

SBIA-DMF Drug Substance Workshop

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API Manufacturing facility Global Distribution and Facility Profile Analysis

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Virtual

PURPOSE

To perform an analysis of the global distribution of API manufacturing facilities supporting NDA and ANDA applications submitted from October 1st 2017 to July 1st 2020.

OBJECTIVE(S)

1. Determine the global distribution of API facilities and their functions supporting GDUFA (generic) submissions over the specified timeframe
2. Determine the global distribution of API facilities supporting PDUFA (innovator) submissions over the specified timeframe
3. Compare the global distribution of API facilities between the GDUFA and PDUFA programs.

METHOD(S)

Facility Data were retrieved from the applications submitted from Oct 1st, 2017-July 1, 2020 using internal database.

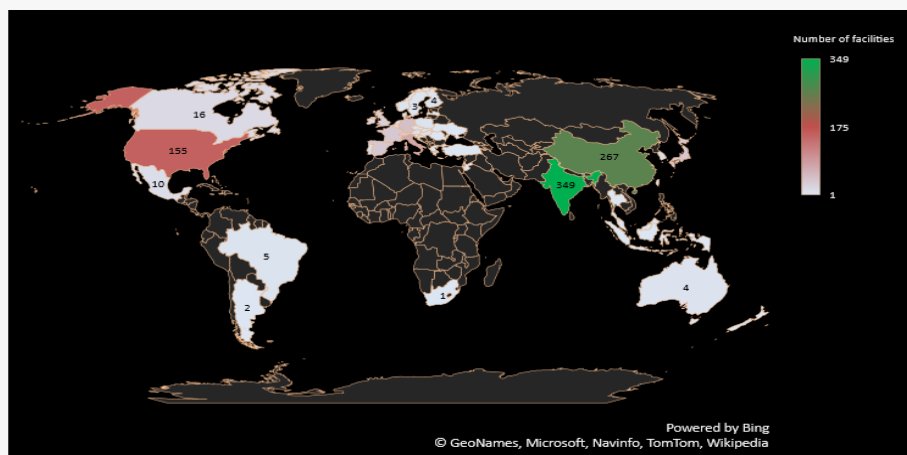
In the last three fiscal years, the agency received 6082 unique application projects across NDAs, ANDAs, and their supplements.

1232 unique manufacturing facilities have been involved in the current study.

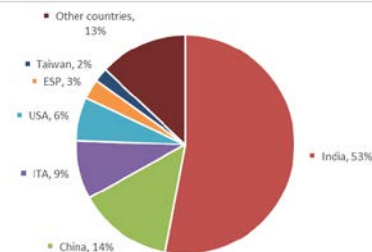
The global distribution analysis was performed based on 6082 unique applications. The same facility can be counted multiple times because it was referenced by multiple applications.

COVID related facility study includes 102 applications submitted before 7/1/2020.

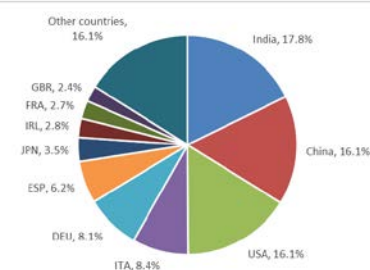
Distribution Map for API Facilities supporting submissions Oct 1st, 2017-July 1, 2020.



Distribution Chart for ANDA API facilities across 5148 submissions



Distribution Chart for NDA API facilities across 934 submissions



CONCLUSION(S)

- Across both NDAs and ANDAs, about 13% of API manufacturing facilities are domestic.
- Distribution of API manufacturing facilities differs between NDA and ANDA submissions:
 - The top three regions for ANDA API manufacturing facilities are India, China, and Italy, accounting for 76% of the total.
 - The top three regions for NDA API manufacturing facilities are India, China and the United States (tie), accounting for 50% of the total.
 - The top three regions for API facilities associated with COVID priority submissions were India, Italy, and China
- Overall the most common manufacturing function in API facilities is Non-sterile API by chemical synthesis accounting for 95% of the profile codes.
- Overall only 1% of applications are associated with sterile API manufacturing facilities.



NOTES ON THE STUDY

Because the data does not systematically capture facilities manufacturing API intermediates or key starting materials, the impact of India and China on the API supply chain is likely more significant than presented here.

