WHERE DO OUR ACTIVE PHARMACEUTICAL INGREDIENTS COME FROM? – A WORLD MAP OF API PRODUCTION

Short Report

Berlin, September 2020

SUMMARY

- **Europe's supply of active pharmaceutical ingredients** is **exposed to various risks**
  - **2/3** of the **currently valid CEPs** for APIs are **held by Asian manufacturers**
  - **Indian and Chinese production sites** are concentrated **in a few provinces**
  - **For 1/6 of the APIs** analyzed in this study, there is **no European production at all**, for more than half of the APIs there are **between 1 – 5 CEPs** and therefore only **very few manufacturers worldwide**
- **Europe** has **lost its strong position** as an **API producer**. Looking at new approvals of CEPs between 2000 and 2020, **Asia significantly outperformed Europe**: **Asian manufacturers** increased the number of their **CEPs from 183 to 2,369**, while **European manufacturers** only grew **from 348 to 1,260 CEPs**
- **Unequal regulatory standards** and **cost pressure** are **main reasons** for this development. **India** and **China** are **actively outperfoming European businesses**
- Today**, European manufacturers focus on specific APIs** (e.g. low production volumes, complex production processes), but **technical know-how and capacities** to **increase European API production** are (still) **available**

CENTRAL QUESTIONS, SCOPE OF THE STUDY AND METHODOLOGY

Central questions

- To what extent does Europe depend on Asia to cover its demand for APIs?
- Objective: Creation of a well-founded database
- What are main drivers for the development within the recent years?

Scope of the study

- Generic APIs with at least one CEP (Certificate of Suitability of Monographs of the European Pharmacopoeia; proof of active pharmaceutical ingredients quality, used for drug approvals)
- Focus on APIs, no consideration of raw materials and intermediates
- In total: 554 APIs with valid CEPs
- Sample selection of 21 APIs from the above-mentioned API database for in-depth analyses

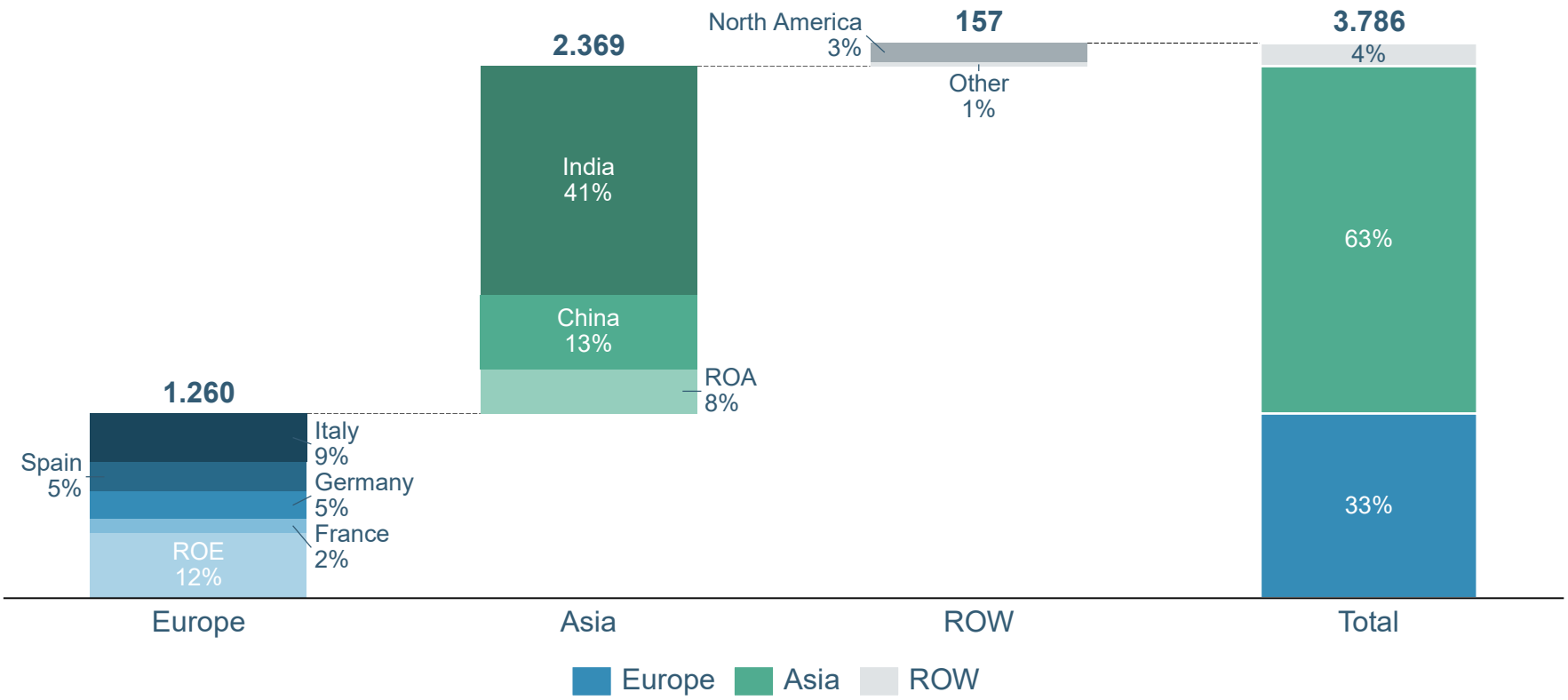
Methodology

- Creation of a cleansed CEP database, enriched with additional manufacturers' information
- In-depth analysis of the data from cleansed CEP database according to various criteria
- Desk Research for further investigations
- Interviews with API manufacturers and stakeholders
    - For quantitative estimation of the coverage of European demand for selected APIs
    - To validate the findings and to confirm observed trends and their causes

