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# University of Texas at Austin International Drug Development Conference

**February 22-27, 2010**  
**Austin, Texas**

**Topic: Challenges Related to Globalization for the  
Pharmaceutical Industry**

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# Outline

- **Introduction**
- **Globalization of the Pharmaceutical Industry**
- **Counterfeit and Substandard Medicines**
- **Ongoing Initiatives and Possible Mitigating Activities**
- **Summary and Conclusions**



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## **Introduction**

- U.S. Department of Commerce (DOC) is the lead advocate in the U.S. government for business and DOC's international trade role is to promote U.S. trade by strengthening industry competitiveness and reducing tariff and non tariff barriers
- I direct the Office of Health and Consumer Goods and my office focuses on medical devices, pharmaceuticals, biotechnology, and a wide array of consumer goods products
- We work closely with industry to understand their challenges and opportunities in overseas markets
- We solicit the assistance of experts (such as USFDA staff) when it comes to finding technical regulatory solutions in many of the markets we focus on



# Introduction (cont')

- During the past two decades there have been significant changes and trends in the global pharmaceutical industry
- These global changes have a significant impact on safety, competitiveness, and the outlook for the pharmaceutical industry and drug development
- During the past several years DOC has been very active in the global battle to stop the spread of counterfeit medicines and we work very closely with U.S. FDA and industry in our activities
- A related problem is the growth of substandard medicines
- Although reliable data does not exist, experts agree that the amount of counterfeit and substandard medicines on the global market is increasing each year



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## **Globalization of the Pharmaceutical Industry**

- With the cost of innovation and the necessity to achieve economies of scale, the pharmaceutical industry is continuously re-organizing on a worldwide scale
- Over the past 20 years, there has been an increase in globalization for both innovative drugs and generic drugs
- Globalization in this sector has occurred with respect to both distribution of medicines in new markets as well as shifting of R&D and manufacturing to lower cost markets



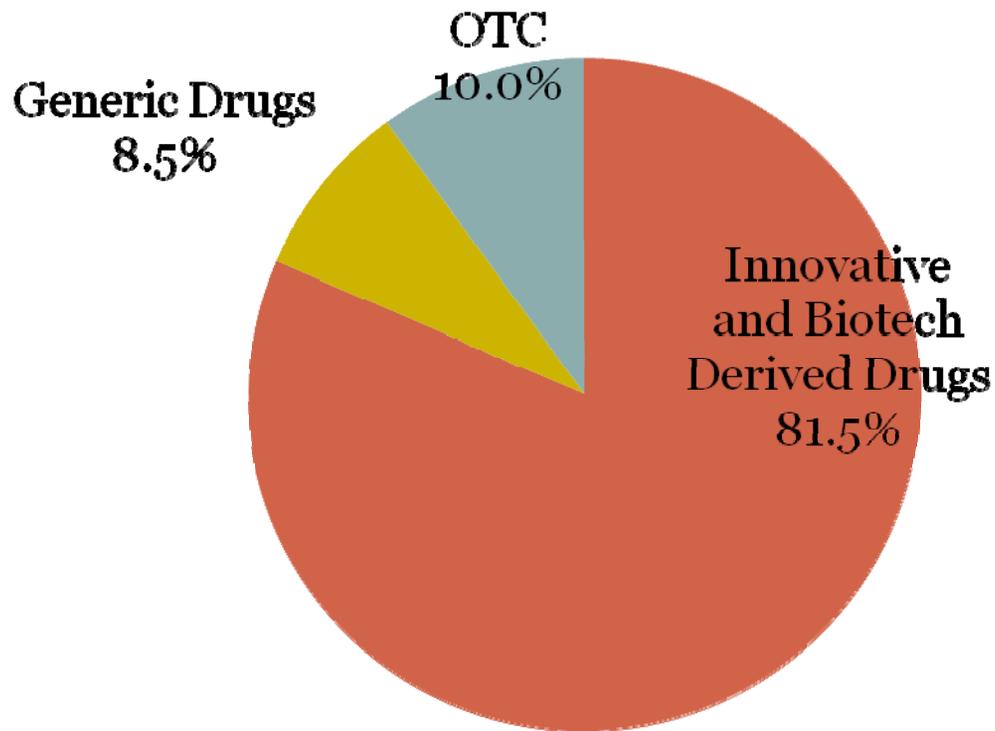
## **Globalization of the Pharmaceutical Industry Long Term Growth**

