

EAHP ACADEMY SEMINAR

19 – 21 October 2018

Warsaw, Poland

**Medicines Shortages –
Causation and
Approaches to
Improvements**

Systematic attempts at a solution

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Disclosure of conflicts of interest

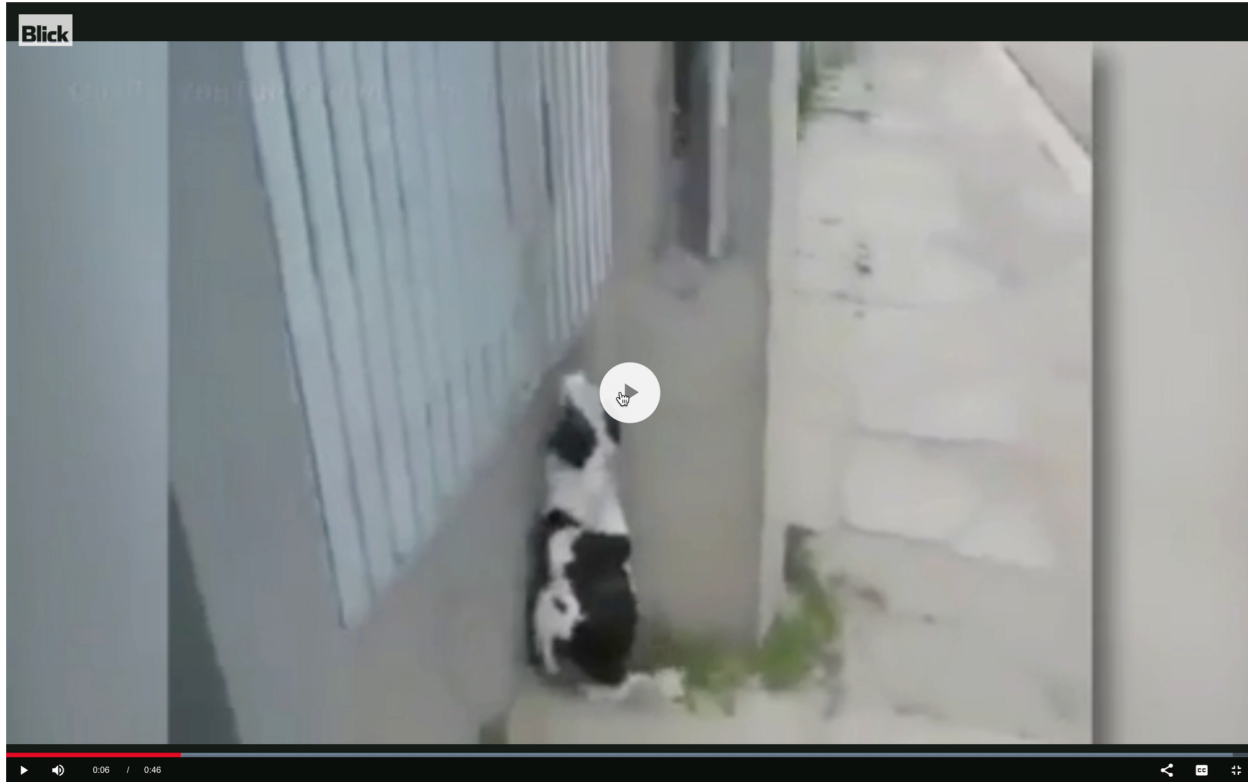
- **Nothing to declare**
- My main interest is the patient's outcome (according to the Hippocratic Oath)
- No research funding from private sources



Contents

- ▶ Coping strategies
- ▶ Supply contracts between the Swiss Federal Office for National Economic Supply and the pharmaceutical industry
- ▶ The importance of being innovative, anticipative and of sharing responsibilities

Where there's a will there's a way



Produce and supply medicines wisely!

Coping strategies:
(In-)Available or (In-)Accessible

Emergency Supplies – Inaccessibility or Inavailability?

- ▶ Foodstuff shortages in case of hazards – immediate international support, but national supply delayed (2 days)
- ▶ Medicines shortages in case of hazards – delayed international support (2 days)
- ▶ Common shortages situations: No support foreseen

Food

Montgomery - eve of Hurricane Sandy



Medicines

Venezuela actual HIV medicines stock



Swissmedic: Multilateral co-operation with international organisations / initiatives

- ▶ <https://www.swissmedic.ch/swissmedic/en/home/about-us/collaboration/international-collaboration/multilateral-co-operation-with-international-organisations---ini.html>
 - ▶ ACSS Consortium (Australia, Canada, Singapore, Switzerland)
 - ▶ to promote greater regulatory collaboration
 - ▶ Bill & Melinda Gates Foundation
 - ▶ to improve and accelerate access to health interventions and therapeutic products in resource-constrained countries
 - ▶ to bringing high-quality, life-saving medicines to patients as quickly as possible
 - ▶ "European Patients' Academy on Therapeutic Innovation" (EUPATI)
 - ▶ funded by the Innovative Medicines Initiative (IMI) of the European Union (EU)
 - ▶ to provide patients with scientifically reliable, objective and comprehensible information on medicines research, development and approval
 - ▶ Council of Europe / EDQM
 - ▶ internationally binding quality regulations for medicines
 - ▶ Harmonisation of Ph.Eur. / Ph.Helv.
 - ▶ International Council for Harmonisation (ICH)
 - ▶ International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)
 - ▶ International Generic Drug Regulators Programme (IGRDP)
 - ▶ To enhance international collaboration in the area of the authorisation of generics

