

FEAM

Federation of the
European Academies
of Medicine



Opportunities and Challenges for Reforming the EU Clinical Trials Directive: an Academic Perspective

Statement

August 2010



The Federation of the European Academies of Medicine (FEAM)

FEAM was founded in 1993 in Brussels with the objective of promoting cooperation between the national Academies of Medicine and of extending to the political and administrative authorities of the European Union the advisory role that the Academies exercise in their own countries on matters concerning medicine and public health. As an umbrella organisation, it brings together national Academies of thirteen European member states (Austria, Belgium, Czech Republic, France, Germany, Greece, Hungary, Italy, Portugal, the Netherlands, Romania, Spain and the United Kingdom) and aims to reflect the European diversity by seeking the involvement of additional Academies and experts in its scientific activities and by collaborating with other European-wide networks on scientific matters of common interest.



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A FEAM Statement

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Summary

The introduction of the Clinical Trials Directive (CTD), intended to harmonise authorisation of EU Clinical Trials on medicinal products and to improve the collection of reliable data, has been controversial. While increased support for multi-national collaboration is very important, the CTD has dramatically increased the administrative burden and costs for academia and has deterred academic clinical research.

There must be urgent reform of CTD legislation together with clarification of definitions and guidance. FEAM advises particular attention should be devoted to the following points:

- The majority of clinical trials are currently based within a single Member State. These must not be subjected to additional bureaucratic burden and costs in consequence of future reform to the authorisation of multi-national studies.
- More streamlined assessment of multi-national studies is essential. The options for voluntary cooperation in assessment between national competent authorities (NCAs) must be thoroughly evaluated. If voluntary cooperation is found to be insufficient, our preferred approach is the “common agreement” whereby a designated lead NCA reviews and approves the trial with other NCAs providing expedited approval for their country. The creation of new, centralised assessment bodies should be avoided.
- The function of national Ethics Committees must also be streamlined to improve their efficiency and their working towards common approaches. FEAM advises that the creation of a system where there is a single Ethics Committee assessment of multi-national trials is not feasible or desirable in the foreseeable future. But there is a lot to be done now to clarify the scope of Ethics Committees and to introduce standardised procedures, training and accreditation across the EU.
- FEAM recommends the introduction of a more differentiated assessment system, based on classification of trial risk-benefit. The appropriate classification of studies according to risk and the implications (in particular, in terms of ethical review, monitoring, safety reporting, drug labelling and insurance) requires much more discussion. It is vital that a proportionate, risk-based approach is agreed and implemented successfully before there is further consideration of extending the scope of the CTD. We advise those who would like to extend the scope that there are many types of clinical research and it is important to retain this flexibility in research design when thinking about the implications of extending the scope of the CTD.



- There are a number of other current problems in the operation of the CTD arising from lack of clear definition, inconsistencies in implementation and, in some cases, weaknesses in the infrastructure for clinical research. Among the main issues that need to be addressed are: (a) Submission of Substantial Amendments – clarification and simplification to focus on what is truly important; (b) Reporting of Suspected Unexpected Serious Adverse Reactions (SUSARS) – creation of a system where key information is acted upon by a responsible body, requiring clarity in assignment of roles but also better methods for safety signal detection; (c) Insurance – development of consistent risk-based insurance systems across the EU; (d) Sponsorship – clarification of options for multiple sponsorship or delegation of responsibilities.
- The further improvement of the clinical trial framework must take account of the needs of special research populations. These include those involved in studies in paediatrics, emergency situations, mental health disorders, and when using radioactivity or controlled drugs.
- Creating a strategy for improving the EU clinical research environment requires much more than reform of the CTD. FEAM recommends that policy-makers also prioritise

action to: (a) Increase funding for academic clinical research and its infrastructure; (b) Identify and implement new approaches to multi-disciplinary research and to partnership between academia and industry; (c) Support clinical research training, career pathways and mobility between the sectors; (d) Develop integrated clinical research databases to register all research and, in due course, document research outputs; (e) Ensure that the clinical academic community has early awareness of impending EU policy developments.



