REPORT OF THE INTERNATIONAL SUMMIT ON MEDICINES SHORTAGE

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fip ADVANCING PHARMACY WORLDWIDE

CONTENTS

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1.

INTRODUCTION

Medicine shortages have become a complex global problem. In some countries medicine shortages tripled between 2005 and 2010. There is evidence that these shortages are worsening with time, creating ever more difficulties for healthcare professionals, and compromising patient safety. Such shortages have also serious implications in terms of additional costs and staff workloads, possibly as much as hundreds of millions of dollars in expenses every year. The causes of these shortages are several and multidimensional in the context of a complex global supply chain. As a result, there is a growing concern amongst healthcare professionals about the future of medicine supplies worldwide.

In light of this growing concern, delegates from around the world gathered in Toronto in June 2013 to attend the first-ever "International Summit on Medicine Shortages" hosted by the International Pharmaceutical Federation (FIP), and co-hosted by the Canadian Pharmacists Association. The purpose of the Summit was to provide a forum to discuss the causes, impacts, and solutions to the global issue of medicine shortages through a multi-stakeholder approach involving representatives from governments, healthcare practitioners and professional bodies, industry, and patients.

2.

EXECUTIVE SUMMARY

The fabric of medicine shortages is multi-layered, with overlapping and interconnected threads of causes. Within a highly complex global chain of supply, manufacturers are generally reliant on a single authorised supplier for key ingredients including active substance. Frequently, several manufacturers are supplied by one source. Very often these sources are situated in only a few countries, such as India or China. This reliance on very few sources is a risk factor, which can cause instability in the global supply chain. Many countries in the world are consumers of only a small percent of overall global consumption of medicines and hence do not have a viable domestic manufacturing industry for medicines. Also most developed countries regularly impose stricter regulations in an effort to improve quality. The surge of tainted drugs and contaminated food, as well as counterfeit medicines, around the world has called for tighter regulation and more frequent audits, often inadvertently contributing to impediment of production flow and temporary or even permanent medicine shortages.

Simultaneously, adding to the complexity of the problem, there is an ever-growing demand for medications, due to ageing communities and availability of more effective treatments. When combined with disruptions in production due to the abovementioned reasons, declining inventories, hoarding by some purchasers, imperfect purchasing policies, and 'grey markets'[1], the frequent result is an inability to supply medicines to where and when they are needed.

As such, in formulating recommendations to address all or any one of the causes of medicine shortages, the FIP Summit firstly established by unanimous consensus the following assumptions:
- Medicines should not be considered as ordinary commodities of trade
- The free market does not always achieve desired social goals in relation to medicines
- There are both short-term solutions (addressing current shortages) and long-term strategies (preventing future shortages)

Upon these assumptions, the Summit then made the following major recommendations:
- Each country should establish a publicly accessible means of providing information on medicine shortages.
- A global process to determine the list of critical/vulnerable products should be developed.
- All procurers of medicines are urged to move towards active procurement processes that assure the continuity of supply of quality medicines.
- All countries are encouraged to remove unnecessary variability of regulatory practices within and between countries.
- All countries should investigate the potential to establish a national body charged with gathering and sharing information about demand for, and supply of, medicines within their jurisdiction.
- All countries are encouraged to develop evidence-based risk mitigation strategies which might include strategic buffer stockpiles, contingency plans, pandemic planning and capacity redundancy, appropriate to their national needs.

1 The grey market is a trade of products through supply channels which, while often legal, is unintended, unofficial, unauthorized by the original manufacturer. Grey market distributors buy available drug supplies and sell them to providers or end purchasers at important mark-ups (e.g. several hundred per cent in USA for instance)

3.

STRUCTURE OF THE MEETING

The Summit benefited from the input of 46 delegates from around the world, including representatives of health ministries, governments and intergovernmental bodies, regulators, pharmaceutical companies, patients and professional associations of pharmacists, medical practitioners and dentists.
The programme extended over two days, and included workshops and plenary sessions.

A. Opening remarks

Dr Michel Buchmann, President of FIP, welcomed the delegates and set the scene for collaboration and brain storming to attain the purpose of the summit, which was to develop recommendations to address the global problem of medicine shortages. The Summit was meant not only to identify solutions to the problem at a global level, but also to develop a community of experts and networks collaborating in deliberations about the problem of medicine shortages around the world.
Dr Cecil Wilson, the President of the World Medical Association (WMA), presented the perspective of physicians worldwide. He spoke about the widespread issue of shortages in medicine supplies and the implications on decision making, impact on patient care and the role of government bodies such as the FDA in the USA. Dr Wilson emphasised the urgent need to work on prevention and mitigation of medicine shortages.
Suzanne Nurse, representing the International Alliance of Patients' Organizations (IAPO), presented the patient perspectives of medicine shortages, giving examples of real people who have experienced shortages and the impact this had on their health and safety. She highlighted that medicines shortages have been associated with lack of transparency, lack of public awareness and lack of data on serious adverse events occurring as a direct result of medicine shortages. Patients have reportedly been left out of the decision-making process, and there exists a climate of suspicion and distrust between patient and healthcare systems. Emphasis was placed on the need for patient engagement at all levels in patient-centred care.

