API Assessment Update &

ePQS update

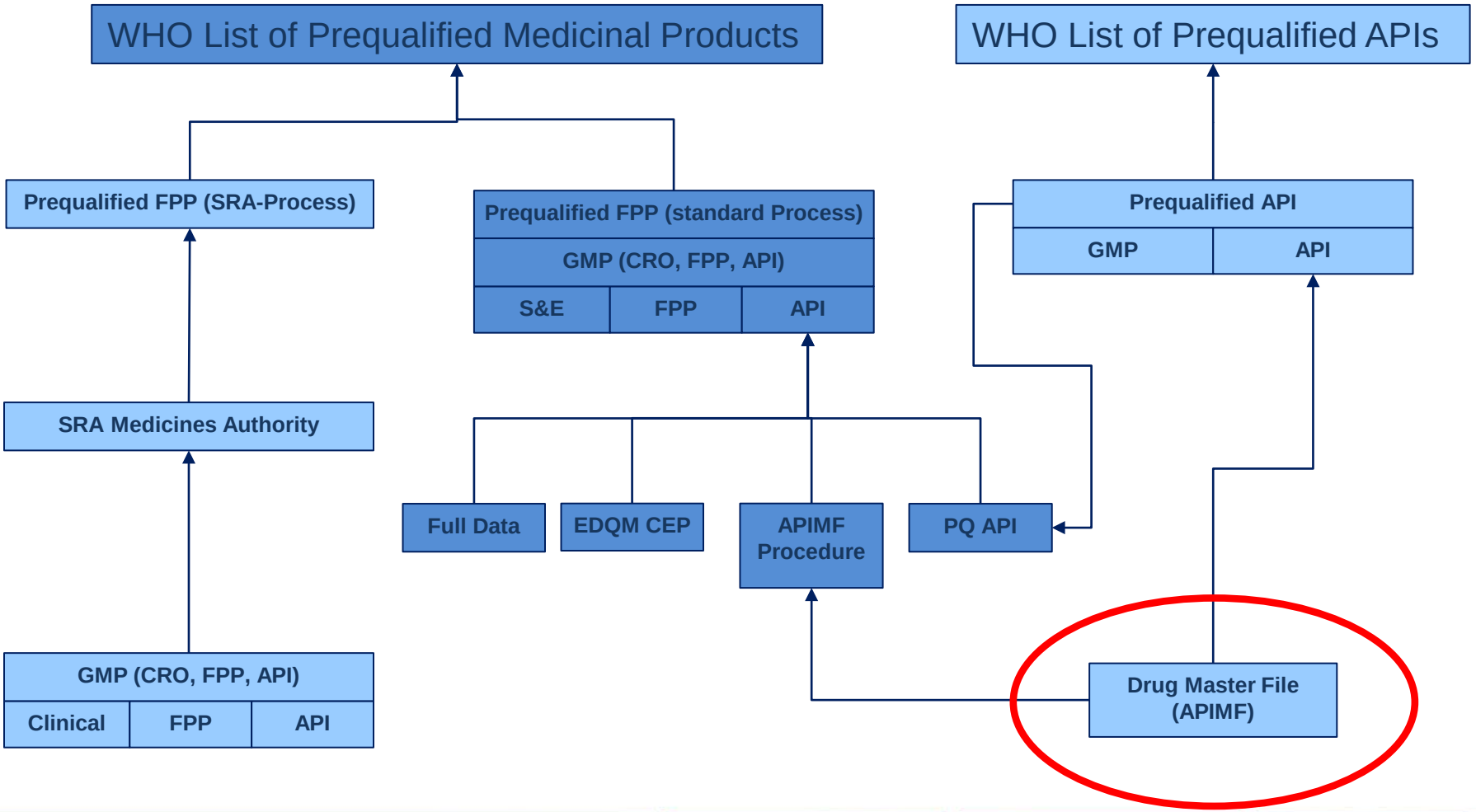
Antony Fake

API assessment within PQT Medicines

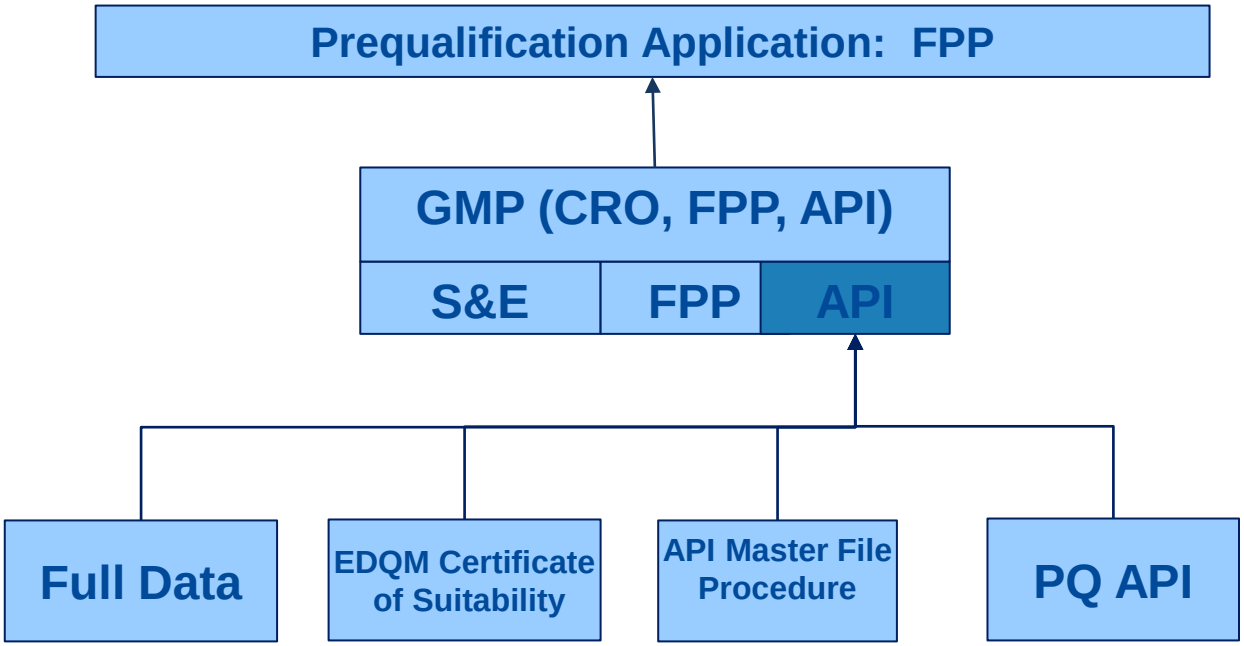
API manufacturers may be involved in two ways.

- Seeking prequalification of their own API.
- In support of a finished pharmaceutical product (FPP) seeking prequalification (4 options).

Prequalification of APIs



API Manufacturers supporting an FPP



Submission of an APIMF

There are 2 uses of APIMFs in PQ:

- APIMF Procedure
- API Prequalification Procedure

- **Both procedures may be used in support of an FPP application**, and both procedures make extensive use of APIMFs. But they are separate procedures.

- **The same APIMF can be used** as part of a submission for API prequalification and as part of a submission for APIMF procedure in support of a FPP application.

- Confidentiality of the API is preserved.

API assessment by the numbers

- 163 Prequalified APIs and 167 APIMFs accepted[1].
- 56 APIs under assessment for Prequalification and 18 APIMFs for the APIMF procedure only and dual use.
- 105 amendment applications received in 2023 to-date.
- 10 APIs PQd in 2023 to-date: median WHO time (~90 days), Manuf time (~220 days).
- This includes the first two prequalified nirmatrelvir APIs.
- 16 API PQ applications received to-date (including 3 for Covid 19)

1. APIMFs used in the APIMF Procedure only, or both API PQ and APIMF procedures

API assessment performance

- We are still receiving and assessing some Covid related applications, but increasingly resources are turning to non-covid applications.
- Clearing of the non-covid applications to improve pipeline performance is the current priority.

API assessment – What is new?

- Nitrosamine policy revision
- QSAR Analysis on impurities

Nitrosamine impurities

Medicines regulatory authorities collaborating under the Nitrosamines International Technical Working Group (NITWG), has published important guidance on nitrosamine impurity AI limits

