1- SESSION
Eudravigilance updates - Experience gathered following one year from the implementation of the new Requirements

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Eudravigilance update: practical experience of a big pharma with the implementation of EVWEB and EVDAS

Dr. Françoise Dumas Sillan
Vice President, Head Global QPPV office – Pfizer
agenda

• The Company description
• The requirements
• Impact analysis/Preparation
• The expected / unexpected challenges
• Last minutes surprises
• Back to Business as usual
$52 BILLION in revenue in 2017

62 MANUFACTURING sites worldwide

175 MARKETS in which Pfizer sells products

9 PRODUCTS with sales greater than $1 billion in 2016

140 NEW R&D COLLABORATIONS in 2016

96,000 COLLEAGUES around the world

As of February 1, 2017
Safety & Regulatory Contributions to Lifecycle Decision-Making

*Throughout the asset lifecycle….*
Regulatory Strategy, Benefit / Risk Assessment, Agency Interactions, Regulatory CMC, Submissions Management, Quality Control, Inspections, Policy & Intelligence.
Support across all platform modalities (small molecules, large molecules/biologics, vaccines, advanced modalities, and drug/device combinations)

**Discovery & Pre-clinical**
**Clinical Development**
**Reg / Launch**
**Post Approval**

**Pharmacovigilance / Safety (FIH through Post Approval/Authorization)**

**Registration / Post - Approval**
- Advertising / Promotion
- Artwork & Labeling
- Publishing & License support
- Rx to OTC switch
Pfizer Processes for Safety surveillance

- Pfizer’s current authorized product portfolio consists of more than 1000 unique substances worldwide
- More than 1 million ICSRs per year in the database
- Post-authorisation Product Surveillance includes:
  - Individual case assessment at case receipt
  - Periodic data review
    - Periodicity based on the known safety profile and the life cycle of the product (1 month, 6 months, quarterly, yearly, adhoc).
    - Periodic review of AEs and cumulative summaries of events (qualitative)
    - Automated Signal Detection (quantitative ~5000 SDRs*/yr)
    - Periodic Literature Review (>100,000/yr)
  - Periodic Adverse Event Product Complaint Review

* signals of disproportionate reporting
EudraVigilance centralized reporting and submissions

New and improved version of EudraVigilance launched 22-Nov-2017, applicable to post-marketing ICSRs from EEA countries (30)

- Implementation of EC Regulation No 726/2004
- Centralized submissions to EV in E2B R3 format
  - All serious and non serious EEA sourced
  - All serious ‘foreign’ sourced
- Central download of ICSRs from EVWEB portal by MAHs, NCA

EU GVP module IX update – 22-Feb-2018 pilot launched for signal monitoring

- Initial pilot only
- Subset of products (Additional Monitoring list as of November 2017)
Eudravigilance Upgrade
Transition Team

• Members from different groups
  – EU QPPV Office (Lead)
  – Drug Safety Units (DSU: European countries and global)
  – Business Management
  – Business Technology
  – Information Management
  – Safety regulatory & Quality – Inspection Management

• Sub teams
  – Business continuity/Roll back planning
  – Argus reporting rules
  – DSU resource analysis
  – Documentation

• Met biweekly
General challenges of EVWEB downloads

• High volume of downloads
  – Approximately 18,000 per month

• High volume of ‘invalid’ ICSRs
  – Downloads based on having at least one EEA EVMPD entry for product
  – Receive ICSRs from markets where company is not MAH
  – Approximately 11,600 (65%)
  – 8-12 FTE’s for initial triage (depending on volume/issues)
High Impact challenges (1)

- Occurred November 2017 (immediately after implementation)
- XMLs missing mandatory date tag (N.1.1)
- EMA solution slow to arrive
- Internal solution developed to populate with pseudo data to allow import into Argus
- Issue continued for a couple of days
High Impact challenges (2)

• Started on 27 December 2017
• 2 specific ICSRs created over 30,000 ICSRs requiring download
• EMA solution slow to arrive
• Internal solution developed
  – Identified duplicate ICSRs
  – Allowed manual rejection before import
  – Rejected approx 80%
• Issue continued for 10 days
Feedback from MAHs (Jan 2018)