B. An overview of medicines shortages

Kasey Thompson, representing the American Society of Health-System Pharmacists (ASHP), reported having dealt with the problem of medicine shortages in the USA for over 14 years. He provided an in-depth overview of the number and duration of medicine shortages in the USA over the years. He shared with the Summit delegates his observations of serious impact on patient care and the lessons learned from the many aspects of the problem, and how it has been managed, highlighting the important role of the US Food and Drug Administration (FDA) and the University of Utah Drug Information Service in collecting vital data and statistics crucial to policy development and tracing progress.

C. Estimates of the consequences of a medicines shortage

The impact of medicine shortages in terms of consequences to human lives, finances, human resources and indirect costs, was then presented from two perspectives: one from developing countries and another from developed countries.
Lisa Hedman from the WHO Department of Essential Medicines and Health Products, talked about the vulnerabilities of low- and middle-income countries in terms of policy, regulation, financing, manufacturing, supply and emergencies, all of which can lead to problems of shortages. She used anti-tuberculosis and antibiotic medicines to illustrate the complexities of interactions between policy changes, cost and demand, as well as the change affecting the internal markets of BRICS countries (Brazil, Russia, India, China and South Africa), which could result in a decrease of the export of medicines from these countries.
On the other hand, Jeff Morrison, representing the Canadian Pharmacists Association, highlighted the differences and similarities between the USA and Canada, and reported the impact of medicines shortages on pharmacists, patients and physicians, elaborating on the approaches adopted in Canada to deal with medicine shortages.

D. Causes and contributing factors of the medicines shortages

Luc Besançon (FIP, The Netherlands) and Andy Gray (FIP, South Africa) then gave a presentation about causes and contributing factors in medicine shortages; placing the issue of medicine shortages into context in terms of place, supply and demand. Delegates were invited to think of the concept of "national accessible stock", which is the overall amount of a specific pharmaceutical product accessible through the whole supply chain, integrating the different levels of stock/inventories (e.g. at national manufacturer/importer level, wholesaler level, public sector pharmacy depot level and at community pharmacy/local hospital level). Issues such as affordability, challenges, vulnerability to change, limited reactivity, and globalisation of manufacture of medicines (whilst regulators remained national), were explored.

Examples were drawn from 17 countries in the world to illustrate the diversity of causes and contributing factors associated with medicines shortages. The presentation concluded with the statement that primary drivers associated with medicines shortages were both economic and technological.

E. Perspective from the Pharmaceutical Industry

Dr Maura Kinahan (Pfizer) presented the pharmaceutical industry perspective. The many complexities of supply and demand variability were highlighted. Several internal Pfizer initiatives to mitigate the risk of medicines shortages or to manage existing shortages were reported. One example is an International Drug Shortage Review Team (DSRT) which reviews issues such as stock numbers on hand, supply interruptions and forecast error, for a set of activities to be taken by local management (at country level). She concluded her presentation with suggestions for future improvement for consideration.

F. Workshops

Delegates were then invited to participate in one of two workshops (looking respectively at the supply and demand sides of the problem) which continued work into the second day of the Summit.
The first part of the workshops was dedicated to deliberating on the reasons for medicines shortage from both supply and demand perspectives. The second day of the workshops focused on best practices to prevent medicines shortages (or to limit their consequences), and concluded by discussing resolutions or recommendations.
(Please refer to point 6 in this Report for details of workshop outcomes).

4.

THE PROBLEM

A. Description

A medicine shortage can be defined a drug supply issue requiring a change. It impacts patient care and requires the use of an alternative agent.
There is insufficient information to assess the magnitude of the problem at an international level. Similarly, the characteristics of medicines shortages vary greatly from country to country, and the lack of reliable information at a global level limits the capability for establishing a global coordinated action.
However, at a few national or regional levels, data have been collected, providing some crucial evidence for the estimation of the extent and depth of the problem of medicine shortages.

For instance, in the USA, data presented at the conference from the University of Utah Drug Information Center, showed an increase in the number of new shortages from 58-88 in 2002-2007 to 267 in 2011, and 204 in 2012. These new shortages are additional to with unresolved shortages from previous years and therefore lead to an increase in the quarterly reports of active medicine shortages from 152 in early 2010 to 300 on early 2013. This clearly demonstrates that, despite the remedial measures taken, the issue is far from declining in the USA.

Most active shortages in the USA are in antimicrobials, chemotherapy, cardiovascular medicines, central nervous system medicine and nutritional supplements. There are now shortages of 11 chemotherapy agents in 2013. In 2011, the IMS Institute of Health Informatics estimated that 89% of the medicines shortages in the USA were in generics and branded generics. In 2012, the University of Utah estimated that 45% of the shortages were injectables and generics.

In Canada, the national drug shortages reporting system (www.drugshortages.ca) listed approximately 300 products (drug, package size, dosage strength, etc.) as of June 2013.

Medicine shortages are not restricted to Northern America. In Europe, 346 hospitals were surveyed by the European Association of Hospital Pharmacists and found 98.8% participating hospitals were found to have experienced shortages over the past 12 months, while 63% reported that problems associated with shortages occur at least weekly. The most frequent medicines in shortage were from the following therapeutic groups: Oncology, Emergency, Cardiovascular, Haematology, Respiratory and Paediatrics. Such shortages were frequent both among generic products (57%) than original/brand products (43%), reflecting that a higher proportion of brand products are affected by shortages in the European market vs. in Northern America.