API Manufacturing facility Global Distribution and Facility Profile Analysis

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Background and Data Source



- The outsourcing of the drug development and manufacturing is a growing trend for the global pharmaceutical industry. The detail of manufacturing facility distribution has not been studied yet. Our study is focused on the API manufacturing facilities supporting both NDA and ANDA applications from Oct 1st, 2017-July 1, 2020. This study only covers the facilities referenced by the prescription drugs.
- The facility Data were retrieved from the filed applications using internal database. The report contained 9296 projects. We note that multiple submissions might be counted during one review cycle. To treat each application equally, the duplicate submissions within one review cycle were removed. After the removal, there are 6082 unique projects left. There are 1232 unique manufacturing facilities from 49 countries have been involved in the current study.



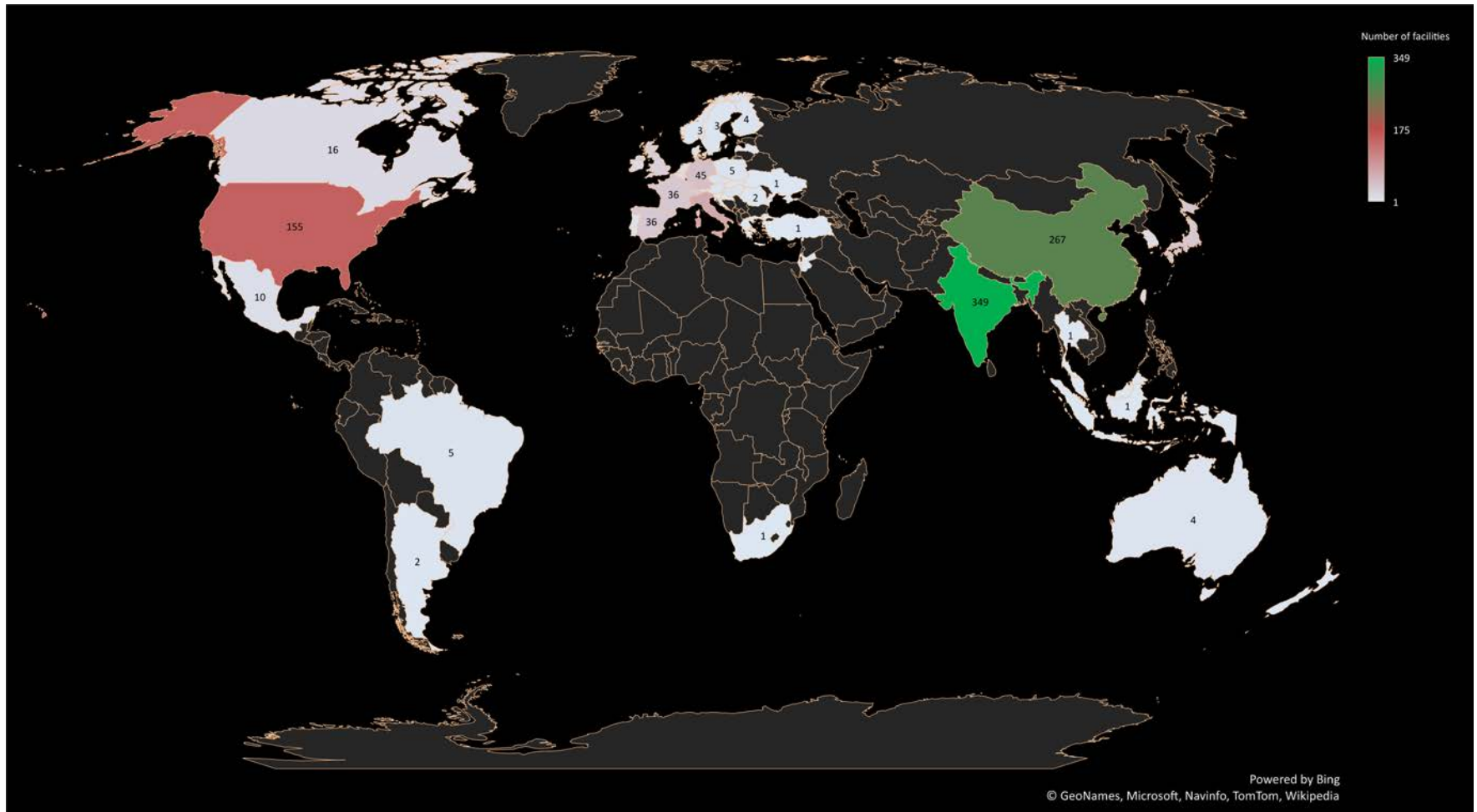
Background and Data Source



- Any submissions after July 1, 2020 are not included in this study.
- The global distribution analysis was performed based on 6082 unique applications. Same facility can be counted multiple times because it was referenced by multiple applications.
- 102 unique applications, which were submitted before July 1, 2020, were determined by FDA as COVID-related applications. There are 83 unique manufacturing facilities from 19 countries were included this COVID-related manufacturing facility study