1

Introduction

In a Statement published in 2004¹, the Federation of European Academies of Medicine (FEAM) welcomed the potential benefits for multinational collaboration in clinical research that could result from the Clinical Trials Directive (CTD) but raised concerns about the inflexible application to academic, non-commercial trials (Investigator-Driven Clinical Trials, IDCT).

To a significant extent, these initial concerns have been substantiated and a negative impact has been compounded by variable implementation of the CTD by Member States, leading to inconsistencies in practice. The CTD has not solved the problems it was designed to do, **but has dramatically increased administrative burden and costs for academia**, resulting in a deterrent effect on new clinical research. Clinical trials are essential in the development of medicines to address hitherto unmet societal needs and are also a vital part of improving current medical care. But as a consequence of the CTD, **the EU has become a less attractive location for such research.**


The CTD introduced legislation aimed at harmonising the way in which clinical trials conducted in the EU are authorised and at

improving the reliability of the data generated in these trials. However, we are not aware of evidence indicating a systematic improvement in patient protection as a consequence of the CTD nor are we aware of any quantifiable evidence to document the claim that the CTD has resulted in important improvements in the ethical soundness of review across the EU. The European Commission could support future discussions by collecting and validating such evidence. In addition, updating the evidence base to document the negative impact of the CTD will be of great importance. The net impact on the number of clinical trials varies between different Member States, according to the data collected by the project 'Impact on Clinical Research of European Legislation' (ICREL)² with a slight overall decrease in IDCT. The markedly negative experience in the UK on the number of trials may not initially have been shared by other countries. But there is reason to believe that a negative impact is now also being seen more widely in the EU for commercial trials (latest data in Eudract database) and the experiences described by individual researchers suggest that the problem for non-commercial trials is also worsening. Thus, there is rising concern about IDCT in the clinical academic research sector³.


1 "Recommendations to the European Commission on the clinical trials directive", www.feam.eu.com

2 Report of project "Impact on Clinical Research of European Legislation" December 2008 on www.efgcp.be/downloads/icrel_docs/Final_report_ICREL.pdf

3 Typical concerns arising from research experience in academia are described in the following literature; many but by no means all come from the UK: AD McMahon et al, The unintended consequences of clinical trials regulation, PLoS Medicine 2009 3 (11) doi: 10.1371/journal.pmed.1000131; P O'Donnell, Disharmony stifling research in Europe, Applied Clinical Trials online 2009 August 1, <http://appliedclinicaltrialsonline> ; A Burton, Special report: Is paperwork suffocating British clinical research? Lancet Oncology 2009 10 749-750; A Gulland, Number of clinical trials done in UK fell by two thirds after EU directive, BMJ 2009 doi: 10.1136/bmj.b1052; L Duley et al, Specific barriers to the conduct of randomized trials, Clinical Trials 2008 5 40-48; A Hemminki & P-L Kellokumpu-Lehtinen, Harmful impact of EU clinical trials directive, BMJ 2006 332 501-502; CD Hanning & P Rentowl, Harmful impact of EU clinical trials directive. Trial of alerting drug in fibromyalgia has had to be abandoned, BMJ 2006 332 666; M Watson, Harmful impact of EU clinical trials directive ...and so has trial of melatonin in cancer related weight loss, BMJ 2006 332 666; CD Mitchell, Harmful impact of EU clinical trials directive... while paediatric oncology is being scuppered, BMJ 2006 332 666



Our main message is that there must be **urgent** reform of the CTD legislation together with early clarification of definitions and guidance. We emphasise some guiding principles for regulatory aspects of clinical research and it is essential that changes to the framework for clinical trial regulation conform to these principles:

- Clinical research must be recognised as an essential component of high quality health care systems and IDCT must be supported.
 - The effective management of safety is critically important and the right balance must be achieved between protecting research participants, ensuring reliability of data and supporting the development of new or improved health care.
 - The regulatory supervision of a clinical study should be proportionate to the risks to the participant.
 - The roles, responsibilities and support mechanisms for sponsors, researchers, ethical reviewers and national competent authorities (NCAs) must be clarified to ensure coherence and consistency in practice.
 - Reforms should aim to reduce administrative burden and costs for researchers, streamline processes and avoid duplicate review by allocating responsibility for review to the most experienced and capable organisations.
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2