ASIA CURRENTLY HOLDS ALMOST TWICE AS MANY CEPS AS EUROPE

OVERVIEW: GLOBAL DISTRIBUTION OF CURRENTLY VALID CEPS (2020*)[1]

Number of CEPs



*) Data collection: 30.04.2020, applies to all subsequent analyses

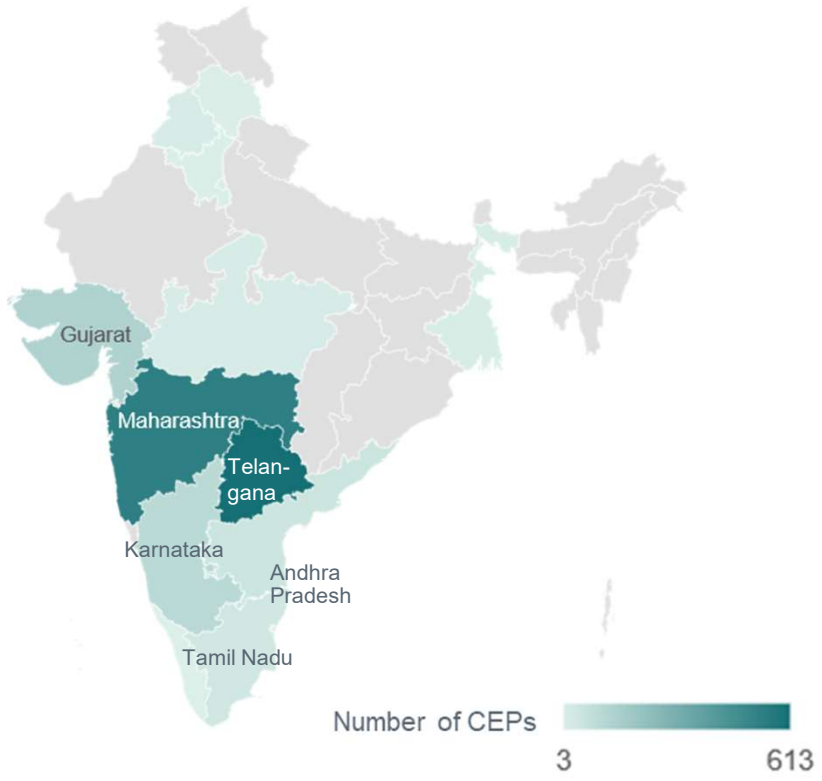
1) Number of all valid CEPs in the respective calendar year for the APIs under consideration (expired / withdrawn CEPs are already excluded)

Source: Certificate Database, European Directorate for the Quality of Medicine & Healthcare, Date: 30.04.2020

HIGH CONCENTRATION OF MANUFACTURERS IN SPECIFIC PROVINCES OF INDIA AND CHINA POSE A HIGH RISK, E.G. IN TIMES OF COVID-19

GEOGRAPHICAL ALLOCATION OF ASIAN CEPS (2020)[1]

