WHO Prequalification of medicines

Setting the Context
Advanced GMP Workshops
12-20 November 2018, India

Presentation outline

- Introduction
- Prequalification process
- Contribution
- WHO' recent initiatives
- Concluding messages

1. Introduction

PQTm: A United Nations Programme managed by WHO

- Started in March 2001 as a pilot project to facilitate access to quality medicines used in the treatment of HIV/AIDS.
- Partners included WHO, UNAIDS, UNICEF, UNFPA and supported by World Bank.
- Quickly expanded to include Tuberculosis, Malaria, Reproductive Health (2006), Influenza and others
- Current donors – mainly UNITAID and Bill and Melinda Gates Foundation.
- Fees were introduced on 1 Sept 2013 and reviewed in January 2017- aims to cover 50% of the PQT budget.

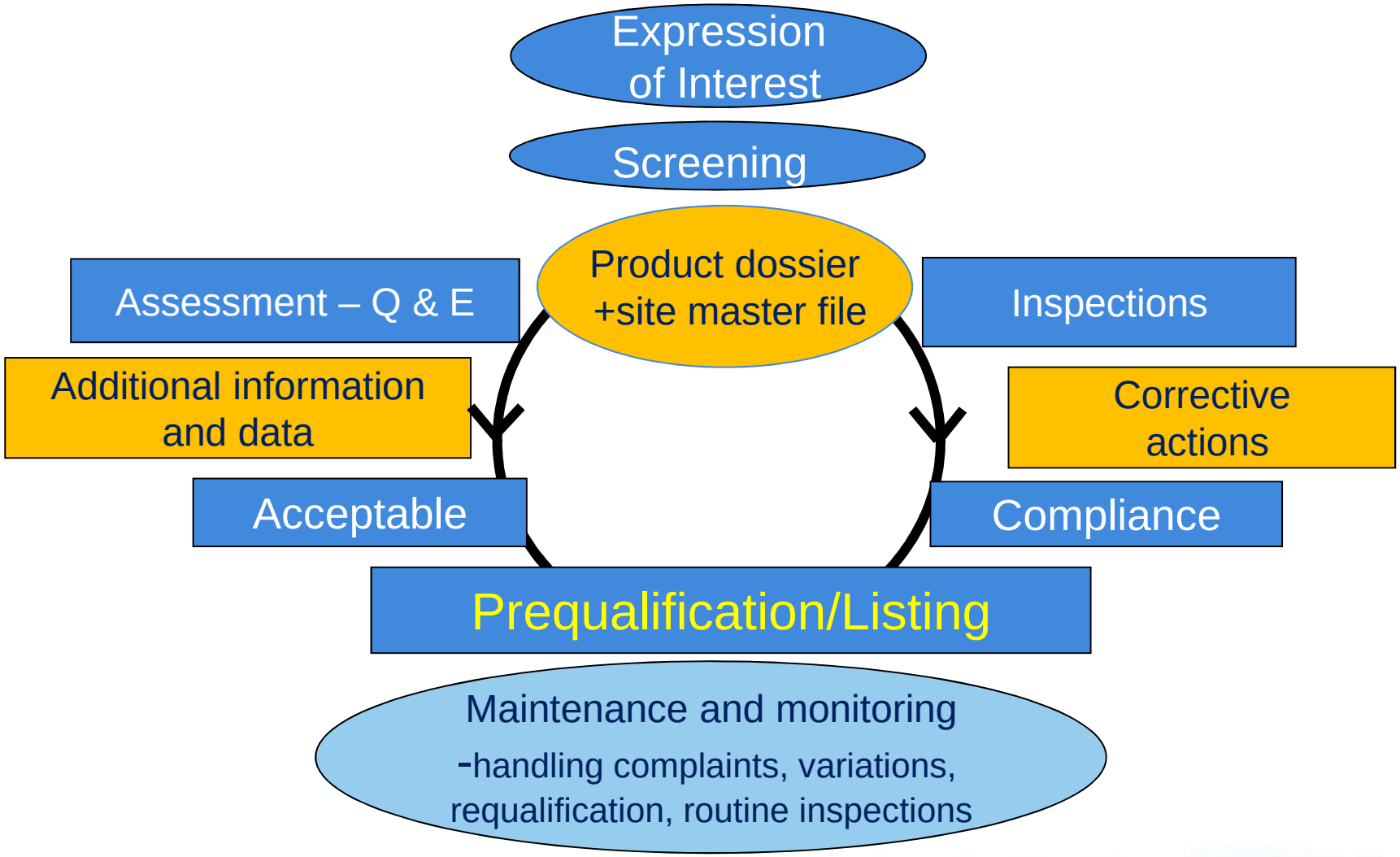
Why prequalify medicines?