Present situation: multiple assessments and inconsistencies

There are current problems arising from the multiple assessments of multi-national trials. One of the most important issues to resolve is whether it will be possible to devise a system for a single Clinical Trial Application (CTA) and, in attempting to resolve this issue, we commend the work of the Road Map Initiative⁴. We suggest that the European Commission should support further discussion based on the outputs from the “Single CTA Workshop⁵” and the other ongoing activities of the Road Map Initiative but, as we describe subsequently, FEAM is not in favour of setting up new centralised assessment bodies.

It is very important to ensure that any changes to the processes for regulatory or ethical review for multinational trials do not, inadvertently, increase the burden on trials organised within a single Member State.

There have been major adverse impacts since the introduction of the CTD in terms of increasing administrative costs for clinical trials and causing delays before recruiting patients, as quantified in the ICREL report. Because these impacts have been felt in most Member States, we conclude that they are a direct consequence of the CTD itself relating, for example, to the requested double approval, Investigational Medicinal Product Dossier (IMPD) and safety reporting requirements as well as partly attributable to variable Member State implementation approaches. Further problems have arisen because of the lack of clear definition in the current legislation for some terms and procedures.

We are aware that some Member States do not use their resources efficiently insofar as

they impose multiple assessments of protocols that may lead to contradictory as well as burdensome implications for researchers. In some Member States, there are multiple assessments of a single study by different Ethical Committees and other (governmental/hospital) organisations, who may ask for different information and provide different advice. These Member States could use resources more efficiently by simplifying and minimising their demands for duplicate review.

Among the main issues that cause difficulties for researchers, particularly in IDCT, are the following:

2.1 Insurance

Variability in Member State insurance arrangements is a particular problem. This variability is associated with increased bureaucracy and costs without a beneficial impact on quality of science or safety. We suggest that the community should aim for consistent risk-based insurance conditions throughout a multinational trial.

Among the possible options for change proposed by other groups are the creation of a not-for-profit insurance organisation for clinical trials and exploration of the feasibility of insuring studies through the national public health systems in all Member States. However it is vital that care is taken not to introduce further unnecessary bureaucracy. Because of the complexity of the current situation and the need to create a better system that is flexible enough to cover insurance needs for both national and international trials, we

⁴ A Road Map Initiative for Clinical Research in Europe”, October 2008, www.efgcp.be

⁵ A multidisciplinary workshop on “A single CTA in multinational clinical trials – dream or option?” was held in July 2009 and the report has been published on www.efgcp.be



endorse the proposal by the European Science Foundation (ESF)⁶ to constitute a multinational task force of experts with a mandate to advise on how to harmonise insurance requirements.

Other variations in Member State interpretation and definitions also cause inefficiencies and complexities in operationalising trials. Two significant operational difficulties relate to the processes for making Substantial Amendments and for reporting SUSARS (Suspected Unexpected Serious Adverse Reaction).

2.2 Substantial Amendments

There must be much more clarity in definition and interpretation between countries but this must also be accompanied by a re-assessment and an extensive reduction to what is submitted as an amendment for approval so as to focus on what is truly a substantial change. The sponsor's responsibility to judge what is truly substantial for the protection of study participants should be strengthened. We welcome current efforts by the European Commission to increase clarity⁷.

