

# Local production of pharmaceuticals as measure to overcome medicine shortages

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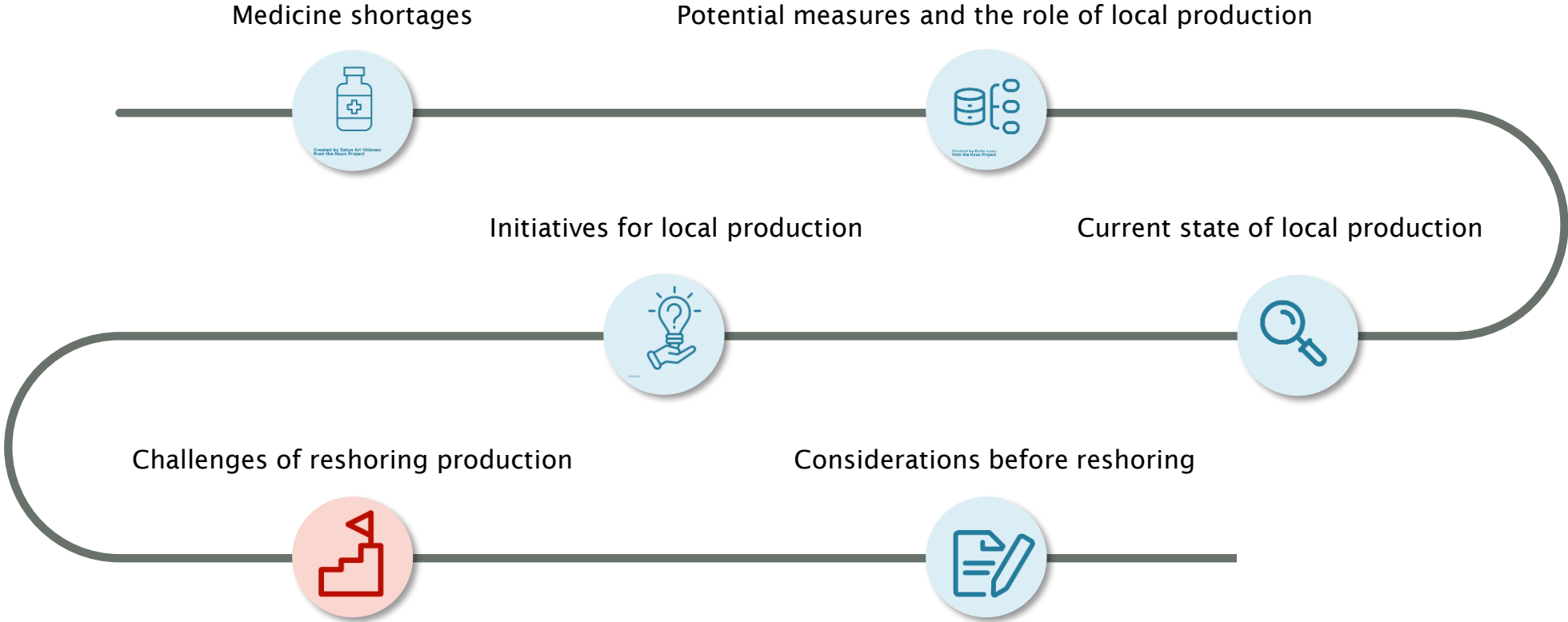
Gesundheit Österreich  
GmbH 

# Conflict of Interest

**Nothing to declare\*!**

\* Except that I have a high interest that our health care system is working (better) and will be working in the future.

# Content



# What is what?



Picture: pixabay

## Medicine shortage

- Synonyms: drug shortage
- Various definitions
- What is meant:  
demand > supply
- Medicine shortages can lead to delayed treatments



Picture: Adobe Stock

## Reshoring

- Synonyms: backshoring or relocating
- Not: onshoring or nearshoring
- What is meant: bringing manufacturing back to a region (or country)