Swissmedic: Multilateral co-operation with international organisations / initiatives (continued)

- ▶ International Medical Device Regulators Forum (IMDRF)
 - ▶ regulation of medical devices through the Mutual Recognition Agreements (MRAs)
- ▶ International Pharmaceutical Regulators Forum (IPRF)
 - ▶ to develop best practices and strategies for dealing with a constantly changing regulatory environment
 - ▶ to provide an overview of global regulatory developments with the aim of being able to share information, experience and ideas
 - ▶ to promote further international cooperation in areas not already covered
- ▶ Organisation for Economic Co-operation and Development (OECD)
 - ▶ to promote policies that will improve the economic and social well-being of people around the world
 - ▶ Restore confidence in markets and the institutions that make them function
 - ▶ Re-establish healthy public finances as a basis for future sustainable economic growth
 - ▶ Foster and support new sources of growth through innovation, environmentally friendly 'green growth' strategies and the development of emerging economies
- ▶ Pharmaceutical Inspection Co-operation Scheme (PIC/S)
 - ▶ To implement harmonised GMP standards and compliance with them
- ▶ World Health Organisation (WHO)
 - ▶ To notably participate in expert commissions for the development of new guidelines or support for training projects

Memorandum of Understanding between the Swiss Agency for Therapeutic Products (Swissmedic) and the Bill & Melinda Gates Foundation

- ▶ The BMGF *“has as one of its missions the reduction of global health inequities by accelerating the development, deployment, and sustainability of health interventions that will save lives and dramatically reduce the disease burden in developing countries”*
- ▶ To strengthen regulatory systems in resource-constraint countries
- ▶ to accelerate access to important health interventions for diseases that disproportionately affect populations living in these countries

Supply contracts between the Swiss
Federal Office for National Economic
Supply and the pharmaceutical
industry

Filling gaps in supply - constitutional or private task?

▶ Task of the **National Economic Supply** (Art 102 Federal Constitution)

- ▶ *“The country is supplied with essential goods and services in the event of the threat of politico-military strife or war, or of severe shortages that the economy cannot by itself counteract.”*
- ▶ *“In exercising its powers under this Article, it may if necessary depart from the principle of economic freedom”*

▶ **Essential goods and services**

- ▶ i.e. foodstuffs and drinking water, energy, therapeutic products, logistics, information and communication technologies

▶ **Subsidiarity**

Providing the country with goods and services is normally the responsibility of the private sector. Only when the private sector is no longer able to meet this responsibility the state intervenes to regulate

▶ **Partnerships**

- ▶ Swissmedic (<https://www.swissmedic.ch>)
- ▶ Science Industries (Business Association Chemistry, Pharma, biotech, <https://en.scienceindustries.ch>)
- ▶ Helvecura (self-help organisation of stockpiling industry in the frame of national economic supply, <http://www.helvecura.ch>)

Filling gaps in supply (from compulsory stocks) and controlling demand (prioritised distribution, quotas)

- ▶ Globalisation
 - ▶ concentrates suppliers and production sites worldwide
- ▶ Stocks reduced at all levels for cost reasons
- ▶ Interest of FONES: Early warning system for the rapid detection of disruptions in the supply of critical human medicines
- ▶ Legal frame set in force by Federal Council in June 2017
 - ▶ FONES - private sector collaboration
 - ▶ looking at how to increase the resilience of supply infrastructure
 - ▶ making flexible instruments available to deal with severe supply shortages
- ▶ Both **prevention** and **intervention**
 - ▶ to increase the resilience of supply processes so that state intervention can be avoided for as long as possible
 - ▶ to bridge partial shortfalls (supply management)
 - ▶ measures to reduce demand
 - ▶ distribution of available goods and services at a reduced supply level
- ▶ Partners are storing agreed amounts of medicines for **4 months**

Compulsory stocks of therapeutic products for national economic supply

III. Neuraminidasehemmer (Humanmedizin)

ATC-Code	Wirkstoff (Nr.)
J05AH	Oseltamivir (9801)