2.3 SUSARS

We do not believe that the current complex situation – characterised by variability between Member States in definition and reporting – helps to improve patient safety. There is a false sense of security in maintaining the current system, partly because those SUSARS reported to EudraVigilance are not then acted on. We recommend that a common definition of SUSARS is used in all countries but, even more importantly, that a system is created

where the SUSARS are entered by the sponsor into EudraVigilance with a copy sent to one responsible body (together with the study coordinator/Principal Investigator) who act on SUSARS alerts, cascading the information to others, as appropriate. This means that in a multinational trial, one NCA (e.g., the sponsor's country) should be given the responsibility to act for all Member States, irrespective of the location of the SUSARS, instead of the present system where the NCA generally sees its role as only applicable to its own Member State. To be successful, this increased responsibility must be accompanied by better capacity for safety signal detection (methods to provide an early indication of potential adverse events) and appropriate Information Technology (IT) tools should be developed to allow the competent authorities to evaluate SUSARS, per study, per drug, per therapeutic area, and per country. Moreover, in the present system, SUSARS are reported to Ethics Committees, who do not act on this information. It would be better for the Ethics Committees to receive only the annual safety report and be aware that the NCA is discharging its responsibility to act on SUSARS.

The unnecessary burdens on researchers dictated by excessive reporting of Substantial Amendments and SUSARS do not improve patient safety. In fact safety outcome may be undermined because the committees that assess the reports are overloaded with reportable data. Safety is further undermined because one consequence of the increasing costs of applications for academics and smaller companies (evidence presented in ICREL report) is a limitation on affordable trial size and, hence, the study power and ability to detect side effects.

6 Report from the European Science Foundation, 2009 "Forward Look. Investigator-driven clinical trials" on www.esf.org. Further analysis of the issues and identification of options for improving the insurance framework is also being taken forward in an EORTC-organised workshop (June 2010).

7 Some clarification is already available in the Communication from the Commission 2010/C 82/01 (March 2010).

3

Reforming National Competent Authority roles for multi-national studies

Approximately 70% of clinical trials are currently based within a single Member State. It is vital not to introduce further changes that will increase the bureaucratic burden and cost of these national trials. Researchers in a single or national multi-centre study centre should apply, as now, to their NCA for robust national approval.

FEAM fully supports streamlining of the assessment process for multi-national trials. The current system of voluntary cooperation (Voluntary Harmonisation Procedure - VHP) would be valuable if it could be comprehensive. This may be difficult to institute in practice as we note that some Member States are already opting out, but it is worthwhile continuing to explore feasibility. The system could be improved in two ways: (a) Reducing the number of requested reviewers to avoid duplication of effort in all Member States who are involved; mutual recognition of the review would have to be ensured; (b) Acceptance of the same submission dossier by all Member States to avoid the need for individualisation of the subsequent national submission dossiers.

If, after further evaluation, it is concluded that the VHP cannot be made to work satisfactorily, an international multi-centre study would proceed via a reformed procedure.

FEAM recommends that the creation of a new centralised assessment body should be avoided. Our preferred option is the formalised “common agreement” whereby a designated lead NCA reviews and approves the project (usually the NCA in the country of origin of the trial) while other NCAs provide expedited approval. If, in the longer term, there are pressures for a wholly centralised route for a multi-national study, then this option should be rigorously piloted in selected therapeutic areas, perhaps those requiring particularly complex scientific expertise, and taking into account current best practice from individual Member States.

Regardless of the assessment mechanism, what does need to be achieved in any community-wide streamlining process is that the responsible bodies must appoint rapporteurs on the criterion of appropriate expertise rather than seeking to achieve geographical balance in distribution of tasks. Both the ESF report and Road Map Initiative provide further guidance on what is needed if streamlined assessment is to succeed and we recommend that the European Commission, together with experienced organisations such as the European Organisation for Research and Treatment of Cancer (EORTC) and its partners in the Road Map initiative, facilitates further discussion based on these analyses. FEAM and its member Academies are very willing to participate in this further discussion.

4

Reforming Ethics Committee roles

FEAM also supports the streamlining of the function of national Ethics Committees to improve their efficiency and to work towards common approaches. Furthermore, it is vital that researchers and ethical reviewers appreciate that they share a common goal in facilitating research conducted in an ethical manner, by contrast to some current perceptions where researchers view Ethics Committees as an impediment to research.

The roles and responsibilities of the Ethics Committees should be clarified and there should be better coordination between them and NCAs. Ethical review should proceed in parallel with regulatory review, but this is not currently the case in some Member States. We believe that the alignment of information reviewed by the Competent Authorities and Ethics Committees will drive other improvements and enable technology-driven review.