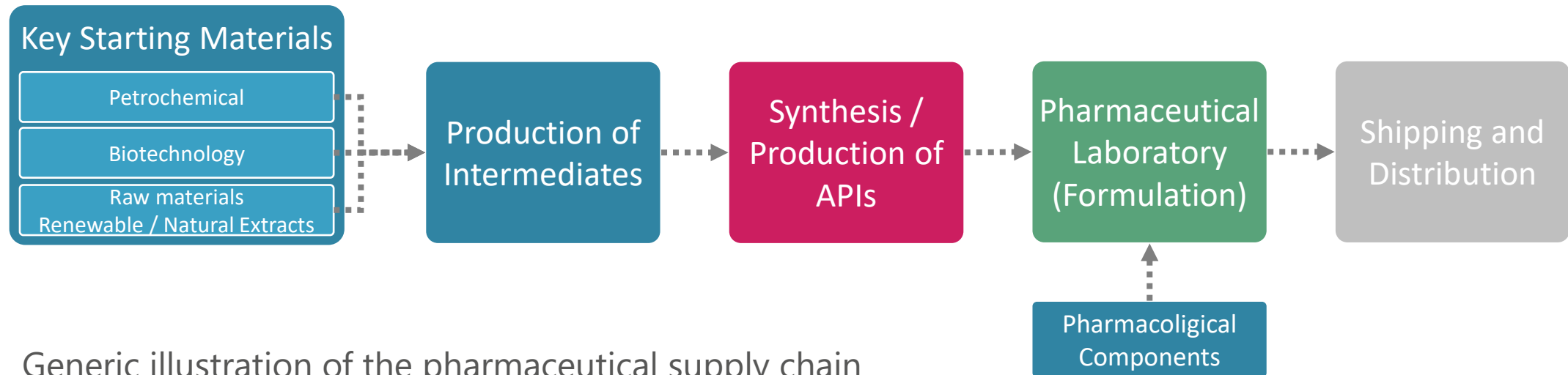


Picture: precisionnutrition.com

## Local production

- Synonyms: national / domestic
- What is meant: describe a more close-by production
- Can refer to a certain region (EU, Europe, Austria, etc.)

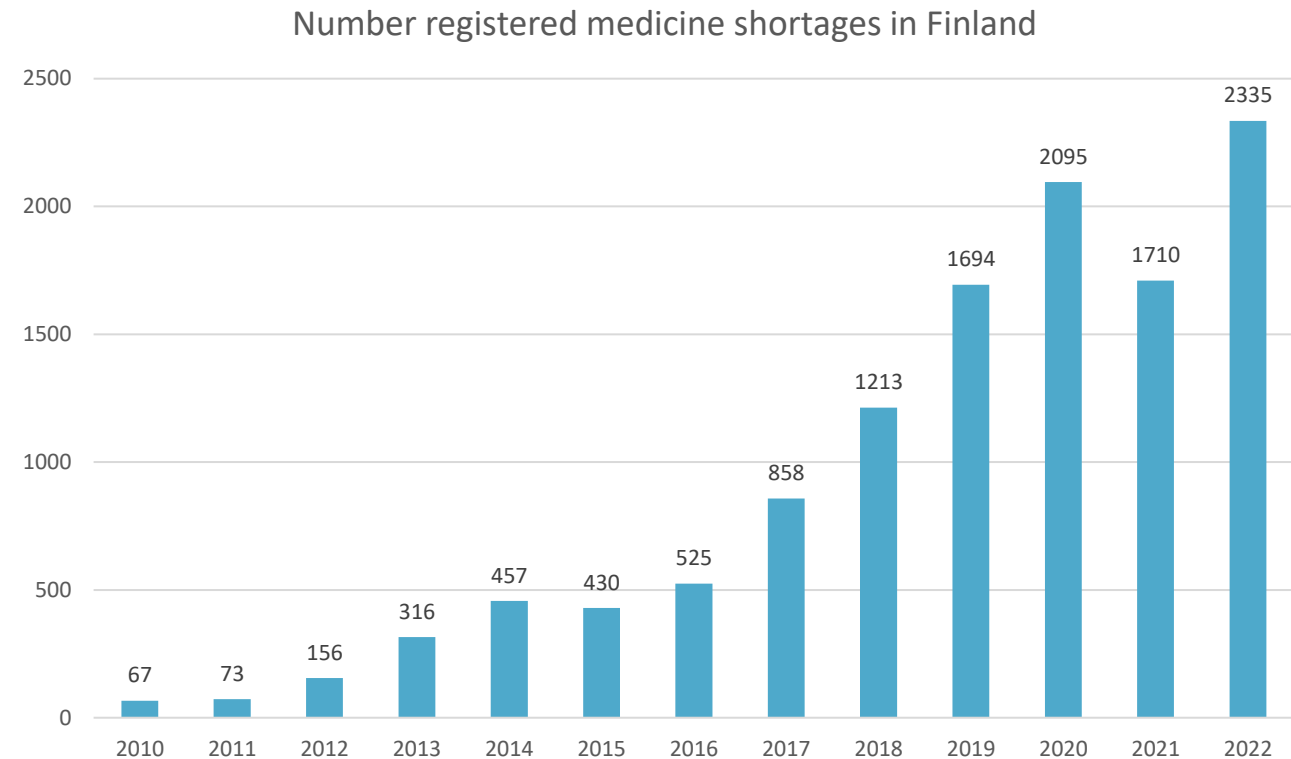
# What is what?



