# Response Evaluation In Neurofibromatosis Schwannomatosis
# INTERNATIONAL COLLABORATION

- If sharing any data or information from these slides generated by the REiNS International Collaboration, please acknowledge the authors, group chairs, and specific working group.
- If using any information presented with a citation, please reference the primary source.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

# Support for developing medicines to address unmet medical needs of patients with a rare disease

Introduction to offerings and invitation to further exchange

Response Evaluation in Neurofibromatosis and Schwannomatosis (REiNS)
2022 Winter Meeting

Presented by Ralf Herold 5 December 2022, Regulatory Science and Innovation Task Force

# Disclaimer

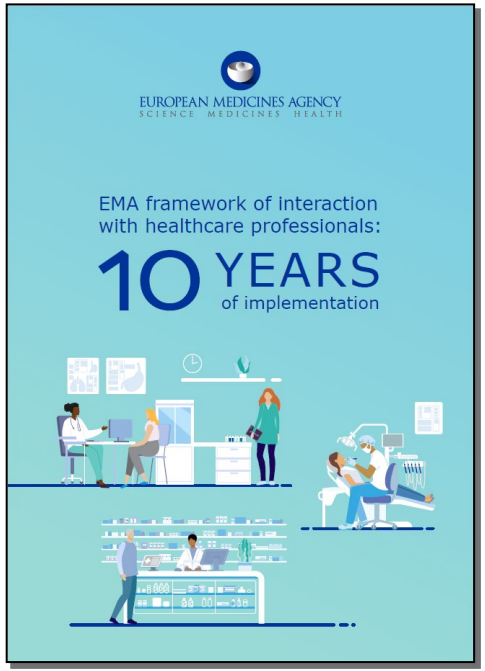
The views expressed in this presentation are the personal views of the author(s) and may not be understood or quoted as being made on behalf of or reflecting the position of the European Medicines Agency or one of its committees or working parties.

# What does the EMA do and why do we exist?

- Support research & innovation of medicines
- Facilitate development of medicines
- Enable timely access to new medicines
- Evaluate marketing authorisations
- Monitor medicines during all their life cycle
- Provide reliable information on medicines with high level of transparency
- Advance regulatory science and practices
- Foster scientific excellence in the evaluation and supervision of medicines, for the
- Benefit of public and animal health in the European Union (EU)

https://www.ema.europa.eu/en/documents/other/laboratory-patient-journey-centrally-authorised-medicine_en.pdf

# EMA systematically engages with stakeholders

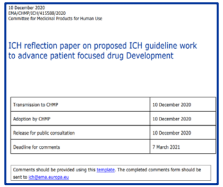



- A successful model of engagement built between regulators, patients, consumers, academics, healthcare professionals
- Engagement strengthened in crisis
- Academic stakeholders >80 EU organisations registered
- **Many academics, healthcare professionals and patients registered as EU External experts, contributing to regulatory evaluations of medicines**

https://www.ema.europa.eu/en/documents/report/stakeholder-engagement-report-2020-2021_en.pdf

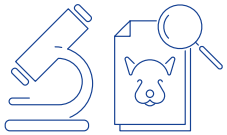
# EMA stakeholder workshop patient experience 2022



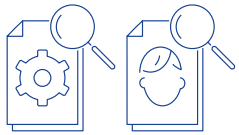



- Reinforcing patient relevance in evidence generation is key priority
- Guidance work ongoing at ICH for global harmonisation
- EU Multi-stakeholder approach for defining robust and meaningful Patient Experience Data for regulatory decision-making
- EMA to work on a reflection paper how to best generate and collect PED
- Robust methodology needed to capture and analyse what matters most to patients, to optimise medicines development, regulatory decision- making and HTA assessments
- New digital tools for clinical data generation and DARWIN offer wide opportunities for optimising clinical data generation and analysis to 2030

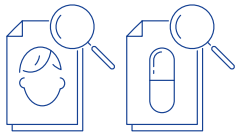
# Entry points for academia developers to **get support**