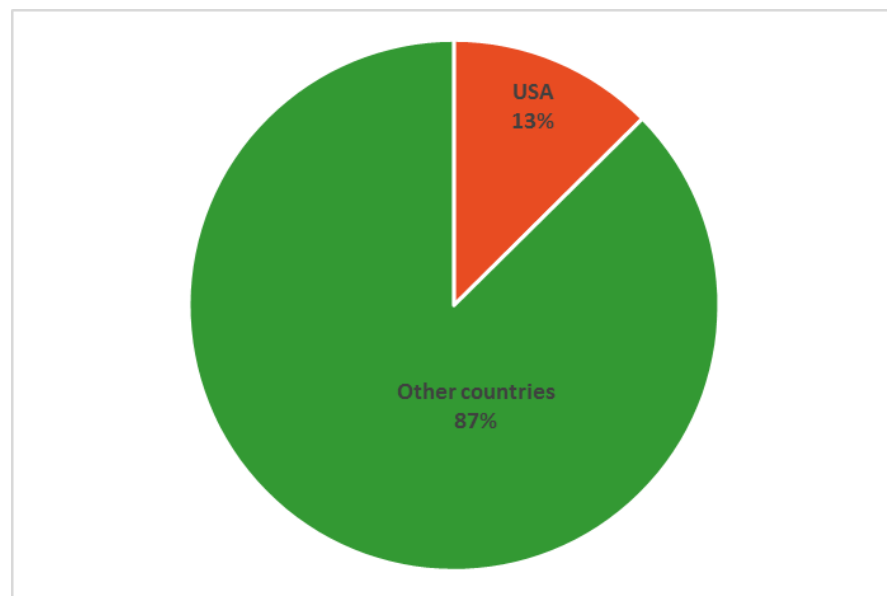


GDUFA II API Manufacturing Facilities Map

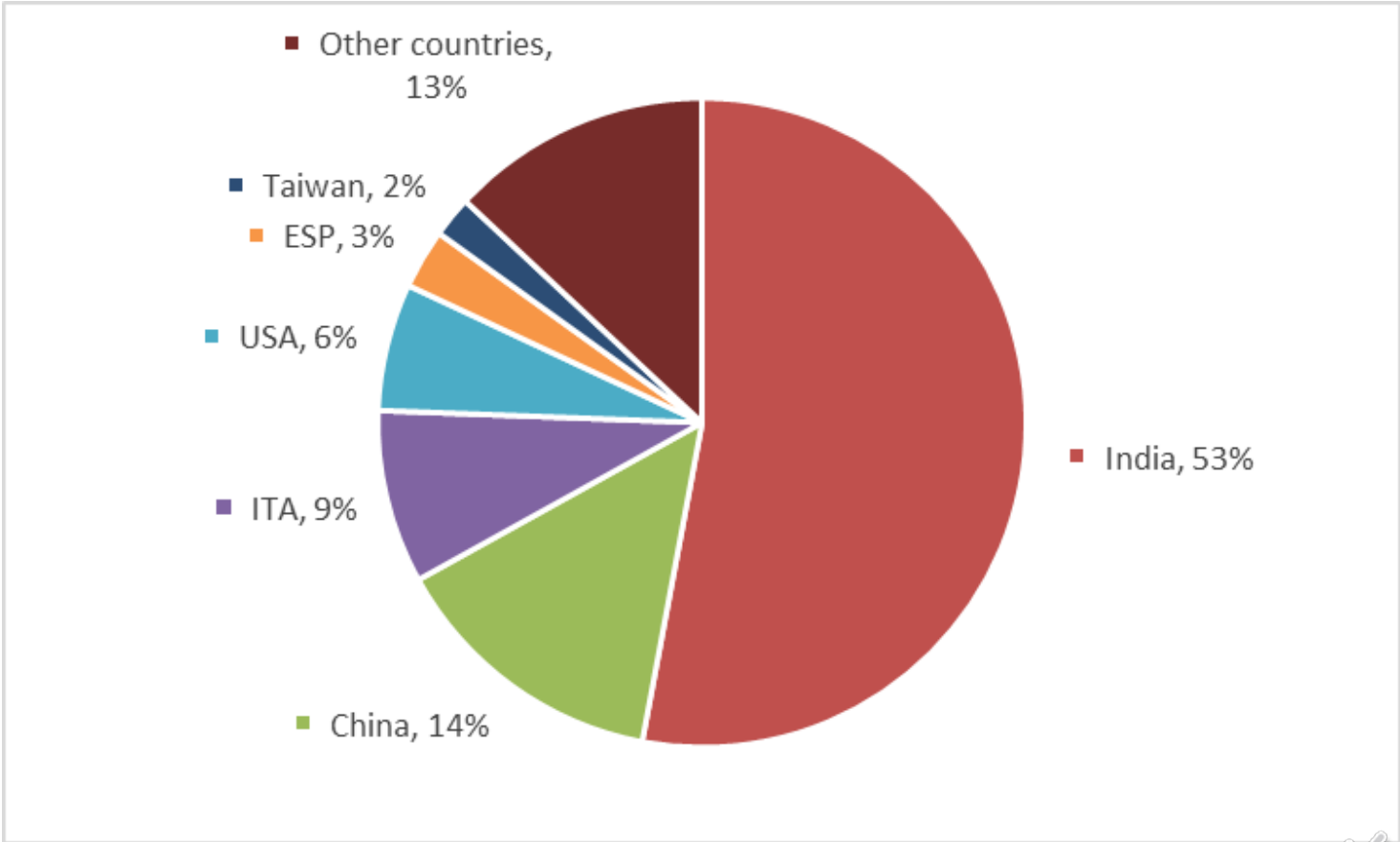


API Manufacturing Facilities Distribution Analysis (10/1/2017~7/1/2020)

- 1232 API manufacturing facilities locate in 49 countries