IV. Starke Analgetika und Opiate (Humanmedizin)

ATC-Code	Wirkstoff (Nr.)
N02AA01	Morphin (10002)
N02AA03	Hydromorphon (10005)
N02AA04	Nicomorphin (10007)
N02AA05	Oxycodon (10003)
N02AA51	Morphin, Kombinationen (10002)
N02AA55	Oxycodon, Kombinationen (10003)
N02AB02	Pehidin (10006)
N02AB03	Fentanyl (10001)
N02AB52	Pethidin, Kombinationen, exkl. Psycholeptika (10006)
N02AB72	Pethidin, Kombinationen mit Psycholeptika (10006)
N02AC52	Methadon, Kombinationen, exkl. Psycholeptika (10004)
N02AG01	Morphin und Spasmolytika (10002)
N02AG03	Pethidin und Spasmolytika (10006)
N02AG04	Hydromorphon und Spasmolytika (10005)
N07BC02	Methadon (10004)

V. Impfstoffe (Humanmedizin)⁹

ATC-Code	Warenbezeichnung
J07AG	Haemophilus-influenzae-B-Impfstoffe
J07AH07	Meningokokkus C, gereinigtes Polysaccharid-Antigen, konjugiert
J07AH08	Meningokokken A, C, Y, W-135, tetravalent, gereinigtes Polysaccharid-Antigen, konjugiert
J07AJ	Pertussis-Impfstoffe
J07AL02	Pneumokokken, gereinigtes Polysaccharid-Antigen, konjugiert
J07AM	Tetanus-Impfstoffe
J07BC	Hepatitis-Impfstoffe
J07BD	Masern-Impfstoffe
J07BF	Poliomyelitis-Impfstoffe (Kombinationen mit D/Te/Per oder Hib unter J07CA)
J07BG	Tollwut-Impfstoffe
J07BK01	Varicella, lebend abgeschwächt
J07BM	Papillomvirus-Impfstoffe
J07CA	Bakterielle und virale Impfstoffe, kombiniert

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⁹ Änderung vom 21. Juni 2016, in Kraft seit 1. Oktober 2016

⁹ Änderung vom 21. Juni 2016, in Kraft seit 1. Oktober 2016

For APIs in addition: direct GSASA – industry agreement on API provision



Absichtserklärung

der Verbände der pharmazeutischen Industrie in der Schweiz:

- **ASSGP** (Schweizerischer Fachverband für Selbstmedikation),
- **Intergenerika** (Verband der Hersteller- und Vertriebsfirmen von Generika/Biosimilars in der Schweiz),
- **interpharma** (Verband der forschenden pharmazeutischen Firmen der Schweiz),
- **scienceindustries** (Wirtschaftsverband Chemie Pharma Biotech),
- **vips** (Vereinigung Pharmafirmen in der Schweiz)

gegenüber folgenden Organisationen in der Schweiz:

- **FMH** (Verbindung der Schweizer Ärztinnen und Ärzte),
- **GSASA** (Schweizerischer Verein der Amts- und Spitalapotheker),
- **H+** Die Spitäler der Schweiz,
- **pharmaSuisse** (Schweizerischer Apothekerverband).

Im Bewusstsein, dass

- die Versorgung mit Arzneimitteln, die individuelle Herstellung von Arzneimitteln für bestimmte Patienten und die defekturemässige Herstellung von Arzneimitteln in kleinen Mengen (gemäss Art. 9 Abs. 2 HMG) zu einem wesentlichen Teil von Apotheken gewährleistet wird,
- für bestimmte Patientengruppen (Pädiatrie, Geriatrie) geeignete Arzneimittel-Anwendungsformen nicht als Fertigpräparate verfügbar sind,
- es weder ethisch vertretbar noch gesundheitspolitisch erwünscht ist, die Versorgung mit Arzneimitteln unangemessen einzuschränken,

und unter Berücksichtigung der in diesem Zusammenhang massgebenden staatlichen Vorschriften erklären die oben erwähnten Verbände der pharmazeutischen Industrie Folgendes:

1. Diese Verbände und ihre Mitgliedsunternehmen setzen sich dafür ein, dass die Apotheken in der Schweiz mit Wirkstoffen beliefert werden, die sie zur individuellen oder defekturemässigen Herstellung von Arzneimitteln brauchen, die für die Versorgung der Bevölkerung notwendig, als Fertigpräparate jedoch nicht verfügbar sind.
2. Diese Verbände empfehlen ihren Mitgliedsunternehmen, Apotheken, Ärzte und Spitäler auf Anfrage hin über laufende Patente eines Wirkstoffs (Laufzeit und Indikation) und autorisierte Bezugsquellen zu informieren sowie in oben erwähntem Zusammenhang auf die Durchsetzung von Patentrechtsansprüchen zu verzichten. Im Einzelfall können Lizenzgebühren erhoben werden.