B. Impact of medicine shortages

All delegates at the Summit emphasized that patient care was at the centre of all deliberations, and agreed there was a substantial degree of compromise in patient care as a result of medicine shortages.
Medicine shortages can result in delayed or unavailable treatment, or a change to an alternative, often less effective drug. And there are safety implications to consider, including those incurred through errors from the use of alternative medicines, and adverse patient outcomes as a result. The following table summarizes the results of a survey among US hospitals estimating the impact of a medicine shortage on patient care:

IMPACT	ALWAYS	FREQUENTLY	RARELY	TOTAL
Patient treatment was delayed	3%	17%	62%	82%
Patient received a less effective drug	0%	11%	58%	69%
Patient did not receive a recommended treatment	1%	10%	52%	63%
Patient experienced an adverse outcome	0%	3%	32%	35%

Adapted from: AHA analysis of survey data from 820 non-federal acute care hospitals. Survey completed in June 2011

These issues indicate there are often painful decisions to be made by physicians. Some circumstances may also require medical doctors to choose which patients to treat and which may need to delay (or cancel) treatment. Medicine shortages can also result in the patient's condition worsening or requiring hospitalisation and may even cause death: there is evidence that at least 15 deaths in the USA could be attributed to medicine shortages in 2010-2011.

Similar consequences in patients have also been reported in Canada, where 68% of medical doctors and 78% of pharmacists surveyed concluded that drug shortages have consequences for patients.
Shortages also result in additional costs for healthcare systems, as the cost of alternative medicines could be higher as the purchasing is usually made off-contract, sometimes even from the 'grey' market.

To limit the impact of medicines shortages as much as possible, healthcare professionals spend substantial amounts of their time trying to find solutions. For instance, in a 2011 study, it was reported that pharmacists spent 9 hours per week trying to manage medicine shortages, pharmacy technicians 8 hours per week and medical doctors 30 minutes per week.

This also means that medicine shortages divert healthcare providers from direct patient care activities. In a survey undertaken in Canada in January 2013, 67% of the medical doctors stated that shortages have a negative impact on their practice, while 75% of pharmacists reported a significant impact on their practice and on their workload.

Premier Healthcare Alliance reported that the cost to US hospitals of shortages was $416 million (consisting of $200 million purchasing more expensive alternatives and $216 million in labour costs). It was however pointed out that we do not know the global cost of medicine shortages annually, nor the cost related to under-treatment of patients because of medicines shortages.

5.

CAUSES AND CONTRIBUTING FACTORS OF THE MEDICINES SHORTAGES

The University of Utah estimated that 36% of the medicine shortages occurring in the USA in 2012 were related to manufacturing reasons, 8.3% related to supply/demand reason, 7.8% were attributed to the discontinuation of a product and 3.9% to lack of raw materials. However, for 44%, no specific reason was reported.
When looking at reasons for injectable medicine shortages occurring in 2012, 42% were found to be related to quality assurance, manufacturing delays or capacity issues, 35% to issues with GMP (Good Manufacturing Practices), 7% to increase in demand, 7% to discontinuation of product, 5% related to procurement of raw materials and 4% to the loss of a manufacturing site.

The European Association of Hospital Pharmacists (EAHP) found that there are usually several explanations for medicine shortages experienced in Europe. They reported that 52.4% of the medicines shortages were related to having a single (or limited number of) supplier(s), 43.7% were related to shortages of raw materials, 43.7% due to manufacturing quality problems and 41.7% were related to the size of the market (small country with limited market).

Through the presentations and cases discussed at the Summit, it became clear that, while the issue of medicines shortage often involves issues in manufacturing, there are clearly additional factors involved in destabilising the market and increasing the likelihood of medicines shortages.

The reasons and contributing factors have been classified into two different groups:

A. Causes and contributing factors on the demand side

In terms of demand, it is often difficult to predict fluctuating market demand, which may be affected by price, tenders and surges in epidemics or certain disease states necessitating emergency medicines.

Changes in demand
The changes in demand can affect (and sometimes lead to) medicine shortages. For instance, the increasing demand in penicillin G in Australian hospitals lead to rationing of this product, as the only provider was unable to meet a sudden surge in demand. Similarly, in Brazil, the increasing demand of benznidazole (used to treat Chagas disease) could not be met by the sole world manufacturer (which is state-owned) and resulted in medicines shortages.

Of course, when a product is subject to a shortage, this will most likely result in an (unexpected) increase in demand for therapeutic alternatives, which can consequently be subject to shortages as well. In addition, when a patented product is about to go off-patent, the reliability of market share forecasts (and the substitution rate) is greatly reduced.

There is a global movement towards developing formularies and guidelines, which could help ensure improved predictability of demand. However, if these guidelines are not adhered to by prescribers, this can also lead to medicines shortages. Similarly, demand can be affected by changes in guidelines and new scientific evidence from clinical trials. When a product gains a new indication, this may also increase its demand. The manufacturer may have little time to adjust its manufacturing capacity to meet the increase in demand.

The situation in neighbouring countries also has a documented impact on a national situation: for instance, during the Libyan war, rebels were procuring medicines from Tunisia (increased export), whilst a number of refugees arrived in Tunisia with a need for medicines (increased interior demand). These two elements lead to medicine shortages in Tunisia.

As an important role is being played by emerging economies in manufacturing Active Pharmaceutical Ingredients (APIs) and finished pharmaceutical products, special attention should be given to the increased demand of their internal market. If not met appropriately with increased manufacturing capacities (as currently seen in China, South Africa, Russia and Brazil), this may create tensions between the provision of the internal (national) market and international markets.