India: Geographical Allocation of CEPs by Province



China: Geographical Allocation of CEPs by Province

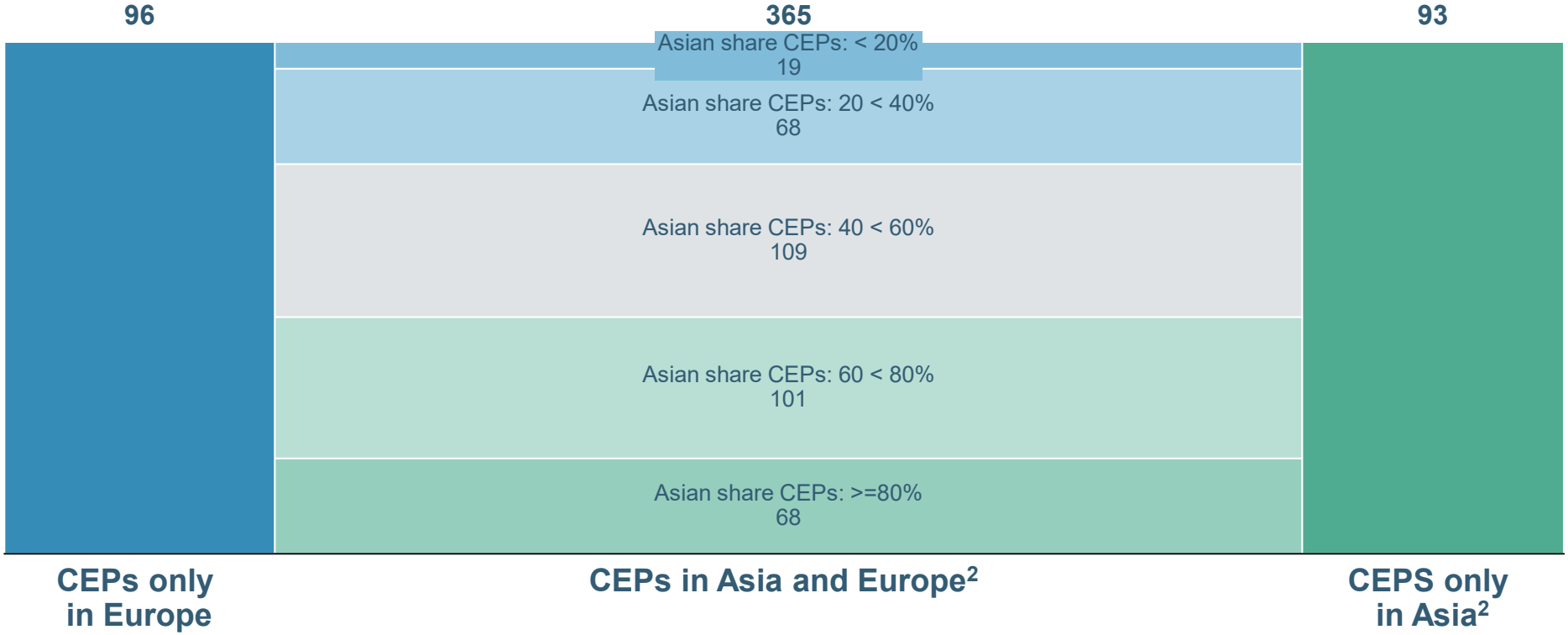
[1)] Number of all valid CEPs in the respective calendar year for the APIs under consideration (expired / withdrawn CEPs are already excluded)
Source: Certificate Database, European Directorate for the Quality of Medicine & Healthcare, Date: 30.04.2020

FOR 1 OUT OF 6 APIS NEEDED IN EUROPE THERE ARE NO EUROPEAN CEP HOLDERS AT ALL

OVERVIEW: GLOBAL DISTRIBUTION OF API PRODUCTION (2020)[1]

