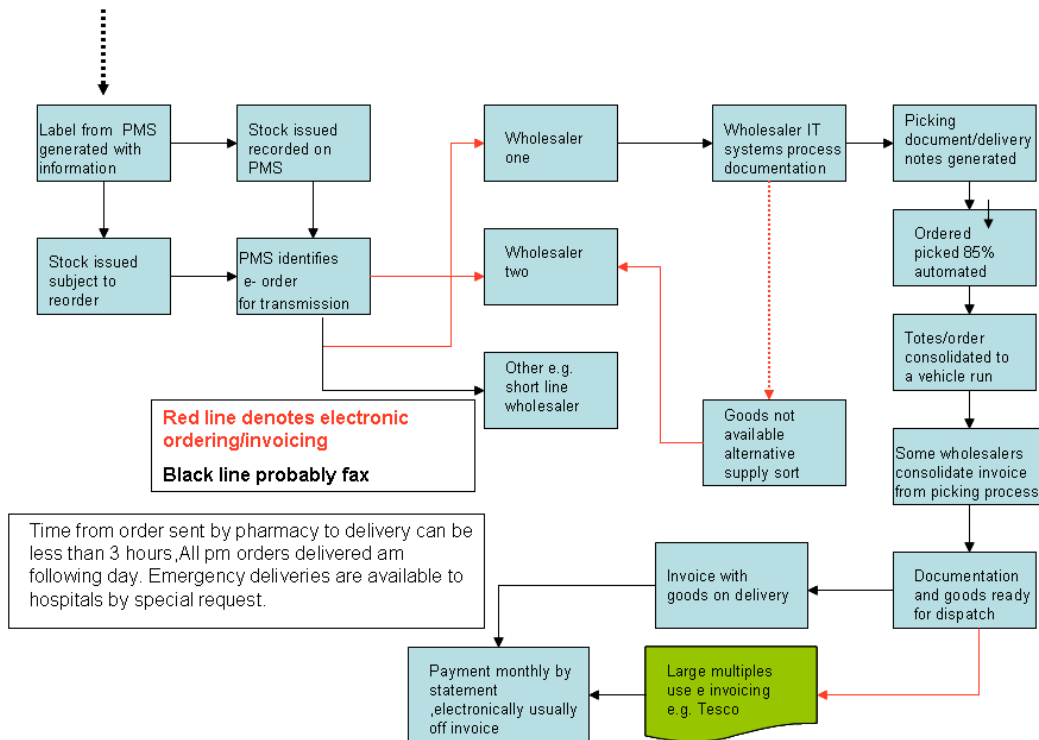


Figure 8

APPENDIX

Introduction to organisations with an interest in pharmaceutical supply

The diagram below shows organisations that are involved with management of medicines in England .

- **Red** boxes are organisations linked to the DOH which undertake a statutory requirement.
- **Blue** boxes are organisations involved mainly in primary care and community pharmacy
- **Green** boxes are pharmacy organisations both regulatory and supply chain
- **Yellow** boxes relate to service providers of logistics and technology
- **Purple** boxes represent pharmaceutical industry organisations.