Similarly, when the donor founding to a country is reduced, this can impact the supply in other countries: India represents around 70% of the global demand of cycloserine and this demand is supported via donor funding. Currently, the global market is above the sustainable production level but as India will no longer receive donor funding from 2015, it is predicted that the demand will then drop below the sustainable production levels and may lead to medicines shortages in all other countries.

Overall, forecasting of demand is constantly challenging for all stakeholders in the supply chain (industry, wholesalers, pharmacies/hospitals), as it often relies on seasonal trends and scarce historical data.
This prevents these stakeholders and partners from being able to adjust their production and stock accordingly to help prevent the occurrence of medicine shortages.

Perceived limited financial purchasing capability
From an economic point of view, affordability and capability to pre-finance the purchase of medicines are also important factors to consider in relation to medicine shortages. It was reported that in Zambia, donors suspended their financial support for HIV drugs on suspicion of corruption, which ultimately lead to a serious shortage in HIV medicines.

Similarly, the limited access to foreign currencies in Iran (as a consequence of International sanctions pursuant to UN resolutions) lead to several shortages. In other countries, like in Madagascar, insufficient funding for the purchase of medicines, combined with the currency exchange rate variation also led to medicines shortages.

In Greece, hospitals have been unable to pay for past orders to manufacturers, and the pharmaceutical industry has requested to have the debt paid before they deliver any new orders. In some parts of Spain also, governments of autonomous communities had major delays (up to 1 year) in reimbursing medicines costs to community pharmacies, which in turn prevented pharmacies from procuring subsequent stocks from wholesalers.

Structure of the demand
It was mentioned that the way demand by tender is structured (primarily to decrease costs) can affect the predictability of such demand and could be seen as a contributing factor for medicines shortages. Increased business risks relating to capability and predictability make the tender process less attractive for manufacturers to participate in.
For instance, when a tender policy awards exclusivity to a market for the cheapest product(s) to be reimbursed, it naturally leads to the exclusion of other players in the market, which consequently reduces alternatives if the selected manufacturers experience shortages.
Similarly, when “mega tenders” for several hospitals or large health systems are employed, the predictability of demand is affected, as they inevitably result in demand peaks.
The use of short-term tenders may also affect the predictability of demand and consequently increase the business risk.

On the other hand, if tender processes are bypassed (usually supported by corruption), this can lead to shortages, as was the experience in Papua New Guinea.

Some tender practices may impact the capacity of the manufacturer to forecast demand. If the contract is won, the manufacturer may have to withdraw resources from other lines in order to meet contractual obligations, which can affect the capacity to meet demands for other products, especially when the delivery of the products is to be made shortly after the contract is won.
Changes in rules for tenders (and import contracts and requirements) can also facilitate medicines shortages, as experienced in Senegal.
Examples of other elements affecting the attractiveness of the tender market could also be the nominated reference price and the lack of consideration given to guaranteed continuous access to medicines. The size of the market and lack of regulatory harmonization (leading to fragmentation of markets), also affect tender processes, as well as the rate of cross-subsidization with non-drug products, which keep prices artificially low.
Therefore, responsible contracting is crucial to ensure healthy, fair competition and to avoid shortages in supply of medicines.

Non-traditional demands
Similarly, exporting/parallel trade can also affect the availability of products: the National Institute of the Czech Republic reported that 20% of the medicines for the national market are exported (through parallel trade), resulting in shortages.
In France, the Académie Nationale de Pharmacie estimated that 4% of medicines shortages in France are associated with exports (parallel trade).
Some unscrupulous players in the supply chain can also stockpile products at risk of being in shortage, as a speculation. They could then sell their stock at extremely high prices once the shortages are experienced. This trend is also referred to as the ‘grey market’ in the US and other countries.

B. Causes and contributing factors on the supply side

As highlighted earlier, manufacturing reasons are often associated with the appearance of medicine shortages.

Manufacturing Finished Products

Several reasons can explain why a manufacturing site of finished pharmaceutical products has reduced or stopped the production of medicines.

Such decisions can be related to deficiencies in the quality of the medicines detected:

- By the manufacturer itself, through its quality assurance, resulting in batches not released onto the market, as happened in South Africa for Amphotericin B;
- By the inspection team of a medicines regulatory authority which may suspend the licence of a site, until the problem is solved. Moreover, inspections themselves can delay production.

Corrective measures may take some time and may require the manufacturer to decrease production at the affected site.

It may be more complicated to identify the most appropriate corrective measures when there is a lack of consistency between the regulators (when a manufacturing site produces for several markets) or there are differences in interpretations. In some cases, rigid regulatory frameworks are restrictive.

Ample notice of regulatory changes is important to ensure sufficient time for needed adjustment. Similarly, when a manufacturing licence is suspended, there could be a delay in performing the re-inspection to allow the manufacture to re-start its production.

There are other reasons explaining why a manufacturing site has stopped or dramatically reduced its production: for instance, in Japan, the tsunami of 11 March 2012 severely damaged or destroyed several pharmaceutical manufacturing sites. Similarly, as facilities age, it is crucial to ensure regular maintenance. If such operations are not properly planned (e.g. the manufacturer has not produced sufficient stock of the line to cover the period whilst it is closed and/or is faced with an unpredicted increase of the duration of maintenance), it can result in medicine shortages. Many factories run on a continual basis (24/7), and therefore the capacity to increase production to compensate for an incident in another factory, is quite limited and would also require authorizations by medicines regulatory authorities if the second site is not already listed.

