# Summary of the HMA/EMA Big Data Taskforce priority recommendations and plan for implementation

Session 1 - Implementation of the HMA-EMA Big Data Task Force priority recommendations

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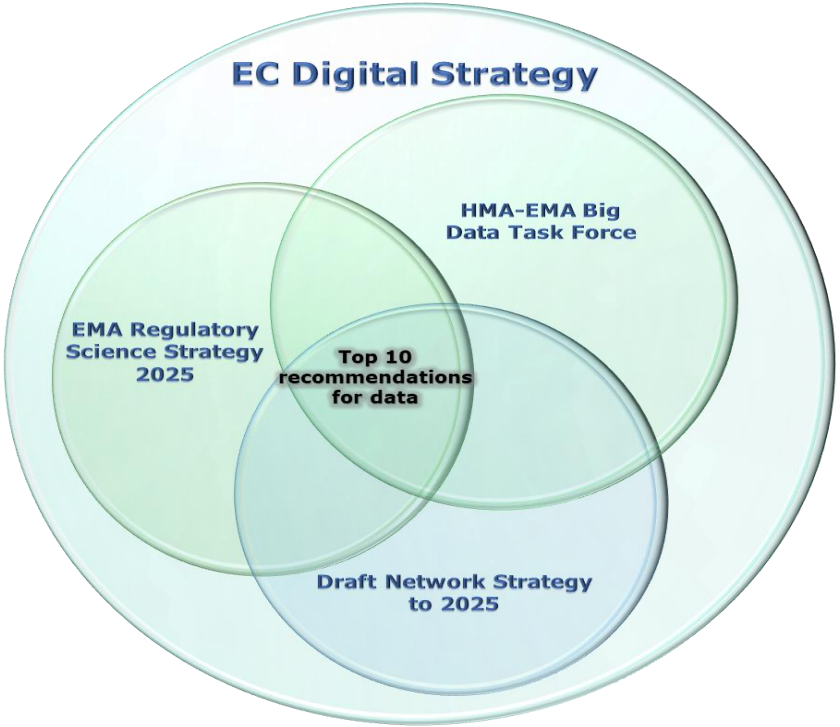
Co-chair of Big data steering group

# The timing is now

- Commission digital strategy: **"EU health data space"**
- Joint HMA EMA Big Data Task Force **Top-ten data recommendations**
- **EMA Regulatory Science Strategy to 2025**
- **EU Network Strategy to 2025** includes data and digital pillar
- EC **Pharma Strategy** and **Health Union**




Vision: innovate to turn data into decisions on medicines that create a healthier world

# Planning a world ……beyond COVID-19

March 2020 COVID-19 pandemic

Priorities:

- Maintain core business
- Rapid and robust opinions on COVID-19 vaccines and therapeutics
- Prepare for post COVID-19 transformation…..including data-driven regulation

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# Big Data: from Task Force to implementation

## Jan. 2020

'Ten recommendations to unlock the potential of big data for public health in the EU'

## Sep. 2020

Making best use of big data for public health: publication of the Big Data Steering Group workplan for 2020-21