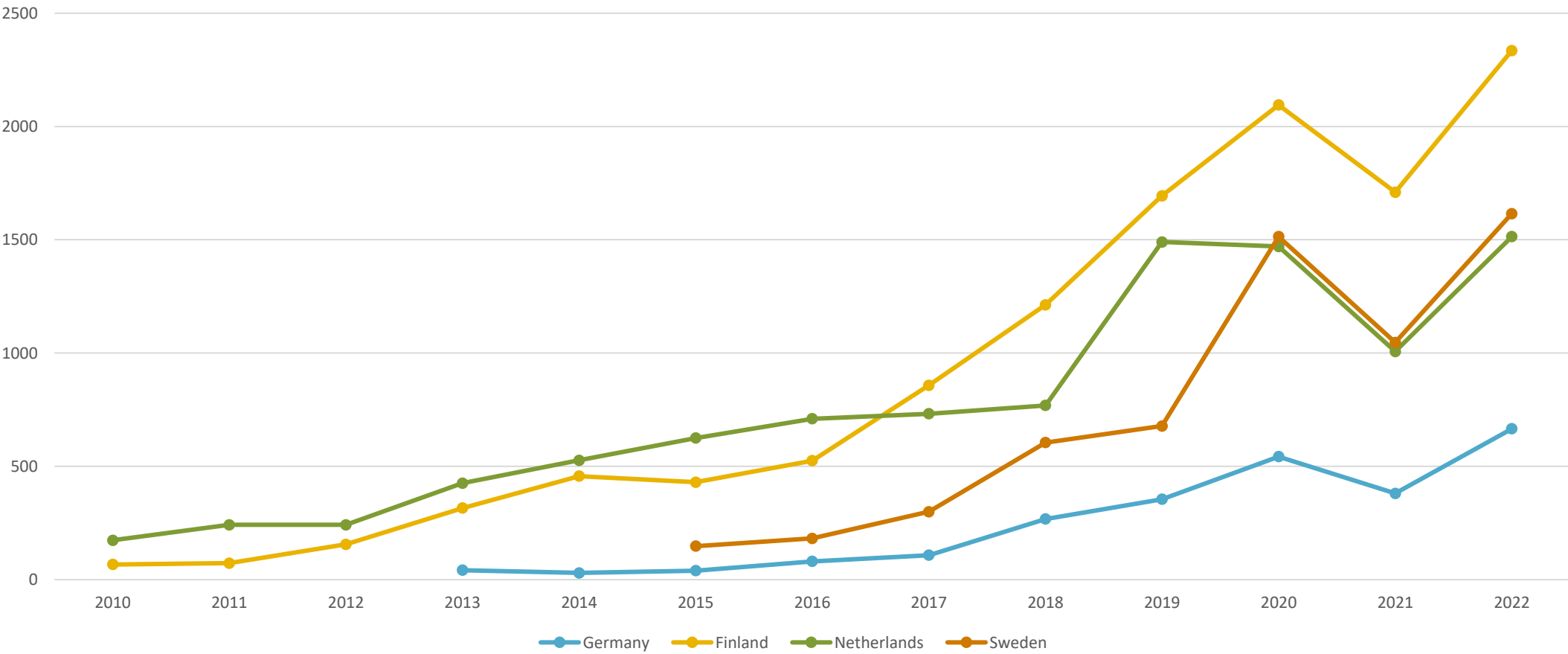
Generic illustration of the pharmaceutical supply chain

# Medicine shortages: Is it new?

- Not a new phenomena
- First reported medicine shortage affected insulin a century ago
- But: the extent of shortages intensified over the past 20 years
- During the COVID-19 pandemic the issue became more visible and urgent, when shortages for certain critical pharmaceuticals emerged
- From 2000 to 2018 there has been a 20-fold increase in recorded drug shortages in Europe



# Medicine shortages: Situation in countries



# Causes of medicine shortages

- Very complex and often not one single reason
- Possible causes:
  - Unexpected temporarily increased demands  
(e.g. during flu season)
  - Issues in the supply chain  
(e.g. limited number of suppliers due to high complexity of the production, making the supply chain less resilient)
  - Quality problems  
(e.g. contaminations during manufacturing)
  - Disruptions during transportation  
(e.g. when it comes to freight issues, as happened in 2021 in the Suez Canal)





# Potential measures to address shortages

- Obligation for industry to report shortages to authorities and the creation of national reporting systems (in several countries)
- Supply reserve stocks (e.g. in Finland)
- Notification of parallel exports (e.g. in Poland)
- Collaborative projects with stakeholders such as representatives of the pharmaceutical industry, wholesale and pharmacies (e.g. in Italy)



All these measures are reactive – and not proactive!