- 2010 estimate market - \$825 Billion (estimate)
- 2013 estimate market - \$975 Billion (estimate)
- Factors leading growth
  - world population growth
  - increasing elderly population
  - rising incidences of chronic diseases
  - higher disposable incomes
- Fastest growing global markets – China, India, Brazil, Turkey, Indonesia, Mexico, South Korea and Russia



# Globalization of the Pharmaceutical Industry (con't)

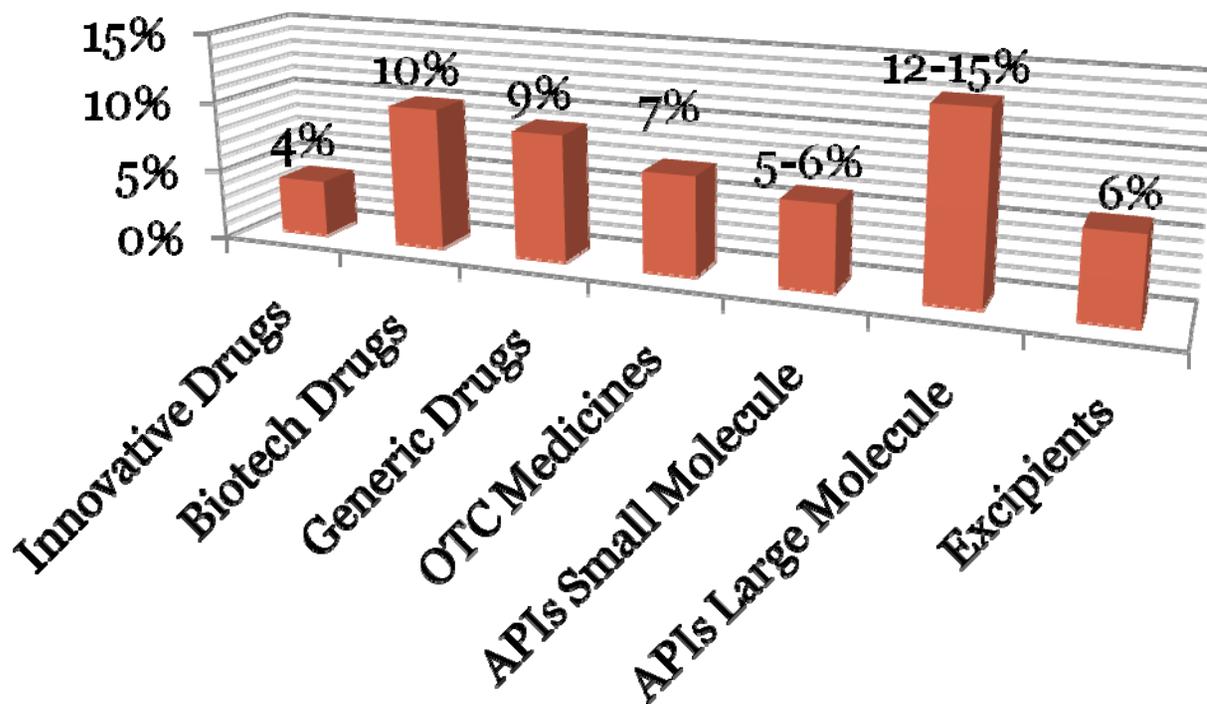
## Global Pharmaceutical Market



Source: IMS Health, BCC Research and Frost and Sullivan



## Globalization of the Pharmaceutical Industry Growth Rates



Source: IMS Health, BCC Research and Frost and Sullivan



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## **Globalization of the Pharmaceutical Industry Reasons for Declining Innovative Drug Growth**