- 155 Domestic API manufacturing facilities have been referenced since Oct 1, 2017
- About 87% API manufacturing facilities are international manufacturing facilities



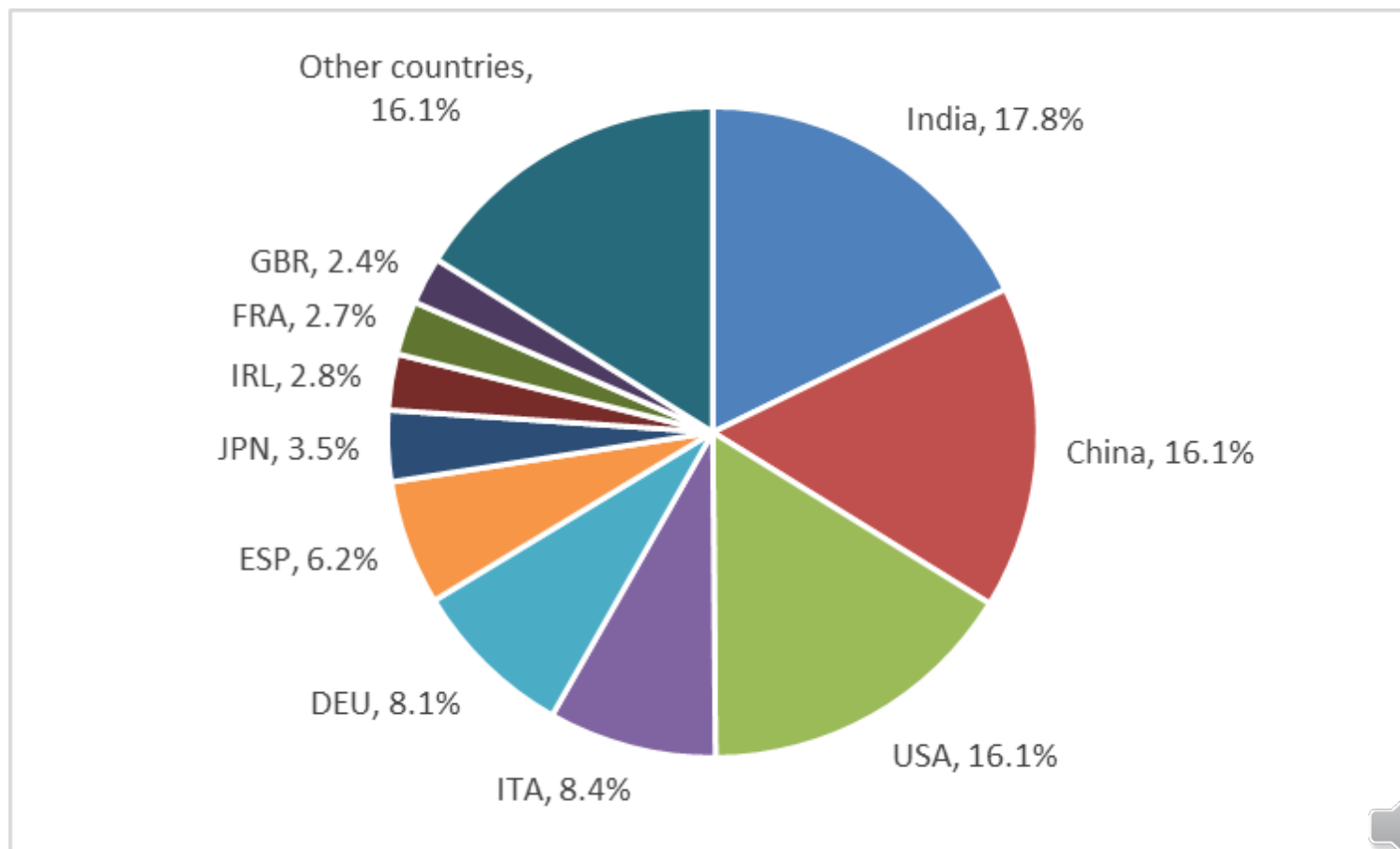
The Distribution of API Manufacturing Facilities Referenced by 5148 ANDA Submissions