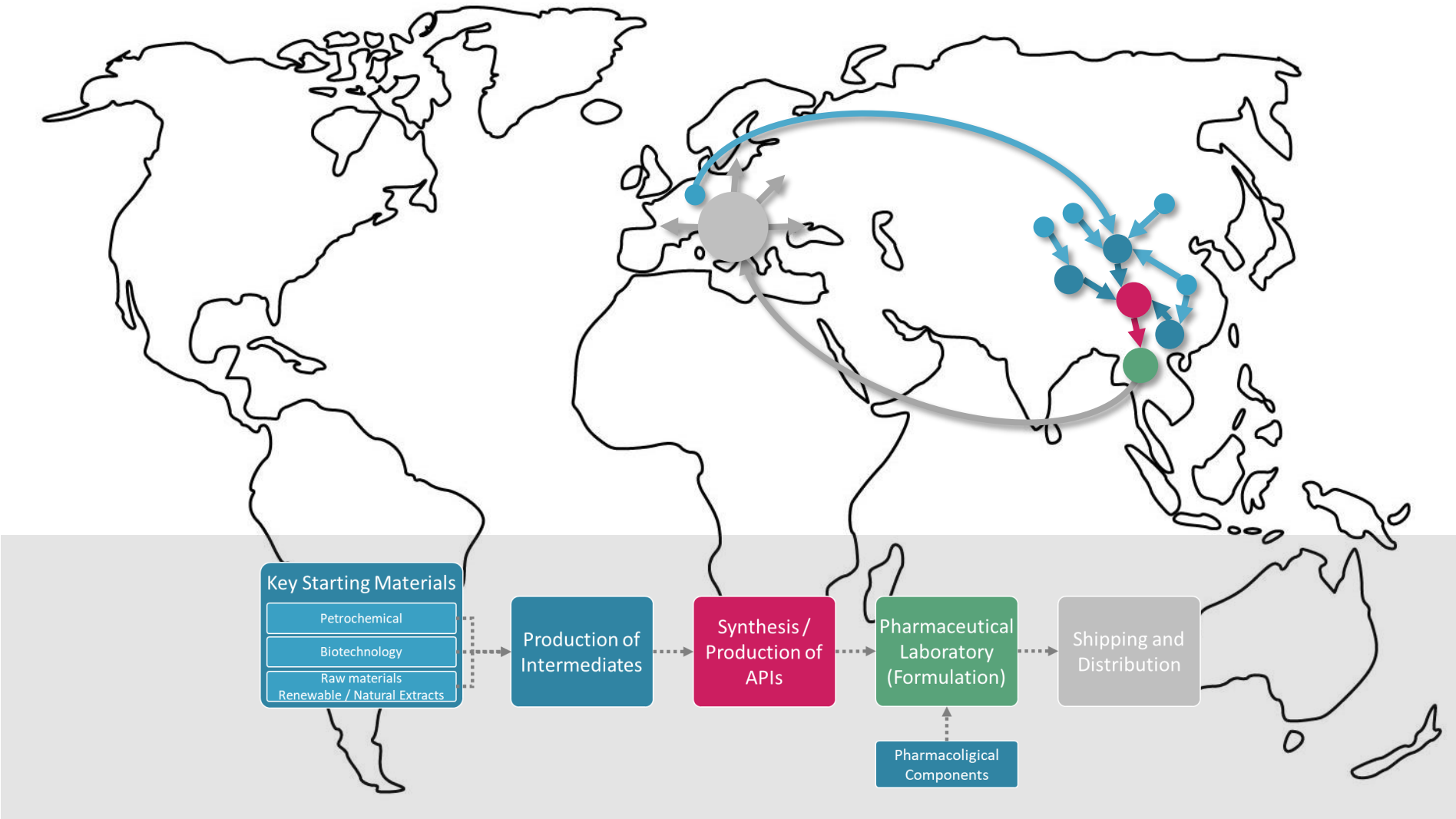
# Potential measures: Approach of local production

- Conception:
  - Pharmaceutical supply chain is complex and globally interwoven
  - More local production would reduce complexity and dependency
- Background:
  - Until 1950s: Europe was global leader in medicines manufacturing
  - In 1960s: emerging economies of India and China started to set up pharmaceutical production capacities to cover own needs and became independent from other countries
  - Over time, Indian and Chinese manufacturers became very competitive in the world market and exerted price pressure on manufacturers in the Western countries, resulted in a transfer of global production of pharmaceuticals towards Asia

# Potential measures: Approach of local production

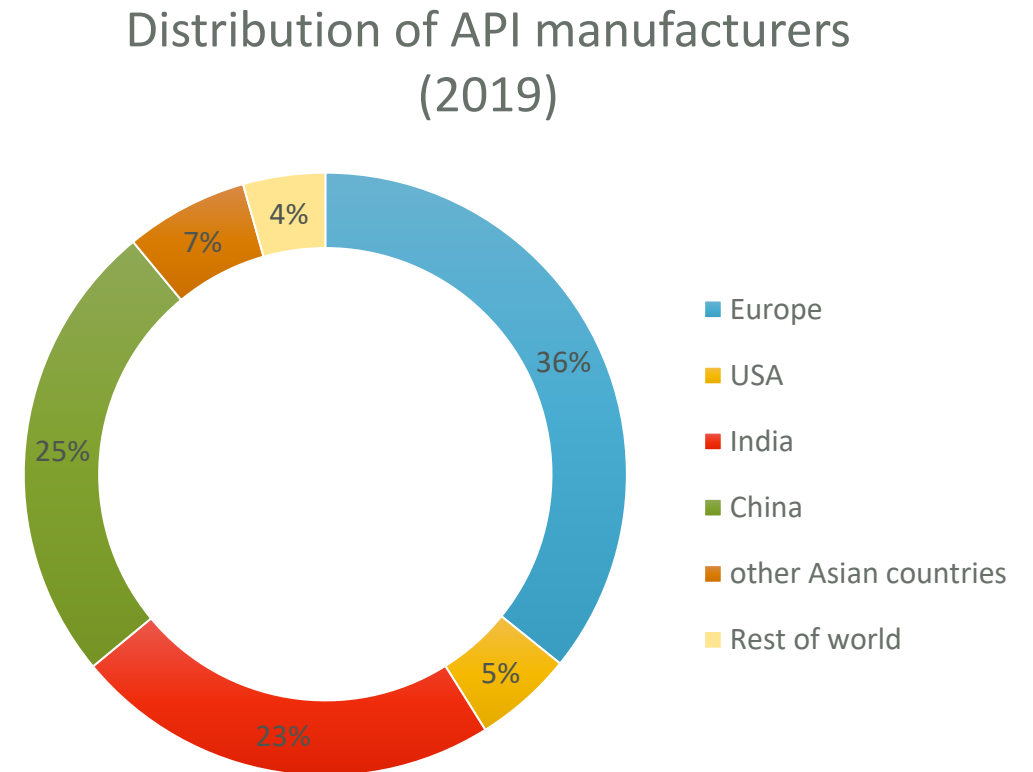
- Situation today:
  - Pharmaceutical production left Europe more and more
  - Concerns medicines as finished products, raw materials and active pharmaceutical ingredients (APIs)
  - Changes have resulted in a globalisation of the pharmaceutical supply chain
  - Nowadays, China is the world's main supplier of raw materials, including key starting materials (KSMs), intermediates and APIs
  - India is a major producer of finished products, particularly generics, but is highly dependent on imports for approximately 32% of its production needs, for which China is the major supplier
- Possible solution:
  - Reshore pharmaceutical production back to Europe and
  - Facilitate local production

