



EU initiatives for simplifying clinical trial approval

Concerns and Initiatives: An Overview

The Voluntary Harmonisation Procedure – a step towards quicker approvals?



Approximately 30% of all clinical trials conducted in EU are multinational studies.

The Voluntary Harmonisation Procedure (VHP) can be used for all clinical trials of medicinal products involving three or more EU Member States.

A single application, submitted to the Clinical Trials Facilitation Group (CTFG) in English, is evaluated in a single procedure by the competent authorities of those Member States where the clinical trial is to be performed.

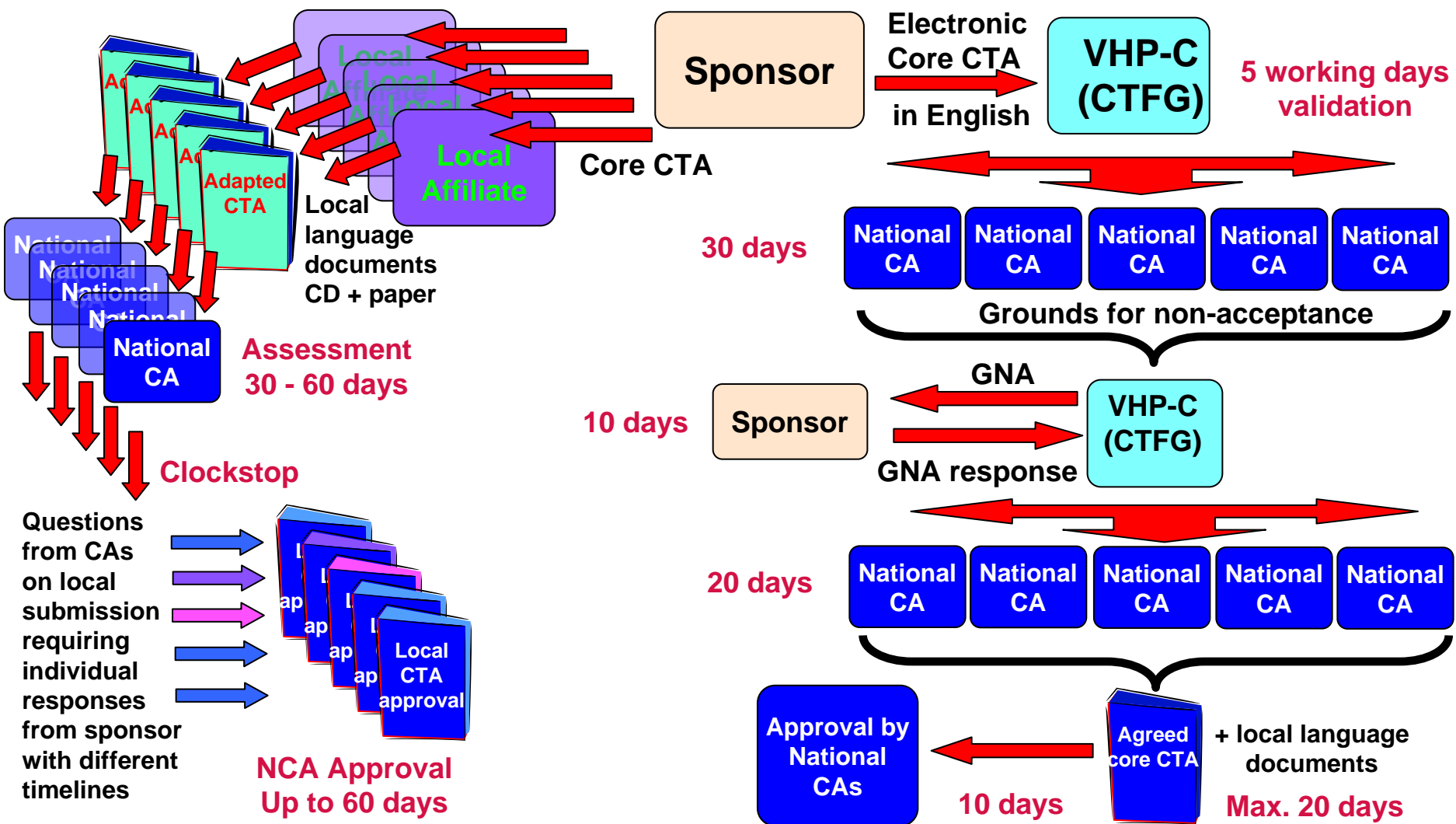
The Voluntary Harmonisation Procedure – a step towards quicker approvals?