Moreover, some products require specific facilities and knowledge to produce, such as for sterile injections and products that require high or complex standards of quality assurance in production processes, e.g. lyophilisation. Transfer of production sites can also increase the likelihood of medicines shortages, if approval by authorities is delayed.

Whatever the reason, whenever a manufacturing plant stops production, it can have a major impact on the supply of the market. When one manufacturing plant closed in 2010 for example, the impact was on 49 medicines - 18 of which were cancer chemotherapy products.

The launch of new products is sometimes associated with the discontinuation of old products, particularly those with very low prices and/or complex manufacturing processes, inadvertently causing a medicine shortage

Other reasons were mentioned at the Summit, such as a lack of coordination of production capacity and the lack of an ethical framework for decision-making in supply/distribution.

Raw materials

Sometimes, the issue is not related to the manufacturing site of finished pharmaceutical products but to the availability of raw materials.

When there is a single source of raw material for production of a medicine, if this source experiences a manufacturing problem, it is highly likely to impact on all manufacturers of finished pharmaceutical products based on this raw material.

Whilst 20 years ago 90% of APIs were manufactured in the USA, today the situation is very different, where 40% of medicines are manufactured abroad. Most APIs are sourced from India or China, making it difficult to replace such sources at short notice.

For instance, when a decision to make a significant price reduction of protamine sulphate was taken in China, several local active pharmaceutical ingredients manufacturers decided to stop its production, as it was then perceived to be not (sufficiently) profitable.

Similarly, the raw materials, especially excipients (or their precursors) may not only be used to produce medicines, and as such, there is always a competition between their different uses, guided by the price offered by the different sectors.

Moreover, an inherent vulnerability of raw materials also originates from the fact that their production might be seasonal (as they may rely on natural products as precursors). Lack of quality standards and the fact that inspections/reports are not shared with the rest of the world, have been considered as contributing factors as well.

Batch recall
When quality assurance is deficient, a product may be recalled due to concerns about contamination or faulty raw materials, causing a sudden gap in supply with an inevitable shortage.

Market structure
In many cases of generic medicines shortages, the products had single or limited suppliers, which increased the risk of shortage. For instance, in the USA, the majority of the injectable generic products market is supplied by only seven major manufacturers.

Inventory
Inventory practices can have a profound role in preventing or enabling medicines shortages, given that the national accessible stock (i.e. the overall amount of a specific pharmaceutical product through the whole supply chain) can play an important role in buffering incidents at the manufacturer level. For instance, the Académie Nationale de Pharmacie in France estimated that while 12% of the orders of wholesalers were not delivered by the pharmaceutical industry, only 4-5% of the orders of community pharmacies were not delivered, illustrating the positive role of buffers of the supply chain.
When conditions on minimum stock are removed (e.g. public service obligation of having a minimum stock to cover a specific-time demand), this may also affect the likelihood of medicine shortages as the buffer effect is then decreased.
Too often, inventory is "just-in-time", that is: waiting until there is high demand to order, instead of maintaining a lean inventory, contributes to the impact of medicine shortages. Similarly, too often, contingency plans are not robust and stock piling is in place in only a few countries (and they are often limited to a few products).

Other contributing factors for medicines shortages were mentioned: no proper framework for fair allocation of medicines in shortages, or failure to follow best practices in relation to distribution in such a situation, the increasing complexity of the distribution models (and who owns the inventory), and the allocation rules.

Information management
It was also mentioned that the lack of oversight and an absence of systemic indicators pointing to potential outages anywhere along the supply chain can also contribute to medicines shortages, as well as the lack of information on current cases of drug shortages.

6.

SOLUTIONS AND BEST PRACTICES TO PREVENT AND MITIGATE SHORTAGES

Solutions and best practices were discussed in depth at the Summit (in particular during the workshop) and then translated into a series of recommendations (see next chapter).

A. Solutions on the Demand side

Short-term and long-term strategies were discussed to address the problem of medicine shortages from a demand perspective.

During the Summit deliberations, the concept of "quality value" was recurrent, i.e. how much the supply chain and the consumer value the quality and certainty of a continuous supply.
This concept would imply a new model of purchasing:

a. Promoting multi-source contracts (not only the use of different pharmaceutical companies, but also requiring at least 2 suppliers of APIs and 2 manufacturing sites)
b. Not be solely based on price (and include consideration for quality and multi-sourcing). Indeed, a commitment to quality and supply can be made if pricing policy promotes it.

Multi-source contracts could also include provision for contingency plans.
Similarly, given ethics consideration, the procurement bodies should consider carefully before using the grey market for supply, where such options exist.

New models for purchasing should be developed to ensure a reasonable profit in exchange for guaranteed supply of drugs and encourage investment in facilities. Governments will have a key role in developing these new models.

Through incentives, global risk of medicines shortages can be reduced while manufacturing capacity redundancy could be promoted.

Improving forecasting could also have a positive impact. To ensure more accurate forecasting, the following options could be considered:

a. Develop a framework for forecasting
b. Take into account and minimise possible distortions (i.e. anything that would impact on predictability)
c. Consider the long-term trends of all countries, especially the ones involved in pharmaceutical manufacturing.
d. Involve all stakeholders for more credible forecasts, based on reliable information

With accurate forecasting, the industry will be able to adjust its capacity more easily.

