The Hague Centre for Strategic Studies
TNO
STRATEGY & CHANGE

MEDICAL SCARCITY

INCREASING SCARCITY OF MEDICATION

Over the past five years, the pharmaceutical supply chain has grown increasingly unreliable. According to the US Food and Drug Administration (FDA), the figure of drug shortages has tripled between 2006 and 2010 (see Figure 1 and Figure 2[1]). In 2010 alone 211 cases were recorded, while in 2011 up to 89 cases were recorded as early as March.[2] These shortages range from cancer medication to antibiotics, anesthetics, painkillers, anti-depressants and emergency care drugs. Shortages have grave implications for the provision of healthcare, with hospitals not able to provide the right care causing patients to become ill or even perish. Drug scarcity has also been experienced in Europe where reports have surfaced of shortages in cytarabine, a leukemia drug, Thyrogen, used to treat thyroid cancer, and in Cerezyme and Fabrazyme, essential for the treatment of enzyme deficiency disorders.[3] The rise of drug shortages has raised concerns among health care providers and requires effective monitoring by national authorities with possible intervention. Increasing scarcity of medication is a worrying trend, which is likely to continue for the coming decades.

EXAMPLES OF RECENT DRUG SHORTAGES

CANCER MEDICATION: CYTARABINE, CISPLATIN, CARBOPLATIN, DAUANOR UBICIN, DEXAMETHASONE, DOXORUBICIN, ETOPOSIDE, LEVOLEUCOVORIN, VINCRISTINE, TAXOL, ETC.
ANTIBIOTICS: PENICILLIN, TETRACYCLINE, ERYTHROMYCIN, CEPHALEXIN, DOXYCYCLINE, CLINDAMYCIN, CIPROFLOXACIN, GENTAMICIN, ETC.
ANESTHETICS: PROPOFOL, PENTOTHAL, ETC.
PAINKILLERS: MORPHINE AND FENTANYL, ETC.
ANTI-DEPRESSANTS: ELAVIL, STEMETIL, ETC.
EMERCENCY CARE DRUGS: NOREPINEPHRINE, DIGOXIN, ETC.
MEDICAL ISOTOPES: TECHNETIUM 99M

FIGURE 1 'EXAMPLES OF RECENT DRUGS SHORTAGES'

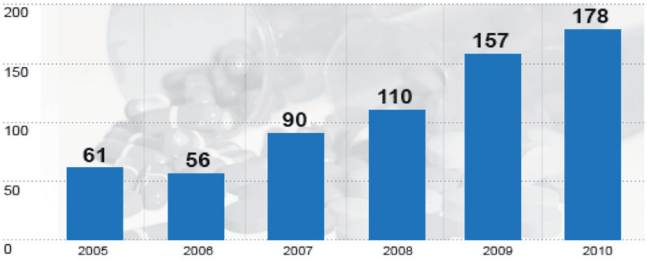

FIGURE 2 'NUMBER OF SHORTAGES IN THE UNITED STATES' (2005-2010) BASED ON 2010 DATA COLLECTED BY FDA THROUGH 12/13/10; SOURCE FDA; PHOTO THINKSTOCK

RISING DEMAND

Demand is likely to continue to increase in the short, medium, and long term future, driven by a number of developments.

Governments in Europe, Asia and the US are confronted with an aging population. It is expected that the global number of people of over 60 years of age will increase from 739 million in 2009 to more than 2 billion by 2050. Chronic diseases will become more prevalent and the increasing number afflicted will require medication for a longer period of time. These problems are not only related to aging, but also to life-style choices and increasing urbanization. Obesity is rapidly overtaking hunger as the world's biggest health problem. Furthermore, exposure to environmental pollution is causing more people to suffer from airway diseases such as asthma and COPD. Moreover, shortages also contribute to rising medication costs. With people getting older and unhealthier, the demand for adequate health care is projected to not only increase, but also to become far more expensive.

SUFFERING SUPPLY

There are a number of factors which cause disruptions to the supply of medicines that need to be taken into account:

QUICK TOPIC REPORTS

Quick Topic Reports are a series of briefs produced by the Strategy & Change Program. The briefs in the series identify emerging strategic issues that are relevant for the four themes of Strategy & Change: security, technology & innovation, economy & society, and sustainable development (see strategyandchange.nl/).