- Decline in the number of new innovative drugs coming to the market
- Number of innovative drug applications submitted for FDA approval has declined from nearly 60 submissions in 1995 to low 205 in recent years
- Increased substitution rates from (generic drugs)
- Drugs coming off patent protection
- Increasing R&D costs
- Cost of litigation



## Globalization of the Pharmaceutical Industry: Top 10 Pharmaceutical Markets 2008

	Sales US\$BN	Market Share %
Pfizer (incl. Wyeth)	63.2	United States
GSK	43.0	United Kingdom
Sanofi-Aventis	38.7	France
Merck (incl. SP)	37.8	United States
Novartis	36.0	Switzerland
Astra-Zeneca	31.6	United Kingdom
Roche (incl. Genentech)	31.5	Switzerland
J&J	24.6	United States
Eli Lilly	19.3	United States
Bristol-Meyers Squibb	17.7	United States

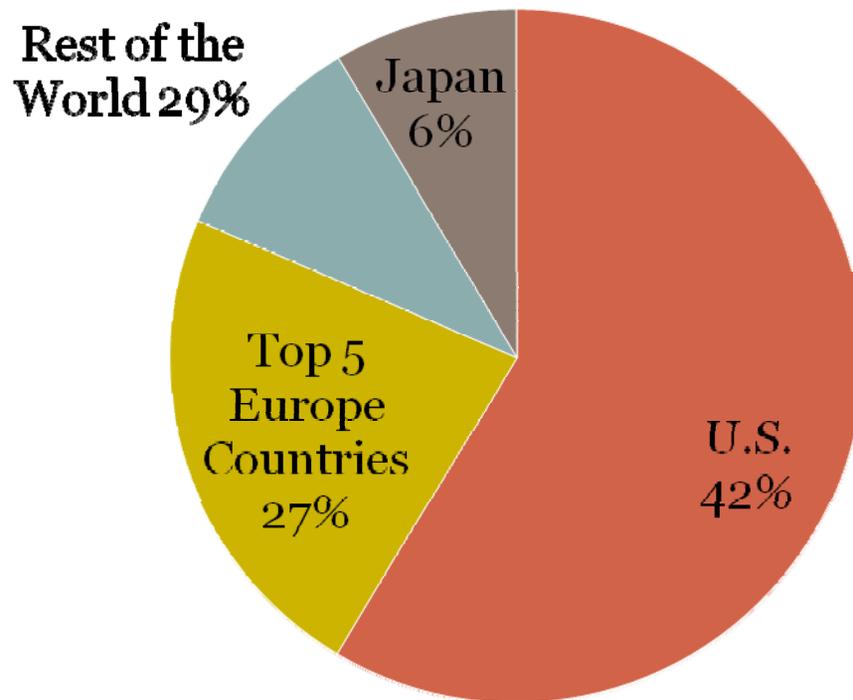
(Source: IMS 2008)



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## Global Generic Market

(Source: Global Generic Market Report 2009) BCC



Source: BCC Global Generic Market Report 2009



## Global Pharmaceutical Market Growth to 2012 (US\$ Constant)

<b>Mature Markets 2007-2012</b>	
USA	3-6%
Japan	1-4%
France	3-6%
Germany	3-6%
Italy	2-5%
UK	2-5%
Spain	5-8%
Canada	5-8%

Source: IMS Health Market Diagnosis



## Global Pharmaceutical Market Growth to 2012 (US\$ Constant)

<b>Emerging Markets 2007-2012</b>	
China	18-21%
Brazil	8-11%
Turkey	13-16%
Russia	16-19%
India	11-14%
Korea	8-11%
Mexico	6-9%



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# Globalization of the Pharmaceutical Industry Trends

- U.S. and Europe firms have long dominated the global pharmaceutical industry
- Largest generic manufacturing – India, China, Israel
- Pharmaceutical manufacturing continues to move out of U.S. and Europe
- Fastest growing pharmaceutical manufacturing centers – India, China, SE Asia, Korea, Brazil, Middle East, and Russia
- Large innovative pharmaceutical firms are diversifying in generic, biotech, vaccine, OTC etc.