# Local production: Current state



# Local production: Current state (focus on API production)

- 36% of API manufacturing sites are in Europe
- 55% of manufacturing sites are in Asia
- EU's share of global generic API production is 24%, compared to 66% in Asia Pacific (India and China)
- In 2021, China brought 18 new active substances for the first time onto the market (worldwide) and nearly equalled Europe (19 new active substances)



# Local production: Current state (focus on API production)

## Europe

- Europe is still a strong competitor, especially when it comes to global pharmaceutical manufacturing leadership
- European manufacturers are specialised in APIs with:
  - low production volumes,
  - technologically complex production processes and
  - products with high quality requirements
- Production of older APIs tends to be strong in Europe and the migration to Asia is still low for these APIs

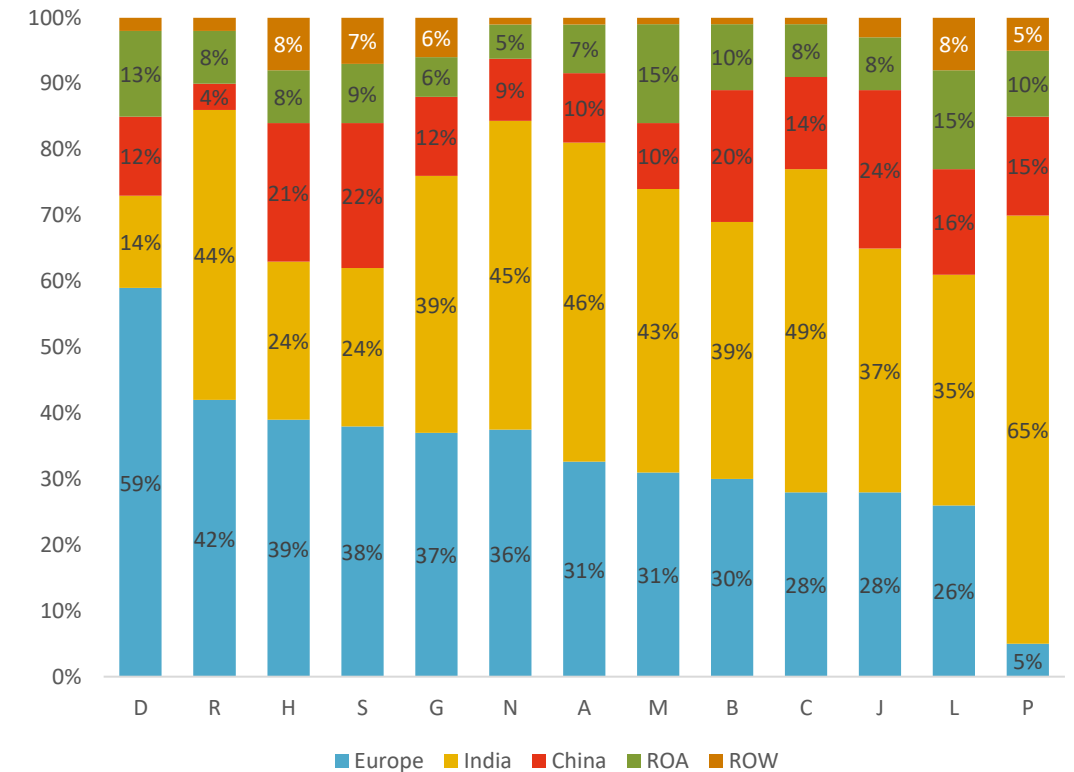
## Asia

- Many manufacturers in India and China have a relatively small API portfolio
- Indian manufacturers tend to be larger and more focused on high-volume APIs
- Newer APIs have a high proportion of Asian manufacturers and / or migration to Asia is faster
- Most APIs are either produced mainly in Europe or Asia, only for a few APIs is the production balanced between Europe and Asia.