1st Big data steering group meeting in May 2020

## May 2020

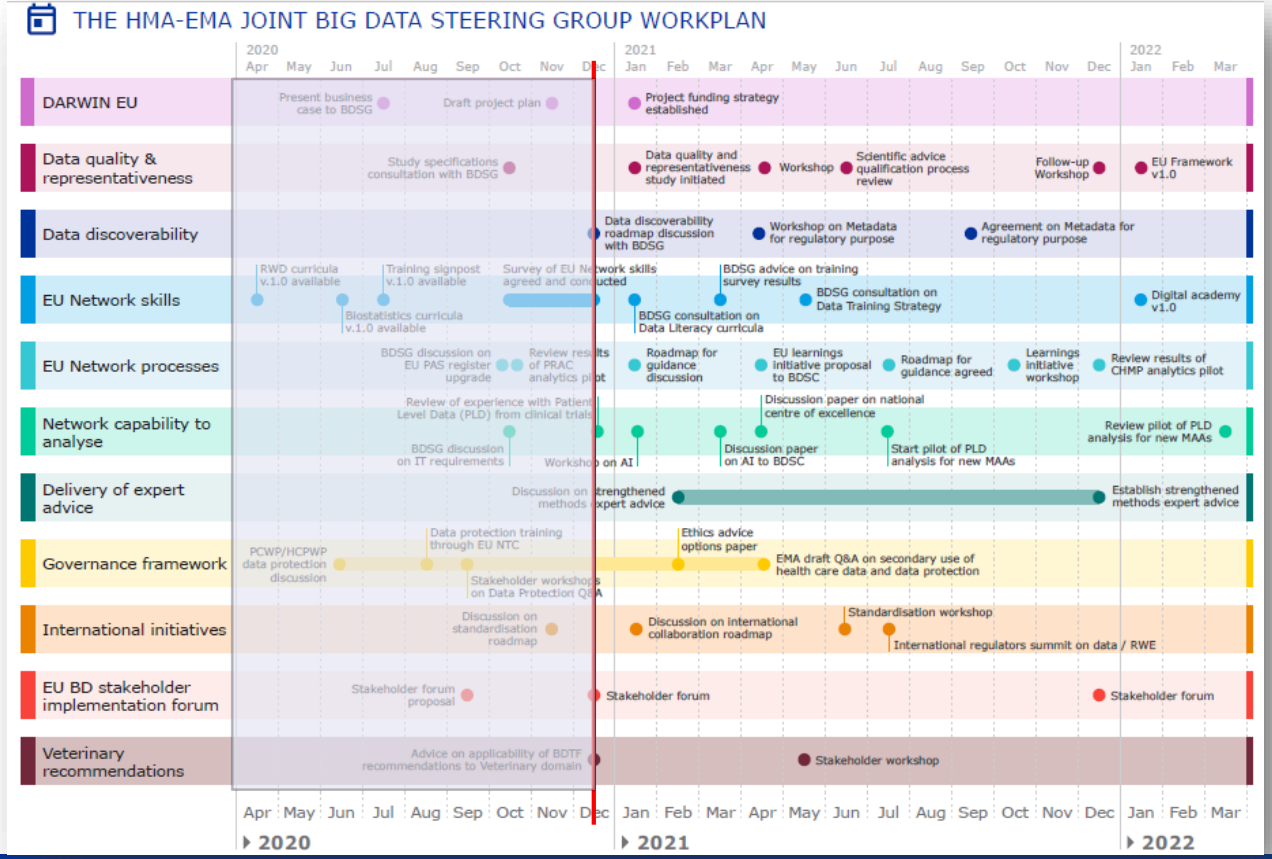
1st Big data stakeholder forum

## Dec. 2020

# Big Data Task Force Priority recommendations

| | |
|---|---|
| 1 | Deliver a sustainable platform to access and analyse healthcare data from across the EU (Data Analysis and Real World Interrogation Network: DARWIN EU) |
| 2 | Establish an EU framework for data quality and representativeness |
| 3 | Enable data discoverability |
| 4 | Develop EU Network skills in Big Data |
| 5 | Strengthen EU Network processes for Big Data submissions |
| 6 | Build EU Network capability to analyse Big Data (technology / analytics) |
| 7 | Modernise the delivery of expert advice |
| 8 | Ensure data are managed and analysed within a secure and ethical governance framework |
| 9 | Engage with international initiatives on Big Data |
| 10 | Establish an EU Big Data 'stakeholder implementation forum' |
| 11 | Veterinary recommendations |

# BDSG workplan:




On track with milestones and deliverables

[Making best use of big data for public health: publication of the Big Data Steering Group workplan for 2020-21]

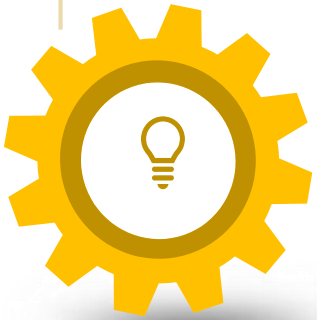
# Ho will the future look …

- **DARWIN EU network as part of the EU Health data space** will support better decision-making throughout the product lifecycle via its network of expertise/partnerships and databases.
- **RWE will be an established source of evidence** as a complement to clinical trials
- **Data will be discoverable and of known quality and representativeness** allowing choice of optimal data source, enabling regulators to expertly assess study results
- **EMA and EU Network will have knowledge and experience** in data science, methods and analytics to advise companies developing products and to expertly assess application dossiers.
- **Learning initiative will allow to continue to** learn and evolve to rapidly be able to answer new regulatory needs, including response to future health crisis.
- **Suite of EU and international guidelines and standards available** to help industry and regulators develop and supervise medicines (built on learnings from submissions of Big Data and enhanced study transparency (EU PAS Register)
- **Full compliance with data protection and ethics** of data sharing
- **Collaboration** with all stakeholders, will be key

# Priority Recommendation – 1 – DARWIN EU

## Why

- Current EU access to healthcare data limited
- Complex and slow analysis

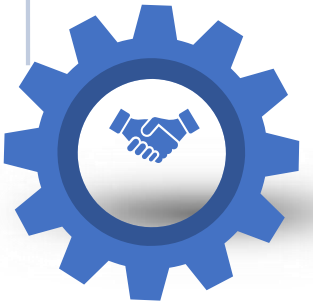


## How

- **Establish a network of data, expertise, and services to support better decision-making by EMA and NCA scientific committees (Data Analysis and Real World Interrogation Network (DARWIN EU))**