Number of APIs with Valid CEPs by Region

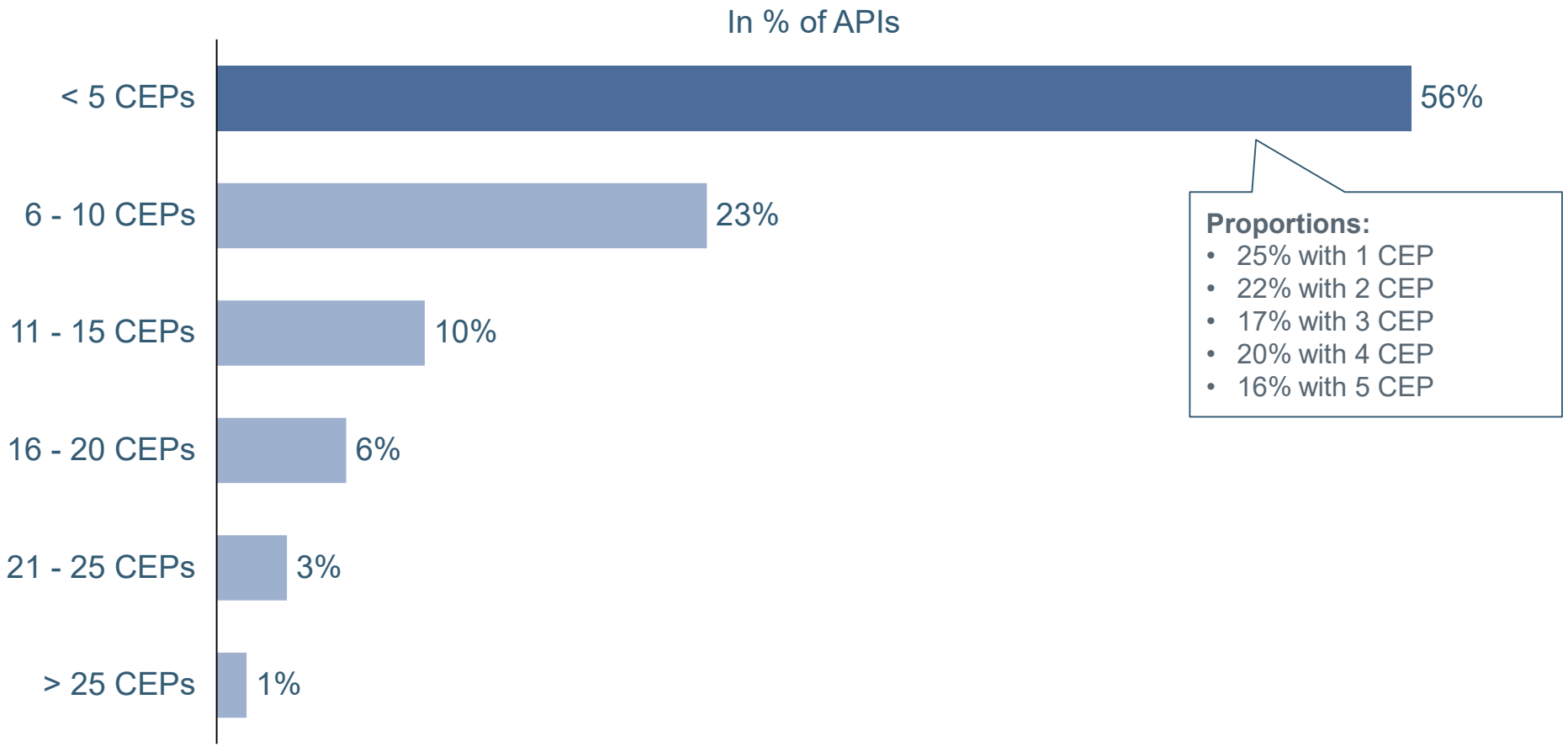
Total APIs: 554



[1)] Number of all considered APIs with valid CEPs in the respective calendar year (APIs with expired / withdrawn CEPs are already excluded);
[2)] Including Rest of World
Quelle: Certificate Database, European Directorate for the Quality of Medicine & Healthcare, Date: 30.04.2020

FOR MORE THAN HALF OF THE APIS THERE ARE BETWEEN 1 – 5 CEPS WORLDWIDE AND THEREFORE ONLY A FEW MANUFACTURERS

OVERVIEW SHARE OF APIS PER GROUP "CEPS PER API" WORLDWIDE (2020)[1]

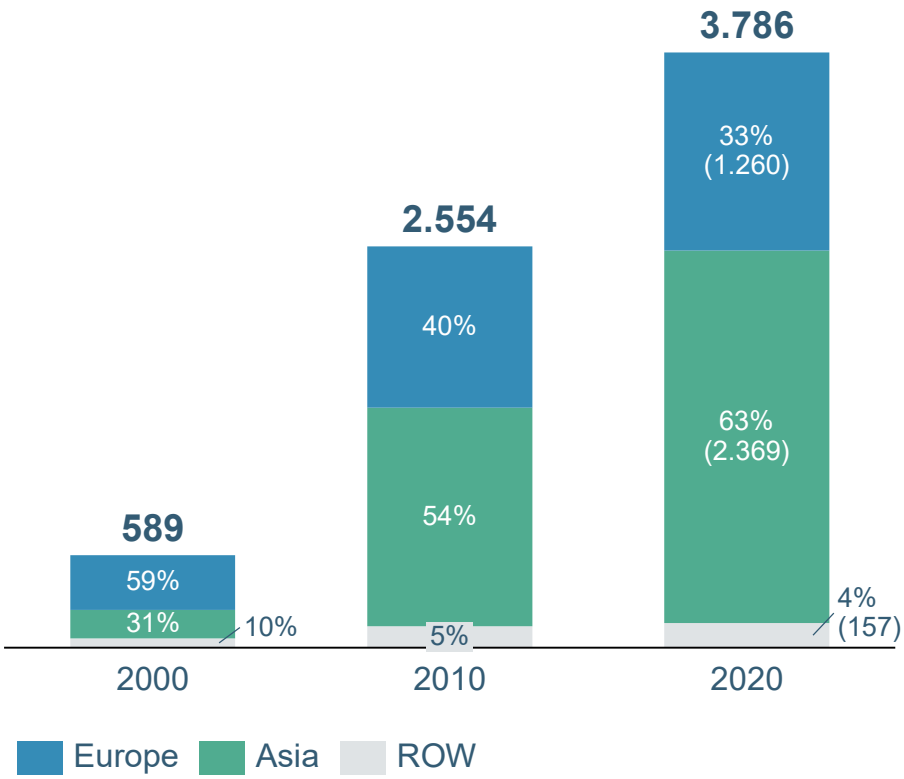


[1)] Number of all considered APIs with valid CEPs in the respective calendar year (APIs with expired / withdrawn CEPs are already excluded)
Source: Certificate Database, European Directorate for the Quality of Medicine & Healthcare, Date: 30.04.2020

THE RATIO BETWEEN EUROPE AND ASIA HAS COMPLETELY REVERSED WITHIN THE PAST 20 YEARS

DEVELOPMENT OF THE NUMBER OF VALID CEPS (2000 – 2020)[1]

Number of CEPs



"There is **high price pressure** on the generics market **due to discount agreements**. As a result, many **generic companies are forced to buy** active pharmaceutical ingredients **at low prices in Asia**"