We doubt that it will be easy to strengthen networks of national or even establish functioning pan-European Ethics Committees as there is little present basis for doing this and there is still considerable variation in practice among the Member States. We agree, however, that benefits would come from greater consistency across Europe and that better organisation and accreditation of Ethics Committees within each Member State is an important first step. There are opportunities now for improvement and standardisation of Ethics Committee working practices, for example, in use of electronic review, development of an agreed template for managing the process of obtaining informed consent to research, and introduction of education and training programmes for all Ethics Committee members.

A good case can also be made for all Member States developing their own centralised Ethics Committees with more expertise, necessary to provide the robust review of more complex trials using advanced therapies (such as gene therapy, stem cell-based therapy, device-therapeutic combinations, clinico-genomic studies in cancer). We doubt, however, that it will be feasible or desirable in the foreseeable future to create a system where there is a single Ethics Committee review for multi-national trials. This is because there are differences between Member States in ethical views on fundamental research areas, for example, embryonic and stem cell research, as well as in the review procedures, and any unifying system would need to take account of these differences.

In the longer term, those centralised Ethics committees within Member States, with demonstrable expertise might be allowed under a mutual recognition system to take a lead in a pan-European review of multinational study protocols, but accompanied by national ethics review of the local issues - that is the investigator, site and information for patients - for each participating Member State. If this model of ethical review were to be developed, it is essential that it is first piloted, rigorously evaluated and based on current best practice from individual Member States. We advise that there is need for further discussion and, as a first step, the European Commission should work with its partners from the scientific community to lay out the options for change.

8 For example, current variation is documented in: AA Schnitzbauer et al, Procedures for ethical review for clinical trials within the EU, *BMJ* 2009 338b1893; R Hernandez et al, Harmonisation of ethics committees practice in 10 European countries, *J Med Ethics* 2009 35 696-700

5

Adopting a risk-based approach in clarifying the scope of the CTD

It is very important to clarify the scope of the CTD, for example to agree the definition of “non-interventional study”, together with more consistent application of guidance relating to what is covered. It is crucial to retain academic sponsors within the scope of the CTD. There must be one conceptual framework, one standard of uniform quality for patient protection.

We acknowledge that some are also calling for further discussion of the longer-term options for changing the scope of the CTD. Already, national law in some Member States has implemented the CTD with a scope broader than trials with medicinal products only, but there is still often lack of clarity in these cases. Furthermore, in some Member States in consequence of the CTD excluding Competent Authorities from reviewing some categories of research, Ethics Committees take on a lot of responsibility for reviewing non-drug trials, for which they are not qualified. However, any increase in formal scope of the Directive can only be contemplated after reform of the CTD is agreed and successfully implemented to introduce a proportionate, risk-based approach. We advise those who are thinking about extending the scope that there are many different types of clinical research and there is need for much further discussion about the implications for that research. It is important to retain flexibility in research if any proposals were to be made to expand the scope of the CTD.

In the current system the requirements set by the CTD are not commensurate with the expected risks. **This weakness is central to the current problems.** We strongly recommend a more differentiated system in terms of risk, although we recognise the difficulty in agreeing a robust classification of risk. The strategic outline of risk

categories in interventional studies has been produced by ESF and by the Road Map Initiative. For example, the Road Map Initiative proposes a framework of categories based on marketing authorisation status although the boundaries are debatable and marketing authorisation can be regarded as a surrogate marker for the amount of quality data available on the intervention. In addition to the further work needed to define the level of intervention associated with each risk category, it is important to be clear on who proposes the risk level for a new study (assumed to be the sponsor) and who validates this assignment (assumed to be NCA or Ethics Committee). We advise that further discussion is needed to clarify the options for developing a risk-based approach and the criteria to be used in establishing a system that is flexible enough to accommodate different types of research.