Making information publicly available to all stakeholders on a regular basis is crucial. This information could cover:

a. Medicine needs (includes tenders/requests for proposals/contracts)
b. Existing stock throughout the whole supply chain
c. Best practices (in terms of tendering, dealing with shortages, etc.):e.g. in Canada, a "Drug Shortage communication protocol" under development by federal / provincial stakeholder committee.
d. Current medicines shortages including the reasons: for instance, in Canada, there is a national drug shortages reporting system (www.drugshortage.ca) which will soon include enhanced links to external drug information resources for health care practitioners. Similarly, in USA, both the FDA and the ASHP have websites with information on shortages to assist healthcare providers.

It was also considered that a list of critical or vulnerable products should be established at national level. Incentives for their production (and subsidization if needed) could then focus on the products on this list. Such products could also be guaranteed with a minimum price per unit.

The expansion of the scope of practice of some healthcare professionals (such as pharmacists) could better equip them to find solutions when facing a medicine shortage (for instance by allowing them to substitute medicines). In this regard, there are effective collaborative practice models in place in a number of settings.

B. Solutions on the Supply side

Regulatory side

The issue of harmonisation of regulation and standards on manufacturing (GMP) and product approval between countries was highlighted, not only between regulators but also within the same regulation framework.
Such harmonisation could help minimise market fragmentation and therefore facilitate reallocation of medicines to a country experiencing a shortage.

Early communication and transparency between regulators and manufacturers, even before official decisions are made, could improve the development of corrective measures before shortages happen, and when decisions which may affect the supply are taken by the regulators, it is crucial that they are communicated to pharmacists and prescribers.

Once a shortage occurs, the regulator may decide to focus its work on specific products (e.g. critical or vulnerable products). In the USA, the FDA's policy is to prevent or alleviate the need for medically necessary products which treat or prevent serious or life-threatening illness – whether off-label or labelled. The US FDA estimated that between 2010 and 2013, it had helped prevent close to 300 shortages.
Regulators' assessment activities are on a case-by-case basis and they can take appropriate measures to alleviate short-term problems, such as by: asking clinicians to be alert and check the availability of medicines, asking other companies to increase production, expediting reviews of new manufacturing plants or products which could provide alternative options' and allowing for imports. To increase the efficiency of the regulators responses, early notification of anticipated shortages by manufacturers (with appropriate penalties in case of noncompliance) and interagency coordination are considered important facilitators.
Clearly, the prevention and mitigation of medicine shortages needs different approaches from the regulators and these can be facilitated by the experience of the medicine regulatory agency.
The World Health Organization and larger regulators can have a key role in supporting less resourced agencies in developing and applying relevant policies for managing shortages.

Production of Finished Products and Active Pharmaceutical Ingredients

Industry could build capacity redundancy (within same company and/or pooled with other companies) and an open dialogue could be established between procurement officials and manufacturers in order to improve the forecasting and planning process.
Manufacturers' corporate social responsibility of manufacturers demands that they provide necessary information on the availability of medicines.
Closer attention should be given to ensuring that APIs meet quality standards. This would imply activities from both manufacturers and regulators and a stronger enforcement of quality standards. Audit reports of API suppliers could be shared between countries or companies.
When quality problems are detected, collaboration between regulators and manufacturers could be established to overcome the problems efficiently and in a timely fashion to avoid extensive medicine shortages.
To ensure a continuous supply of APIs, manufacturers should have more than one API supplier for a given product.

Each pharmaceutical manufacturer and wholesaler should employ a responsible person (e.g. pharmacist) in charge of oversighting the availability and communication..

Stock

The idea of stockpiling of a specific product or legislation on a minimum stock at the producer or wholesalers was discussed.
Similarly, it was envisioned that a demand-sharing agency could be established in order to facilitate the allocations between different countries in the event of shortages.

7.

RECOMMENDATIONS OF THE SUMMIT

Based on the discussion around the causes, contributing factors, solutions and best practices to prevent or mitigate shortages, summit delegates developed the following set of recommendations:

Recommendation 1

In order to advance transparency and increase communication between all stakeholders on existing shortages, each country should establish a publicly accessible means of providing information that is

- Timely
- As complete as possible
- Focused on current shortages and their reasons
- Provides details of expected duration and responses

This mechanism may involve the Ministry of Health, Medicines Regulatory Authority, Professional Bodies and/or, Industry Associations and other stakeholders.
The mid- to long-term aim should be to aggregate this information at the international level.

Recommendation 2

A global process to determine the list of Critical or Vulnerable products should be developed.
This would be most easily done by a multilateral organization within the United Nations structure and with inputs from Ministries of Health, Medicines Regulatory Authorities, Professional Bodies like FIP and Industry Associations.

Definition and criteria for designation as Critical or Vulnerable products would be based on the vulnerability of supply, the complexity of production, number and location of sites of API and finished pharmaceutical products manufacture, medical necessity and the ability to substitute.

This list will require continuous revision and will inform regulatory responses, procurement practices and risk mitigation strategies.

Each country could adapt the list to local conditions.