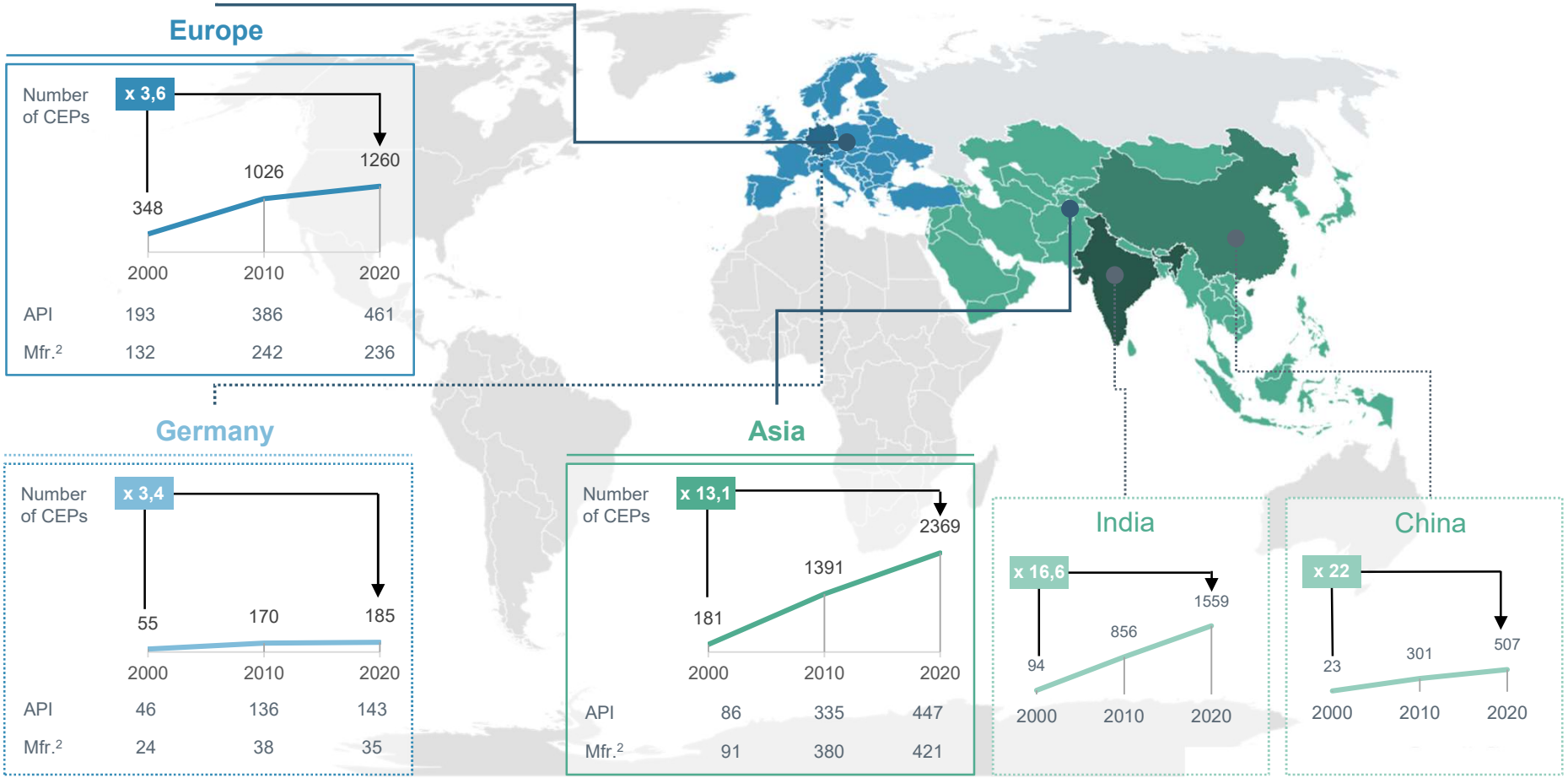
"**Approval process in Europe is too slow**, while **in India** new **facilities** are being **built without problems**"

"**Customers** do not accept that it is important to produce in Europe. They **are not willing to pay more**. **Indian prices can never be undercut** "

[1)] Number of all valid CEPs in the respective calendar year for the APIs under consideration (expired / withdrawn CEPs are already excluded)
Source: Certificate Database, European Directorate for the Quality of Medicine & Healthcare, Date: 30.04.2020