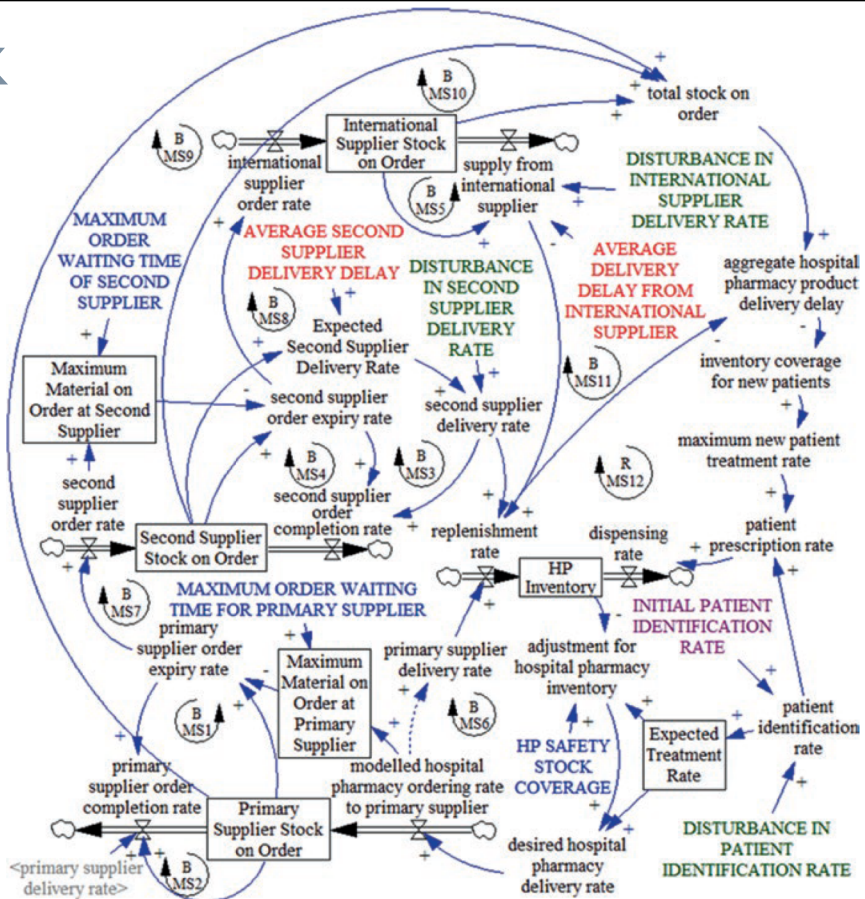
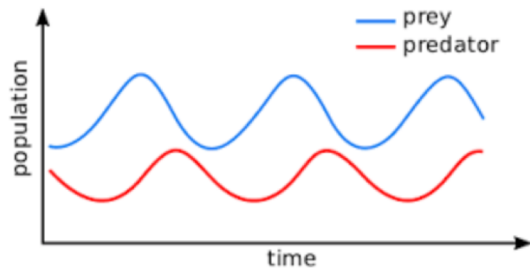
3. Ergeben sich im Zusammenhang mit dieser Absichtserklärung praktische Probleme, so verständigen sich die oben erwähnten Verbände und Organisationen wo immer möglich auf eine geeignete Lösung.
4. Die oben erwähnten Verbände informieren ihre Mitgliedsunternehmen über diese Absichtserklärung.

Organisation	Ort und Datum	Unterschrift
ASSGP Hans-Rudolf Fuhrer	Rothkreuz, 26.8.13	
Intergenerika Dr. Peter Huber	Rothkreuz, 26.8.13	
interpharma Thomas B. Cueni	Rothkreuz, 26.8.13	
scienceindustries Dr. Dieter Grauer	Rothkreuz, 26.09.13	
vips Walter P. Hölzle	Rothkreuz 26/09/13	
FMH Dr. med. Jürg Schlup	Bern, 29.8.2013	
GSASA Prof. Dr. Pascal Bonnabry	Bern, 30/08/13	
H+ Charles Favre	BERN, 3.9.13	
pharmaSuisse Dominique Jordan	Bern, 3.9.2013	

The importance of being innovative,
anticipative and of sharing
responsibilities

No (fore-)sight – high risk

Foresight requests more than just being in the driver's seat
-> it needs lots of information



Aggregate structure of the medicines sourcing section of the hospital pharmacy echelon (Groesser and Duminy 2018, Resilience as Basis for Sustainability, https://doi.org/10.1007/978-3-319-94322-0_9)

Recommendations for improvements of the medicines supply chain (by Federal Office of Public Health, thus *top-down regulation governmental regulation*)

▶ Monitoring

- ▶ Notification on FONES platform
- ▶ Support by FONES, FOPH, Swissmedic, army pharmacy, industry (*no hospitals?*)

▶ Qualification of providers

- ▶ To qualify providers on a capability to satisfy the need (*GMP requirement*)

▶ Storage capacities and practices

- ▶ To conditionally authorise (pre-)wholesalers (*authorisation to be attributed only if full supply is warranted*)
- ▶ Adaption of cantonal legal frames in order to oblige health care providers to keep minimal stocks essentially of life-saving medicines (*stock volumes allocated?*)
- ▶ Increased stock-keeping on all levels covering several weeks (*taxation alleviation or remuneration/ interests of private bound capital*)
- ▶ Contingency planning / allocation of quota
- ▶ Revision of order point and order amounts on all levels