Recommendation 3

All procurers of medicines are urged to move towards active procurement processes that assure the continuity of supply of quality medicines

Elements of high-quality active procurement processes would include:

- Improved quantification including forecasting
- Direct communication between procurement agencies and manufacturers around issues of sustainable capacity
- Deliberate and considered approaches tailored to the specific situation for each product (long-term, short-term, split contracts…)
- Responsible pricing that values quality
- Meaningful binding contracting

Recommendation 4

All countries are encouraged to remove unnecessary variability of regulatory practices within and between countries.
All regulatory authorities need to advance responsible transparency in relation to all regulatory processes.
Manufacturers are encouraged to find a non-threatening means to share non-competitive aspects of audits of suppliers and contractors in order to improve transparency and enable coordinated responses.

Recommendation 5

All countries should investigate the potential to establish a national body charged with gathering and sharing information about demand for and supply of medicines within their jurisdiction.
This body could also develop an ethical framework for decision making relating to resource allocation at times of scarcity.
This body could also coordinate the dissemination of information about the national available stock disseminated through the whole supply chain.

Recommendation 6

All countries are encouraged to develop evidence-based risk mitigation strategies which might include strategic buffer stocks and stock piles, contingency planning, pandemic planning and capacity redundancy, appropriate to their national needs.

8.

CONCLUSION

In conclusion, the FIP Toronto Summit on Medicine Shortages achieved its main goal as articulated by Dr Buchmann: to identify both long-term and short-term solutions to the problem of medicine shortages at a global level, and to develop a community of collaborating experts and networks concerned and involved with this issue.

The issue under investigation, that is, the timely and affordable availability of medicines, has an impact on health status, human quality of life, and mortality. Reasons for medicine shortages are several, and often multidimensional involving industry capacity and capabilities, legislative frameworks, market policies and fluctuating demand. Some reasons overlap and perpetuate the problem, often causing a domino effect, whilst others are unique or stand alone, such as those resulting from natural disasters. Alternative options for substitution of medicines are fraught with risk, inequity of efficacy and lack of availability.

However, whatever the causes and impact of medicine shortages, it is in the best interests of the global community, governments, healthcare professionals, patients and the pharmaceutical industry, to work together in collaboration, transparency and understanding of the factors influencing the issue, in order to prevent or mitigate the evolution or worsening of the longstanding global trend of medicine shortages. The Summit culminated in the provision of six major recommendations for countries around the world to consider adopting, regardless of whether they have experienced major shortages of medicines to date or not, as the global structure of the medicines supply chain renders most countries similarly vulnerable.

In so doing, FIP and collaborating organisations participating in this Summit on medicine shortages, encourage governments and health ministries around the world to acknowledge and engage in the dialogue around the issue of medicine shortages and give careful consideration to implementation of the recommendations provided in this report.

9.

ANNEXES

A. List of participants

The following individuals took part in the International Summit on Medicines Shortage:

NAME	ORGANIZATION	COUNTRY
Abramowitz, Paul	American Society of Health-system Pharmacists (ASHP)	USA
Adenot, Isabelle	Ordre national des Pharmaciens	France
Andrews, Emma	Pfizer	USA
Besançon, Luc	International Pharmaceutical Federation (FIP)	Netherlands
Betito, Elie	Apotex	Canada
Boyle, Kathleen	Health Pro Canada	Canada
Buchmann, Michel	International Pharmaceutical Federation (FIP)	Switzerland
Chaar, Betty	University of Sydney	Sydney
Cottrell, Jack	World Dental Federation (FDI)	Canada
de Jong, Henk	International Pharmaceutical Federation (FIP)	France
Gaugh, David R.	Generic Pharmaceutical Association	USA
Gill, Tony	Therapeutic Goods Administration	Australia
Goyal, Neerja	GSK	Canada
Gray, Andy	International Pharmaceutical Federation (FIP)	South Africa
Hakes, Linda	International Pharmaceutical Federation (FIP)	Germany
Harasymuk, Mark	Government of Alberta	Canada
Hay, Terri	Canadian Association of Pharmacy Distribution Management	Canada
Hedman, Lisa	World Health Organization	Switzerland
Johnson, Ian	IMS Brogan	Canada
Kettledas, Ricardo	Ministry of Health	South Africa
Kinahan, Maura	Pfizer	Ireland
Kitts, Jennifer	Canadian Healthcare Association	Canada
Lamarre, Diane	Ordre des pharmaciens du Québec	Canada
Link, Michael	Union Internationale Contre le Cancer – UICC	USA

NAME	ORGANIZATION	COUNTRY
Madigan, Melissa	NABP	USA
Manasse, Henri	International Pharmaceutical Federation (FIP)	USA
McCannos, KJ	Canadian Dental Association	Canada
McIntosh, Keith	Canada's Research-Based Pharmaceutical Companies	Canada
McNeill, Felicity	Department of Health and Ageing	Australia
Midha, Kamal	International Pharmaceutical Federation (FIP)	Canada
Morrison, Jeff	Canadian Pharmacists Association (CPhA)	Canada
Nurse, Suzanne	International Alliance of Patients' Organizations (IAPO)	Canada
Ouimette, Etienne	Health Canada's Health Products and Food Branch	Canada
Paradis, François	Association des pharmaciens des établissements de santé	Canada
Paulino, Ema	International Pharmaceutical Federation (FIP)	Portugal
Pearlstein, Lisa	American Society of Anesthesiologists	USA
Peister, Sherry	Canadian Pharmacists Association (CPhA)	Canada
Philip, Beverly	American Society of Anesthesiologists	USA
Roy, Myrella	Canadian Society of Hospital Pharmacists	Canada
Skinner, Jill	Canadian Medical Association	Canada
Steel, Gavin	Ministry of Health	South Africa
Tam, Julie	Canadian Generics Pharmaceutical Association	Canada
Thompson, Kasey K.	American Society of Health-system Pharmacists (ASHP)	USA
van der Hoeff, Carola	International Pharmaceutical Federation (FIP)	Netherlands
van Kesteren, Rachel	International Pharmaceutical Federation (FIP)	Netherlands
Wilson, Cecil D.	World Medical Association (WMA)	USA