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# Globalization of Pharmaceutical Industry

- Globalization is also leading to shift in R&D and manufacturing of both innovative and generic medicines
  - Innovative research is being conducted in countries like China and India
  - Research partnerships are developing between innovative companies in developed and developing countries; also between innovative and generic companies
  - Increased use of Contract Research Organizations (CROs) located in developing countries
  - API and finished dosage manufacturing are shifting to countries like China and India



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# Globalization of the Pharmaceutical Key Non-Tariff Barriers

- Cost contaminant – reimbursement and pricing issues in global markets (DOC 2004 Drug Pricing Study)
- IPR issues
  - Protection of confidential test data
  - Reliance on data
  - USTR identified 12 countries in need of IPR reform including China, India, Russia, Thailand, Indonesia,
- Growth in counterfeit and substandard medicines
- Lengthy regulatory review times and redundant regulatory testing



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# Globalization of the Pharmaceutical Key Non-Tariff Barrier (con't)

- National regulatory systems that are not harmonized with international best practices (ICH)
- Competition against “local” quality products
- Lack of supply chain distribution systems
- Tariff rates for medications in some countries



# Counterfeit and Substandard Medicines

- Factors leading to this increase in counterfeit and substandard medicines includes:
  - An increasing number of criminals, and sophistication of criminals producing counterfeit medicines
  - High profit level (profit levels for counterfeit medicines are significantly larger than for narcotics)
  - The internet provides an easy and lucrative marketing vehicle for counterfeiters to distribute counterfeit medicines
  - Lack of penalties and coordinated law enforcement and prosecution activities have created conditions for counterfeiting to grow

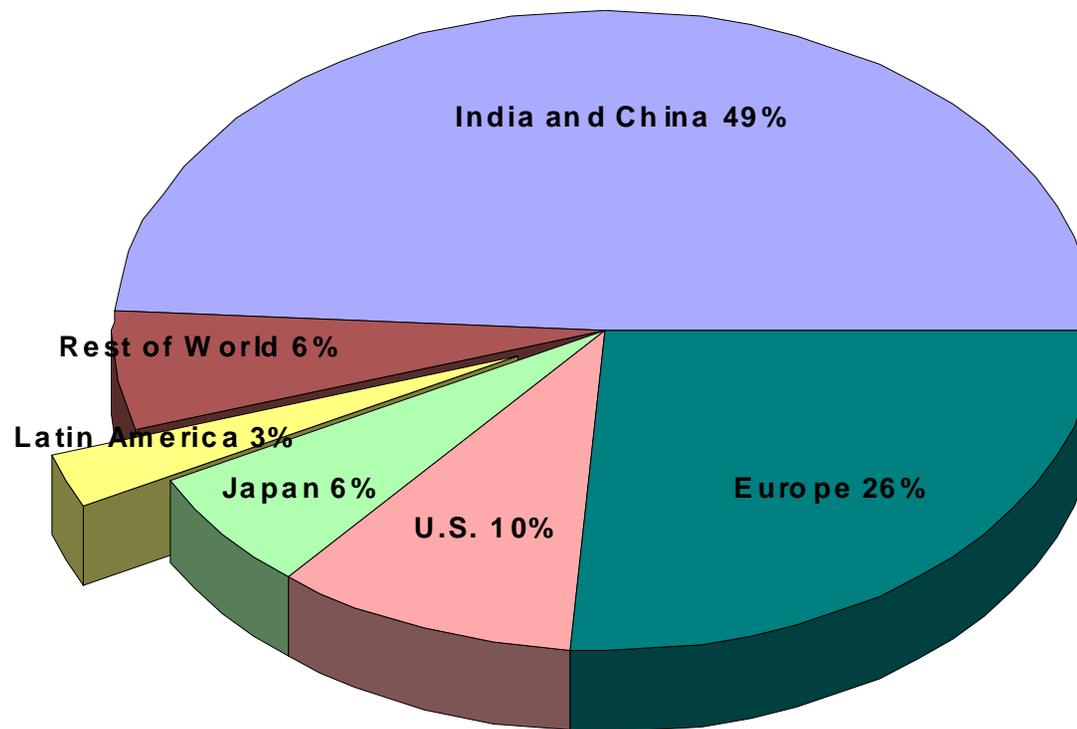


# Counterfeit and Substandard Medicines

- The globalization of the pharmaceutical industry has contributed to the ready supply of APIs to counterfeiters
- The globalization of the pharmaceutical industry has also contributed to the growth of substandard medicines, as manufacturing of APIs and finished dosage forms, shifts from developed to lesser developed countries
- Counterfeiting impacts all aspects of the pharmaceutical industry – – patented drugs, generic drugs, biotech drugs, and OTC medications



