Prequalification Team – Medicines (PQT/MED)

Update

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PQT Medicines 2023

- ✓ Some updates/news
- ✓ Performance
- ✓ Issues/challenges
- ✓ Future direction, not least collaborations

So far in 2023…

- A number of “firsts” prequalified, for example products against Ebola Virus Disease, insulin analogues, bedaquiline, generic rifapentine, certain pediatric products…
- Face-to-face assessment sessions for more than a year now
- Continue to use virtual platforms frequently
  - Advisory/pre-submission meetings
  - Annual workshops for manufacturers (4-day quality workshop and biotherapeutics/biosimilar workshop, both in Sept)
- Updated invitations (EOIs)
- New EOIs
- Coordinated Scientific Advice (CSA) procedure
- Launch of a new pathway to increase insulin access
- Ever increasing number of variations due to increasing number of prequalified products and requalification applications – *still PQT/MED is meeting its timelines*

EOIs - updated or new since January 2023

- Ebola disease (25 May 2023) - *updated*
  - A combination of atoltivimab, 483.3 mg, maftivimab 483.3 mg, and odesivimab 483.3 mg per 14.5 mL (higher strength added)
- Reproductive health (19 October 2023) - *updated*
  - tranexamic acid 100 mg/ml – 5ml added
- Malaria (19 October 2023) - *updated*
  - Tafenoquine, 50 mg dispersible tablets; 150 mg tablets
- Treatment of multi-drug resistant bacterial infections (30 March 2023) – *new EOI*
  - Cefiderocol 1 g in vial (as sulfate toxylate) lyophilized powder
- Products for cessation of tobacco use (14 Aug 2023) – *new EOI*
  - Nicotine replacement therapy (chewing gum and transdermal patch)

PQT/MED: Scope

Priority medicines in 15 therapeutic areas:

- HIV/AIDS
- Tuberculosis
- Malaria
- Reproductive health
- Influenza
- Neglected Tropical Diseases
- Diarrhoeal disease
- Hepatitis B and C
- Infections in newborn and young infants and childhood pneumonia
- Insulins and insulin analogues (BTPs)
- Certain cancers (BTPs)
- COVID-19 (BTPs and small molecules)
- Ebola Virus Disease (BTPs)
- Treatment of multi-drug resistant bacterial infections **(2023)**
- Products for cessation of tobacco use **(2023)**

Type of products:

- ✓ Finished Pharmaceutical Products
- ✓ Active Pharmaceutical Ingredients
- ✓ Biotherapeutics, incl biosimilars

Pathways:

- ✓ Full assessment of generics/biotherapeutics, including those that may be facilitated by access to SRA/WLA assessment reports
- ✓ Abridged pathway for innovator or generic/biotherapeutics products approved by an SRA, or in future ML4 WLA

Expert Review Panel (ERP) for FPPs and BTPs

PQT Medicines guidances

PQT/MED develops *and* updates guidances on an ongoing basis:

- ✓ **Product specific guidance,** eg Zinc products, DMPA inj
- ✓ **Therapeutic area specific guidance**, eg RH products
- ✓ **Common/frequent deficiencies in quality, or in BE protocols**
- ✓ **Q&As**
- ✓ **Screening checklist**
- ✓ **Comparator products list**
- ✓ **BE design advice for invited medicines (NDBS)**

Note, PQT/MED will review your final draft BE protocols, before study start (*most reg authorities do not do that*)

Pre-submission meetings

- Pre-submission meetings are mandatory for applicants new to PQT/MED
  - Generally when the applicant has generated at least 1-2 months stability data on submission batches
  - Important to have early interaction to plan the pre-submission meeting, or to address specific questions
- Pre-submission meetings are encouraged for any applicant especially if unusual products/products with particular issues
- PQT/MED can provide advice at any stage before, or after submission - *PQ is accessible. You should use this opportunity*