We also advise that there must be a focus on benefit-risk rather than safety alone. Elucidation of risk categories requires much more analysis and sharing of perspectives and we recommend that the European Commission stimulate further discussion on the nature of the risk involved in different types of study and on the implications for risk-based governance of research. In particular, to determine what would be the consequences for a research study in terms of ethical review, intensity of monitoring, safety reporting, insurance requirements, quality assurance and other issues for study medication provision, commensurate with its assessed risk.

The regulatory burden on low-risk trials must be decreased. We suggest that studies viewed as minimum risk would require only Ethics Committee oversight (assuming that Ethics Committees are standardised and accredited as described previously), for example, where the risk involved is similar to that of “usual care”.

6

Other key issues

6.1 Sponsorship

While there had been initial concern expressed from the academic sector about the challenges inherent in acting as a single sponsor for a multinational study, it now seems that the problems may not be so formidable⁹.

Nonetheless, we urge consideration of a flexible system which permits multiple (co-) sponsors¹⁰: the UK has already interpreted the CTD to achieve this situation. We recommend that a multi-sponsor system should be based primarily on functionality, that is involving different sponsors, where appropriate, for functions such as protocol construction and data collection. It is also important to clarify sponsorship under conditions where the funder of the trial is different from the operational management: it should be made very clear that the sponsor should have operational management responsibility which includes ensuring adequate funding for the trial from whatever source. Instituting a multi-sponsor system requires clear definition and agreement of responsibilities, defined in a contract and recognising that there will always be joint liability. It would be helpful to have available a standard EU contract template for co-sponsored trials and a summary of the current practice in sponsorship in every Member State.

At the same time, it is necessary to build academic capacity to act as a sponsor – this has implications for researcher education, training

and funding. The ESF report offers detailed suggestions for what kind of support should be provided to academic institutions who act as sponsors.

6.2 Special research populations

6.2.1 Paediatrics research

FEAM strongly supports the encouragement of good quality paediatric research and such encouragement is more likely if it is not automatically assumed that the research will fall into a higher risk category. In addition, however, support for paediatric research requires public funding and the EU could learn from the initiatives of the NIH in the USA and the Programme Priority Medicine for Children in the Netherlands to encourage this area.

6.2.2 Emergency research

Similarly, FEAM supports good quality research in emergency situations and we recommend the development of guidelines to incorporate the current best practice that allows research in defined circumstances with request for patient consent subsequently as soon as is practically possible. There is one particular point that needs to be clarified – whether or not study-related data must be withdrawn if the subject does not consent subsequently (this may have implications for the Data Protection Directive).

⁹ Roadmap Initiative multidisciplinary workshop on “Innovative approaches to clinical trial co-sponsorship in the EU” was held in September 2009 and the report has now been published on www.efgcp.be

¹⁰ There is another alternative – a single sponsor with delegating powers to share responsibilities. This option was discussed in detail in the final workshop of the Road Map Initiative (March 2010, www.efgcp.be).

6 Other key issues

6.2.3 Other particular research designs

FEAM notes three other clinical areas where research is difficult in some Member States:

- First, research using radioactivity (for example, imaging studies) – where there are accepted international norms which need to be taken into account by all Member States.
- Secondly, research using controlled drugs (those substances that are addictive or liable for mis-use and are subject to specific national regulation), where we recommend that conditions (including insurance requirements) across the EU should be harmonised according to current best practice.
- Thirdly, research in mental health disorders where there are particular challenges, for example in obtaining patient consent to participate under conditions where there may be fluctuating ability to consent. Lessons learned in initiatives in some Member States to encourage such research should be shared across the EU. A broader analysis of mental health policy issues, including the support of research, will be published by FEAM later in 2010.

7

Procedural options for change

There is no substitute for a full review of the CTD. Lesser options run the risk of returning to a scenario where there is no harmonisation, core process or common documentation. In our view, there must be both short-term action, in modifying guidelines to improve the current environment as far as is possible, together with changes to the CTD to ensure long-term sustainability of an improved system. The early review of guidelines requires clarity in definitions as discussed previously. Clear guidelines with definitions and examples would enable NCAs, first, to determine whether a trial is covered by the CTD and, secondly, to ensure that requirements are proportionate to the risk involved. Guideline review must take into account the need to make them sufficiently compelling so as to enable similar practice within a short period of time in all Member States, even if this requires changes to national legislation and ordinances. For revision of guidelines to be effective in the short term, we consider that there is a major concomitant responsibility for those Member States who are most experienced in clinical research to provide leadership to ensure the supportive environment for trials. This has implications for availability of resources and for legislation in some Member States.