THERE ARE MORE CEPS AND MORE MANUFACTURERS IN ASIA, BUT ABOUT THE SAME NUMBER OF APIS AS IN EUROPE

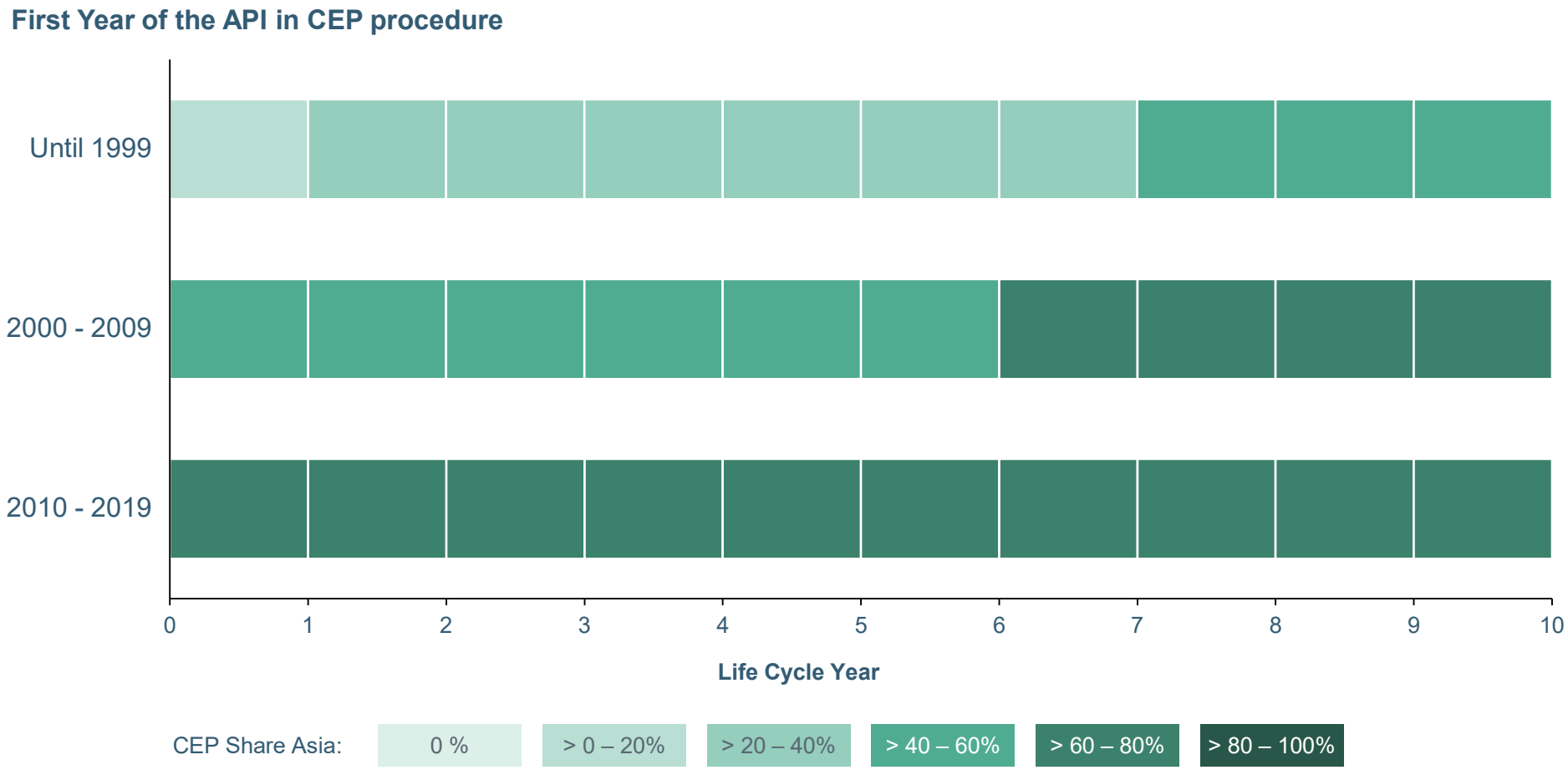
OVERVIEW CEPS, APIS AND MANUFACTURERS BY REGION (2000 – 2020)[1]



[1] Number of all valid CEPs in the respective calendar year for the APIs under consideration (expired / withdrawn CEPs are already excluded)
[2] Mfr. = Manufacturer
Source: Certificate Database, European Directorate for the Quality of Medicine & Healthcare, Date: 30.04.2020