B. Programme of the Summit

Thursday 20/06/2013

08:30 - 12:30

1. Opening remarks (30 min)

- For the pharmacists: Michel Buchmann, President of FIP (International Pharmaceutical Federation)
- For the physicians: Cecil D. Wilson, President of WMA (World Medical Association)
- For the patients: Suzanne Nurse, IAPO (International Alliance of Patients' Organizations)

2. An overview of medicines shortages (60 min)

Compilation of data on the number (and duration) of medicines shortages/scale of the problem/trajectory over time: Kasey K. Thompson, ASHP (American Society of Health-system Pharmacists)

Coffee break (30 min)

3. Estimates of the consequences of a medicines shortage (60 min)

Two country case studies (30 min each), one from developing countries (Lisa Hedman, Essential Medicines and Health Products, WHO), the other one from developed countries (Jeff Morrison, Canadian Pharmacists Association, Canada).
In terms of:

- Human lives;
- Financial consequences (more expensive therapeutic alternatives);
- Human resources and indirect costs (time spent by medical doctors and pharmacists to cope with a shortage).

4. Causes and contributing factors of the medicines shortages (60 min)

Introduction presentation: The main causes and contributing factors of medicines shortages:
Luc Besançon (FIP, The Netherlands) & Andy Gray (FIP, South Africa)

14:00 - 17:30

1. "Reasons for medicines shortage" (workshops run in parallel; 2h)

Discussion around practical examples/experience of participants through two parallel workshops:

The workshops will also aim to identify profiles of products which are more likely to be at risk of medicines shortages

WORKSHOP 1	WORKSHOP 2
Demand reasons: e.g. parallel trade and non-traditional distributors, unexpected increases in demand and shifts in clinical practice, incapability to adjust demand based on supply (no notification). Other reasons.	Supply reasons: e.g. raw and bulk material unavailability, manufacturing difficulties and regulatory issues, voluntary recalls, change in product formulation or manufacturer, manufacturers' production decisions and economics, industry consolidations, restricted drug product distribution and allocation, inventory practices and natural disasters.

Coffee break (30 min)

2. Wrap-up session: Each group will report its findings (1 hour)

Friday 21/06/2013

08:00 - 12:00

1. Best practices to prevent medicines shortages (or to limit its consequences): (2h30)

Workshops (run in parallel: 2h30): Discussion around solutions adopted by governments, private sectors and healthcare professionals to limit the consequences of a medicines shortage, to prevent future medicines shortages and to prevent the transfer of drug shortage issues to/from another country through massive importation.

This workshop will also consider the following questions:

a. What specific actions need to be taken globally to better respond to medicines shortages?

b. What role do national governments and multinational organizations have to play in addressing medicines shortages?

WORKSHOP 1	WORKSHOP 2
Solutions to demand reasons: e.g. parallel trade and non-traditional distributors, unexpected increases in demand and shifts in clinical practice, incapability to adjust demand based on supply (no notification). Solutions to other reasons.	Solutions to supply reasons: e.g. raw and bulk material unavailability, manufacturing difficulties and regulatory issues, voluntary recalls, change in product formulation or manufacturer, manufacturers' production decisions and economics, industry consolidations, restricted drug product distribution and allocation, inventory practices and natural disasters.

2. Wrap-up session: Each group will report its findings (1 hour)

13:30-14:30

1. Summary of the recommendations (45 min)

During lunch time, a working group will take the conclusions of each workshop and develop a short list of key recommendations to prevent or limit the impact of medicines shortages. The next steps for this Summit will also be discussed.

2. Concluding remarks (15 min)

Sherry Peister, CPhA incoming President

Michel Buchmann, FIP President

C. Acknowledgements of sponsors

FIP would like to thank Pfizer, Interpharma and Canada's Research-Based Pharmaceutical Companies (Rx&D) for their generous support to organise this International Summit on Medicines Shortages, highlighting their interest and commitment to this topic.

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Founded in 1912, the International Pharmaceutical Federation (FIP) is the global federation of national associations of pharmacists and pharmaceutical scientists. As a Non-Governmental Organisation (NGO), FIP has been in official relations with the World Health Organization (WHO) since the founding of the latter in 1948. Through its 127 member organisations, FIP represents and serves two million pharmacy practitioners and scientists around the world.

Throughout the 100 year history of FIP its priorities have expanded both literally and figuratively to meet the needs and expectations of the profession of pharmacy, of pharmaceutical scientists and of society in general. Its mission is to improve global health by advancing pharmacy practice and sciences to facilitate the discovery, development, access to and safe use of appropriate, cost-effective quality medicines. The emergence of Pharmacy Practice as a cornerstone of the profession has led FIP to become globally visible for its advocacy of the role of the pharmacist in the provision of healthcare, while still maintaining and developing a strong basis in the pharmaceutical sciences.
The membership of FIP has evolved into the most extensive global pharmacy and pharmaceutical sciences network, and the organization continues to expand its presence and influence through partnerships with other leading healthcare, educational and scientific institutions.