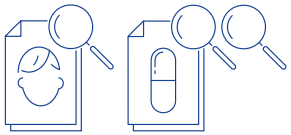
**Early Research**



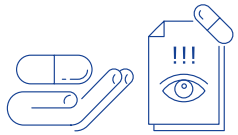
**Non-clinical and First in Man**



**Clinical exploratory**



**Clinical confirmatory**




- **Authorisation**
- **Access decision**
- **Post-licensing evidence**

**Innovation Task Force and EU-IN**

**Scientific Advice/Protocol Assistance**

**PRIME support**

**ATMP certification**

**Orphan Drug Designation**

**Paediatric Investigation Plan**

**Qualification of Novel Methodologies**

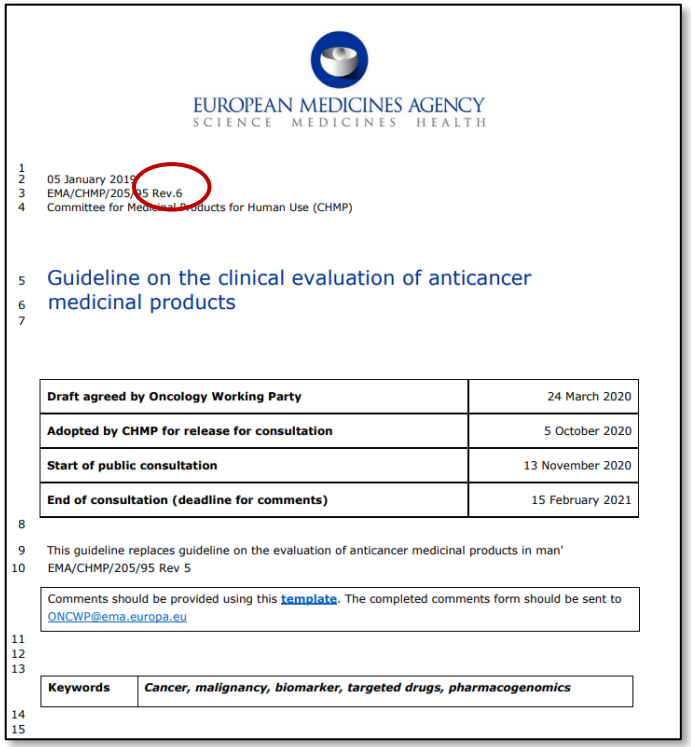
**SME briefings**



EU-IN = EU Innovation Network

# Guideline on anti-cancer products

- Trial design considerations
- Time to event endpoints (PFS, ...)
- Single-arm trials
- External controls
- More than one experimental medicine
- Harmonised safety reporting
- Patient reported outcomes
- Minimal residual disease (MM so far)
- Paediatric and special populations
- Histology and site-independent indications



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

05 January 2019
EMA/CHMP/205/95 Rev.6
Committee for Medicinal Products for Human Use (CHMP)

Guideline on the clinical evaluation of anticancer medicinal products

| | |
|---|---|
| **Draft agreed by Oncology Working Party** | 24 March 2020 |
| **Adopted by CHMP for release for consultation** | 5 October 2020 |
| **Start of public consultation** | 13 November 2020 |
| **End of consultation (deadline for comments)** | 15 February 2021 |

This guideline replaces guideline on the evaluation of anticancer medicinal products in man' EMA/CHMP/205/95 Rev 5

Comments should be provided using this **template**. The completed comments form should be sent to ONCWP@ema.europa.eu

| | |
|---|---|
| **Keywords** | ***Cancer, malignancy, biomarker, targeted drugs, pharmacogenomics*** |

https://www.ema.europa.eu/en/human-regulatory/research-development/scientific-guidelines/clinical-efficacy-safety/clinical-efficacy-safety-antineoplastic-immunomodulating-agents

# EMA guidelines for consideration

- Paediatric population https://www.ema.europa.eu/en/human-regulatory/research-development/paediatric-medicines/scientific-guidelines-paediatrics
- CNS https://www.ema.europa.eu/en/human-regulatory/research-development/scientific-guidelines/clinical-efficacy-safety/clinical-efficacy-safety-nervous-system
- Guideline on registry-based studies https://www.ema.europa.eu/en/guideline-registry-based-studies
- Data Quality Framework for EU medicines regulation; Metadata list describing real world data https://www.ema.europa.eu/en/about-us/how-we-work/big-data
- Guideline on computerised systems and electronic data in clinical trials https://www.ema.europa.eu/en/human-regulatory/research-development/compliance/good-clinical-practice/good-clinical-practice-inspectors-working-group

# Regulators at risk to be misperceived

A maze of requirements and hurdles?

https://unsplash.com/photos/Ctaj_HCqW84

# Assemble elements into compelling picture

Cubism is an early-20th-century avant-garde art movement that revolutionized European painting and sculpture, and inspired related movements in music, literature and architecture.
In Cubist artwork, objects are analyzed, broken up and reassembled in an abstracted form—instead of depicting objects from a single viewpoint, the artist depicts the subject from a multitude of viewpoints to represent the subject in a greater context.