THE LATER AN API ENTERS THE CEP PROCEDURE, THE LOWER THE SHARE OF EUROPEAN MANUFACTURERS

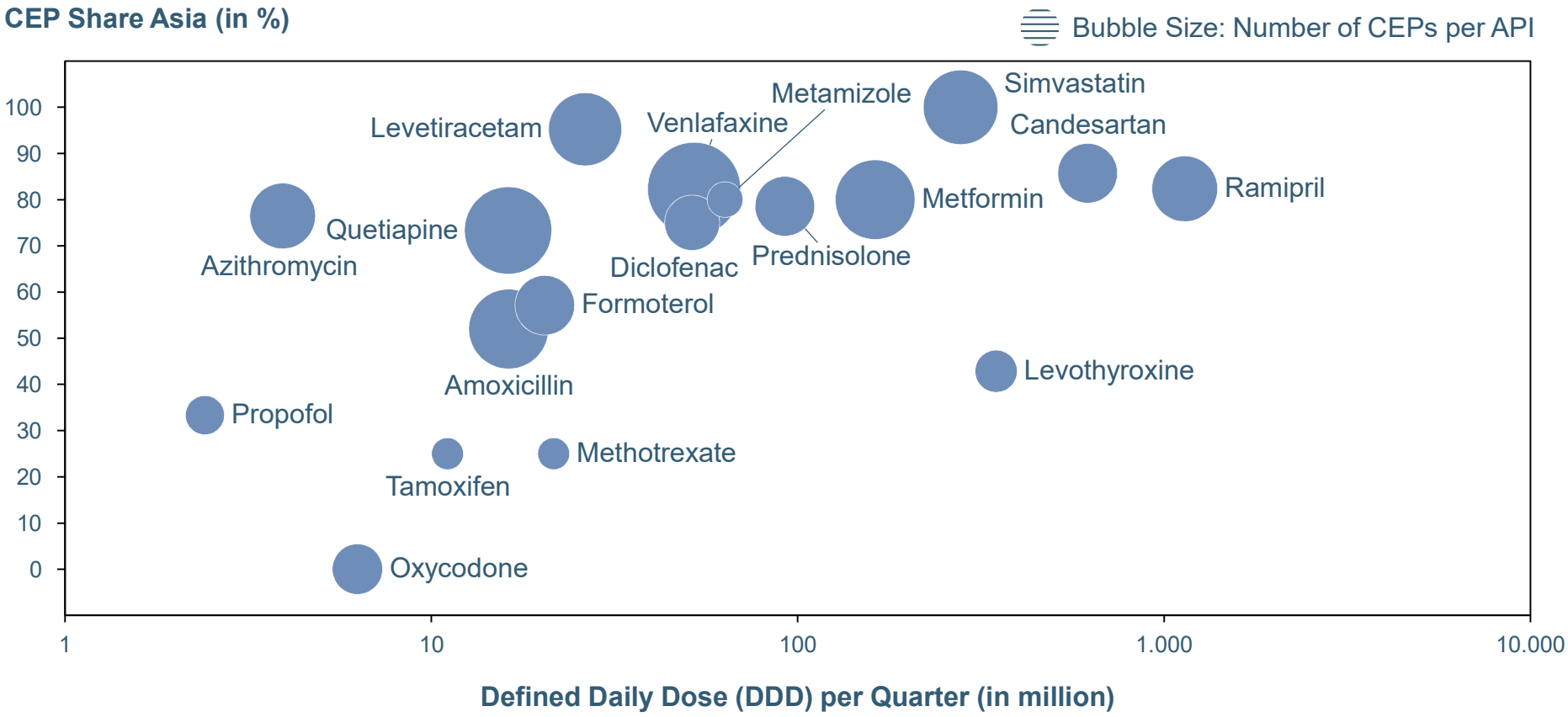
DEVELOPMENT OF THE SHARE OF ASIAN MANUFACTURERS BY LIFE CYCLE



Source: Certificate Database, European Directorate for the Quality of Medicine & Healthcare, Date: 30.04.2020

IN-DEPTH ANALYSIS: THE HIGHER THE VOLUME OF AN API, THE HIGHER THE PROPORTION OF ASIAN CEP HOLDERS

SELECTED APIS: CEP SHARE ASIA IN RELATION TO DEFINED DAILY DOSES (2020)[1,2]



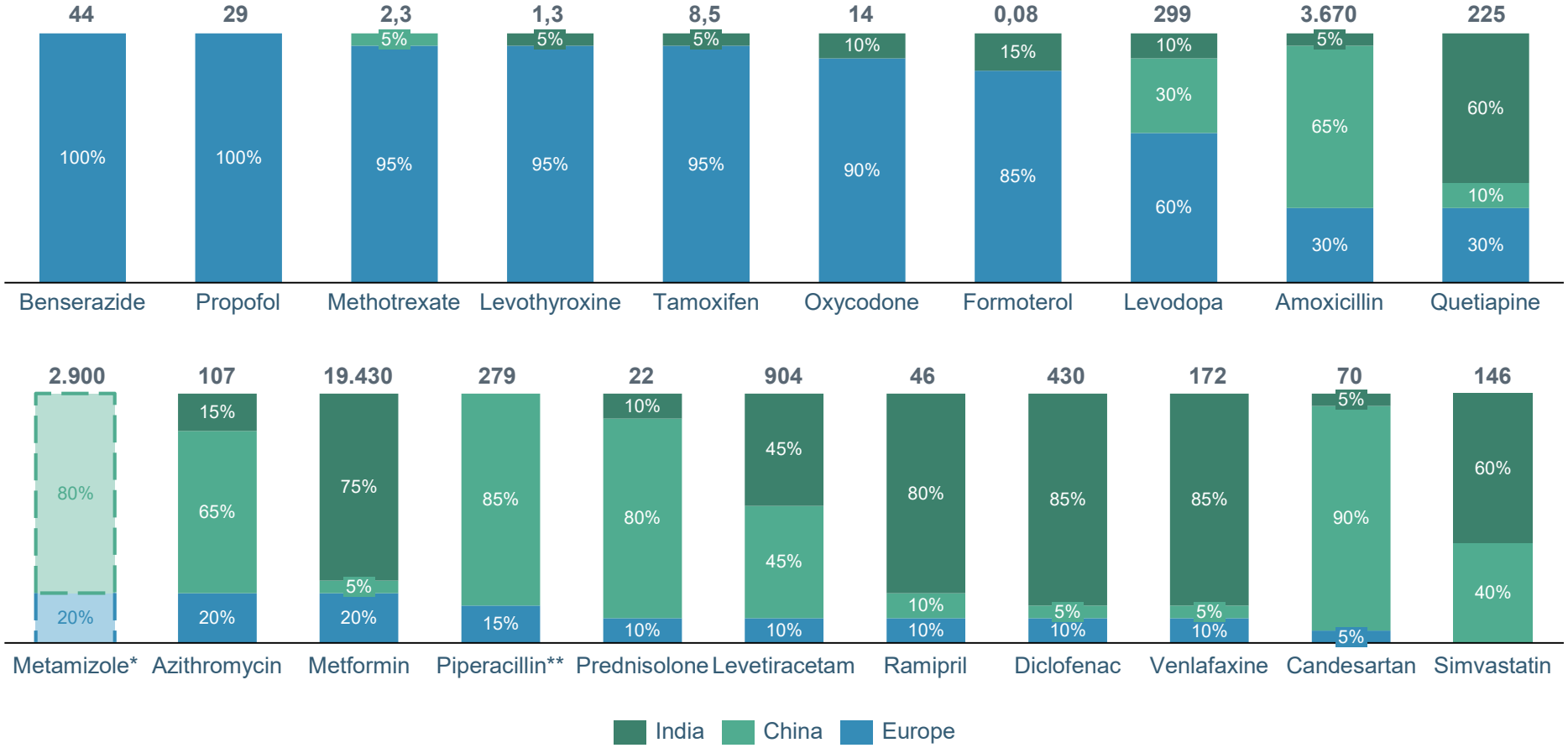
[1)] Number of all valid CEPs in the respective calendar year for the APIs under consideration (expired / withdrawn CEPs are already excluded)
[2)] API sample selected by defined daily dose Q4 2019 > 1 million DDD in retail (exclusion of: Piperacillin, Benserazide, Levodopa); n = 18
Source: Certificate Database, European Directorate for the Quality of Medicine & Healthcare, Date: 30.04.2020; Basic List Pro Generika