## Benefits

- Supports the development, authorisation and supervision of medicines

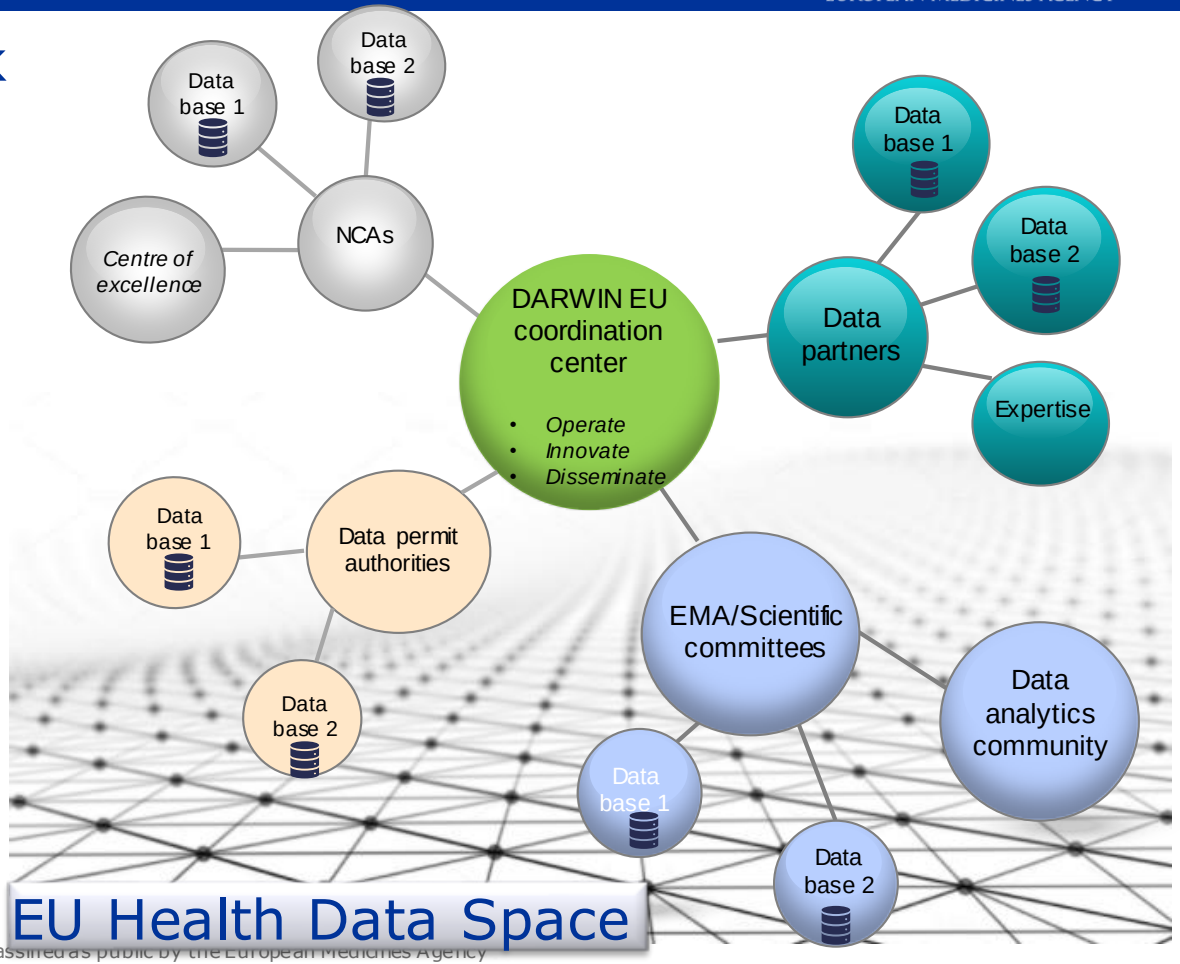


# DARWIN EU: deep dive

- Vision: Establish a network of data, expertise, and services to support better decision-making by EMA and NCA scientific committees on the benefits and risks of products via rapid access and analysis and increased reliability, validity and representativeness of EU health data

# The DARWIN EU network

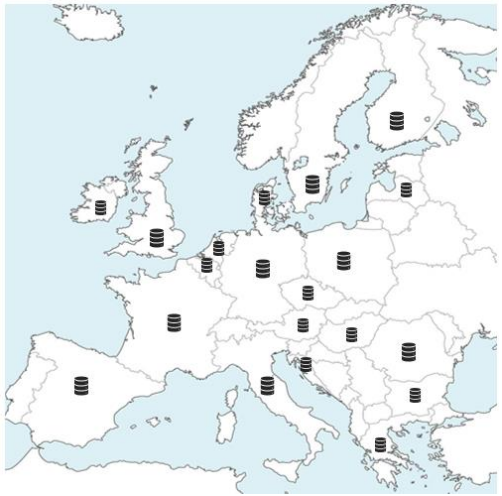
- Distributed data access for fast analysis
- Federated network - Data stays local, exchange anonymous data and queried remotely
- Hybrid approach:
  - Use of a common data model for fast analysis
  - Use a common protocol
  - Use of rapid analytics software
- 3rd party Coordination centre
  - data management / quality activities,
  - study analyses
- Will leverage the EU Health data Space initiative and fully integrated into EC Digital strategy.