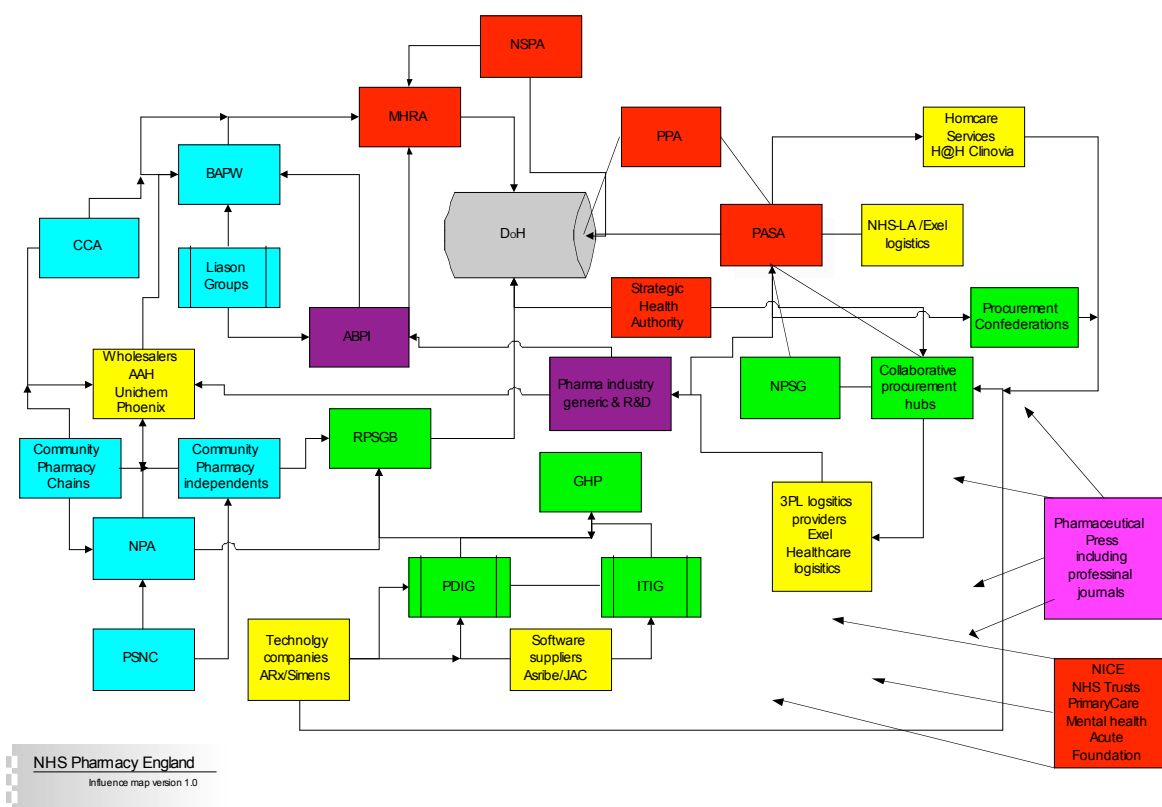


Figure 9

- DH Department of Health
- NPSA National Patient Safety Agency
- PPD Business Services Division –Prescription Pricing Division
- PASA Purchasing and Supply Agency
- MRHA Medicines and Healthcare products Regulatory Agency
- NPSG National Pharmaceutical Supplies Group
- GHP Guild of Healthcare Pharmacists
- PDIG Procurement and Distribution Interest Group

- ITIG Computer Technology/Software Interest Group
- RPSGB Royal Pharmaceutical Society of GB
- ABPI Association of British Pharmaceutical Industry
- BAPW British Association of Pharmaceutical Wholesalers
- PSNC Pharmaceutical Services Negotiating Committee
- NPA National Pharmacy Association
- SHA Strategic Health Authority
- CCA Company Chemists Association

DEPARTMENT OF HEALTH

Agencies who implement strategy including

- NICE clinical and value
- NPSA for safety and Risk
- MHRA for regulation and Control
- PASA Procurement
- PPC Drug tariff and reimbursement
- SHA targets efficiency – capital allocation.

NHS AGENCIES

MHRA

The Medicines and Healthcare products Regulatory Agency (MHRA) is the government agency which is responsible for ensuring that medicines and medical devices work, and are acceptably safe.

No product is risk-free. Underpinning all their work lie robust and fact-based judgements to ensure that the benefits to patients and the public justify the risks.

MHRA controls licensing of premises and auditing of CDs and use of software.

PPD

The NHSBSA Prescription Pricing Division processes over two million prescription items per working day, determining reimbursement and remuneration levels through to payment. Annual payments to contractors made on behalf of the NHS now total around £7 billion. These payment services centre on the direct reimbursement and remuneration of pharmacy contractors in England, the provision of payment schedules covering dispensing doctors and personal administration by GPs in England and schedules for Jersey and Guernsey.