Any values less than 2.0% were combined as other countries

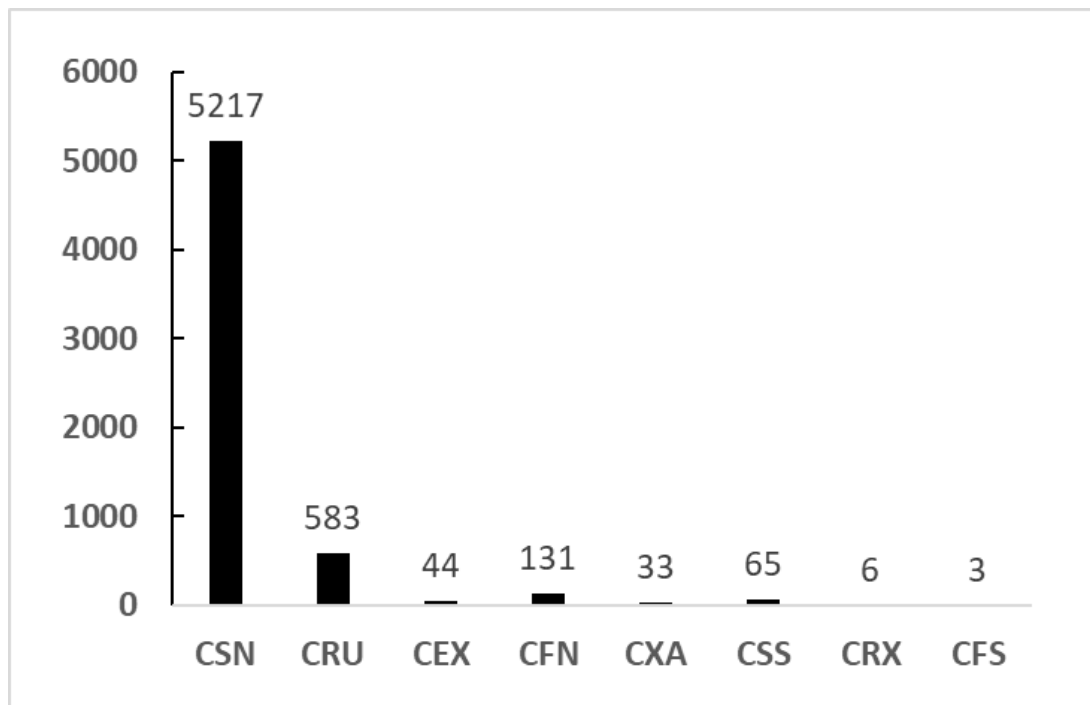


The Distribution of API Manufacturing Facilities Referenced by 934 NDA Submissions