- Increasing demand for generics, several players, substandard products on the market.
- Lack of well established drug regulatory systems (50% have varying capacity and level of development, 30% minimal or limited regulation).
- Lack of quality assured medicines can have serious consequences – ineffective treatment, drug resistance, side effects etc.
- Provide quality products for UN procurement, but also other partners (Global Fund, NGOs and country procurement).

Scope of prequalification

- Limited to priority medicines as published in Invitations for Expression of Interest (EOI) on PQT website
- 8 Therapeutic areas
  - ✓ **HIV/AIDS**
  - ✓ **Malaria**
  - ✓ **Tuberculosis**
  - ✓ **Reproductive Health**
  - ✓ **Influenza**
  - ✓ **Acute diarrhoea in children (zinc)**
  - ✓ **Neglected Tropical Diseases (NTDs)**
  - ✓ **Hepatitis B and C**
- Potential for other categories if there is the need

2. Prequalification of medicines process

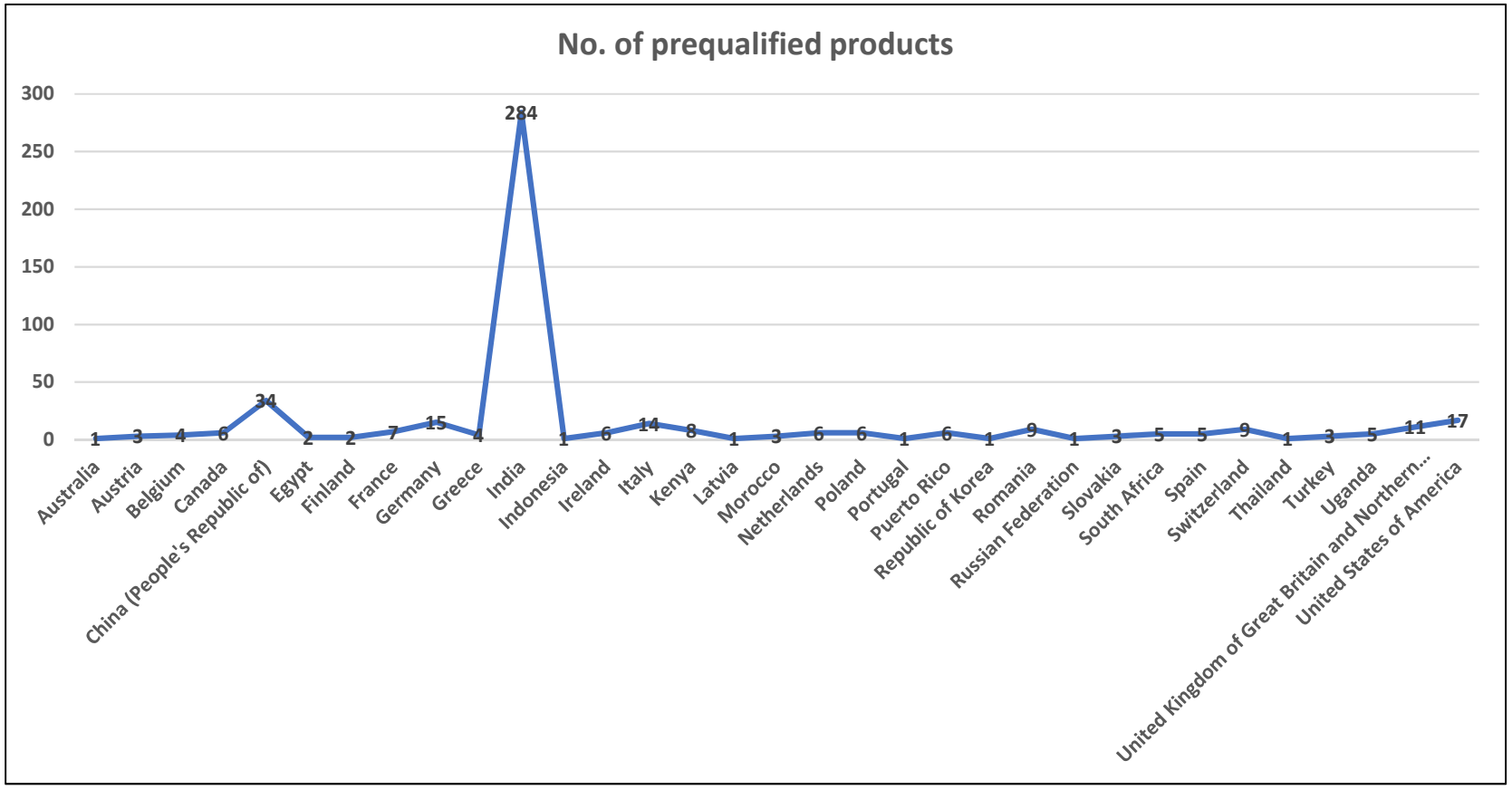


3. Contribution of Indian Pharmaceutical Manufacturers to WHO PQ-[1]

Indian manufacturers	APIs	FPPs
Currently on the PQ list	70 out of 123 **(57%)**	368 out of 533 **(69%)***
Under assessment	30 out of 44 (68%)	80 out of 125 (64%)

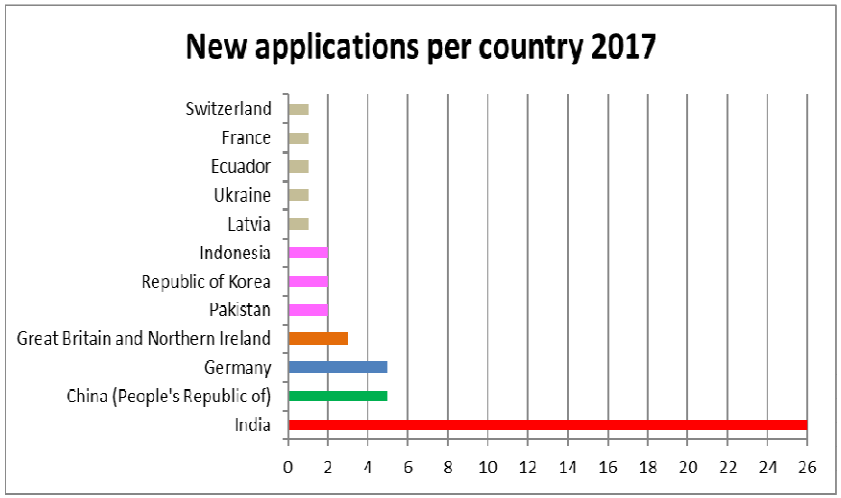
*includes those that are listed based on alternative listing route (the number for those prequalified by WHO (full or SRA route) is 270 out of 427= 63%)

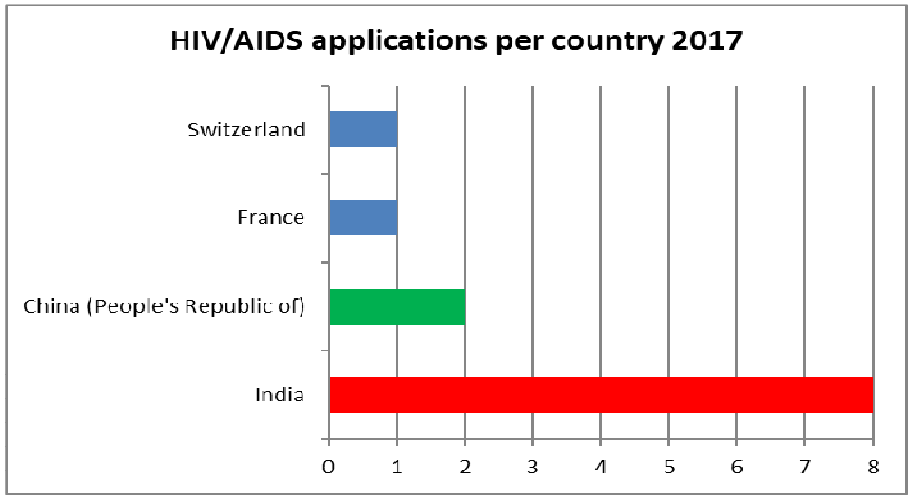
Contribution of Indian Pharmaceutical Manufacturers to WHO PQ-2