# DARWIN EU as pathfinder initiative in EU Health Data Space: evolution

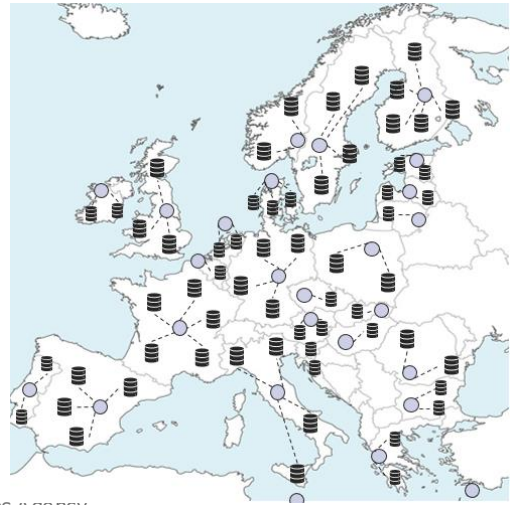
## DARWIN EU **2023**

- Coalition of existing datasets
- Federated access data analysis



## DARWIN EU **evolution**

- Node in the EHDS
- Includes Data Permit Authorities ( )



# DARWIN EU network operation: EMA/National Agency initiates an analysis

## EMA/NCA Committees

Question that impacts committee opinion

## EMA or NCA

Evaluates relevance and feasibility of RWD

Define the research questions

## Coordinating centre

Create protocol and programming code

Contact relevant DBs holders

Manage specific study governance

## Data holders (may include NCA/EMA)

Receive and run the code on their own DBs

Aggregate data and results sent to the coordinating centre

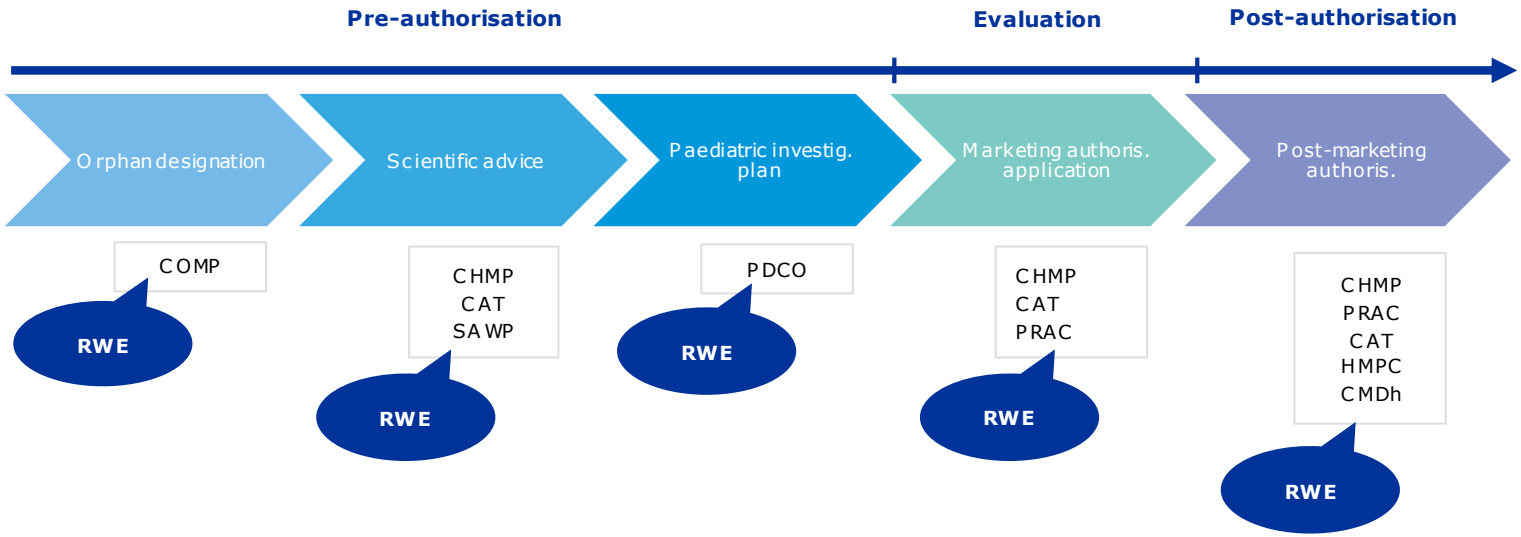
Receive, check, analyse aggregate data

Compile the results in a study report

Share aggregate data and reports with committees (and support integration/assessment)

Integrate data and reports in the assessment report

# Regulatory use cases through the life-cycle



# DARWIN EU benefits: bears fruit

- **Complements clinical trials**
- **Increase quality** of decision-making
- **Faster access** to safer, more effective and innovative medicines to patients
- Optimised **safe and effective use** on the market

- **Increase access** to data: GP, registry, claims and hospital data
- **Increase power, representativeness** and spectrum of **use cases** to support decision making
- **Rapid evidence generation**
- **Increased quality** of the evidence generated to a data quality framework tailored to EU data sources

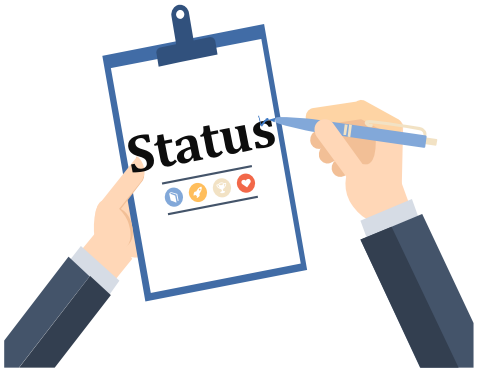
- **Enhanced support for industry through scientific advice and qualification procedures using RWE**
- DARWIN EU studies will replace studies done by companies when imposed, **reducing duplications** (e.g. generics, o questions affecting a class of products)