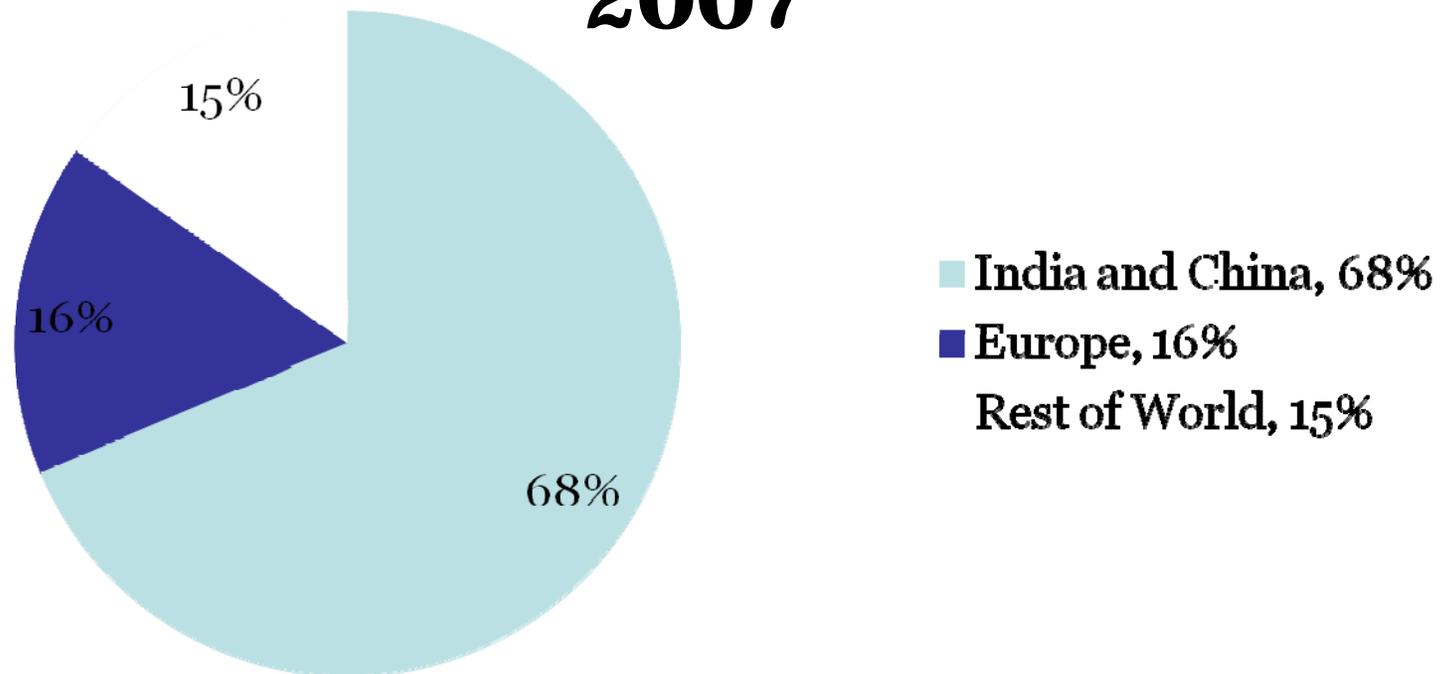
# Globalization of API Manufacturing 2004