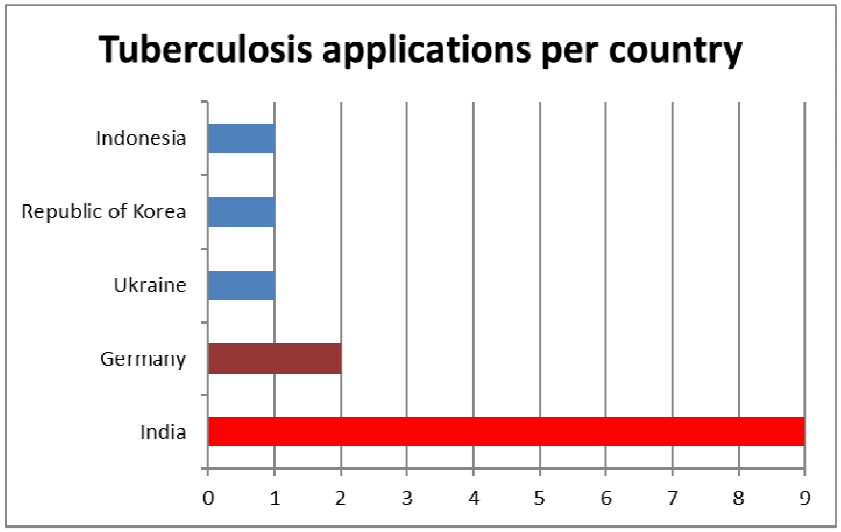


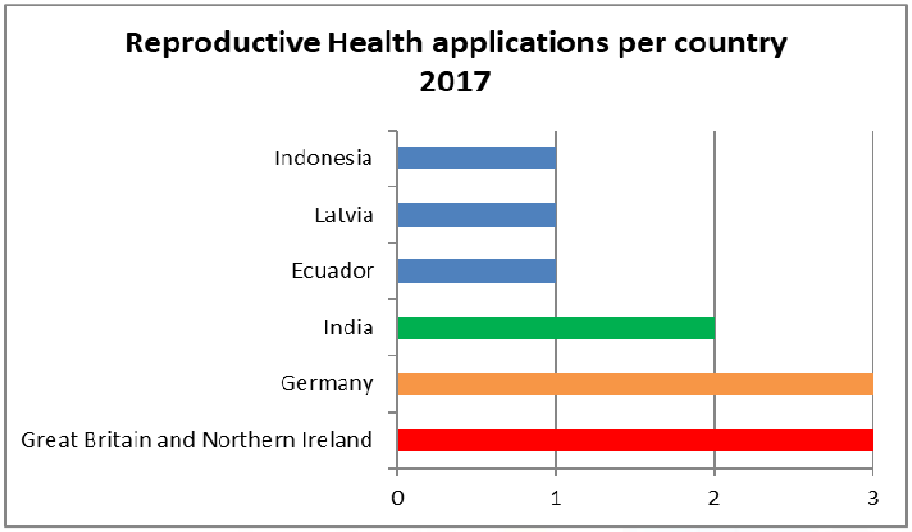
Note: total number 484 but actual number is higher because several products manufactured in more than one country

Contribution of Indian Pharmaceutical Manufacturers to WHO PQ-3









Contribution of Indian Pharmaceutical Manufacturers to WHO PQ-4

On 31 October 2018, WHO Prequalification Team - medicines (PQTm) added the below products to its "List of Prequalified Products".