For each of these issues, we explore policy implications across the four themes. To identify these issues, Strategy & Change employs an innovative approach analyzing a wealth of forward looking resources available the Internet. This process is supported by *Leximancer* text mining software. For a full description of the methodology, please see strategyandchange.nl.

- **Shortages of resources**: Many natural materials used in medicines are concentrated in a few countries, most notably China, but also India.[4] These countries may invoke decrease in biodiversity or other national interests to instate export restrictions, leading to shortages elsewhere. Dr. Yusuf Hamied, the chairman of Cipla, one of the world's most prominent suppliers of pharmaceutical ingredients, stated *'[i]f tomorrow China stopped supplying pharmaceutical ingredients, the worldwide pharmaceutical industry would collapse'*.[5] This concentration of resources has proven hazardous, with instances of contamination in one country disrupting the entire global supply chain of a drug. Shortages also occur for synthetic or chemical substances, such as medical isotopes used in medicine tests.

- **Decreasing innovation**: Despite growing R&D expenditure during the last ten years, output of medicines has been decreasing. In 2010, worldwide expenditure on R&D decreased for the first time by 3%. Reasons for dwindling R&D include the expiration of patents and availability of generic medicines as well as the financial crisis. In addition, there is a shift visible from Big Pharma towards smaller companies, through a practice of in-licensing.

- **Industrial developments**: The emergence of global innovation networks and consolidation of the pharmaceutical industry have made the supply chain vulnerable. A reduction in the number of suppliers due to mergers and acquisitions has resulted in the narrowing and discontinuation of product lines, cost control efforts and higher costs for R&D. Moreover, more companies are shifting to 'just in time' production, while pharmacies keep lower buffer stocks, increasing the vulnerability of the supply line to supply shocks.

- **Medicinal quality**: Instances have occurred in the past where drugs were recalled due to contamination, impurities and stability changes. For instance, a shortage of heparin, an anti-clog drug used in dialysis and surgery, emerged in the US when the product originating from China appeared to be contaminated. With Chinese standards still inferior to American and European standards, these problems are unlikely to diminish in the near future.

- **Governmental regulations**: Stringent compliance requirements and extensive approval programs make it more difficult for companies to launch new medicines onto the market. Review boards have been found wanting in accommodating sudden shortages and speeding up processes to allow imports or approve new suppliers. Furthermore, these bodies are often not equipped to enforce the production of certain medication, and lack data on medical shortages as suppliers only have to inform on imminent shortages under minimal conditions.

It is often an interplay of different factors that leads to a shortage, as can be seen in Figuur 3[6].

CASE OF STERILE INJECTABLE DRUG SHORTAGES IN 2010

IT IS OFTEN AN INTERPLAY OF DIFFERENT FACTORS THAT LEADS TO A SHORTAGE. AN EXAMPLE IS THE STERILE INJECTABLE DRUG SHORTAGES OF 2010. IN THIS CASE, 42% OF SHORTAGES COULD BE ATTRIBUTED TO PRODUCT QUALITY ISSUES, 18% TO DISCONTINUATIONS OF PRODUCTS, 9% TO RAW MATERIALS ISSUES, 5% TO THE SHUTDOWN OF A MANUFACTURING SITE, AND 4% TO THE INCREASE IN DEMAND CAUSED BY SHORTAGES OF OTHER DRUGS.

FIGUUR 3 'CASE OF STERILE INJECTABLE DRUG SHORTAGES IN 2010'

GOVERNMENT INTERFERENCE

Government policy influences the drugs market in several ways. First, governments can provide incentives for innovation through policies on price regulation, such as reference pricing, on free competition, data protection, and manipulation of the branded period. Secondly, they can influence the market through government acquisition policies of drugs, in which they have to balance cost containment measures with rising demand. As a result national authorities are increasingly buying and supporting generic medication, and looking for cost-effective products, which does not provide a good incentive for pharmaceutical innovation. Thirdly, the current innovation gap requires better coordination of funding, research objectives and societal needs for medication and health care. Coordination between companies and authorities is lacking, often resulting in misallocation of funding and overlapping research programs.

