

# Strengthening of work sharing on clinical trials in Europe

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# Clinical trials: a major stake

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- **Innovation in healthcare, produced by academia and industry;**
- **Providing patients with new medicines to improve converge of medical needs;**
- **Contribution to preserving industrial capacity in the healthcare area;**

## Europe in the field of clinical trials: still significant but declining role

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- **Still a substantial flow of clinical trials in Europe, around 5000 each year;**
- **Among them, 75% single states clinical trials, 25% multi-states clinical trials;**
- **But double shift:**
  - **Inside Europe, from countries with a strong pharma tradition to emerging or strengthening sites;**
  - **From Europe to distant sites, mostly Asian, but also Latin American and African;**
  - **Keep in mind that such shifts are to some extent natural: geographical spread of activities formerly restricted to European and North American countries is one of the drivers of economic and social progress at worldwide level;**

# A range of attractiveness factors on which Europe should capitalize or further work

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- **Well beyond smoothness and consistency of procedures at National Competent Authorities (NCA) level;**
- **Smooth functioning of ethics committees, which are independent from NCAs, and interaction with NCAs;**
- **Functional infrastructures (transportation of medicines, samples...);**
- **Competence of investigators and Clinical Research Organizations (CROs);**
- **Easiness and speed of patients and healthy subjects inclusion;**
- **Quality of operational and administrative links with health centers;**
- **Level of costs...**

# Clinical trials evaluation and monitoring: a key activity for national agencies in their four-level involvement<sup>5</sup>

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- International cooperation exchange of information and training, joint inspection of remote clinical trials sites;
- Contribution to centralized tasks at EMA level: production of scientific and inspection guidance;
- Coordination of national assignment within Europe: assessment, authorization, decisions, clinical trials vigilance;
- Purely national tasks: authorizing some clinical trials sites, checking compliance with ethics;

# Implementation of the European clinical trials regulatory framework: significant progress and remaining difficulties (1/2)

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- Improved standards of quality (good clinical and manufacturing practices GCP-GMP);
- Improved communication and exchanges between member states authorities (assessors and inspectors);
- Enhanced protection safeguards for subjects ;
- Common technical requirements;
- Progress with regard to timelines in decision-making;

# Implementation of the European clinical trials regulatory framework: significant progress and remaining difficulties (2/2) <sup>7</sup>

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- **Persisting lack of harmonisation in some areas (requirements on CTA dossiers, a few definitions (substantial amendment, non-interventional trial...), safety reporting, IMP/NIMP concept;**
- **A few divergent decisions for multi-states EC (true but limited issue = less than 0,1 % mostly linked with clinical practice difference);**
- **Not enough risk-based approach to take account of the diversity in clinical trials;**
- **Inadequate basis for multiple sponsorship;**
- **Room for progress with regard to transparency;**

# Heads of Medicines Agencies (HMA) reflexions<sup>8</sup> and initiatives to address the remaining difficulties

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- **First discussions at HMA regular meetings in the first semester of 2007;**
- **Spurred by results of the 3 October 2007 European Commission/EMA workshop;**
- **Resulting in a new mandate for CTFG (January 2008) and then an action plan (July 2008);**

# Main orientations of CTFG new mandate and action plan 2008-2009

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- **Strengthen coordination or sharing of scientific assessment of multinational clinical trials and safety data ;**
- **Harmonise processes and practices ;**
- **Develop data-sharing and information systems ;**
- **Improve communication on NCAs CT regulatory activities ;**

# Some significant achievements to date

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- Valuable improvement of assessment coordination, though the voluntary harmonised procedure (VHP): simplified CTA process, single opinion for several member states, controlled timelines, enlargement of the scope of VHP to all kinds of multinational CT and to substantial amendments (HMA approval October 2009);
- A few steps forward in telematic information sharing between NCA with EMA support, and CTA submission form;
- Moves toward better communication both within the CT regulatory network and with the stakeholders;

## action plan 2010-2011 endorsed by HMA in April 2010

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- Implement VHP version 2 with enlarged scope;
- Coordinate CT safety informations on a risk based line: by prioritising annual safety report (ASR),; assessment when the Development safety update report (DSUR) is released by ICH; by promoting work sharing on Susars;
- Bring input in the development of EU legislation and harmonised interpretation in close connection with the European Commission which both prepares revised legislation and updates CTA guidance;
- Adopt process according to a risk based approach,
- Further improve information systems to facilitate work-sharing and simplify process;
- Keep improving communication to stakeholders to assist them in conducting CTs in EU;
- Liaise with other European Commission and EMA groups;

## The prospect of a revision process by end 2011 should not stop or inhibit the work in progress for reaching operational and concrete improvement

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- Still much room for improvement within the current CT legal framework;
- Provided that is interpreted in a constructive and pragmatic way, with a view to facilitating daily operation of sponsors and regulators alike as much as possible on the basis of the current provisions;
- Operational headway too crucial for promotion of CT in Europe to be postponed or made contingent on the future (2012-2013?) and uncertain outcome of a revision process;

## The revision of the 2001/20/CE directive should build on recent operational initiatives while solving issues that require legislative input

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- Spirit of the HMA response to the Commission's consultation on review of the CT directive (January 2010);
- Give robust legal ground to the coordinated DCP like approach of the VHP;
- Provide firm basis for a risk-based approach;
- Help clarify division between NCA and Ethical Committees (EC) to avoid duplication of work;
- Strengthen safeguards to ensure compliance with GCP performed in third countries (65% of CT supporting centralized submissions at EMEA are completed there);

# Conclusion

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- **NCA and HMA are fully aware of the stakes and keen to foster further operational improvements without waiting for a revised directive that will nevertheless be useful;**
- **This major issue will be emphasized in the Strategy Paper N°2 currently prepared by an HMA task force;**
- **Coordination and simplification should be further improved without weakening protection of subjects nor undermining quality of data;**
- **We hope this meeting in Paris – after the April meeting in Bonn and before the November meeting in Brussels – will bring about better understanding of the work in progress and possibly give birth to further ideas of improvements.**