Common elements of the CTA review process in National Competent Authorities

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LÄKEMEDELSVERKET
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Role of National Competent Authority

Protection of subjects

Scientifically valid and ethical trials

Reliable data

Prevent fraud

through

- stating provisions and guidelines
- supervision and inspections
- information, education and advice

All NCAs demand

A clinical trial should be

- safe
- evaluable
- address a clinically relevant question

The Clinical Trials Directive 2001/20/EC

Pre Clinical Trials Directive

- Individual demands for contents of a CTA in 27 countries
- Variety of procedures and extent of CTA assessment
- Phase I studies not assessed in some countries
- Time to approval unpredictable
- Ethics review according to various procedures

With Clinical Trials Directive in place

- Approximation of laws, regulations and administrative provisions in Member States
- Common databases (EudraCT and EV CTM)
- Clear focus on patient safety and GCP
- Guidance and networking to enhance harmonisation
- Formal and informal interaction with multinational trials

However

- Implemented with somewhat varying interpretation

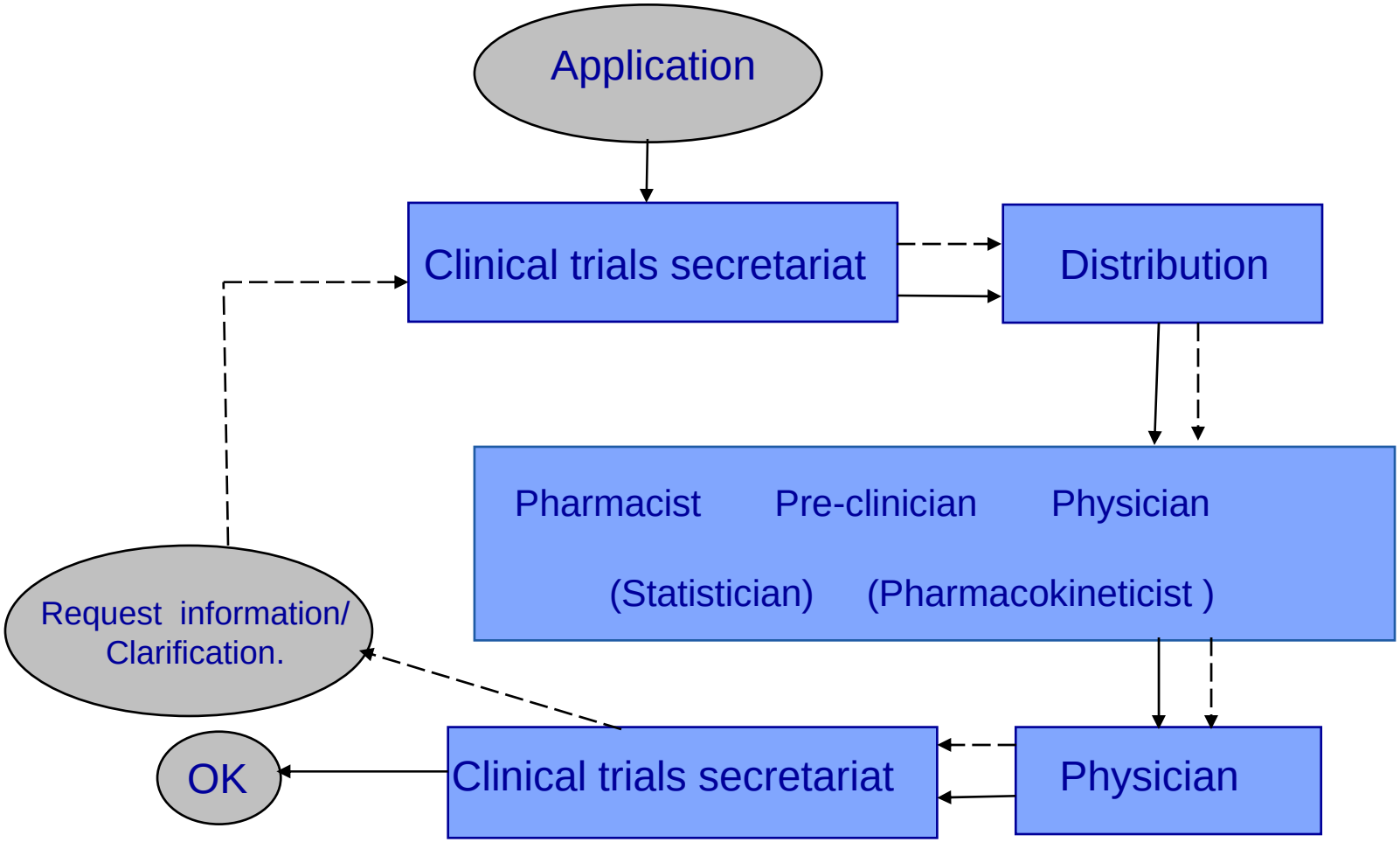
CTAs under the Clinical Trials Directive

- Same set of documents submitted to all NCAs
- Same principles for assessment in all NCAs
- One possibility to request information/clarification
- Defined timelines (up to 60 days)
- Communication between NCAs
- CAs expected to arrive at the same conclusion for multinational studies (approval/rejection)

List of documentation to be included in CTA

- **Cover letter**
- **Clinical Trial Application Form**
- **Protocol**
- **Investigator Brochure (IB) or approved SPC**
- **Investigational Medicinal Product Dossier (IMPD)**
- **Non-Investigational Product Dossier (if applicable)**
- **Content of IMP labelling**
- **Copy of EC opinion (when available)**
- **If applicable**
  - Information on Scientific Advice
  - Copy of agreement on Paediatric Investigational Plan

Procedural aspects, an example



Procedural aspects

All NCAs assess

–The same set of documents

–According to the same principles

With different volumes of CTAs

–Some NCA have dedicated staff for clinical trials

–In other NCA same staff review CTs and MAs

–Some NCA use external consultants

Request for information during assessment - Some examples, most common areas

Toxicology

- Repeated dose toxicology
- Photosafety

IMP related

- Labelling
- GMP/manufacturing licence

Clinical

- Dose
- Inclusion/exclusion criteria

EU guidande for CTAs

- Detailed guidance on the submission to competent authorities of a request for authorisation of a clinical trial on a medicinal product for human use (update in progress)
- Detailed guidance on the European clinical trial database (EudraCT)
- Detailed guidance on the collection, verification and presentation of adverse reaction reports arising from clinical trials on medicinal products for human use
- Detailed guidance on the European database of Suspected Unexpected Serious Adverse Reactions (SUSAR) (update in progress)

www.eudra.org

Hurdles for SMEs

- **Secure Regulatory understandig and competence**
  - In house or insourced
  - When insourcíng choose carefully
- **Understand regulatory "need and must" for product development**
- **Acknowledge there are no quick , easy and cheap trails**

A market plan, however brilliant, is not sufficient!

Service provided by NCAs and EMA

- **Detailed information "step by step" from webpage**

  Including reference to CT directive, legislation, ordinance, provisions, guidelines, Q&A

- **NCA Scientific Advice**

  - development program- or protocol level

- **EMA Central Scientific Advice at EMA**

  - product development level

Summary

For clinical trials, all NCAs assess the same documents according to the same principles in order to secure clinical trials are

- safe
- evaluable
- address a clinically relevant question