The role and responsibilities of a national competent authority in the development of modern therapies

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MHRA
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What are the role and responsibilities of a NCA?

The MHRA’s mission is to enhance and safeguard the health of the public by ensuring that medicines and medical devices work, and are acceptably safe.
What are the role and responsibilities of a NCA?

Part of the activity in enhancing and safeguarding the health of the public is by supporting the development of new medicines.
What can a NCA do to support the development of new medicines?

The two main areas are

in our role as regulator

in our role as providers of advice
What can a NCA do to support the development of new medicines?

in our role as regulator

provision of clinical trial authorisations in a timely fashion, with robust, consistent decisions
What can a NCA do to support the development of new medicines?

- in our role as providers of advice
- to provide both regulatory and scientific advice which is readily available and easily accessible
How do we do this?

providers of advice

scientific advice meetings

to provide both regulatory and scientific advice which is readily available and easily accessible

web site

specific areas for clinical trials including special interest groups
How do we do this?

as regulators

meeting statutory timelines

participation in European initiatives

CTFG
Commission ad hoc group
VHP
Voluntary Harmonisation Procedure

Key features:
• HMA CTFG initiative in response to industry
• Offer to sponsors to get one clinical trial approved in a number of Member States
• Will be given a priority by NCAs
• Currently no fees payable during the VHP phase
• Electronic documents sent to one address only
• Only core documents required, (e.g. Protocol, IB, IMP Dossier, manufacturer’s authorisations, labelling)
• Fixed timelines for Sponsor and Member States

• Harmonised scientific discussion resulting in harmonised applications in the Member States concerned
Launched March 2009
• 3 phases
  - ‘Formal’ Request (fixed dates)
  - Assessment
  - National submission

• Limited entry criteria
  - IMP without MA in the EU
  - ‘critical’ trial design or IMP (e.g. FTIH)
  - Large multi-state CTs >5 MS

July 2009
• Concept of “Lead Member State” introduced
VHP version 2

Launched March 2010

- Still 3 phases but process simplified:
  - No ‘formal’ request phase
  - Submit anytime
  - All trials >3MS (although trials with 2 MS have been accepted)
  - Validation time included in assessment phase
  - Shortened timeline by up to 4 weeks

- Includes process for Amendments
VHP-Phase 1: Request for a VHP

- Request by sponsors at any time
- Core documentation submitted electronically to co-ordinator
- Identification of the potential participating NCAs

Package sent to participating NCAs by co-ordinator
- NCAs accept/decline the VHP validate the submission within 3 days
- One NCA agrees to act as Lead Member State

The process previously contained a fixed date for submission of a letter on intent and a formal acceptance by CTFG into the process
<table>
<thead>
<tr>
<th>Task</th>
<th>Day (max)</th>
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<tbody>
<tr>
<td>Acknowledgement of receipt (validation)</td>
<td>3</td>
</tr>
<tr>
<td>Assessment by P-NCAs</td>
<td>21</td>
</tr>
<tr>
<td>GNAs sent to VHP co-ordinator (or VHP approvable)</td>
<td>22</td>
</tr>
<tr>
<td>Consolidation of GNAs by Lead MS</td>
<td>26</td>
</tr>
<tr>
<td>Teleconference (if required)</td>
<td>28</td>
</tr>
<tr>
<td>Inform Sponsor of GNA points</td>
<td>30</td>
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<tr>
<td>Sponsor’s response to GNA due by</td>
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<tr>
<td>Assessment of response by NCA</td>
<td>47</td>
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<tr>
<td>End of VHP after GNA when resolved</td>
<td>50</td>
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<tr>
<td>If GNA are not resolved –Inform P-NCA</td>
<td>50</td>
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<tr>
<td>TC on outstanding GNA</td>
<td>57</td>
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<tr>
<td>End of VHP / final info to Sponsor</td>
<td>60</td>
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</tbody>
</table>
VHP-Phase 3: National CTA application

- Formal CTA applications sent to NCAs within 21 days.
- Documentation should reflect that which has been approved via VHP. No further scientific discussion.
- CTA approval by NCAs within short timelines (10 days)
- New MSs (ie not part of the VHP) can be selected and may accept the VHP outcome
- Where conditions imposed are not acceptable to the sponsor, they may choose not to proceed with Phase 3
VHP experience April 09 – Feb 2011

65 applications received

- 54 standard VHP;
- 11 accelerated VHP (Pandemic Influenza Vaccines)

Only 1 procedure had a negative outcome (GNA not addressed)

2 procedures were withdrawn (before dossier submission)
1 was not submitted nationally to any MS (sponsor modified development plan post VHP)
VHP experience April 09 – Feb 2011

2009 (Mar-Dec): 14 (standard) applications → 1.4 per month

2010 (Jan-Dec): 27 applications → 2.25 per month

2011 (Jan-Feb): 13 applications → 6.5 per month
[to 10th March: 17 applications]
Lead Member State Jul 2009 to Feb 2011

- No LMS
- Joint LMS (DE, FR)
- BfArM (3)
- PEI (8)
- France (11)
- UK (16)
- Denmark (2)
- Czech Republic (2)
- Spain (1)
Effect of LMS on number of GNA points issued

Average % reduction in 2010

Note: Parentheses indicate no of times MS was lead
Denmark was lead for 1 VHP and reduced 4 GNA points to 1
### Summary results of standard VHP (ex flu)

[Data provided by the VHP co-ordinator (PEI) for Mar 2009 to Nov 2010]

<table>
<thead>
<tr>
<th>Category</th>
<th>Value</th>
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<tbody>
<tr>
<td>Average time for the process</td>
<td>51 days</td>
</tr>
<tr>
<td>(Range 29-68)</td>
<td></td>
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<tr>
<td>Average number of Member States</td>
<td>7</td>
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<tr>
<td>(Range 2-18)</td>
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<tr>
<td>Time to national application submission</td>
<td>~30 days (UK ~19.5 days)</td>
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<td>(Range 1-139 days)</td>
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<tr>
<td>Time for national approval</td>
<td>~19 days (UK ~7.5 days)</td>
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<td>(Range 0-101 days)</td>
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<tr>
<td>Commercial applicants</td>
<td>85%</td>
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<tr>
<td>Non-commercial applicants</td>
<td>15%</td>
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<tr>
<td>Biologicals</td>
<td>43%</td>
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<tr>
<td>Chemicals</td>
<td>57%</td>
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</table>
Sponsor advantages

• Single application
  - One set of core documentation
  - No MS-specific requirements

• Single, consolidated set of questions
  - GNAs reduced by over ~50%

• Single decision agreed by all concerned MS
  - Sponsor can decide not to submit nationally if a MS raises a specific condition not acceptable to the sponsor

• Addresses many criticisms of Clinical Trials Directive
  - Don’t need to wait for new legislation
Future of VHP?

VHP numbers are growing rapidly!
Further streamline the process
   Rap/Co-Rap system?
   EU portal for submission?
   remove need to re-submit documentation for national submission

Longer term: EC Concept paper on the revision of the Clinical trials Directive 2001/20/EC introduces the concept of a ‘coordinated assessment procedure’ (CAP),

[if you have a comment on the concept paper respond by 13 May 2011]
Conclusion

Although National Competent Authorities may historically have been seen as the rate limiting step for the development of new medicines, this is not the case.

In the EU, there are a number of initiatives by NCAs individually and collectively to play a positive role in protecting public health by supporting the clinical trials of new medicines.