# Local production: Current state (focus on API production)

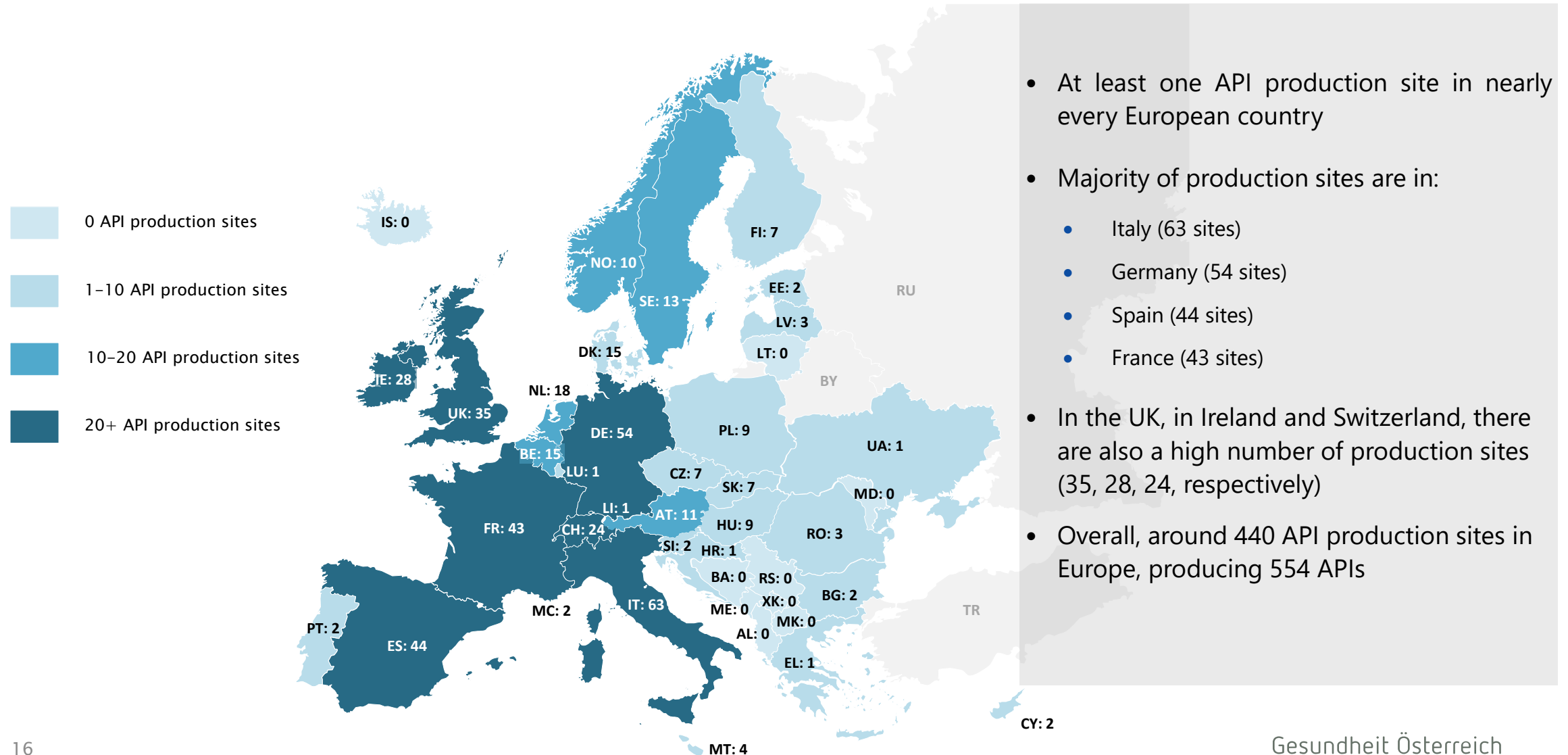
- For more than half of the APIs that are placed in the EU market, there are only 1-5 manufacturers with a valid CEP (globally)
- For certain indications, the share of API production in Europe is higher (i.e. APIs with valid Certificates of Suitability of Monographs of the European Pharmacopoeia / CEPs)
- For some APIs the demand is fully covered by European production (e.g. Benserazide and Propofol)
- There are other APIs that are exclusively produced in Asia (e.g. Simvastatin)

Certificates of Suitability of Monographs of the European Pharmacopoeia for APIs (per ATC-code)



ATC classifications: A – Alimentary tract and metabolism; B – Blood and blood forming organs; C – Cardiovascular system; D – Dermatologicals; G – Genito urinary system and sex hormones; H – Systemical hormonal preparations, excl. sex hormones and insulins; J – Antiinfectives for systemic use; L – Antineoplastic and immunomodulating agents; M – Musculoskeletal system; N – Nervous system; P – Antiparasitic products, insecticides and repellents