- Additional benefits as EU stakeholders participate:
  - European Commission – **delivers on European Health Data Space**
  - **National governments** supports health policy and delivery of healthcare
  - **HTA bodies and payers** supports decisions on cost-effectiveness
  - **EU health agencies** – e.g. health crisis preparation and response
  - Opportunities for **international collaboration**

# DARWIN EU: Status

## Achievements 2020

- Project initiated
- Funding identified including revised EMA fees regulation
- Preliminary delivery model established
- Support Commission to plan pilot with EU Health Data space




## Looking forward to 2021

- Develop network skills and processes
- Initiate coordinating centre service establishment
- Governance: DARWIN Network Coordination Group established
- Pilot with EU Health Data space initiated

# Priority Recommendation – 2 – Data quality

## Why

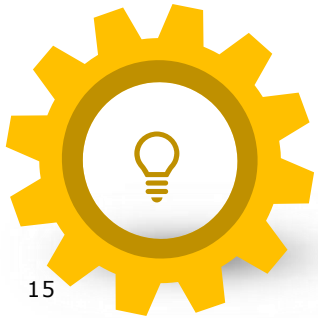
- Limited information on quality of data sources and their representativeness
- Need to identify appropriate real-world data sources

## How

- **Establish an EU framework for data quality and representativeness**
- Develop guidelines and **a strengthened process for data qualification through scientific advice**
- Promote across Member States the uptake of electronic health records, registries, genomics data, and secure data availability

## Benefits

- Recommend best data source to generate evidence for marketing authorisation through scientific advice
- Judge evidentiary value of the results when assessing marketing authorisation applications
- Help NCAs to know their national data including its quality and relevance to regulation by strengthening links to national healthcare data sets



# Developing a Data Quality framework – steps


A comprehensive review of existing data quality framework initiatives

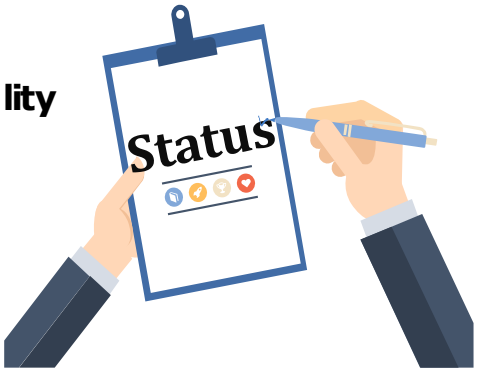
Stakeholder engagement and consultations and workshops in workplan 2021

Draft of the Data Quality Framework 2022

# Data quality and representativeness: status

## Achievements 2020

- Project initiated
- Scope defined for a **data quality framework**




## Looking forward to 2021

- **Workshop and consultation** on a data quality framework
- **Scientific advice qualification process review** planned

# Priority Recommendation – 3 – Data discoverability

## Why

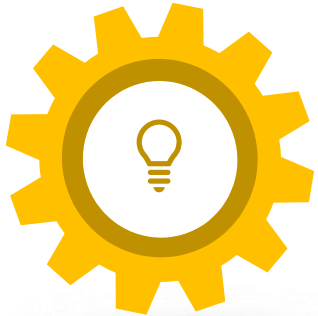
- Lack of knowledge of data in the MSs
- Lack of knowledge on characteristics of such data

## How

- **Enable data discoverability** via an external study to **agree key (meta) data that describe a data source**;
- Include key (meta) data in an **enhanced EU resources database** as a sign-posting tool for the most appropriate data,
- Promote the **use of the FAIR principles** (Findable, Accessible, Interoperable and Reusable)

## Benefits

- MSs, industry, and academia will have a more comprehensive knowledge of data sources available.
- Supports better drug development and choice of data source for post-authorisation studies.



# Data discoverability - metadata

- Metadata are descriptive data that characterise other data to create a clearer understanding of their meaning and to achieve greater reliability and quality of information*

*American Health Information Management Association (AHIMA). 2012, Chicago, IL: AHIMA Press.

# Data discoverability – External studies

**Phase 1: 1-year study (2021)**

- Definition of metadata
- Definition of criteria to include a data source in the EU Resource database
- PoC for the collection of metadata

VS

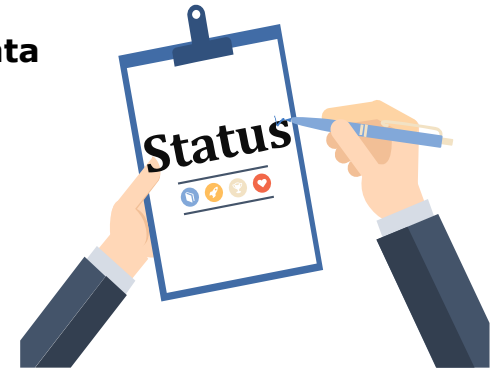
**Phase 2: 4-year study (2021-2025)**

- Identification all relevant data sources
- Collection of metadata from all eligible data sources

# Data discoverability: Status

## Achievements 2020

- Project initiated
- Scope defined for a **Meta data study and collection POC**




## Looking forward to 2021

- Initiate project to develop **EU Resources database**
- External Meta data study completed
- Stakeholder workshop on Metadata for regulatory purposes
- **Good practice guide**, e.g. Recommendations on the use of metadata

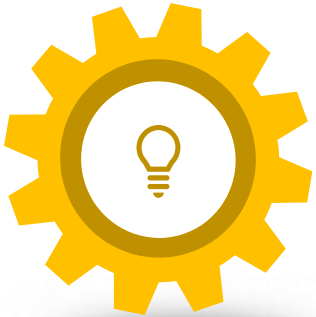
# Priority Recommendation – 4 – EU Network skills

## Why

- Currently limited skills and knowledge in the EU Network in key Big Data areas, including: statistics, epidemiology, data science, 'omics, advanced analytics / AI / ML.

