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Leuven, Belgium

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Regulatory perspectives: What's needed for acceptance?

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Clinical value of intestinal ultrasonography

Intestinal ultrasonography (IUS) – established diagnostic value comparable with MRI and/or CT

(ECCO-ESGAR Diagnostics Guidelines [2018]

Advantages:

- Easy to use
- Inexpensive
- No limitation in repeated use
- Safe
- Immediate interaction with patients
- Characterisation of inflammatory infiltration of bowel wall layers and peri-intestinal abnormalities

Disadvantages for use in clinical trials:

- Lack of regulatory guidance
- Consistency
- Limited experience in monitoring
- Various value with regards to disease site
- Definition and validation of endpoints

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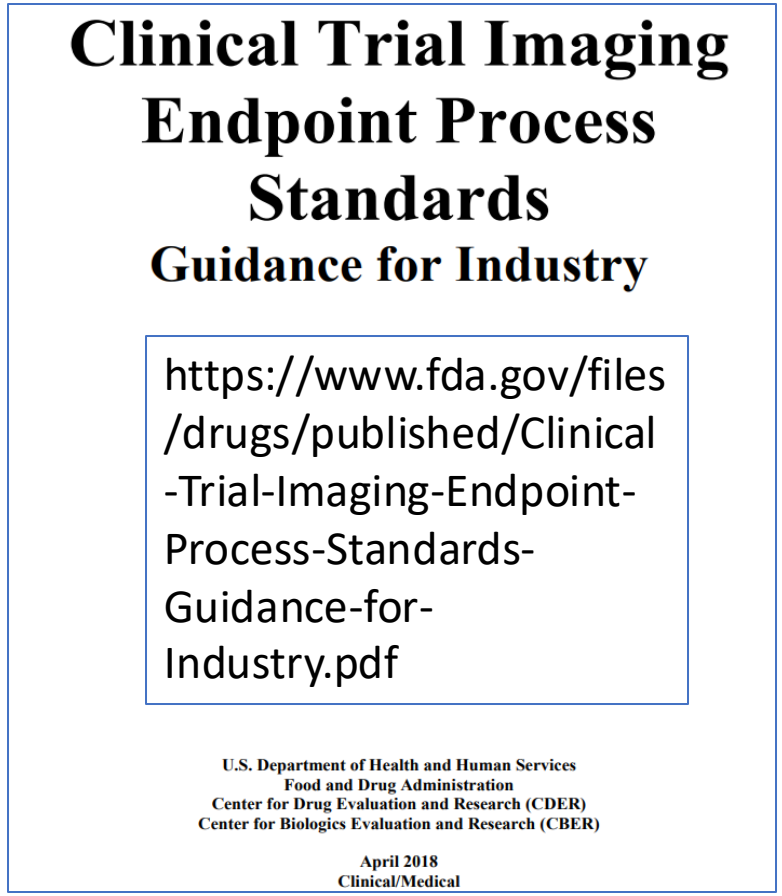
Regulatory guidance

The purpose of this guidance is to assist sponsors in optimizing the quality of imaging data obtained in clinical trials intended to support approval of drugs and biological products.
This guidance focuses on imaging acquisition, display, archiving, and interpretation process standards that FDA regard as important when imaging is used to assess a trial's primary endpoint or a component of that endpoint.



Clinical Trial Imaging Endpoint Process Standards

Guidance for Industry

https://www.fda.gov/files/drugs/published/Clinical-Trial-Imaging-Endpoint-Process-Standards-Guidance-for-Industry.pdf

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

April 2018
Clinical/Medical

Minimisation of variability may enhance clinical trial's ability to detect treatment effect by

- Compliance with CT protocol
- Quality of data among clinical sites
- Verifiable record

This guidance does not address whether specific imaging measures would be acceptable in submissions used to support approval of a drug or biologic. These considerations should be discussed with the FDA review division responsible for drug development.

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Variability

- The images typically achieve the **medical practice's** diagnostic purposes even though the acquisition, display, and interpretation methods **may vary** somewhat among imaging facilities and imaging professionals.
- This variability may have **little or no impact** on the ability to provide a diagnosis **in medical practice**, yet in a **clinical trial**, imaging process variability may result in increased variability in endpoint measurements and may **compromise the ability** of the trial to achieve its objectives.

Create **trial specific** imaging process standards?

Choice of imaging equipment

- Certification and regulatory compliance
- Performance and uniform use of parameters
- Ideally same equipment for use in clinical trial

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Prevention of bias in reading

- Centralised reading and interpretation
- Blinding to clinical data and treatment assignment
- Identical imaging frequency and timing in all CT arms
- Timeliness of the off-site reading

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Standardisation

- Imaging modality **availability** and **variation** across trial sites
- **Performance features** of the imaging modality
- **Qualifications** of the imaging technologists
- Any unique **image acquisition** features of the trial design
- Image **quality control** standards
- Procedures for **imaging display and interpretation**
- Nature of the **primary endpoint** image measurement,
- Image **archiving**
- Potential for imaging modality **upgrades** or modality **failures**
- Precedent for use of the imaging-based primary endpoint

- **Creation of the imaging charter**

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Development of IUS endpoints for use in CTs

- Definition of the endpoint for clinical trials
  - Bowel wall thickness (BWT)
  - Vascularity (Doppler)
  - Other IUS features
    - Loss of haustration
    - Loss of bowel wall stratification
    - Ascites
    - Mesenteric lymphadenopathy
    - Mesenteric fibro-fatty proliferation

(Maaser C et al Gut 2020)

- Development of specific IUS scores
- AI augmented technologies
- Validation
- **Regulatory qualification**

EMA qualification procedure

Qualification of novel methodologies for medicine development

Share

The European Medicines Agency (EMA) offers scientific advice to support the qualification of innovative development methods for a specific intended use in the context of research and development into pharmaceuticals.