FEAM does not ask for a Regulation to govern the changes detailed elsewhere in this Statement. But to expedite CTD reform, we do ask that the European Commission now organises regular meetings on the key issues to be addressed and involves the European Parliament at the earliest opportunity. FEAM reiterates its willingness to be involved and we anticipate that the newly acquired responsibility of DG Sanco for pharmaceutical policy will facilitate these discussions. While we seek CTD revision as soon as possible, it is vital to introduce well-conceived and relevant changes so we acknowledge that significant further debate is needed.

At the same time, further thought should also be given to other ways of streamlining the organisation and monitoring of trials in the EU. A case can be made for developing academic Clinical Research Organisations (CROs) to improve the quality of trial conduct and monitoring (and to save costs). FEAM will encourage its member Academies to explore what role they might play in stimulating the development of academic CROs and in identifying other options for streamlining monitoring. For example, greater emphasis might be placed on central statistical monitoring of trials coupled with targeted site visits rather than the current practice of frequent, routine site visits.

8

Building the European clinical research environment

It is necessary for public policy-makers to do more than reform the existing legislation, highly important though that is, if the European clinical research environment is to be sufficiently improved. Creating a strategy for this improvement requires further discussion across several Directorates-General. FEAM intends to catalyse further discussion on the wider issues during the next year. Among these key issues are:

- It is vital at both EU and national levels to increase funding for clinical research and its infrastructure and to explore opportunities for joint programming. For example, we suggest that the scope of the European Research Council might be extended to include translational and clinical research.
- It is also important to support approaches to interdisciplinary working across the research spectrum and to find ways to build and sustain research partnerships between academia and industry in order to address capacity and competency issues for the research enterprise and translational medicine. The independence of the academic researcher in such partnerships must be maintained and may need to be strengthened, for example in research agenda priority-setting.
- Development of new research capacity must be accompanied by better understanding of the skill sets necessary for clinical research. This requires new initiatives in education and training, particularly to support clinical academic career pathways and mobility between the public and private research sectors.
- It is important, building on the proposal in the FEAM 2004 Statement, to develop integrated clinical trial databases that register all research, not just commercial studies involving Investigational Medicinal Products (IMPs). This may well not need new clinical registration databases but, rather, more coherence and coordination for the existing databases (including EUDRACT) and extending the scope to include, for example, observational clinical studies¹¹. We ask the European Commission to take a lead in instituting global discussion to rationalise the reporting. Furthermore, databases should, in due course, provide the results from trials for access and use by all researchers, but it should be appreciated that the results from long, complex studies may take a number of years to complete. It should also be taken into account that academic research data may have economic value for healthcare providers and subsequently for companies (including Small and Medium Enterprises (SMEs) that spin out from the academic research group); it is important that intellectual property and data protection issues be considered further when designing databases that provide access to research results.
- Finally, the academic clinical research community must ensure that it has early awareness of impending EU policy/legislative developments (for example, currently, Directives that will be relevant to the governance of cell and tissue engineering). FEAM and its member Academies acknowledge that they share the responsibility to alert the research community to developments in regulatory frameworks that either intentionally or inadvertently impinge on research.

11 E Loder, T Groves & D MacAuley, Registration of observational studies, *BMJ* 2010 340, 375-376

Appendix: FEAM procedures and Contributing Individuals

This FEAM statement draws on material provided previously in the FEAM response (January 2010) to the European Commission's Consultation on the Functioning of the Clinical Trials Directive. A FEAM Working Group met in November 2009 and drafts of the present Statement were discussed by Working Group members and Academy reviewers during the period January-March 2010 with final comments contributed during a FEAM meeting in Bucharest (March 2010).

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