• Prior to implementation of EV Access
  ➢ Stakeholder training & webinars: appreciated & helpful
  ➢ Documentation: appropriate & comprehensive
  ➢ Communication via EV EWG: largely adequate & effective

• Post-implementation of EV Access
  ➢ Issues identified by MAHs not resolved in a timely or complete manner
    • Technical
    • Operational
  ➢ Impact: Process failures, MAH resources & late reports
Lower Impact Challenges

• Companies resubmitting erroneously to Eudravigilance
  – ICSRs require review to check for presence of real new information
  – Some cases have over 100 FUs, database performance impacts
  – Impacts resources at triage and processing

• No narrative visible
  – Potential clinically important information missing
  – Follow up for cases with specific regulatory commitments

• Still exporting in R2 vs R3
  – Foetal cases appear invalid to EMA as age group foetal not exported in R2
  – Receive questions on quality checks, resources required to review
EVDAS PILOT GO LIVE

Getting into the pilot using eRMRs

- **22 Nov 17**
  - EV go-live

- **22 Feb 18**
  - Start of pilot

- **22 Mar 18**
  - Deadline for first monthly screening

- **22 May 18**
  - Deadline for first 3-monthly screening

- **31 Aug 18**
  - Deadline for first 6-monthly screening

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**Reference period for first monthly eRMR**

**Reference period for first 3-monthly eRMR**

**Reference period for first 6-monthly eRMR**

(fixed: 1 February – 31 July)
Preparation for Monitoring EVDAS
November 2017 and 22 Feb 2018

• Confirmed Access to EVDAS, Set up Accounts
• Identified Pfizer Products for Pilot Period from additional Monitoring List (~17); determined the frequency for which they will be reviewed (1mo, quarterly, 6 monthly)
• Update internal policies and procedures
• Update signal tracking log to identify signals detected in EV, as well as other minor changes to align with GVP module IX
• Internal Training for Safety Physicians and Scientists
General challenges of Monitoring EVDAS

• Multiple products for Pfizer on the additional monitoring list (17)
  – Manual download of eRMRs and LL monthly
  – Large volume of Drug Event Combinations (DECs) to review
  – Merging data with in-house safety database

• Only 5 users in EVDAS

• Needed to develop processes for:
  – guidance/criteria for reviewers to aid the selection of DECs for further review
  – Archival of eRMRs and LL
  – Documentation the review occurred
  – Requesting case reports if required and databasing
EVDAS Pilot signal management
Feedback from first months

• Metrics collected by MAHs, for the EMA quarterly:
  – % observations of disproportional reporting (ODRs) from EVDAS (eRMR) which result in a validated signal and result in a signal being reported as Emerging Safety Issues, stand-alone signals, variations or in PSURs

• So far no new confirmed and new signal identified

• Pilot prolonged beyond February 2019, report to EC on September
**New EudraVigilance Access Management Portal (IAM2)**

- **Implemented 26th July 2018**
  - aim of simplified access, exiting users to be migrated automatically
  - very little EMA feedback to those MAHs involved in pre-testing

- **Migration issues led to:**
  - industry-wide prolonged deactivation of user accounts
  - lack of EV access resulted in extensive backlogs
  - with both workload and ROW compliance issues for many MAHs
  - Pre and post-live guidance and communication not optimal
  - EMA Helpdesk responses very slow and many incomplete
  - Solutions founded within MAH network
  - several MAHs needed/received direct support from IAM2 Team
IAM2 Impact for Pfizer

- EU QP and Affiliates not linked to parent organisation
  - Users unable to request correct EVWEB access
  - Support from EMA was slow
  - Inability to download ICSRs for 5 days resulting in ‘backlog’
- Once re registration process followed no access issues for eRMR reports and line listings
- But no access to case narratives (L2B access)
  - Finally solved October
- Access OK for all virtual Affiliates except one
  - Legacy entity
  - Finally solved early November
CONCLUSION

- Huge and ambitious changes in one year
- EMA provided a lot of preparation support (meetings, trainings, communications)
- Impact on workload for MAH Pharmacovigilance
- MAHs preparation did not avoid bad surprises and unexpected challenges
- EMA has proposed solutions, situation is improving
- Wait for the next episodes post Brexit
Thank you for the attention