https://extranet.who.int/prequal/medicines/pre-submission-meetings

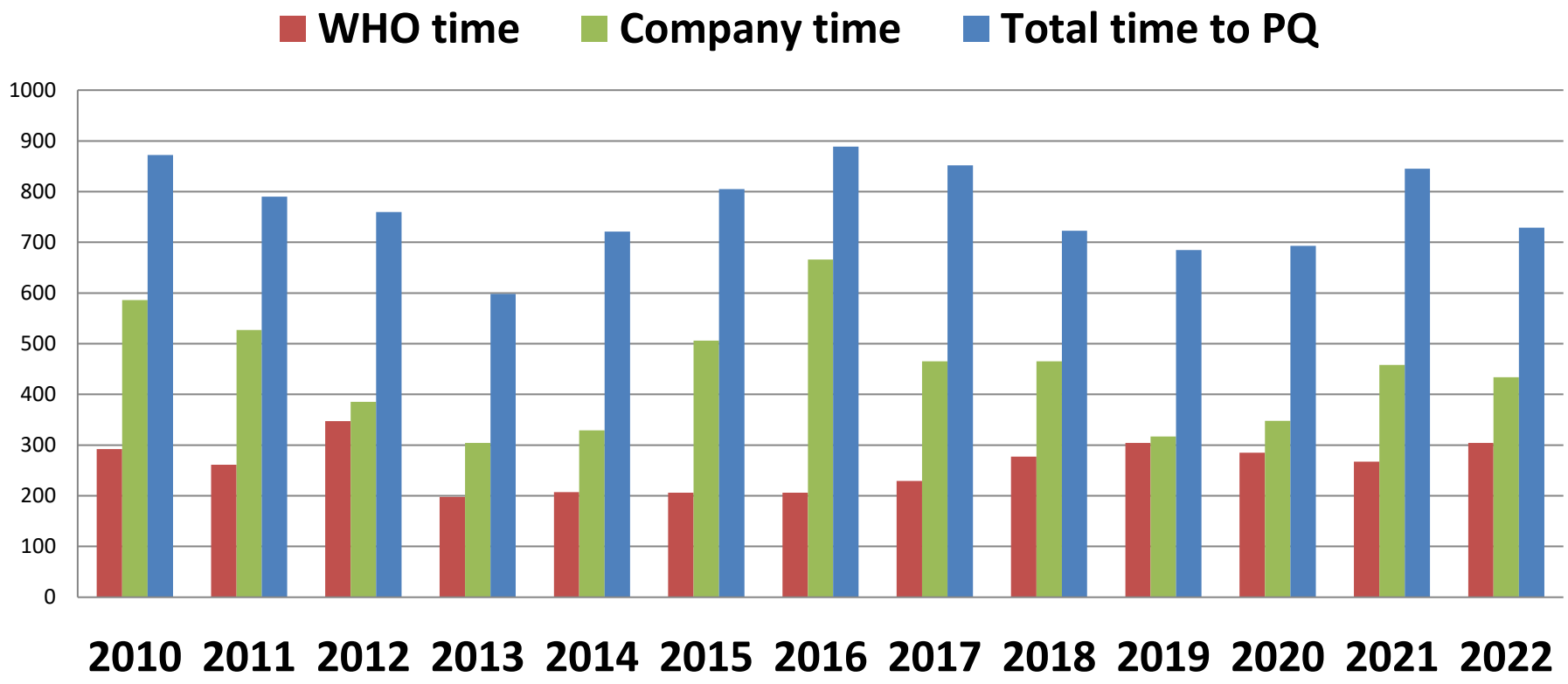
PQT/MED: Some of our key performance targets

- ✓ Screening: 80% of applications screened within 30 days (2022: 90%; 2023 Q1-Q2: 100%)
- ✓ WHO time to PQ for FPPs (Full) – less than 270 days for 50% of FPP (2022: 29%*, median time 304 days; 2023 Q1-Q2: 67%**)
- ✓ WHO time to PQ for FPPs (Abridged) – less than 100 days for 90% of FPPs (2022: 100%; 2023 Q1-Q2: 100%)
- ✓ WHO time to PQ for APIs – less than 270 days for 40% of APIs (2022: 38%; 2023 Q1-Q2: 50%)
- ✓ First action for variations to FPPs – completed for 80% within the timelines stated (2022: 83-100%)

