The European Regulatory Network and The Liver Forum

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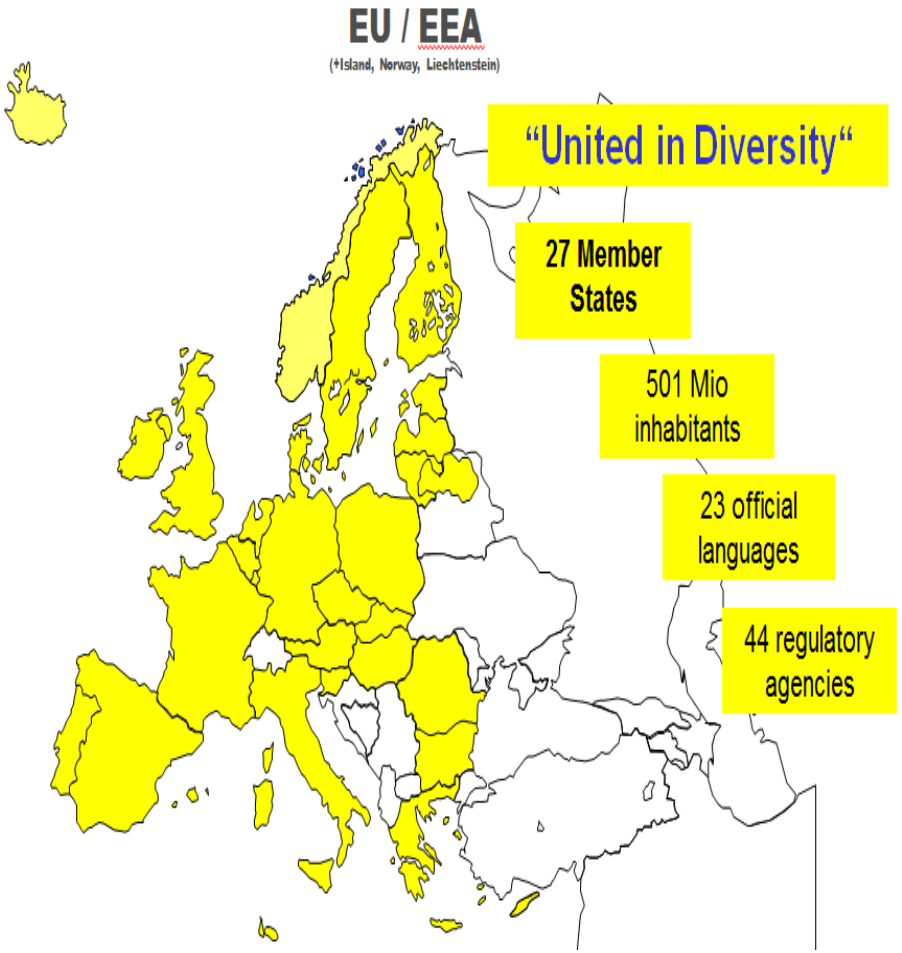
The EU regulatory network

- European Medicines Agency (EMA)
  - "Networking agency"
    - About 3,500 national experts
  - Staff No. ~500
- Committee for Human Medicinal Products (CHMP)
  - Responsible for preparing Agency's opinions concerning all human medicines
  - Mandating Working Parties
- Scientific Advice Working Party (SAWP)
  - Appointed by CHMP
  - Facilitate access of medicinal products to patients by optimising research and development
- Gastroenterology Drafting Group
  - Appointed by CHMP
  - Preparation of Scientific Guidelines for drug development



The Scientific Advice Working Party (SAWP)

- Scientific Advice is given by CHMP based on the recommendations of the SAWP

Scope and Aims:

- Advice is given on the appropriate tests and studies in the development of a medicine. This is designed to facilitate the development and availability of high-quality, effective and acceptably safe medicines
- Can be given at any stage of development
- Independent of liability to Centralised Procedure
- Intended to avoid major objections regarding the design of the tests raised during evaluation of the Marketing Authorisation Application (MAA)
- Advice is given by answering questions
- Prospective in nature; focussed on development strategies rather than pre-evaluation of data
- Not legally binding.
- Protocol assistance: Scientific Advice for companies developing designated orphan medicines.
- Parallel advice with HTA bodies possible
- Parallel advice with FDA possible




Biomarker Qualification Procedure

("Qualification of novel methodologies for medicine development")

- **Given by the CHMP on the basis of recommendations by the SAWP.**
- **Leads to a "Qualification opinion" or a "Qualification advice"**
  - **Qualification Opinion:**

    - The CHMP can issue an opinion on the acceptability of a specific use of a method, such as the use of a novel methodology or an imaging method in the context of research and development. The method can apply to non-clinical or to clinical studies, such as the use of a novel biomarker.
    - Before final adoption of qualification opinion, the CHMP makes its evaluation open for public consultation by the scientific community. This ensures that the CHMP shares information, as agreed with the applicant, and is open to scientific scrutiny and discussion.

  - **Qualification advice:**

    - The CHMP can issue advice on protocols and methods that are intended to develop a novel method with the aim of moving towards qualification
    - The advice is based on the evaluation of the scientific rationale and on the preliminary data submitted to the Agency.

Regulatory Experience with the indication NASH/NAFLD

- Previous applications for Marketing Authorisation: 0
- Procedures within Scientific Advice: 3
- Substances under development (with SAWP involvement): 1
- No regulatory guidance documents available
- Experience with other chronic liver diseases (other than viral hepatitis):
  - Primary biliary cirrhosis (PBC)
  - Primary sclerosing cholangitis (PSC)

Regulatory Experience with the indication NASH/NAFLD

Scientific Advices:

- **NASH was accepted as valid indication for medicinal products**
- **Under discussion:**
  - Potential design of phase II and phase III studies
  - Necessary duration of studies (both phases)
  - Endpoint in phase III: Histology as such accepted, but should mainly be based on fibrosis development
  - How to deal with standard non-pharmacological treatment (weight reduction), especially when compound also has effects on body weight

Thank you for your attention!