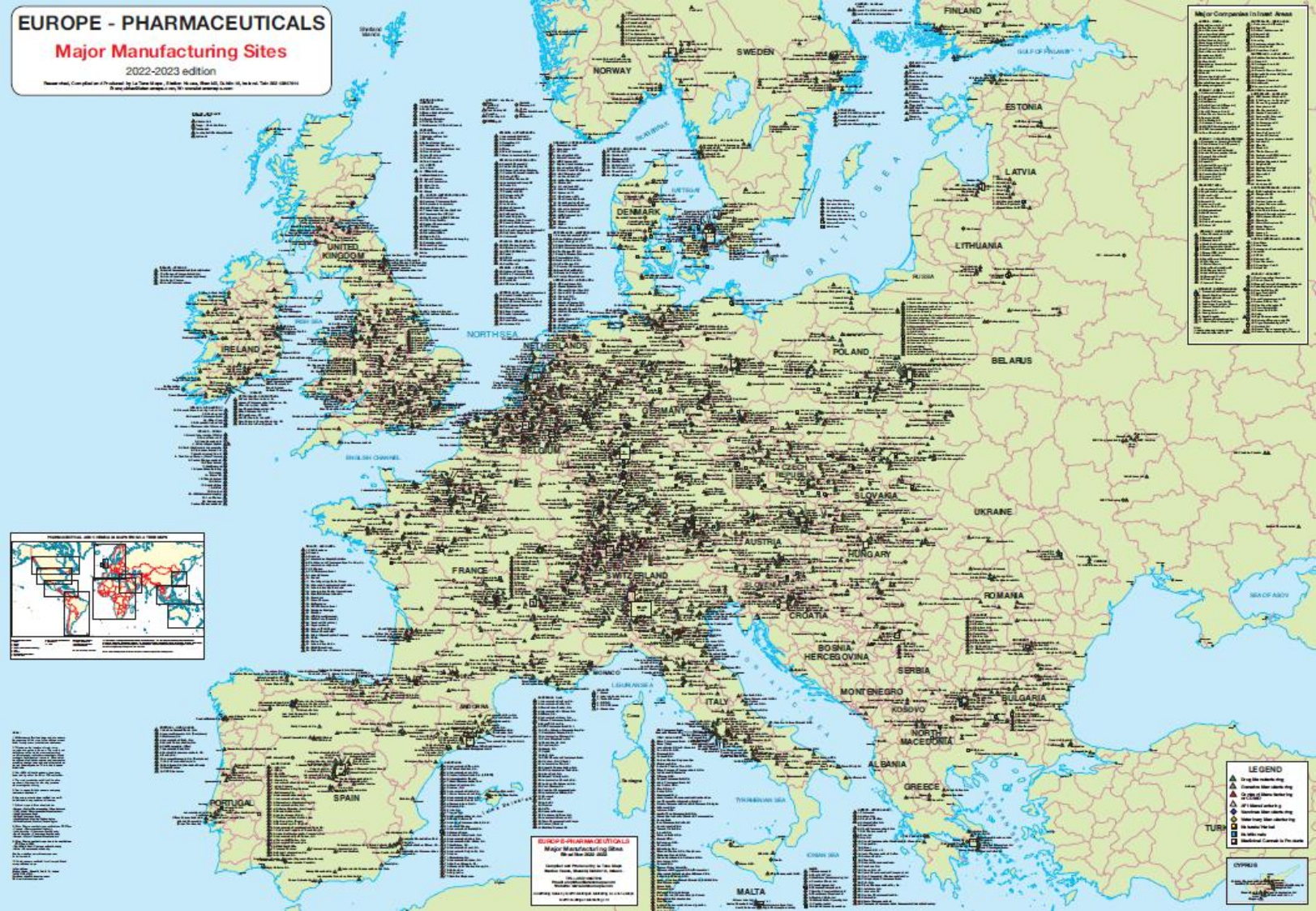
# Local production: Current state (focus on API production)



- At least one API production site in nearly every European country
- Majority of production sites are in:
  - Italy (63 sites)
  - Germany (54 sites)
  - Spain (44 sites)
  - France (43 sites)
- In the UK, in Ireland and Switzerland, there are also a high number of production sites (35, 28, 24, respectively)
- Overall, around 440 API production sites in Europe, producing 554 APIs



# Local production: Current state (why focus on API production)



Picture: La Tene Maps

# Initiatives for local production (examples)



## Kundl (Austria)

- Expansion of the local API production at the manufacturing site for penicillin in Kundl in Tyrol
- Partly funded by the Austrian government (50 million Euro from government, 100 million Euro from industry)



## EuroAPI (France)

- European manufacturer of APIs (originated from Sanofi)
- French government holds a share of 12% through the French public investment bank "EPIC Bpifrance"
- Bank committed to a lock-up of 24 months on EuroAPI shares (starting June 2022)