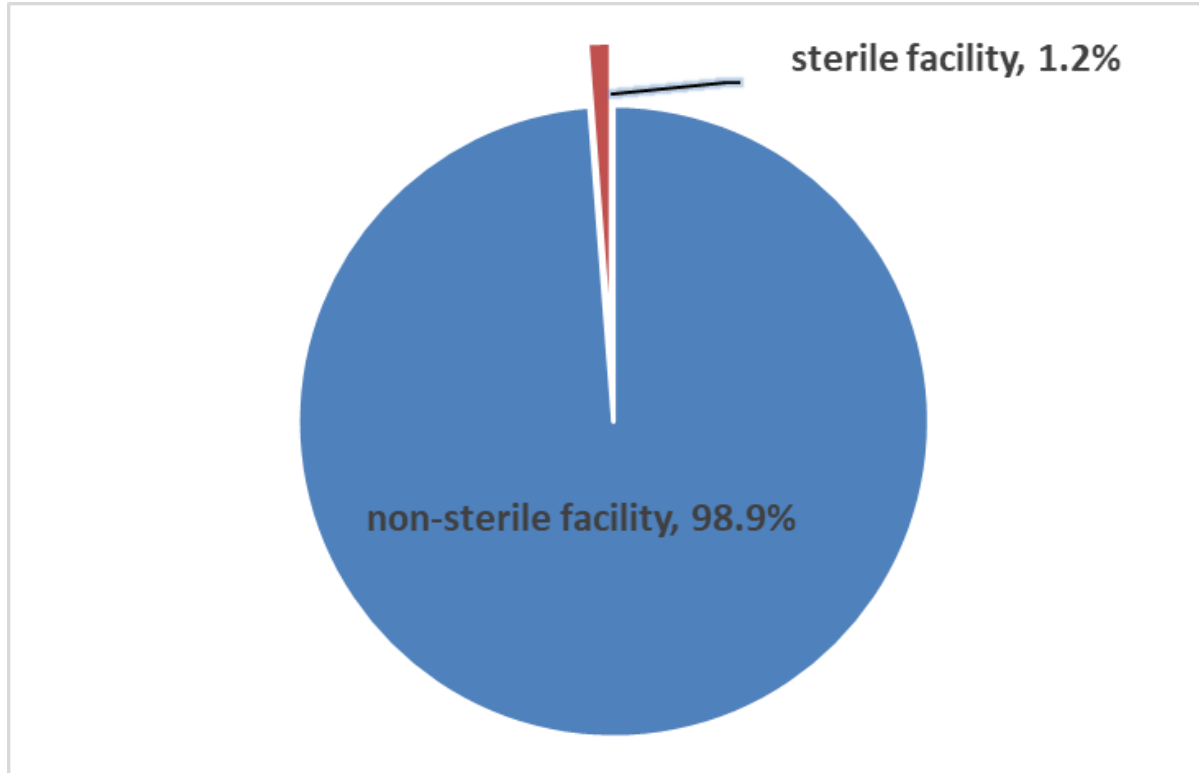
Any values less than 2.0% were combined as other countries

API Manufacturing facility Profile Analysis (10/1/2017~7/1/2020)