▶ Manufacturing

- ▶ As stipulated in the Revision of the Therapeutic Products Act and its 4 ordinances packages / cantonal legal frames (26!)
 - ▶ Hospital Pharmacies should be adequately equipped to produce formula products exempt of market admission
- ▶ Revision of mandates imposed to health care professionals and institutions
 - ▶ Allocation of manufacturing equipment for formula medicines
 - ▶ Revision of the role of the Swiss Army Pharmacy as producer of deregistered medicines (*2nd priority only*)
 - ▶ Increasing manufacturing capacities in bigger hospitals
- ▶ Licensing of medicines to third parties in case of deregistration pressure
- ▶ Enlargement of production capacity (*needs investments*)

Recommendations for improvements of the medicines supply chain (made by Federal Office of Public Health, thus *again a top-down regulation approach on governmental level*) (cont.)

▶ Market admission

- ▶ Facilitated importation (*major time loss, mainly for controlled medicines*)
- ▶ Facilitated market admission (*in consultation for setting in force with upcoming ordinances package*)
 - ▶ *Well-established use* medicines
 - ▶ *Traditional use* OTC
- ▶ Incentives for admittance owners to licence deregistered medicines to third parties
- ▶ Electronic patient information (2D-barcode)
- ▶ Optimisation of communication between Swissmedic and FOPH as related to medicines being deregistered
- ▶ Admission of more than only one manufacturing site per API / medicine (*is one of the most effective prevention options*)

▶ Pricing and reimbursement

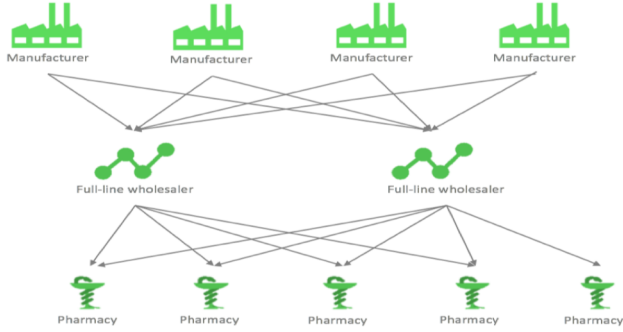
- ▶ Considering availability and supply security in the course of introduction a reference price system (planned for 2018-2019)
- ▶ Support pricing of relevant medicines having added therapeutic and/or economic value and being under deregistering pressure for economic reasons
- ▶ Pre-financing of the whole supply chain
 - ▶ 500 million CHF
 - ▶ 40 days stocks
 - ▶ Management of demand and allocation of quota

Coping Strategies to reduce vulnerability (behavioural approach) (as proposed by V. Hargaden, COST Action CA15105)

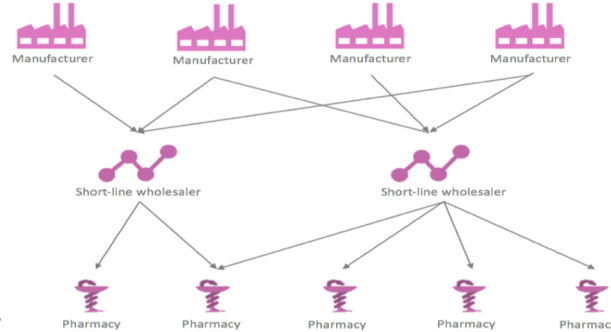
- ▶ Flexibility in sourcing
 - ▶ Modular product design
 - ▶ Multiple uses - multiple sources
 - ▶ Supplier contract flexibility
- ▶ Flexibility in order fulfilment
 - ▶ Alternate distribution
 - ▶ Risk sharing
 - ▶ Multi sourcing
- ▶ Capacity and efficiency
 - ▶ Reserve capacity
 - ▶ Redundancy / excess capacity
 - ▶ Backup sources and communications
- ▶ Visibility (knowledge of the status of operating assets and the environment)
 - ▶ Business intelligence and people visibility
 - ▶ Information technology
 - ▶ Information exchange
- ▶ Adaptability
 - ▶ Monitoring early warning signals
- ▶ Recovery from shortages and damaged reputation
 - ▶ Crisis management
 - ▶ Disperse and distribute decision making
 - ▶ Collaborative forecasting
 - ▶ Customer management
- ▶ As a Summary: Anticipation, creativity, and innovation

Governmental mantra (Many stocks - minimal quantities per stock) makes supply chain vulnerable