## How

- **Develop big data training curriculum and strategy** based on a skill analysis across the Network, roll-out training, targeted recruitment, collaboration with academia.



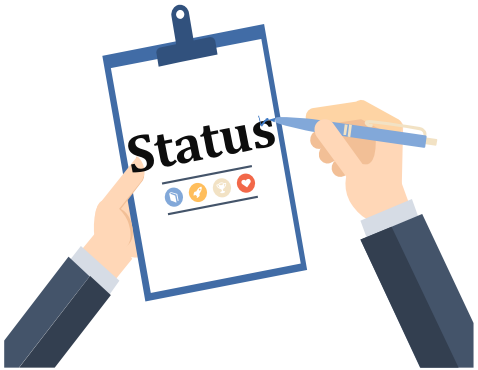
## Benefits

- EU Network assessors have the knowledge and experience to advise on Big Data sources, to conduct analyses in house, to support assessment of MA applications,
- Enable the EU Network as a reference for data-driven regulation.

# Status

## Achievements 2020

- **Big Data Training Sign Post**
- Epidemiology curriculum
- Biostats curriculum
- Planning for data science and academy



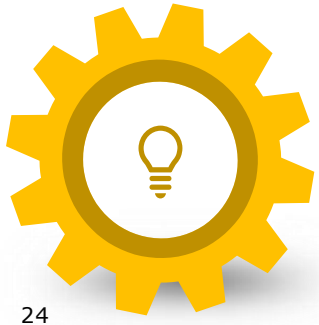

## Looking forward to 2021

- Training curricula published
- at least **one module delivered per curricula** (stats, epidemiology, data science)

# Priority Recommendation – 5 – Regulatory processes

## Why

- Currently we have limited experience of scientific advice and of MA application assessments that include Big Data.
- We do not systematically track and learn from the applications we do have.



## How

- **Strengthen EU Network processes for Big Data submissions**
- Launch Network "**Big Data Learnings Initiative**" - track and learn from relevant Big Data applications through the product life-cycle and feed learnings to reflection papers and guidance.
- Enhance transparency of Big Data study methods through the **EU Post-Authorisation Studies Register**.

## Benefits

- Forms the foundation of guidance for the industry.
- Each submission received and study posted in the register feeds the knowledge of the EU Network and its assessors.

# PRAC real-world evidence pilot initiated

- Pilot on Rapid Data Analysis supporting PRAC procedures started in November 2019
- Several requests and analyses performed relating to:
  - Drug utilisation: use in pregnancy
  - Occurrence of certain events after exposure
  - Drug utilisation: off-label use

➢ Recent signal of psychiatric events with exposure to hydroxychloroquine (HCQ)/ chloroquine (CQ) supported by rapid data analyses

# CHMP review of RWE 2018 and 2019

- Review of RWE/RWD submitted in MAAs and type II variations/line extensions, 2018 and 2019
- Started in August 2020

| Number of products included: **311** | Outcome of application: | Scientific advice: | Orphans: |
|---|---|---|---|
| • 158 new MAA<br>• 153 type II variations/line extension for change of indication or new indication | • 211: positive opinion<br>• 2: negative opinion<br>• 29: withdrawn application<br>• 62: still under evaluation | 289 products (93%) with previous SA | • 70 products (22.5%) |

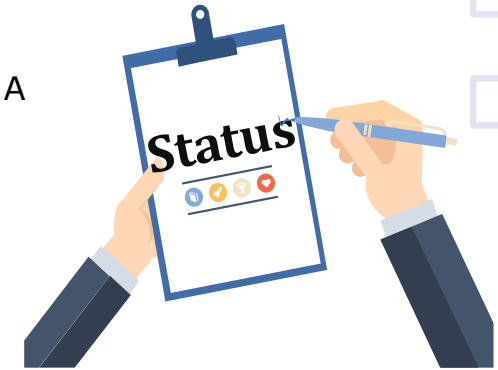
# Next steps: **Prospective 'learnings initiative'**

- Informed by retrospective study
- Topic of stakeholder workshop in 2021
- Ensure we capture and learn from relevant applications to the EU regulators

# Status

## Achievements 2020

- **PRAC RWE pilot initiated**
- **CHMP review of RWE submissions initiated** in MA applications 2018-2019



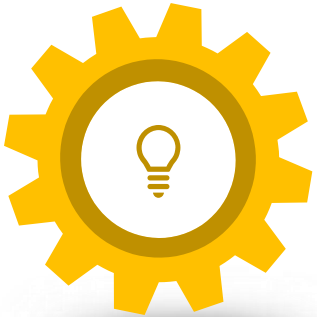

## Looking forward to 2021

- Publish learnings from **review of RWE submissions** (+ workshop)
- learnings from **committee RWE analytics pilot**

# Priority Recommendation – 6 – Technology and 'raw' data

## Why

- Currently the Network has limited IT capacity and staff experience to manage and analyse 'raw' data (both patient level data from clinical trials and real world data from health records).