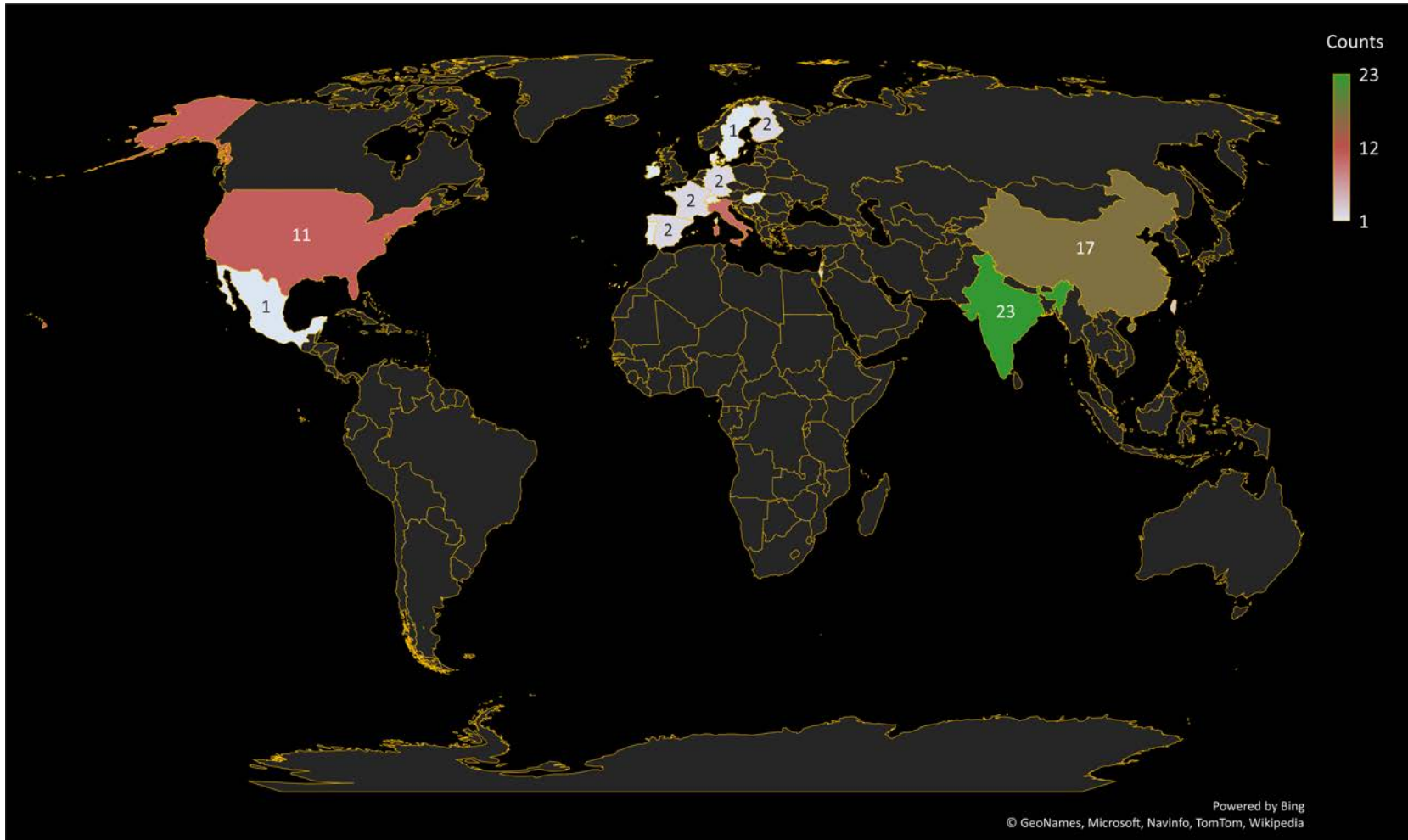


• CSN: Non-Sterile API by Chemical Synthesis	• CRU: Non-sterile intermediate NEC inorganic/ mineral
• CEX: Plant/Animal unpurified (SM or intermediate)	• CFN: Non –Sterile API by Fermentation
• CXA: Plant/Animal Extraction Purified	• CSS: Sterile API by Chemical Synthesis
• CRX: Sterile API/API intermediate/NEC inorganic/mineral	• CFS: Sterile API by Fermentation