**Total Global Number of API Manufacturers Sites approximately  
2,000**



# Globalization of API Manufacturing (con't) 2007



**Total Number of API Manufacturing Sites approximately 1,144**

\*Source: Newport Horizon Sourcing, October 2007



## **Counterfeit and Substandard Medicines**

- Global API production was estimated at \$78 billion in 2007
- Experts agree that China and India currently account for approximately 68% of the global production of APIs
- China and India are expected to account for 80% of global API production within the next 10 to 20 years
- Italy also major a producer of APIs, but expectations are that Italy's global percentage will decline



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# Counterfeit and Substandard Medicines

- Lack of vigilant oversight can lead to supply chain vulnerability
- Supply chain vulnerability, in turn can lead to the introduction of counterfeit and substandard drugs into legitimate distribution channels
- Contributed to providing a supply of APIs for counterfeiters
- Notably, there is a significant difference between counterfeit and substandard drugs
- WHO's website defines counterfeit drug as “a drug that is deliberately mislabeled with respect to identify and or source”



# Counterfeit Substandard Drugs

- Notably, there is a significant difference between counterfeit and substandard drugs
- WHO 's website defines counterfeit drug as “a drug that is deliberately mislabeled with respect to identify and or source”
- Counterfeit drugs are produced by criminals and meet the “fraudulent and the deliberate” aspects of the WHO definition of counterfeit medicines
- Substandard drugs are made by manufacturers, are registered, and do not meet established standards of safety, quality and efficacy
- Substandard drugs are not included in the WHO website definition of counterfeit drugs



# Counterfeit Substandard Drugs (con't)

- However, neither counterfeit or substandard medicines generally meet regulatory requirements such as cGMPs, bioequivalence, or pharmaceutical equivalence
- The public health impact of substandard and counterfeit medicines is the same since both can have correct APIs, wrong APIs, no APIs or less than effective APIs



# Counterfeit and Substandard Drugs (con't)

- In our view all counterfeit and substandard medicines have the potential to cause unnecessary harm to patients and are unsafe
- The substandard and counterfeit medicines problem varies significantly among countries and regions
- Countries and regions with weak regulatory oversight are more likely to have a significant amount of to substandard and counterfeit medicines on their market



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# Counterfeit vs. Substandard Drugs (con't)

- 10-20 years ago most counterfeit medicines had no APIs
- Now an increasing number of counterfeit medicines contain real APIs
- The most expensive drug is the one that does not work



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# Counterfeit and Substandard Medicines Challenges

- Need better statistics to measure global impact
- Lack of global regulatory harmonization system
- No common global definition of the term counterfeit medicine
- Limited budget and resources



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# Ongoing Initiatives and Possible Mitigating Activities

- WHO IMPACT initiative
- Partnership for Safe Medicines
- SafeMeds Alert System: [www.safemedicines.org](http://www.safemedicines.org)
- APEC Life Science Innovation Forum (LSIF)
- U.S. - China Pharmaceutical and Medical Devices JCCT Subgroup
- U.S. - India HTCG Biotechnology and Life Sciences Working Group



## Mitigating Activities

- Global cooperation among health regulators, customs, law enforcement and industry
- Establish a single point of contact (SPOC) within each APEC economy to facilitate the
- Develop a strong legal framework within APEC economies to combat counterfeit medical products and to arrest and prosecute counterfeiters
- Enhance medical training by conducting judges on the counterfeit medical products problem; Conduct training on laboratory detection of counterfeit medicines
- Organize a workshop on the regulations of APIs and the need for global cooperation to stop the availability of APIs to counterfeiters



## Mitigating Activities (con't)

- Continue global harmonization efforts, including training and harmonized standards (ICH and country or region specific activities)
- Global cooperation on plant inspections/audits
- Manufacturers need to be responsible for product quality; regulators need to enforce standards, and take action against poor performances
- Continue to focus on regional dialogues – APEC, ASEAN, PAHO, WHO, PANDRA, etc.
- Risk of doing nothing – prevalence of counterfeit medicines will continue



# Summary and Conclusions

- **Pharmaceutical industry has become globalized and complex in recent years**
- **Industry changes provide opportunities as well as challenges**
- **Challenges require a coordinated and global approach**



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# Thank You!

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