Jean Metzinger 1910, cited in Wikipedia 2022

Pablo Picasso: Three musicians https://www.moma.org/collection/works/78630

# Innovation Task Force

- Open for any applicant, in particular for consortia with academia +/- companies
- Multidisciplinary group of scientific, regulatory and legal experts
- Forum for early dialogue on innovative aspects of development of enabling technologies or medicines
- **No fees**

https://www.ema.europa.eu/en/human-regulatory/research-development/innovation-medicines#ema's-innovation-task-force-(itf)-section

# Scientific advice

- EU harmonised advice; informs subsequent steps (e.g., clinical trial authorisation)
- To any developer (consortia, companies)
- On appropriate tests, studies, trials for development of a medicine
- Any stage of development
- Prospective
- Also for qualifying novel methodologies for specific uses in the R&D of medicines, with platform for public consultation

- **Parallel advice by FDA and EMA can be requested**
- Academia seeking advice on developing an orphan medicinal product: 90% fee waived
- Academia developing a PRIME (Priority medicine)-designated product: no fee

https://www.ema.europa.eu/en/human-regulatory/research-development/scientific-advice-protocol-assistance

# Summary

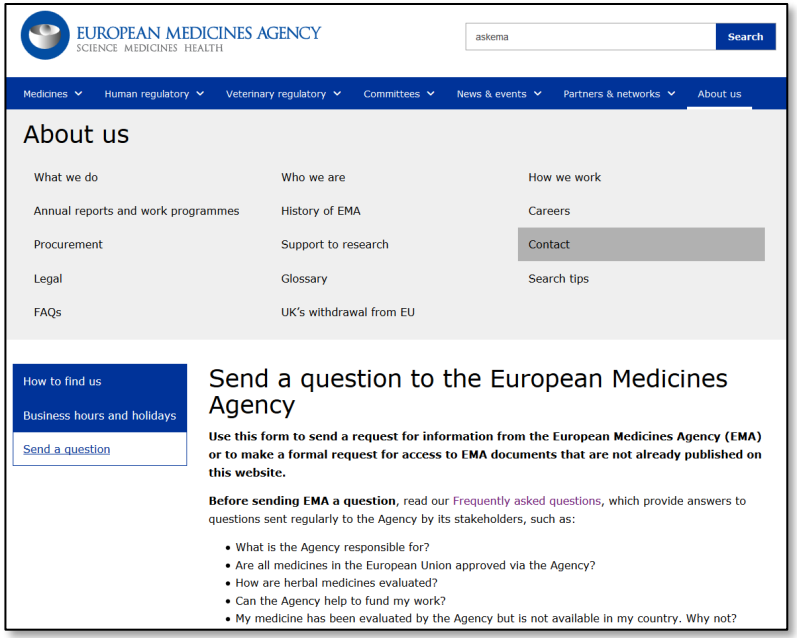
- Regulators fully build on existing basic and clinical science
- Expectations are case dependent and require dialogue on the basis of scientific briefing information with assembly of data and synthetic argumentation
- Academia and non-commercial developers are invited to use EMA's support offers
- EMA provides support through our network of experts across EU and across relevant subject matter relevant for supporting the development project internationally
- Important practicalities concern how academia developers collaborate with pharmaceutical companies, how generated data can be submitted to regulators, how developing new methodologies and medicines goes hand in hand, possibly fees

# Contact us

- Write to academia@ema.europa.eu or go to

https://www.ema.europa.eu/en/about-us/contact/send-question-european-medicines-agency

- Request for information
- Support to navigate regulatory system
- EMA will reply by email