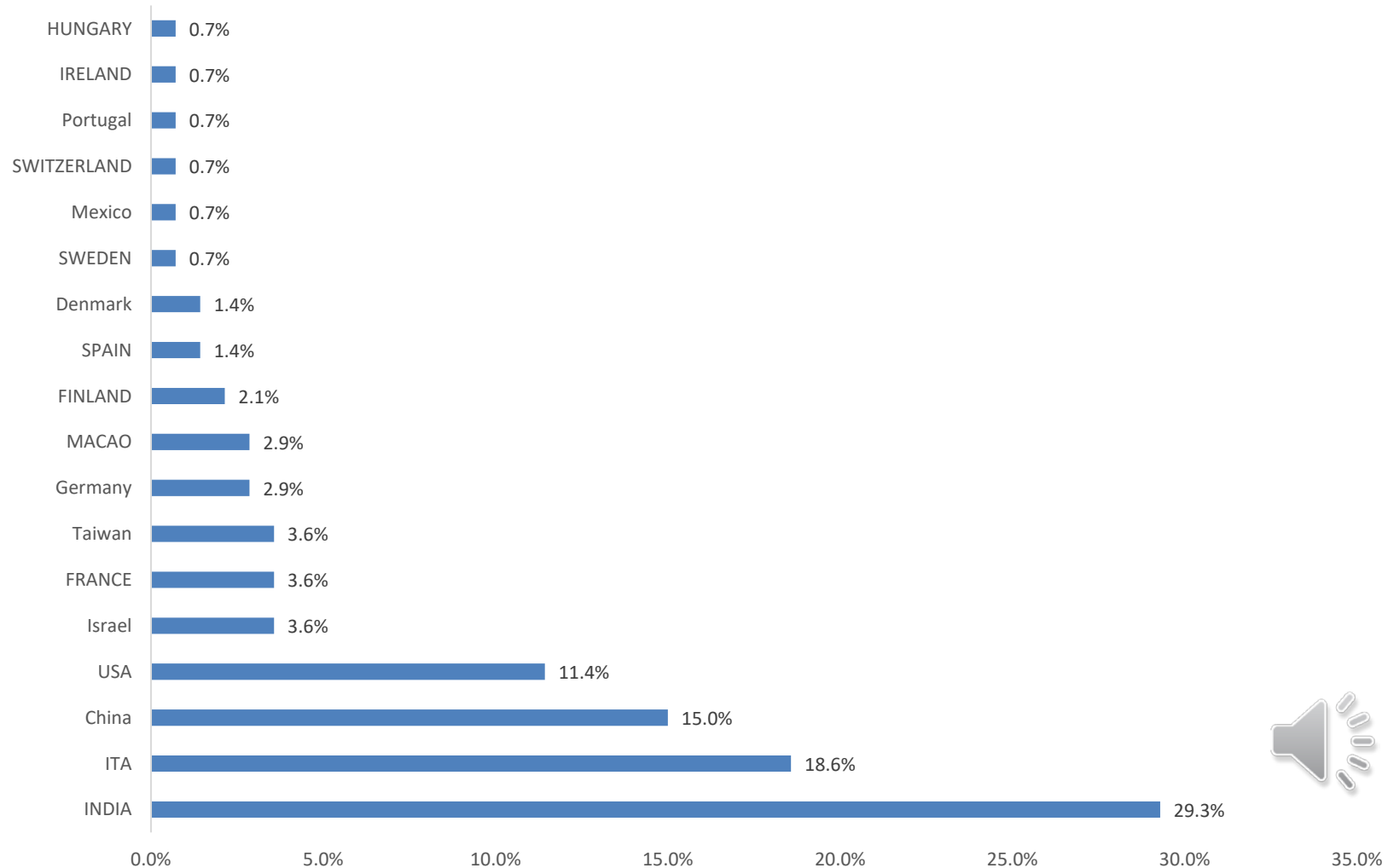
Comparison of Non-sterile API facilities vs. Sterile API facilities referenced by Unique Applications



Distribution Map for API Facilities Supporting COVID 19 Applications



API Manufacturing Facilities Referenced by 102 COVID-19 Related Submissions



Conclusions-1

- Due to limited information, the manufacturing facility profile study only provides a partial view of current drug supply chain. Current study didn't capture the manufacturing facilities for Key starting materials or intermediates. Therefore, the impact of Indian and Chinese facilities may be under estimated.
- Non-sterile chemical synthesis (CSN +CRU) is the most common practice for preparation of API, which counts 95% of the entire submission.



Conclusions-2



- Only 1% of applications are associated with sterile API manufacturing facilities.
- Compared to the NDA applications, ANDA applications associated API manufacturing facilities are more concentrated in India and China.



Conclusions-3

- India, China, and Italy are the top three regions for supporting ANDA API manufacturing. India, China and the United States (tie) are the top three regions for supporting NDA API manufacturing.
- Among entire submissions in last three years, 13% of API manufacturing facilities are domestic. The COVID 19 submission study also indicates 11.3% of API manufacturing facilities are domestic.
- A more systematic facility study, including the intermediate facilities, the testing facilities, and the drug product facilities, is needed for better understand the global drug supply chain distribution.



Acknowledgement

- Ying Zhang, Supervisory Chemist,
Division of Pharmaceutical Manufacturing
Assessment (OPMA), FDA



Thank You!

- Send questions regarding this poster to:
DMFWorkshop2021@fda.hhs.gov by 2/15/2021 for inclusion in the poster Q&A session on March 4th.
- Follow-on webinar for both posters/presentations on April 9, 2021. Questions can be sent to the above email by 3/19/2021 for inclusion in the webinar.
- Please refer to the following presentations on March 3rd and 4th for additional information:
Drug substance facilities – Hidden and critical intermediate by Wei Liu,
Facility Inspection by Jay Jariwala