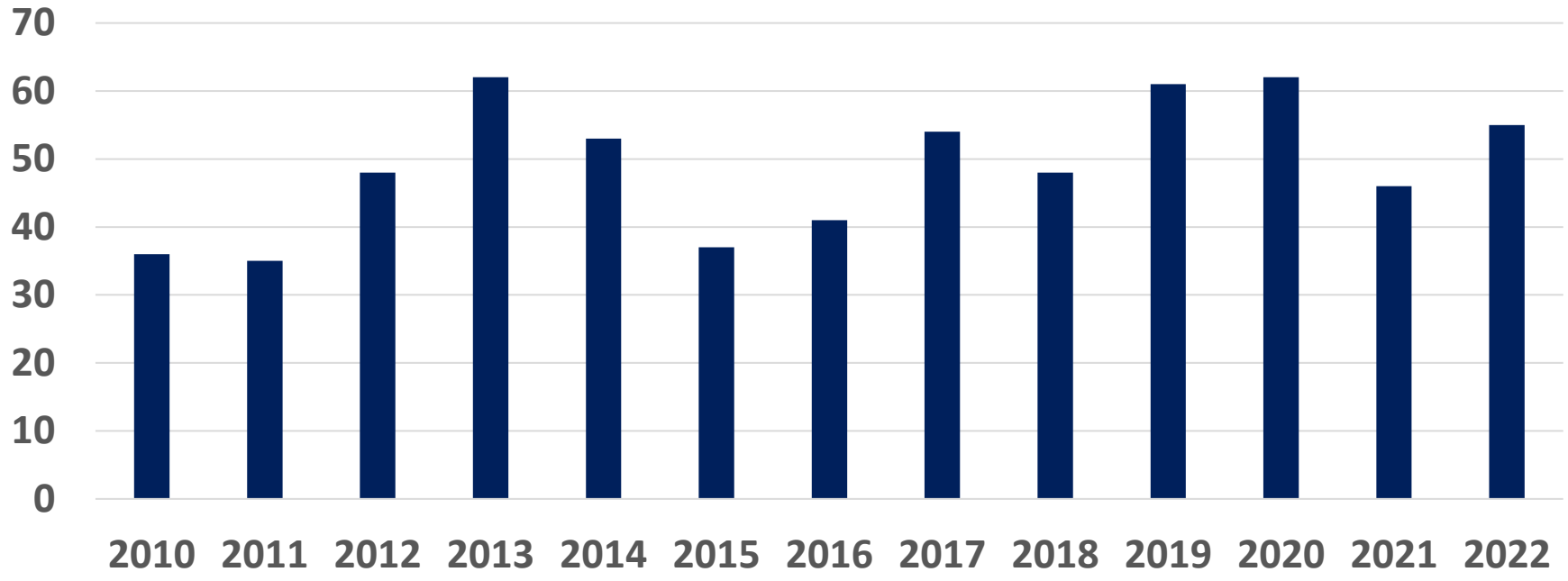
*competing COVID-19 submissions and increased number of assessment rounds due to incomplete manufacturer responses (possibly linked to COVID-19 restrictions since 2020)

** fewer products prequalified compared to previous semesters

Time (days) to prequalification of medicines (FPPs, median, full assessment) 2010-2022



Number of prequalified products (FPPs) per year since 2010



Prequalification of BTPs/SBPs

- Pilot project involving prequalification of trastuzumab/rituximab (16 products prequalified - 2019-2021) created a platform for prequalification of biotherapeutics in other therapeutic areas:
    - Therapeutics against COVID-19 (IL-6 inhibitors and neutralizing antibodies): 3 tocilizumab products prequalified in Feb 2022.
    - Therapeutics against Ebola Virus Disease: two products prequalified in Nov 2023
    - Human insulin and insulin analogues: 4 human insulin dossiers prequalified (2 fast-acting and 2 intermediate acting) and 2 insulin analogue (Insulin glargine) products prequalified in May 2023
    - The human insulin Master File procedure (h-IMF) is an innovative pathway announced on 28 Aug 2023 to facilitate access to h-insulin.
    - TB skin tests – medicines for diagnostic purpose. EOI yet to be established
- The pilot project also facilitated the development of an Expert Review Panel (ERP) mechanism for biosimilars - to aid procurement decisions

https://extranet.who.int/pqweb/medicines/pilot-prequalificationbiotherapeutic-products

New IT platform (ePQS)

- ePQS consists of four elements: ePQS Database (Salesforce); an external Portal; a linked Document Management system; an eCTD repository
- The ePQS database has been used internally for over a year.
- The DMS and eCTD repository are being finalized currently.
- New electronic WHO Prequalification System (ePQS) Portal to be launched in 2024

Nitrosamines – ongoing issue

- PQT/MED collaborates with other regulators, e.g., Nitrosamines International Strategic Group
- PQT/MED provides ongoing updates to stakeholders, eg when levels above the AI are found (currently rifampicin and rifapentine products)
- Latest update (September 2023):

https://extranet.who.int/prequal/news/update-n-nitrosamine-impurities

Challenges

- Additional workload due to emergencies and emerging issues (e.g., risk assessment for the presence of nitrosamines) – *both for manufacturers and PQT/MED*
- Some increase in WHO time due to COVID-19 submissions (competing for available assessment resources) + incomplete responses due to legacy of the pandemic.
- Inspection backlog post-pandemic needs to be cleared, therefore increase in onsite inspections + impact of GMP/GCP non-compliances?; delayed response submissions always a factor to consider