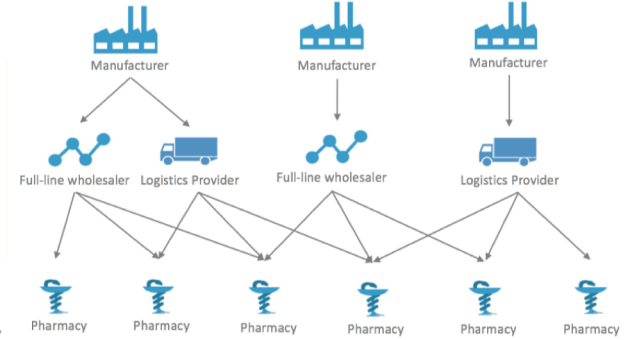
Full-line wholesalers



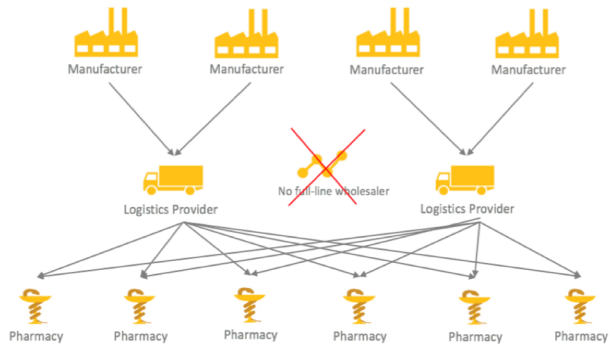
Short-line wholesalers



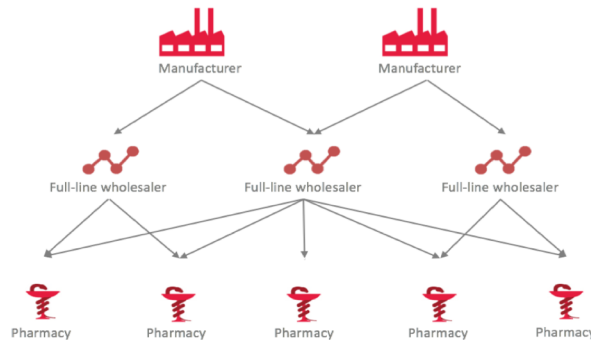
Direct sales



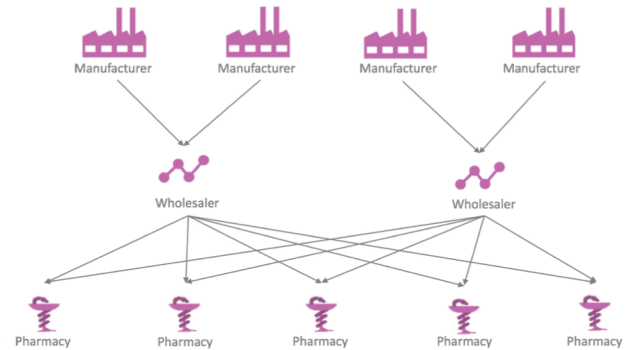
Direct-to-pharmacy



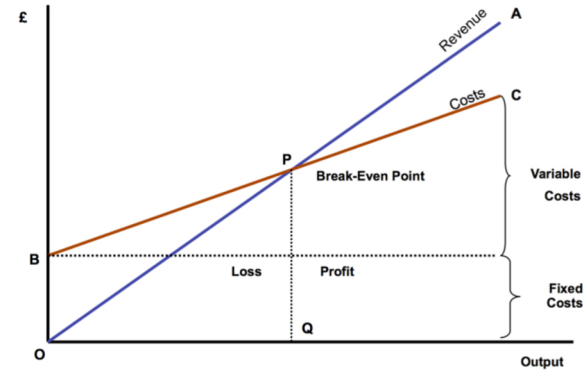
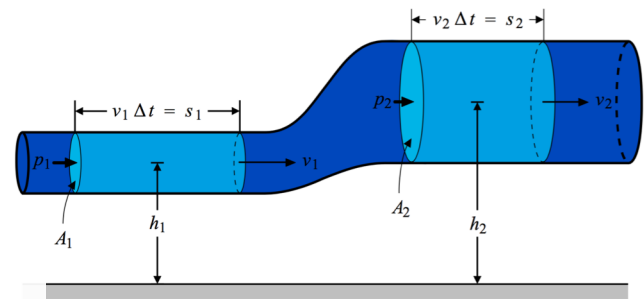
Reduced wholesale arrangement



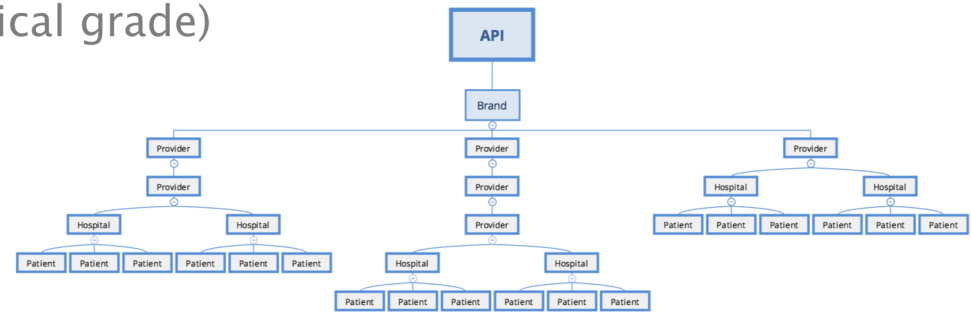
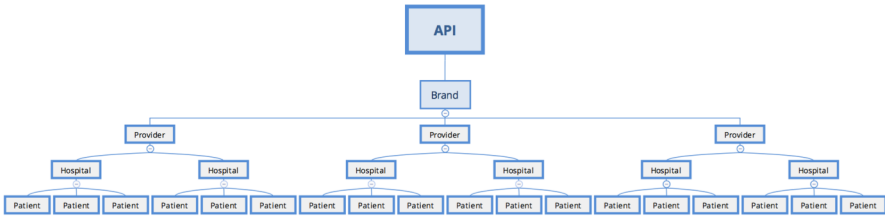
Single channel system