## Seqens (France)

- Support of French government (94€ million in 2021) through "EPIC Bpifrance"
- Continuously extending its capacities and portfolio
- Multi-purpose units, producing non-good manufacturing practice (GMP) intermediates in the short term, APIs in the long term



# Initiatives for local production (details)

	Year	API / medicines affected	Stakeholders involved	Public resources spent	Impact / success	Challenges and issues
<b>Kundl</b> (Novartis/Sandoz)	2021 (announced)	Penicillin	<ul style="list-style-type: none"> <li>• Novartis/Sandoz</li> <li>• Austrian government</li> </ul>	50€ million (100€ million from industry) (announced)	<ul style="list-style-type: none"> <li>• Increase in production</li> <li>• Potential to produce penicillin for the entire demand in Europe</li> </ul>	Unclear (long-term data missing)
<b>EuroAPI</b> (Sanofi)	2021	<ul style="list-style-type: none"> <li>• Steroids</li> <li>• Alkaloids</li> <li>• Sartans,</li> <li>• Antihistamines</li> <li>• Antipyretics</li> <li>• Vitamin B12</li> <li>• Anti-infectives</li> <li>• Prostaglandins</li> </ul>	Shareholders: <ul style="list-style-type: none"> <li>• Sanofi (30,1%)</li> <li>• EPIC Bpifrance (12%)</li> <li>• L'Oréal (5,5%),</li> <li>• Free float (52,4%)</li> </ul>	unclear	<ul style="list-style-type: none"> <li>• \$770 million sales for APIs in 2021</li> <li>• Specialised production</li> <li>• Capable of producing &gt;80% of new drugs</li> <li>• Building additional capacity for vitamin B12, vrostaglandins &amp; hormones</li> <li>• Multiple growth avenues including cross-selling, pricing enhancements, new clients, broader repatriation trends</li> </ul>	Agility and responsiveness to demand
<b>Seqens</b>	2022	<ul style="list-style-type: none"> <li>• Paracetamol</li> <li>• Others</li> </ul>	Shareholders: <ul style="list-style-type: none"> <li>• SK Capita</li> <li>• Bpifrance,</li> <li>• Nov' Santé Actions Non Cotées</li> <li>• Mérieux Equity Partners</li> <li>• Ardian</li> <li>• Eximium</li> </ul>	94€ million in 2021	<ul style="list-style-type: none"> <li>• Capacity to produce 10,000 tonnes of paracetamol per year</li> <li>• High-performance, innovative and competitive installation</li> <li>• €1 billion in sales, 24 industrial sites, 7 R&amp;D centers and more than 3,000 employees</li> </ul>	Unclear (long-term data missing), in 2020 still depending on Asian intermediates

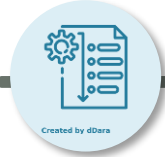
# Challenges of reshoring production

Dimension	Description	Potential solution
<b>Sourcing of intermediate or key materials</b>	(Key) materials needed for API synthesis should come from reliable (and regional) sources	<ul style="list-style-type: none"> <li>• Supply agreements with local chemical suppliers</li> <li>• Development of synthesis design for materials availability</li> </ul>
<b>Fiscal</b>	Impact of local fees and taxes	<ul style="list-style-type: none"> <li>• Federal or local governments need to consider fee or tax benefits for regionally sourced and produced products</li> </ul>
<b>Technology</b>	Implementation of alternative manufacturing procedures and use of advanced technologies to reduce personnel costs	<ul style="list-style-type: none"> <li>• Acceleration of automation and robotisation</li> <li>• Development and adaptation of technologies, such as continuous manufacturing (CM)</li> <li>• Use of strategies for hybrid CM and batch operations</li> </ul>
<b>Environment</b>	API manufacturing use of solvents and their waste generation and handling	<ul style="list-style-type: none"> <li>• Operations that are designed to minimise the use of solvents and waste generation</li> <li>• Provide local and federal economic incentives to encourage the use of environmentally friendly technologies</li> </ul>
<b>Workforce</b>	There is limited (skilled) workforce availability for API manufacturing	<ul style="list-style-type: none"> <li>• Academia can contribute to the creation of training and academic programs to address workforce needs</li> </ul>
<b>Regulatory</b>	Applications for advanced manufacturing	<ul style="list-style-type: none"> <li>• Ensure alignment of existing policies and with authorities</li> </ul>

# Reshoring: What should be considered?

## **Priorisation:**

Concentration on medicines that are crucial for patients



## **Feasibility:**

Concentrate on medicines / APIs for which reshoring is feasibly and reasonable



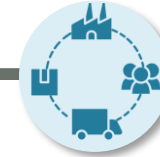
## **Consideration of further dimensions:**

Reshoring process should be eased and shortened



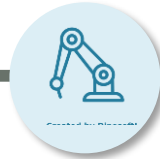
## **Ensuring the Supply Chain:**

Supply of materials and downstream production should be ensured



## **Automatisation and Technology:**

New manufacturing techniques should be adopted



## **Pricing and Reimbursement:**

Manufacturing locations could be a decision criterion



And probably more...

# Thank you for your attention!

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Picture: reddit.com