# Acknowledgments


- Maribel Rico-Salas
- Kristina Larson
- Rosa Gonzales-Quevedo
- Iordanis Gravanis
- Dominik Karres
- Elias Pean
- Francesco Pignatti

# Questions welcome!

## Further information

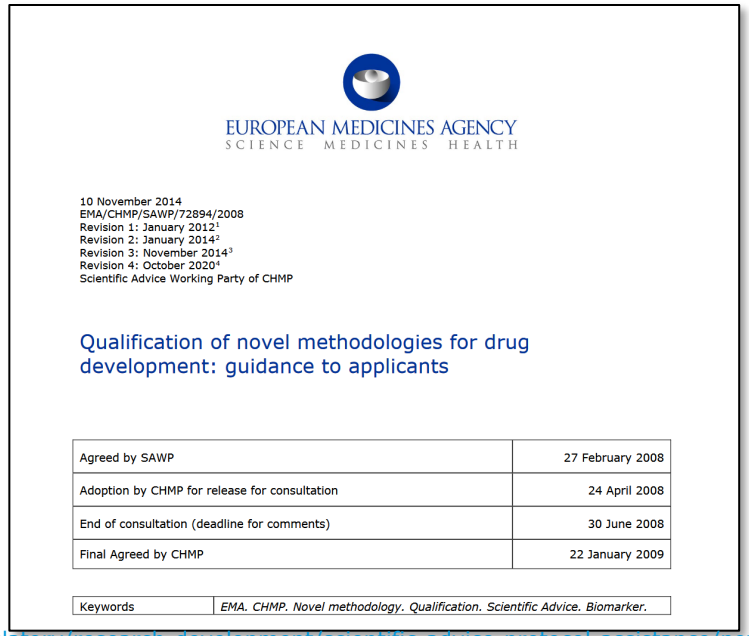
**Official address** Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
**Address for visits and deliveries** Refer to www.ema.europa.eu/how-to-find-us
**Send us a question** Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000

Follow us on **@EMA_News**

# Novel methodologies for medicine development

- EMA offers support for qualifying a new method (e.g., functional, imaging) for a specific use in R&D (non-clinical or clinical)
- Pathway for innovative methods or drug development tools not yet integrated in drug development and clinical management

1. Qualification advice (how to further develop the new method, optional letter of support)
2. Qualification opinion (based on assessment of submitted results data; made public)



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

10 November 2014
EMA/CHMP/SAWP/72894/2008
Revision 1: January 2012[1]
Revision 2: January 2014[2]
Revision 3: November 2014[3]
Revision 4: October 2020[4]
Scientific Advice Working Party of CHMP

Qualification of novel methodologies for drug development: guidance to applicants

| | |
|---|---|
| Agreed by SAWP | 27 February 2008 |
| Adoption by CHMP for release for consultation | 24 April 2008 |
| End of consultation (deadline for comments) | 30 June 2008 |
| Final Agreed by CHMP | 22 January 2009 |

| | |
|---|---|
| Keywords | *EMA. CHMP. Novel methodology. Qualification. Scientific Advice. Biomarker.* |

https://www.ema.europa.eu/en/human-regulatory/research-development/scientific-advice-protocol-assistance/novel-methodologies-biomarkers/opinions-letters-support-qualification-novel-methodologies-medicine-development

# Fees

- See table for orphan-designated medicines
- General info on fees: https://www.ema.europa.eu/en/human-regulatory/overview/fees-payable-european-medicines-agency

| Procedure or service | Fee reduction applicable to | Percentage fee reduction |
|---|---|---|
| Protocol assistance, initial and follow-up requests | SME sponsors for all assistance | 100% |
| | Academia for all assistance | 100% |
| | Sponsors for paediatric-related assistance, other than SME sponsors or academia[1] | 100% |
| | Sponsors for non-paediatric-related assistance, other than SME sponsors or academia | 75% |
| Pre-authorisation inspection | All sponsors | 100% |
| Initial marketing authorisation application | SME sponsors | 100% |
| | Non-SME sponsors | 10% |
| Post-authorisation applications and annual fee, specified in Council Regulation (EC) No 297/95, in the first year from granting of a marketing authorisation | SME sponsors | 100% |
| Pharmacovigilance fees, specified in Regulation (EU) 658/2014 | All sponsors | n/a |