Products added:

- **HA664** - Darunavir (as ethanolate) - 800mg - tablets - Cipla Ltd – INDIA – *This is the first 800mg darunavir tablet to be prequalified*
- **HA678** - Dolutegravir (as sodium) - 50mg - Tablets - Mylan Laboratories Ltd – INDIA
- **HA721** - Efavirenz/Lamivudine/Tenofovir Disoproxil Fumarate - 400mg/300mg/300mg - Tablets - Mylan Laboratories Ltd – INDIA – *This is the first efavirenz/lamivudine/tenofovir disoproxil fumarate 400mg/300mg/300mg tablet to be prequalified*
- **MA113** - Pyrimethamine/Sulfadoxine - 25mg/500mg - Tablets - Guilin Pharmaceutical Co Ltd – CHINA
- **MA132** - Amodiaquine Hydrochloride/Artesunate - 67.5mg/25mg - Tablets - Micro Labs Ltd – INDIA
- **MA133** - Amodiaquine Hydrochloride/Artesunate - 135mg/50mg - Tablets - Micro Labs Ltd – INDIA
- **MA134** - Amodiaquine Hydrochloride/Artesunate - 270mg/100mg - Tablets - Micro Labs Ltd – INDIA
- **RH074** - Medroxyprogesterone acetate - 150mg/ml - Suspension for injection - Mylan Laboratories Ltd – INDIA – *This is the first generic medroxyprogesterone injection to be prequalified*
- **TB289** - Moxifloxacin (as hydrochloride) - 400mg - Tablets - Zhejiang Hisun Pharmaceutical Co Ltd - CHINA
- **TB323** - Linezolid - 600mg - Film-coated tablets - Micro Labs Ltd – INDIA
- **TB349** - Moxifloxacin Hydrochloride (monohydrate) - 100mg - Dispersible tablet - Micro Labs Ltd – INDIA – *This is the first moxifloxacin 100mg dispersible tablet to be prequalified*

For the complete product list please see: https://extranet.who.int/prequal/content/prequalified-lists/medicines

For further information please visit the WHO Prequalification Team - Medicines website at https://extranet.who.int/prequal or contact PQT directly at prequal@who.int

WHO Prequalification Team (PQT)

World Health Organization
Geneva, Switzerland

4. WHO PQ & RSS contribution to Indian Manufactures and recent initiatives

11 **Technical assistance** have been offered to Indian Pharma since 2005

- GMP FPP – 5
- GMP API – 4
- Dossier – 1
- QCL – 1

Rotational inspectors and assessors

PQT-M Quality Workshop for Manufactures

- The first (pilot) Quality Workshop for manufacturers was held in July 2018.
- 60 participants from 30 companies. The feedback was very positive. Significant number of participants from India attended.
- Their questions and perspectives contributed to the value of the workshop for other participants (and also keep PQ assessors and inspectors on their toes!!)
- The 2nd workshop for manufactures is planned for 3, 4 and 5 July 2019. To be announced on the PQ website in the spring of 2019.

5. Conclusion - Key messages-1

- Before Prequalification (PQ), acceptability of the Indian products were questionable. Through the years interaction with PQ has led to an improvement in the quality, safety and efficacy of the products from India.
- PQ has been a learning opportunity for the Indian manufacturers to gain confidence in meeting SRAs requirements and launching to stringent markets
- Indian manufacturers started manufacturing fixed-dose combination (FDC) of ARVs. Together with PQ's innovative approach to accept the concept of FDC products, this has led to reduced pill burden and increased patient compliance.

5. Conclusion - Key messages-2

- More than 50% of prequalified APIs and nearly 70% of prequalified FPPs are from India.
- Nearly 90% antimalarials procured with funds from Global Fund are prequalified and produced in India,
- Model dossier (MD), another good example of collaborative work. The MD was developed by WHO PQ together with an Indian Pharma company,
- Also…Indian pharma has provided valuable input for the development of WHO norms and standards that take industry perspectives and needs sufficiently into account.

5. Conclusion - Key messages-3

In the spirit of continuous improvement, WHO PQ have been seeing some worrying trends:

- Manufacturers work hard to get PQ and then they relax, routine inspections reveal issues, an indication of poor maintenance culture,
- Different sites, different production lines and different standards for different markets e.g. regulated vs non-regulated or less regulated or rest of the world, double standard?
- Data integrity and falsification of data which has led to publication of notice of concerns, statement of non-compliance, warning letters, import alerts, complaints, recalls etc.

Thank you for your attention

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Acknowledgements

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