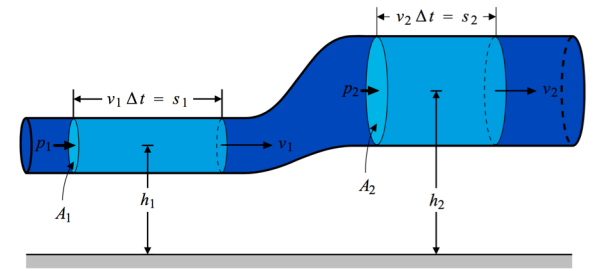
Stabilisation of the supply chain by procedural approach



- ▶ To counter erroneous incentives
 - ▶ To enlarge capacities
 - ▶ To improve coverage over break-even
- ▶ Serial or Parallel Supply preferable / favourable?
 - ▶ Supply Security - 1:1 or n:n?
 - ▶ Direct ways
 - ▶ Multiple channels available
 - ▶ In case of API (PhEur grade) shortage, other qualities to admit (e.b. biochemical or analytical grade)



Stabilisation of the supply chain by considering physical laws



What we need



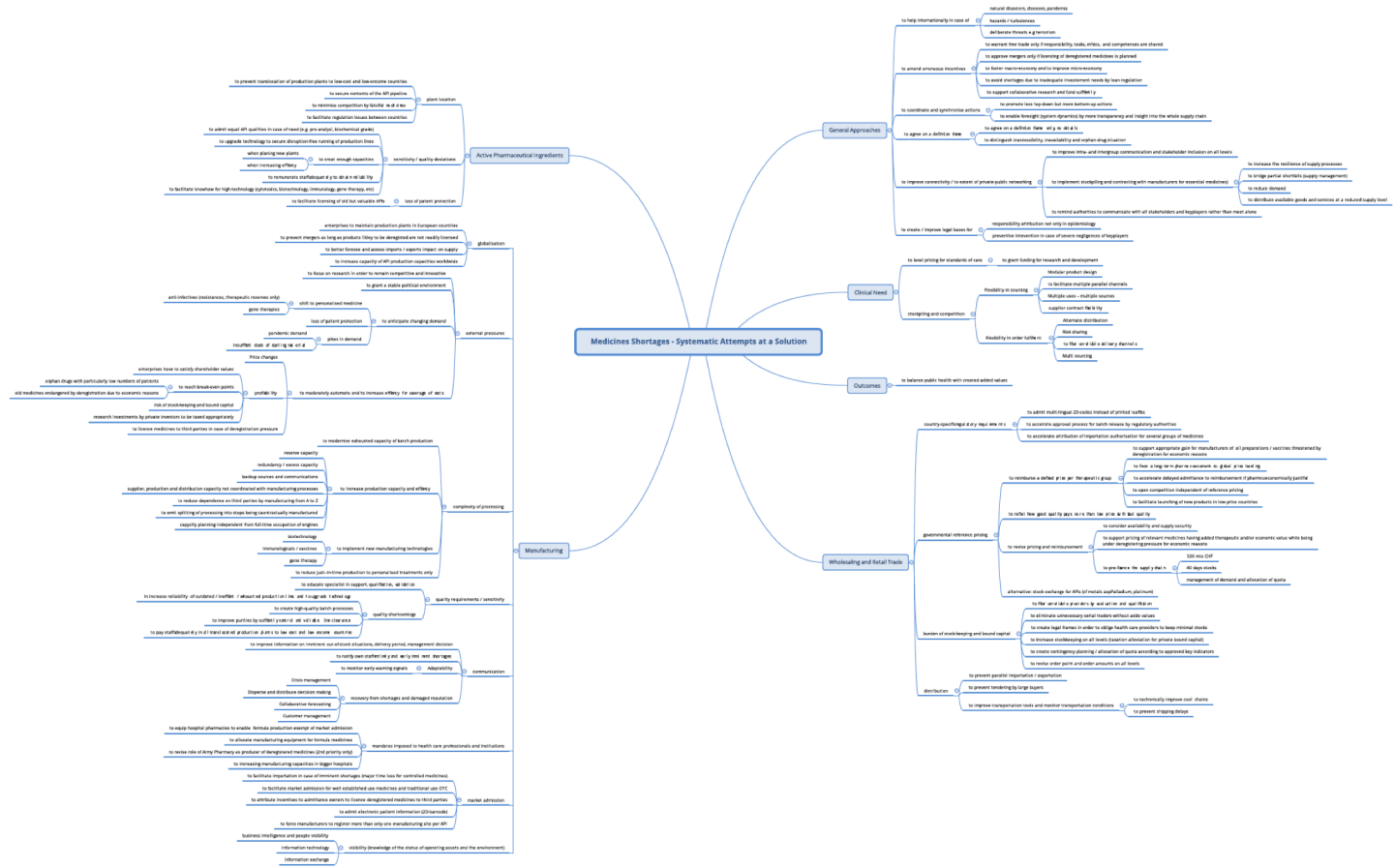
Large tubular cross-sections

What is done



rather than supply-chain bottlenecks

Solutions – Mindmap (6 groups)