POLICY MEASURES

Recent drug shortages have led certain governments, particularly the US, to take up a more interventionist and regulatory role. There are increasing calls for

measures such as stockpiling of drugs and increasing domestic production to secure supply. These measures, however, do not always provide durable solutions and have the potential to actually amplify the shortage problem. Even if mitigation of shortages improves, the prevention of shortages to occur in the first place is of large importance.[7] For instance, the temporary disappearance of the cancer drug prochlorperazine led to a price increase of 56% upon its return.

- **Stockpiling**: Governments may resort to stockpiling during times of shortage or to pre-empt a shortage. However, stockpiling is often not a desirable option given that the shelf-life of medication can be relatively limited and predictions can prove inaccurate. Moreover, stockpiling creates artificial shortages as short term pressures on the market increase.

- **Substitutes and imports**: The use of substitutes and imports may offer temporary relief. However, in the long term, it can lead to a snowballing of scarcity of (substitute) drugs. Moreover, (imported) substitutes are seldom as effective in treatments as the original product.

- **Early notification**: A strengthening of notification rules for imminent shortages by suppliers may prevent or curtail shortages. Thanks to early notification, the FDA has been able to intervene and prevent shortages of at least 24 products in 2010. While the US is taking the lead in data gathering, Europe is still lagging behind in monitoring shortages.

- **Government supervision and regulation:** Initiatives have been taken to strengthen the role of supervisory institutions and to increase their convening power over the pharmaceutical industry. This may require overhauling current principles in the pharmaceutical industry, such as the fact that in some countries supply lines are considered a trade secret, as well as increasing awareness among the public and private sector that medical scarcity touches on national security.

- **Domestic production**: In the US there has been a surge in efforts to (re)establish domestic production methods. However, domestically manufactured products would still require recources from countries such as China and India. Moreover, the creation of domestic industrial capacity is a costly and lengthy procedure with domestic producers often unable to compete in the global market.

- **Government incentives for innovation**: Incentives for R&D include greater pricing flexibility, guaranteeing market exclusivity, extending the branded period, and securing price premiums for innovative products during the branded period. A smooth transfer to cheaper, generic versions can be facilitated by supporting their development during the branded period.

- **Improved public-private cooperation**: Better cooperation between national authorities and companies as well as public and private research institutions would save costs and increase chances of innovation breakthroughs. However, coordination efforts are often thwarted by differing objectives.

- **Changes in health management**: Governments, including in China and EU-states, are currently shifting attention and resources towards healthy aging and care, decreasing interest in cure.

EUROPE

The EU recognizes the pharmaceutical sector as one of the high-tech industries at the basis of its knowledge economy and has expressed the goal to restore Europe's role as a leading and 'natural home' for pharmaceutical innovation in its Europe 2020 strategy. However, the pharmaceutical industry in Europe suffers from a fragmented market caused by a divergence in standards and pricing and reimbursement schemes, complex regulation procedures, limited access to finance and multiplication of research efforts. Meanwhile, acquisition policies of member states mostly prefer generics.

The EU's policy response to these issues has focused on establishing regulatory boundaries for market access, and supporting trade and internal and external regulatory convergence. An interesting policy trend is the targeting of the entire pharmaceutical supply chain as visible in the 2008 'pharmaceutical package' amendment of 'Pharma Directive' 2001/83/EC. In this directive, brokers and partners were subjected to reforms in manufacture, procurement of active pharmaceutical ingredients (APIs), excipients and finished dosage forms and release.[8]

Although the EU has emphasized the need to 'guarantee access to affordable medicines', which are 'safe and effective', this has received limited attention in actual policy making. Contrary to the US, there is relatively limited information available on shortages in

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the different European member states, let alone on the EU level, although notice of several shortages has been made. This lack of data gathering, information, and coordination is worrisome.

THE NETHERLANDS

For the Netherlands, which has to deal with an increasingly older and unhealthy population, medical scarcity has implications in terms of both supply and demand. It lacks a comprehensive program on assessing the issue of medical scarcity, and developing approaches on guarantees of supply, international standards of security, overarching stockpiling and production, etc. Although attempts are made for a comprehensive approach, actions do not always match intentions. Areas of future shortages are currently insufficiently anticipated and addressed.