PPD are also responsible for the management of the drug tariff

NPSA National Patient Safety Agency

The National Patient Safety Agency (NPSA) is a Special Health Authority created to co-ordinate the efforts of all those involved in healthcare, and more importantly to learn from patient safety incidents occurring in the NHS.

The NPSA helps the NHS learn from things that go wrong and develops solutions to prevent harm in the future.

PASA Purchasing and Supply Agency

PASA's Prime target is to release money that could be better spent on patient care by achieving purchasing savings and improving supply performance across the NHS.

PASA carries out the strategic contracting role for hospital medicines, in conjunction with pharmacy colleagues, under the aegis of the pharmaceutical market support group.

Initiatives include SCEP - Supply Chain Excellence Programme - divided into four projects:

- National Contracts Procurement
- Collaborative Procurement Hubs
- NHS PASA Organisational Review
- Marketing testing of outsourcing of NHS consumables supply chain and procurement service (From 2006 NHS Supply Chain took over the storage and distribution of a wide range of products)

Further responsible for inputs into:

- E commerce –PMS pharmaceutical messaging service
- Bar-coding
- Automation-Robotics

TRADE ASSOCIATIONS FOR COMMUNITY PHARMACY

PSNC - Pharmaceutical Services Negotiating Committee

Negotiates on behalf of the pharmacy community covering England and Wales with the DOH.

The PSNC has thirty one members on its main committee:

- 14 members elected on a regional basis from England
- 1 member elected from Wales
- 5 members from the Board of the National Pharmacy Association
- 7 members from the Company Chemists Association
- 3 members from the Association of Independent Multiple Pharmacies
- 1 representative from the Co-operative Pharmacies Association.

NPA - National Pharmacy Association

The Association ensures relevant and proactive support is available to its members assisting them in the successful alignment of their professional and commercial objectives. By staying close to policy makers and pharmacy bodies, the NPA ensures that members' concerns are considered and their views are voiced.

It provides a conduit for independents into the professional bodies, government agencies and the press.

CCA - Company Chemists' Association

The Company Chemists' Association Ltd aims to work in the interests of community pharmacy and, particularly, to represent the interests of, and add value to, nationally represented UK multiple community pharmacy.

It has representation on the PSNC and links through to the NPA.

DDA -Dispensing Doctors Association

To promote the interests of Dispensing Doctors and the excellence of doctor dispensing for the benefit of patients.

TRADE BODIES – DISTRIBUTION INDUSTRY

BAPW - British Association of Pharmaceutical Wholesalers

The BAPW represents full line pharmaceutical distributors who between them distribute 90% of the nation's medicines, covering all of the UK's population. BAPW provides a forum for discussion across the industries involved in the provision of pharmaceuticals to UK'S health services.

The big three (Alliance Boots, AAH/Lloyds [Celesio], and Phoenix) account for around 90% of all distribution and Mawdsleys a further 5%

EAEPC- European Association of Euro-Pharmaceutical Companies

The European Association of Euro-Pharmaceutical Companies (EAEPC) is the professional and representative voice of pharmaceutical parallel trade in Europe. Through national associations and individual company membership, it encompasses over 70 firms from 16 countries in the European Economic Area (EEA). All products handled by EAEPC members have national or EU regulatory approval and are exclusively sourced from and sold to EEA countries using authorised trade channels.

TRADE BODIES – PHARMACEUTICAL (AND MEDICAL) INDUSTRY

ABPI – Association of British Pharmaceutical Industry

ABPI is the trade association for more than 75 companies in the UK producing prescription medicines. Its member companies research, develop, manufacture and supply more than 80 per cent of the medicines prescribed through the National Health Service (NHS).

It lobbies the DOH, NHS, NICE and the Government with high levels of activity, negotiates the PPRS, Prescription Pricing Regulatory Scheme with the DH and handles PR with organisations such as NICE and the MHRA where there is a collective interest.

ABHI -Association of British Healthcare Industries

The Association of British Healthcare Industries (ABHI) is the lead, and largest, industry association for the medical technology sector in the UK. ABHI represent companies whose output makes up for around eighty percent of the industry's total. Our membership includes some of the leading businesses in the sector in the UK right the way through to small independent companies. ABHI members produce essential products for the NHS - everything from life support machines through to latex gloves.