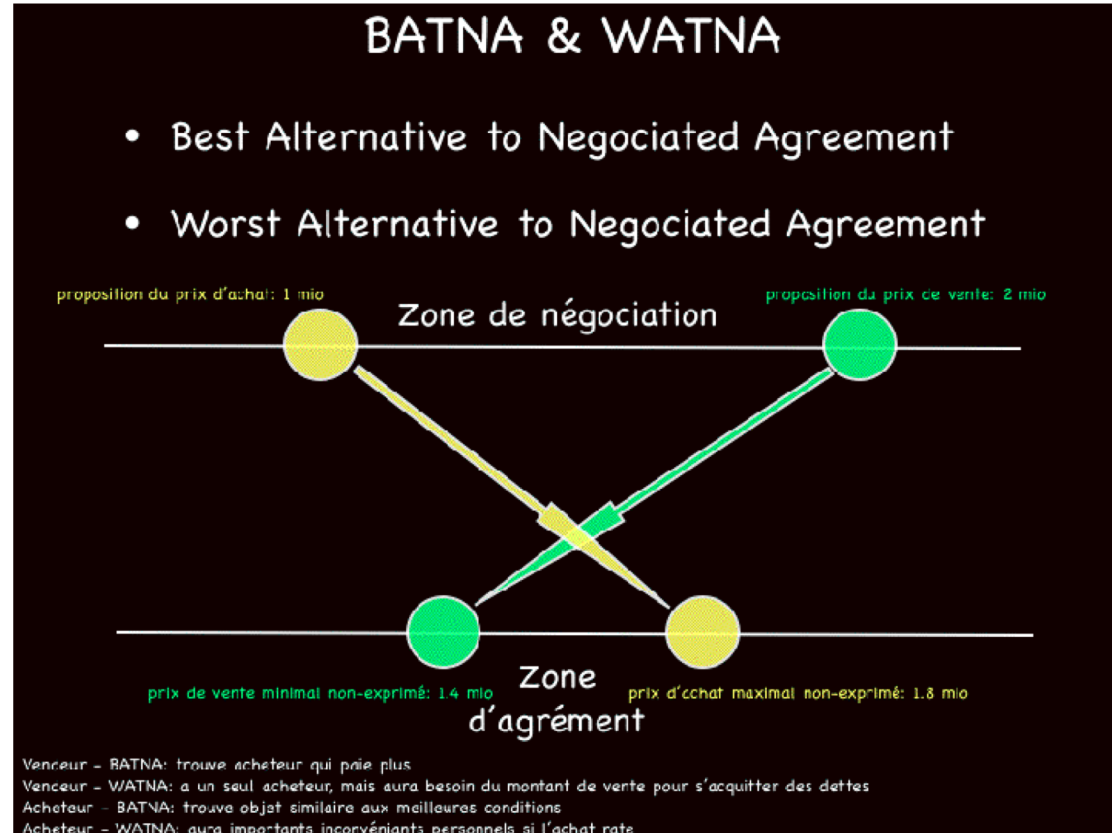
Summary

Conclusion

- ▶ Macro-economy is considered to run well – even on an international level
- ▶ Micro-economy and fine tuning is not considered as priority – **SHARING RESPONSIBILITIES** as a way to improve the shortages problem
- ▶ **NOMINATION OF LEADERS** by Supply Chains step
- ▶ Economic supply is organised within the epidemiology tasks attributed to governments by national constitutions
- ▶ **NON-EPIDEMIOLOGIC INTERVENTIONS** have to be arranged by all stakeholders
- ▶ An **INTERDISCIPLINARY COORDINATED BOTTOM-UP APPROACH** is needed accompanied by facilitated regulation
- ▶ **BETTER REMUNERATION** of threatened medicines
- ▶ New incentives for **MEDIUM SCALE PRODUCTION**

ZOPA – negotiations between BATNA and WATNA

- ▶ ZOPA = zone of possible agreement, BATNA = best alternative to negotiated agreement, WATNA = worst alternative to negotiated agreement
- ▶ Stakeholders in a shared responsibility setting will have to agree on negotiations
- ▶ Negotiation means reframing from emotional and factual levels to a level of common values and ethics
- ▶ A common basis would be the primate of the patient's need and interest before all other interests



That's all folks – questions or coffee break?