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1 PARIJA KAVILANZ, 'DRUG SHORTAGES AT ALL-TIME HIGH,' *CNNMONEY*, JUNE 10, 2011, ACCESSED AUGUST 9, 2011, HTTP://MONEY.CNN.COM/2011/06/10/NEWS/ECONOMY/DRUG_SHORTAGES_FDA/INDEX.HTM.

2 ROB STEIN, 'SHORTAGES OF KEY DRUGS ENDANGER PATIENTS,' *THE WASHINGTON POST*, MAY 2, 2011, ACCESSED AUGUST 9, 2011, HTTP://WWW.WASHINGTONPOST.COM/NATIONAL/SHORTAGES-OF-KEY-DRUGS-ENDANGER-PATIENTS/2011/04/26/AF1AJJVF_STORY.HTML.

3 'GENZYME ANTICIPATES THYROGEN DRUG SHORTAGE,' *PHARMACEUTICAL BUSINESS REVIEW*, MARCH 22, 2011, ACCESSED AUGUST 9, 2011, HTTP://MANUFACTURING.PHARMACEUTICAL-BUSINESS-REVIEW.COM/NEWS/GENZYME-ANTICIPATES-THYROGEN-DRUG-SHORTAGE-220311;
BEN HIRSCHLER, 'EU BODY SEES GENZYME DRUG SHORTAGE UNTIL END-SEPT,' *REUTERS*, APRIL 23, 2010, ACCESSED AUGUST 9, 2011, HTTP://WWW.REUTERS.COM/ARTICLE/2010/04/23/GENZYME-EUROPE-IDUSLDE63M12P20100423.

4 'KLEINE MARKT EN WEINIG TE VERDIENEN: TEKORT AAN MEDICIJNEN LEUKEMIE,' *NOS OP 3*, MAY 17, 2011, ACCESSED AUGUST 9, 2011, HTTP://NOS.NL/OP3/ARTIKEL/241249-KLEINE-MARKT-EN-WEINIG-TE-VERDIENEN-TEKORT-AAN-MEDICIJNEN-LEUKEMIE.HTML;
HELEEN CROONEN, 'DE GEVAREN VAN GENEESMIDDELEN-GLOBALISERING,' *MEDISCH CONTACT* 63, NO. 39 (2008): 1582 HTTP://MEDISCHCONTACT.ARTSENNET.NL/WEB/FILE?UUID=E7A2E8A6-F633-41C3-8083-BDD47D6C720A&OWNER=1D4C113D-91C1-4008-9662-366D54D54DD8.

5 GARDINER HARRIS, 'DRUG MAKING'S MOVE ABROAD STIRS CONCERNS,' *THE NEW YORK TIMES*, JANUARY 19, 2009, ACCESSED AUGUST 9, 2011, HTTP://WWW.NYTIMES.COM/2009/01/20/HEALTH/POLICY/20DRUG.HTML?_R=1&REF=HEALTH.

6 COLEEN CHERICI ET AL., 'NAVIGATING DRUG SHORTAGES IN AMERICAN HEALTHCARE: A PREMIER HEALTHCARE ALLIANCE ANALYSIS,' MARCH 2011, ACCESSED AUGUST 9, 2011, HTTP://WWW.PREMIERINC.COM/ABOUT/NEWS/11-MAR/DRUG-SHORTAGE-WHITE-PAPER-3-28-11.PDF

7 ANDRÉ PICARD, 'WHAT'S CAUSING A SHORTAGE OF COMMON DRUGS?,' *THE GLOBE AND MAIL*, JANUARY 12, 2011, ACCESSED AUGUST 9, 2011, HTTP://WWW.THEGLOBEANDMAIL.COM/LIFE/HEALTH/NEW-HEALTH/ANDRE-PICARD/ARTICLE1867683.ECE

8 'THE NEW PHARMA DIRECTIVE. CONSEQUENCES OF THE AMENDMENTS TO DIRECTIVE 2001/83/EC,' CONCEPT HEIDELBERG, ACCESSED AUGUST 9, 2011, HTTP://WWW.GMP-COMPLIANCE.ORG/DATEN/TRAINING/ECA_NEW_PHARMA_DIRECTIVE_2011.PDF.