## How

- **Build EU Network capability to analyse Big Data (technology / analytics)**
- Build, step by step, through pilots, capacity to analyse for rapid RWD, Clinical Trials PLD, and validation of AI algorithms .
- Where possible, leverage existing EU technology initiatives.
- Support establishment of **analytics centres** linked to regulatory agencies

## Benefits

- Regulators can receive and analyse 'raw' data to validate claims made by the industry, test AI algorithms and investigate major health issues.
- Enables better committee decision-making.
- Establishment of analytics centres of excellence.

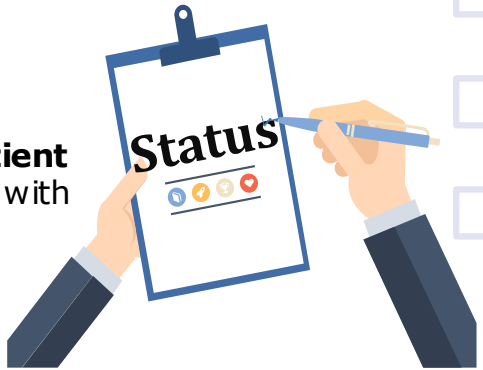
# Clinical Trials-analysis of Patient Level Data: Pre pilot

- An application submitted for MA in October 2020 was identified to gain practical experience as a pre-pilot
  - CHMP agreed on submission of IPD
  - Lessons learned to be reported back to CHMP and inform design for future pilot

# Status

## Achievements 2020

- Rapid analytics software selected for EMA committee support
- **Clinical Trials-analysis of Patient Level Data** – pre-pilot initiated with CHMP



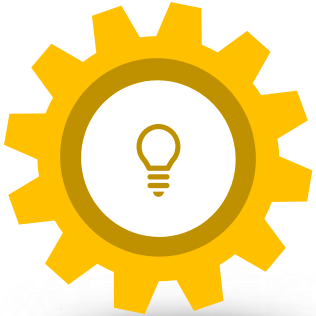

## Looking forward to 2021

- **AI workshop**
- **Patient level data**: pre-pilot becomes **pilot**
- Discussion paper on national centre of excellence

# Priority Recommendation – 7 – Expert advice

## Why

- Current methods advice is fragmented, or absent (no expert fora for real world evidence, advanced analytics or proteomics / metabolomics).



## How

- **Modernise the delivery of expert advice**
- Build on the existing working party structure to **establish a Methodologies Working Party** that encompasses biostatistics, modelling and simulation, extrapolation, pharmacokinetics, real world data and epidemiology;
- **Build an Omics Working Party** that builds on and reinforces the existing pharmacogenomics group.

## Benefits

- Network expertise gaps filled and efficiency of product advice increased.
- New groups receptive to new agile models of guideline development. New groups support training of Network assessors.

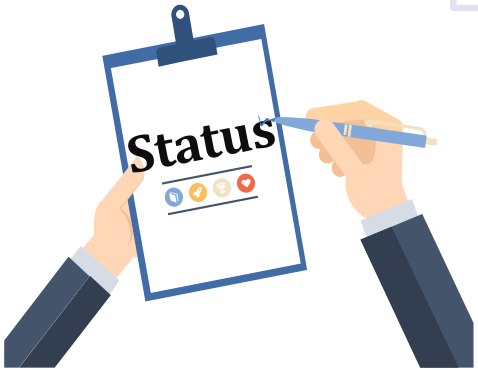
# Status

## Achievements 2020

- **Review of working parties methods domain**: initiated

## Looking forward to 2021

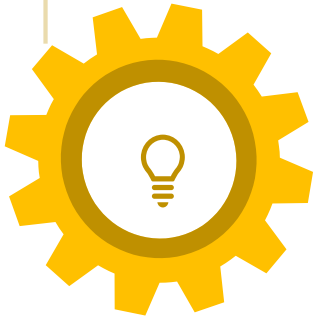
- **RWE and advanced analytics expert advice available**



# Priority Recommendation – 8 – Data governance

## Why

- Data protection critical for secondary use of data
- Any ethical issues should be discuss and addressed.



## How

- **Ensure data are managed and analysed within a secure and ethical governance framework**
- Engage with initiatives on the implementation of EU data protection regulations to **deliver data protection by design.**
- engage with patients, healthcare professionals on data governance.
- Deliver a **Q&A document on data protection in the context of secondary use of healthcare data**
- Discuss an options paper on ethics advice

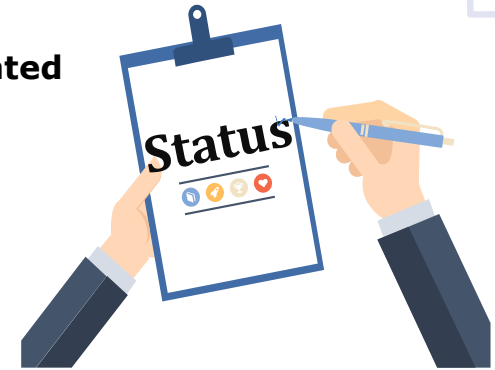
## Benefits

- Clarity for NCAs, EMA, industry and data holders on how to fully comply with data protection while enabling secondary use of healthcare data.
- Patients' views are heard and the Network has expert ethics advice.