BGMA- British Generic Manufacturers Association

The British Generic Manufacturers Association represents the interests of UK based manufacturers and suppliers of generic medicines and promotes the development of the generic medicines industry. Members are normally British based companies whose principal activity within the UK is the manufacture and marketing of generic medicines and manufacture 75% of their generic products by volume in the United Kingdom or the European Union.

BHTA – British Healthcare Trade Association

The aim of the BHTA is to :

- Provide a platform to discuss issues and influence healthcare policy in the UK
- Represent large and small companies across the many sectors of the healthcare industry
- Assist in improving the quality standard within the industry
- Be responsive to the concerns and needs of member companies

PHARMACY PROFESSIONAL BODIES

RPSGB - Royal Pharmaceutical Society of Great Britain

The Royal Pharmaceutical Society of Great Britain (RPSGB) is the professional and regulatory body for pharmacists in England, Scotland and Wales. It also regulates pharmacy technicians on a voluntary basis, which is expected to become statutory under anticipated legislation. The primary objectives of the Society are to lead, regulate, develop and represent the profession of pharmacy. It covers legal and statutory aspects of the pharmacy profession.

Pharmaceutical Journal and Hospital Pharmacist are its publications and main communication channels.

GHP - Guild of Healthcare Pharmacists

Membership of the Guild is open to registered UK pharmacists, pre-registration students or those with reciprocal or equivalent qualifications who hold (or have held) appointments with UK Health Authorities, Health Boards, NHS Trusts, FHSA's or similar institutions.

The guild is part of Amicus, a trade union body, and as such negotiates pay scales and other HR/Payroll issues.

The Guild does support education and training and through its interest groups provides access to the commercial organisations who work with pharmacy.

PDIG - Procurement and Distribution Interest Group

The Group exists to promote Good Procurement and Distribution Practice (GPDP) in the hospital pharmaceutical service.

Members of the Pharmaceutical Industry involved in the area may become affiliates of the group. The Group is managed by a Committee elected from the members and affiliates with two ex officio members nominated by Guild Council.

ITIG - Information Technology Interest Group

The group examines Pharmacy issues with reference to CfH (Connecting for Health) especially electronic prescribing.

They try to establish Standards with regard to use of drug dictionary, EAN codes and bar-coding. There is some overlap with other groups.

NHS SUPPLY CHAIN GROUPS

National Pharmaceutical Supply Group (NPSG)

The role of the NSPG is:

- To provide advice to Chief Executive, NHS Purchasing and Supply Agency concerning the cost effective purchasing and distribution of pharmaceutical products to the NHS in England.
- To act as a focal point for the NHS for pharmaceutical issues of a national nature and provide pharmaceutical advice accordingly.
- To act as a link between Pharmacists and NHS Purchasing and Supply Agency at national level.
- To advise the Department of Health and pharmaceutical industry on significant commercial matters.

NPSG is the strategic focus in the relationships between NHS PASA, the DH, hospital pharmacists and their pharmacy purchasing groups and is the 'point of entry' for any NPSA and MHRA input into contracting dialogue.

Pharmaceutical Market Support Group (PMSG)

PMSG is an operational sub group of NPSG. It consists of pharmacy procurement specialists and NHS PASA category managers.

Amongst other roles, PMSG brings together a national overview of commercial and pharmaceutical expertise to assist NHS PASA coordinate pharmacy purchasing group activity and to advise the pharmacy purchasing groups on the most appropriate award decisions, so as to achieve maximum benefit for the NHS whilst avoiding and managing any introduction of risk to supply.

Collaborative Procurement Hubs

The Collaborative Procurement Hubs (CPH) project is working with trusts and confederations in a phased approach to develop CPHs across the NHS that provide a regional procurement focus.

CPHs will help optimise all commercial spend through collaborative working across all trusts in the local health economy and ensure a strong clinical interface to deliver the right product for local health economies.

[Any queries on the content of this document should be addressed to Mice Associates 01584 881402](#)