Scientific questions on the protocol, the investigators brochure and the investigational medicinal product dossier will thus be clarified by all participating Member States prior to submission of the clinical trial application (CTA).

Subsequently, the CTA is submitted together with the required essential documents to each national Competent Authority (NCA) involved in the VHP and approval should then be provided within 10 days (instead of the 60+ days for normal CTA approvals).

Standard CTA submission - versus – VHP



What is the acceptance of a VHP outcome by Ethics Committees?



- Ethics Committees (ECs) are independent bodies who do not feel bound to or influenced by the outcome of a VHP
- Following a VHP the protocol and/or IB may therefore have to be amended due to subsequent concerns raised by one or more national coordinating ECs
- As ECs are responsible for assessing different documents to the NCAs, other questions may arise e.g. discrepancies between the protocol and patient informed consent documents

What is the acceptance of a VHP outcome by Ethics Committees?



- Local 'country' amendments cannot be made through the VHP, therefore all changes required by national ECs need to be implemented in all countries included in the VHP
- There is no accelerated assessment by the national ECs for a study which has a positive VHP outcome
- Sometimes there are widely differing views between national ECs on 'what is ethical'...

Interaction with national Ethics Committees in multinational EU trials – is complicated!



Germany: 48 different ECs
Regional (county), local (in big counties), and hospital (if universities)
German submission form not identical to EudraCT
Up to 12 paper copies plus CD per EC

Romania: 1 national EC
Submit EudraCT form
1 original on paper

Italy: 247 different ECs
Italian form very similar (but different) to EudraCT
Up to 6 paper copies plus CD per EC

Spain: 132 different ECs
Local (hospital) and regional ECs
Spanish form not identical to EudraCT form
Electronic submission via portal (ECM) + up to 18 paper copies + CD per EC (one EC per participating site)

Interaction with national Ethics Committees in multinational EU trials



Submission Challenges:

- Multiple different 'national' submission forms similar (but not the same as) the CTA form and not in English
- Large amounts of paper to be submitted in some countries
- National electronic submission portals often do not import data from EMA form – it has to be re-entered in the local language
- Requirements vary not only from country to country but also between local ECs within countries

Interaction with national Ethics Committees in multinational EU trials



Differing ethical evaluation regarding e.g.

- Continuation of double-blind studies into an open label follow-up phase
- Informed consent requirements
- Paediatric age groups (not identical to EMA definitions)
- Patient information for children and adolescents
- PIP requirements
- Blood sampling, particularly in paediatrics
- Data protection requirements
- Publication of study results

Concerns...



Van Gogh – Trees and Undergrowth

Can we no longer see the
wood for the trees?

And

Will there be any trees left
if we continue to waste so
much paper?

Options for streamlining clinical trial start-up – a CRO perspective



- All submissions in electronic format *ONLY but please not in different electronic formats*
- A common application form for all NCA and ECs in English and no 'extra' national forms
- One harmonised checklist for national submission documents including Ethics Committees and no local 'additional documents'
- English as only language for all clinical trial regulatory documents - reduce translation requirements to documents for the public and trial participants

Options for streamlining clinical trial approvals – a CRO perspective



- All clarification requests from ECs (and NCAs) in English and all responses to questions in English
- More EU guidance and training for EC members on
 - Advances in protocol design (e.g. adaptive design)
 - Standardising informed consent requirements
 - Requirements and recommendations for paediatric studies
 - EU harmonised data protection requirements
- Integration of EC assessment and feedback into the VHP process and timelines – perhaps with an 'EC coordinator' in analogy to the VHP coordinator?

- Good initiatives for reducing administrative burden at national level e.g. in UK
- However, national platforms for electronic submission can increase submission workload unless the format is harmonised across EU and all paper is abolished
- Cooperation of ECs on initiatives with CTFG at the EMA would be very helpful

Thank you for your attention
...and I hope we have a good discussion!