# Status

## Achievements 2020

- **Dedicated workshops held**
- **Data Protection Q&A initiated**



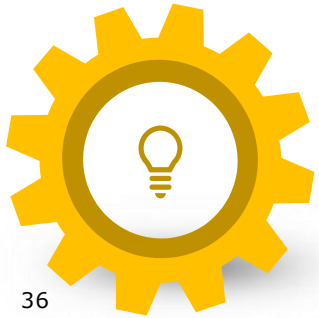

## Looking forward to 2021

- **Publish Q&A on secondary use of health care data and data protection**

# Priority Recommendation – 9 – International collaboration

## Why

- International partners are investing in Big Data including pilot projects, IT capability, networks, training and guidance.
- Opportunity to converge and leverage

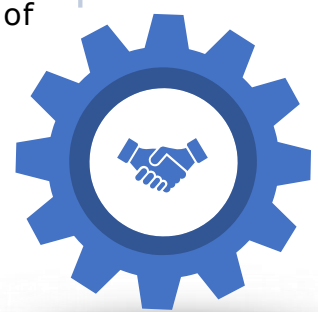


## How

- **Engage with international initiatives**
- Identify opportunities for collaboration including guideline development and sharing of best practice.
- Develop a **Network data standardisation roadmap**.

## Benefits

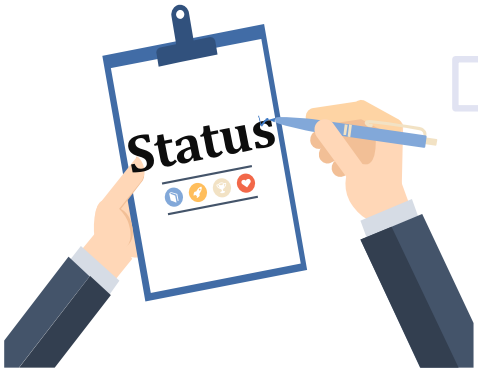
- Learn from the experience of others and leverage their efforts.
- Avoid duplication of effort and deliver coherent, often harmonised guidance for industry.
- International studies deliver greater power and allow cross-fertilisation of skills.



# Status

## Achievements 2020

- **cluster initiated with FDA and Health Canada on a RWE collaboration roadmap**



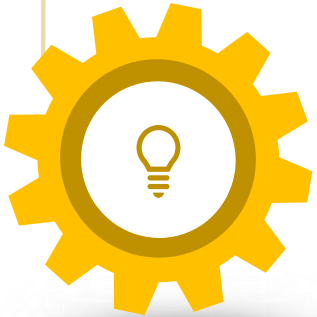

## Looking forward to 2021

- workshop on a **international RWE collaboration**
- **Data standardisation study initiated**

# Priority Recommendation – 10 –EU Stakeholders

## Why

- Need for a platform to discuss Big Data and analytics



## How

- **Establish two-way communication with stakeholders**
- Develop Network communications to articulate the regulatory use cases and requirements for data.
- Ensure active dialogue with key stakeholders, including, patients, HCPs, industry, HTA bodies, payers, and technology companies.
  - 2020: **1st stakeholder forum**
  - 2021: **2nd stakeholder forum**

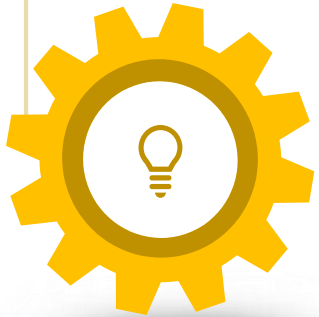
## Benefits

- Forum allows to share best practice, to identify common challenges and to scan the horizon.
- Increase Network influence over those stakeholders who can deliver change.

# Priority Recommendation – 11 - Veterinary

## Why

- BDTF recommendations did not cover veterinary medicines.

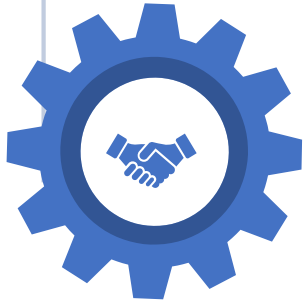


## How

- **Consider the applicability of the recommendations to the veterinary domain:**
  - 2020: **Applicability of BDTF recommendations** to Veterinary domain in preparation
  - 2021: **Veterinary stakeholder data workshop**

## Benefits

- Veterinary domain benefit from learning from Human domain and big data task force recommendations



# Conclusion

- Good progress on implementation of the Big Data recommendations in 2020 and advanced plans for 2021
- BDSG workplan can be delivered while fully supporting COVID-19 pandemic response.
- Implementation will require strong engagement with stakeholders: 2021 will se multiple consultations and workshops.

*"By delivering the vision of a regulatory system able to integrate Big Data into its assessment and decision making, we can support the development of innovated medicines, deliver life-saving treatments to patients more quickly and optimise the safe and effective use of medicines on the market."*

# Any questions?

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