PQT/MED collaboration with WHO clinical departments

- Interaction with WHO treatment programmes (EOIs)
- The Coordinated Scientific Advice procedure (CSA) "*…voluntary…to provide advice to product developers on the generation of robust data for future evaluation towards a WHO policy recommendation and product prequalification, in areas of unmet public health needs*" (https://www.who.int/activities/optimizing-research-and-development-processes-for-accelerated-access-to-health-products/who-coordinated-scientific-advice-for-health-product-r-d)

  The CSA procedure applies to new products, or new/additional data on existing products
- "*Coordination between WHO Living Guidelines and WHO EUL and PQ processes for Therapeutics in the context of COVID-19*" https://extranet.who.int/pqweb/key-resources/documents/coordination-between-who-living-guidelines-and-who-eul-and-pq-processes

  ✓ Invitations for PQ (or EUL) can be issued before a recommendation for use, if data exist that may support a positive WHO recommendation. PQ (or EUL) assessment can then proceed in parallel with the analysis of the totality of the evidence.

  ✓ PQ (or EUL) will not be granted until a guideline recommendation has been made.

Some of our priorities for 2024 and beyond I

- ✓ Collaborate with WHO clinical departments to implement development of treatment recommendations in parallel with prequalification for promising products to promote faster access (as applied for COVID-19 therapeutics), maybe gaining 6-12 months or more.
- ✓ Engage with WHO clinical departments, procurers and partners to expand into new therapeutic areas as per set priorities – *additional expertise needed?*
- ✓ Continue to collaborate with WHO Science division and clinical departments in the WHO Coordinated Scientific Advice (CSA) Procedure for new priority products or new uses of existing products – *additional expertise needed? Collaboration with SRAs?*
- ✓ Expand the abridged procedure to allow prequalification of SRA/WLA approved products (EMA Art 58, Swissmedic's MAGHP and other access programmes) and facilitate their national registrations via CRP

Some of our priorities for 2024 and beyond II

- ✓ Collaborate with the AMA as they establish assessment procedures and practices
- ✓ Collaborate with USFDA to expand the CRP lite pilot
- ✓ Determine how PQT/MED can use the decision/outputs of new WLAs/tWLAs (ML3/ML4 NRAs) in its assessments – *how to ensure harmonized standards across products to reassure procurers and countries.*
- ✓ Implement a new approach to increase availability of quality-assured human insulin: human insulin master file procedure
- ✓ Expand the pipeline on the web to include additional details (as for COVID-19 therapeutics)
- ✓ Collaborations to promote local production
- ✓ Fully implement the new IT solutions (ePQS, incl eCTD)

Meeting PQT/MED?

- ✓ Coordinated Scientific Advice, early point of contact
- ✓ Advisory meetings anytime (before or after submission) https://extranet.who.int/prequal/medicines/technical-advice
- ✓ Pre-submission meetings
- ✓ Annual workshops for manufacturers, usually in Sept.
- ✓ During industry gatherings (e.g., CPHI, procurer organized meetings)
- ✓ *Any questions, e-mail me (stahlm@who.int)*

Thank you!

Collaborations

- Collaborations with WHO Science division and clinical departments (e.g., CSA; updates to EOIs or launching of new EOIs)
- Collaborations with NRAs and regional networks (CRP, participation in PQT assessments; trainings to regulators; joint assessments)
- Collaborations with SRAs (e.g. CRP-lite; EMA; EDQM)
- International collaborations (ICH working groups e.g., M13, Q1 revision; IPRP; NISG/NITWG; USP)
- Collaborations with procurers and related agencies (ERP, regulatory and QA advice to procurers; MPP)
- Industry bodies (IFPMA, IGBA)

Coordinated scientific advice (CSA)

- To provide advice to product developers regarding generation of robust data for future evaluation towards a WHO policy recommendation and product prequalification in areas of unmet public health needs.
- Applies to new products, or new/additional data on existing products
  - For medicines: for example, new chemical entities and new dosage forms/new combinations/new indications for existing molecules
- Advice on quality, non-clinical, clinical aspects
- So far seven CSA sessions completed for medicines. Two ongoing currently

PQT/MED Workshops for Manufacturers

- Two PQT Medicines workshops for manufacturers held in 2023
  - PQT Medicines 6th Annual Medicines Quality Workshop for Manufacturers - 25-28 September 2023
  - PQT Medicines 2nd Biotherapeutic Product (BTP) and Similar Biotherapeutic Product (SBP) Workshop for Manufacturers – 29 September 2023
- Similar workshops planned for 2024 (*dates to be announced on the web*)