Human | Regulatory and procedural guidance | Innovation | Research and development | Scientific advice

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Also on this topic

CHMP qualification opinions

CHMP qualification advice and letters of support

The EMA's Committee for Medicinal Products for Human Use (CHMP) gives opinions on the **qualification** of **novel methodologies** for medicine development based on recommendations that EMA's Scientific Advice Working Party provides.

This qualification process leads to a CHMP qualification opinion or advice.

For more information on EMA's scientific advice and protocol assistance, see:

- Scientific advice and protocol assistance

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]
Revision 5: October 2023[5]
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.*

Qualification of novel methodologies for drug development: guidance to applicants

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EMA qualification process

The EMA qualification process is a voluntary, scientific pathway leading to either a CHMP Qualification opinion or a qualification advice on innovative methods or drug development tools:

- **CHMP qualification opinion** on the acceptability of a specific use of the proposed method (e.g. use of a novel methodology or an imaging method) in a research and development (R&D) context (non-clinical or clinical studies), based on the assessment of submitted data;
- **CHMP qualification advice** on future protocols and methods for further method development towards qualification, based on the evaluation of the scientific rationale and on preliminary data submitted

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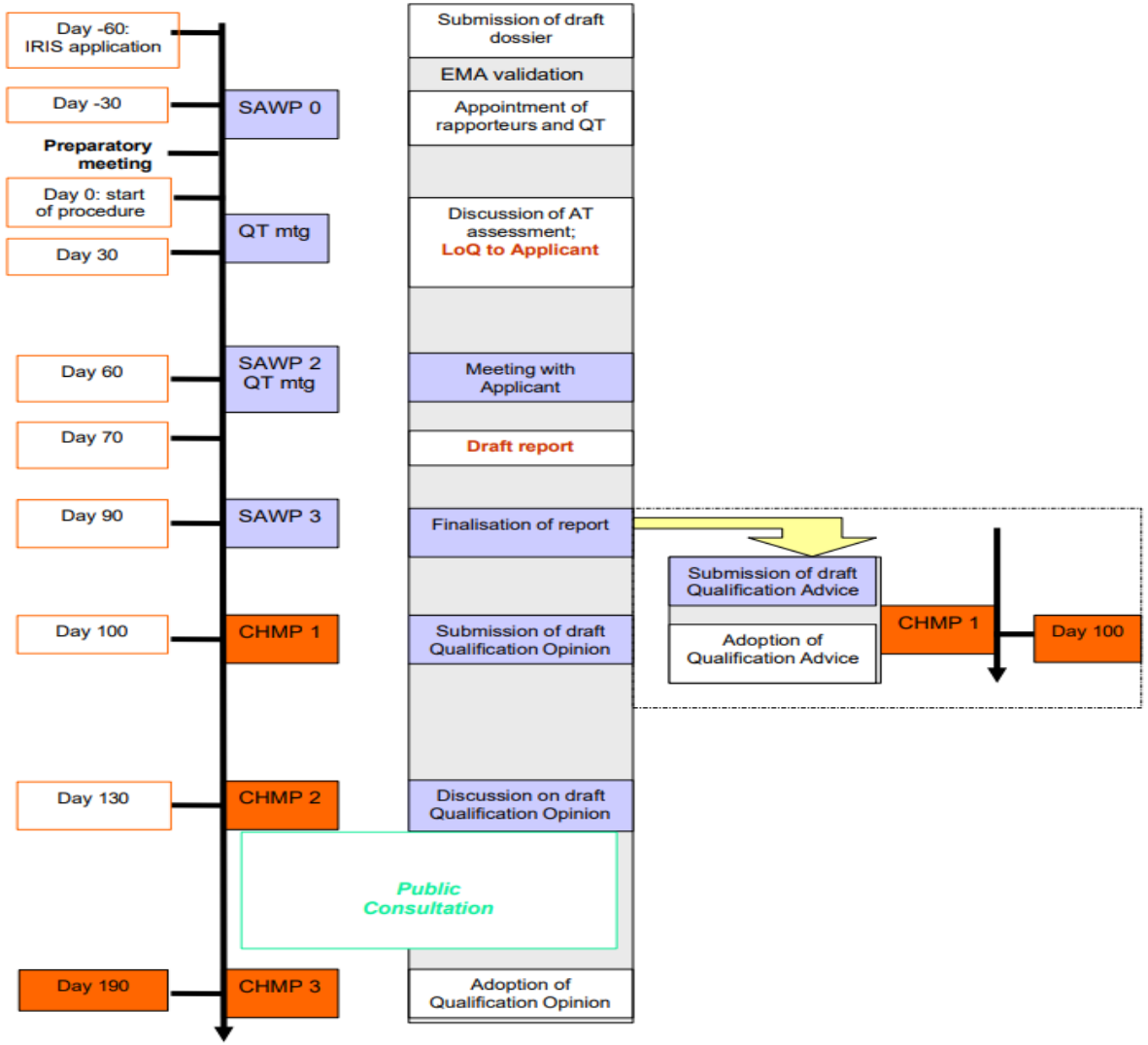
Timelines for EMA qualification procedure



Use of IUS endpoint(s) in clinical trials

- Qualified biomarkers potentially could be used as primary endpoint
- Ad hoc or clinically established IUS parameters more suitable as secondary endpoints
- Determination and suitability to be discussed upfront with regulatory agencies

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Thank you for attention!

Questions?

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