Estimation

IN-DEPTH ANALYSIS: SMALL-VOLUME, COMPLEX APIS TEND TO COME FROM EUROPE, WHILE ASIA IS KNOWN FOR LARGE-VOLUME APIS

ESTIMATED SHARE OF SUPPLY FOR EUROPEAN DEMAND BY REGIONS

Share of supply in % (Above the Pillar: Total European Demand in Tons)

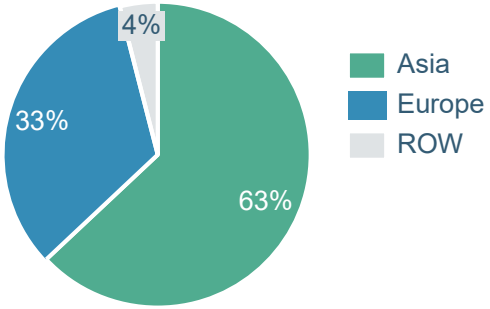


*) Estimation, Data basis limited; **) API mainly in combination with Tazobactam (exclusively produced in Asia).
Source: Supplier Interviews, Import Data Analysis QYOBO Market Platform, CEP Database, Pharmaoffer; IQVIA

TODAY EUROPE FOCUSES ON SPECIFIC APIS; POTENTIAL FOR PRODUCTION EXPANSION STILL EXISTS AND IS ALREADY RECOGNIZED BY POLITICS

Europe focused on specific APIs – Potential for production expansion still exists

Share of valid CEPs by region 2020[1]



"**Complex APIs are competitive**, as **simple ones** are not, because they **can easily be produced by Chinese manufacturers**"

"Some customers pay attention to **production safety** and the **environment** and therefore buy **more expensive European products**"

"The **required production capacities** would be **sufficiently available in the EU** because of empty and multi-purpose plants"

The focus is on strengthening the European network – Example Kundl (Novartis/Sandoz)

- Kundl plant is **the last remaining, fully integrated antibiotics production site** in the **western world**
- Novartis and Austrian government secure **long-term production of key antibiotics in Europe**
- Planned **joint investment of more than EUR 150 million** - Austrian government contributes EUR 50 million

[1] Number of all valid CEPs (expired / withdrawn CEPs are already excluded)

Source: Certificate Database, European Directorate for the Quality of Medicine & Healthcare, Date: 30.04.2020; Supplier Interviews

DR. ANDREAS MEISER

PARTNER

MUNDICARE benefits from Andrea's extensive experience in academic research, strategy consulting, and the setting up and management of biotech start-ups. He works at the interface between science and industry and drives the implementation of new solutions in the biotech environment. Prior to his partnership at MUNDICARE, he was responsible for research and development in various companies and led interdisciplinary consulting projects with large teams.

FOCUS

< Strategy: business development, innovation, market assessment and market entry strategies
< Implementation: Implementation of projects, PMOs in various industries
< Regional experience: Germany, Europe, Asia

MILESTONES

Partner at MUNDICARE

↑

Numerous consulting projects with a broad industry portfolio focusing on business development, implementation of new technologies and the planning/implementation of PMOs

↑

Interim management R&D in a medium-sized pharmaceutical company: Development of new production methods to increase efficiency

↑

Setting up biotechnology start-ups: development and marketing of new technologies in the field of blue (algae) biotechnology

↑

McKinsey & Company: After initially working in a wide range of process industries, he joined the chemical practice as an industry specialist. Afterwards he was a project manager with a portfolio of engagements in the areas of chemicals, climate change and biotechnology. As an industry expert, he supported teams worldwide in biochemicals and bioenergy. Andreas has a global client portfolio with relocation to Asia, is an author of publications and lectures at various international congresses

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Longer research stays in Russia and Latin America

↑

PhD in biotechnology: Commercial production of active pharmaceutical ingredients using a biotechnological approach

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Scientific activity at Fraunhofer Gesellschaft

↑

Study of microbiology/biotechnology

↑

Intensive engagement in chemistry, National Team Chemistry Olympiad

GREAT BY EXPERIENCE:
THREE BRAINS, ONE TEAM, ONE NETWORK

Specialists and team players, forward and lateral thinkers, problem solvers and troubleshooters, analysts and doers - each partner is an expert, the whole team a bridge across the entire value chain. MundiCare combines diversity and multitasking, health industry and management consultancy, consulting approaches and reality.

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