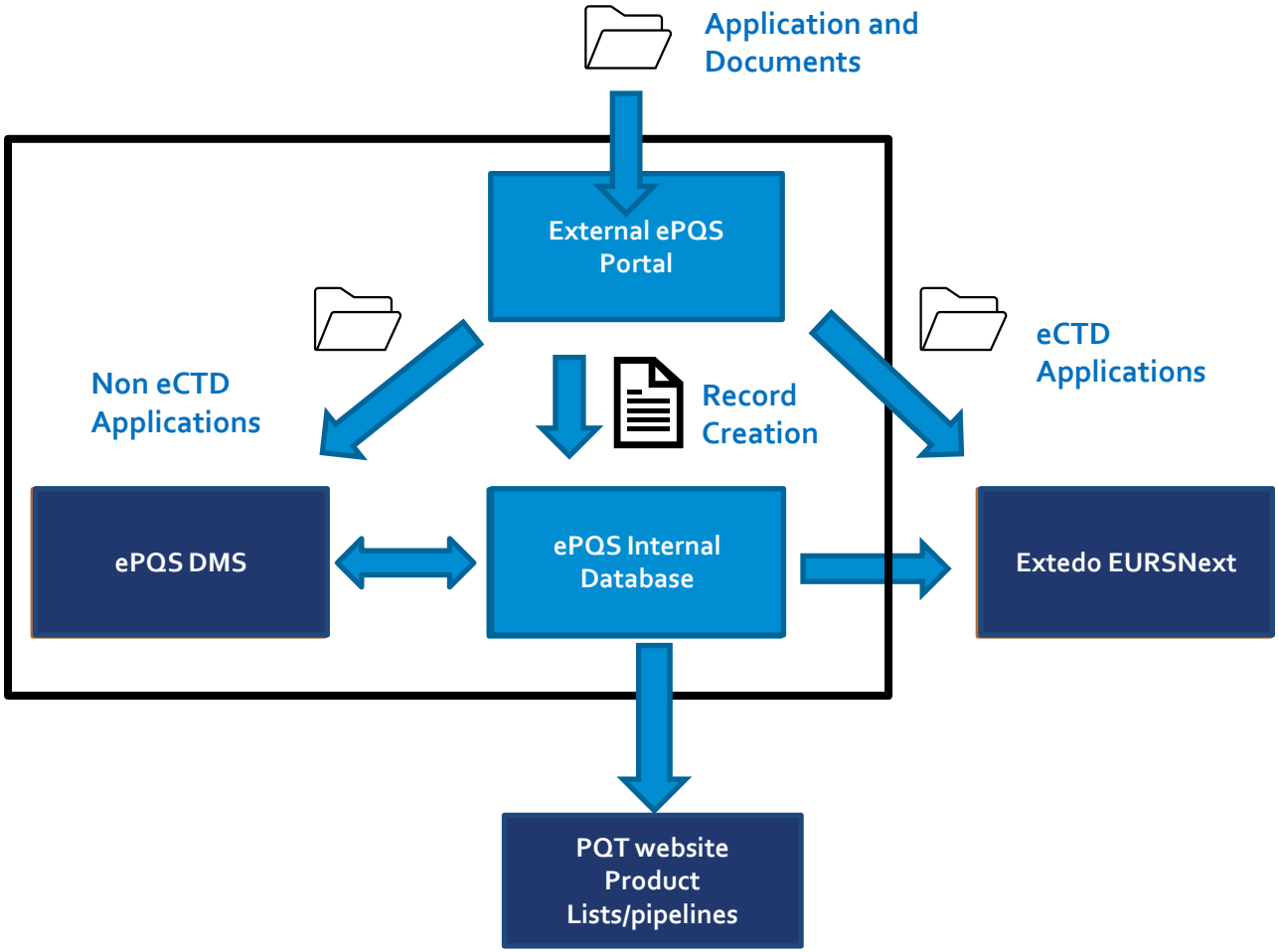
- The Categorization Approach (CPCA) for N-nitrosamines
- Enhanced Ames Test Conditions for N-nitrosamines if levels of a given nitrosamine in a product are found to be above a limit established based on the CPCA.
- These approaches may be used to propose AIs for newly identified N-nitrosamines or for the N-nitrosamines whose current AIs were established based on SAR analysis.
- The CPCA approach is not applicable for N-nitrosamines for which AIs have been established based on toxicological data such as NDMA and NDBA.
- Please refer to our latest update in https://extranet.who.int/prequal/news/update-n-nitrosamine-impurities

QSAR Analysis of impurities

- As per ICH M7 and the M7 Q&A document, there is an expectation that all impurities should be screened using QSAR analysis.
- Within PQT medicines API assessment, it is expected that a table summarizing the QSAR results and for all impurities will be provided in the APIMF.
- Specific QSAR reports and analysis is not expected by default in the APIMF for all impurities only for those that raise potential concerns from the QSAR analysis.

ePQS update

ePQS


Application and Documents
External ePQS Portal
Non eCTD Applications
Record Creation
eCTD Applications
ePQS DMS
ePQS Internal Database
Extedo EURSNext
PQT website Product Lists/pipelines

ePQS consists of several integrated packages

ePQS consists of several integrated software packages.

- A central Salesforce-based database
- An externally facing Salesforce-based community portal
- An integrated Document Management System
- And a related eCTD repository

Current Implementation status

All teams are now using ePQS. IMD migrated last week.

Web Publishing: API, FPP, QCL, VCAI, VCPs, WPEL PQ lists are now coming from ePQS (10 mins refresh). So too the FPP Pipeline page.

The DMS is being finalized and Document migration will follow

Document migration would be the last milestone after which all teams ~~to~~ will be working exclusively in ePQS.

Portal opening will then occur.

Opening of the ePQS Portal

Registration for Portal access will open early 2024

Please continue to check the new ePQS Portal page on the PQT website:
ePQS Portal | WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control)

Guidance information will continue to be added to this page.

Webinars and industry clinics are planned as the portal opens to assist manufacturers.

Contacts and Accounts are more important

- In the portal, access to records will be based upon the user's relationship to an Organization (Account).
    - *For instance, users belonging to Cipla Limited, will only be able to see Cipla Limited's records.*
- Not all contacts need to be external users. But, if they are, their Contact to Account relationship will determine record access.
- Some rationalization of Company contacts and the accounts they belong to is expected to occur as part of the registration process.
- Please check portal webpage for more information

eCTD

- For Vaccine and Medicine Manufactures there will be opportunity to submit in eCTD format.
- Necessarily this will follow the opening of the portal.
- A new eCTD webpage has been added to the PQT website:
  eCTD Portal | WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control)
- Guidance information will continue to be added to this page.
- The Module 1 requirements have been posted to this webpage.
- The first webinar has occurred, and further webinars and industry clinics are planned as eCTD is implemented.

eCTD Transition phases

- Phase 1 (2024): optional eCTD submissions.
- Phase 2 (+1 year): Mandatory for new product applications.
- Phase 3 (+2 years): Mandatory all applications in eCTD.