

Experiences from the first year working in the new regulatory environment: Central Europe

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Central Europe



New member states in Central Europe



Current Status

- All New Member States in Central Europe have officially implemented the new EU directive 2001-20-EC

In preparation of joining the EC, most of them had already adopted relevant parts of the directive as part of their local drug law

Current Status

- The „Detailed guidance for the request for authorisation of a clinical trial on a medicinal product for human use to the competent authorities, notification of substantial amendments and declaration of the end of the trial“ defines the format and content of applications in the new member states.

Detailed Guidance

INFORMATION REQUIRED	CY	CZ	EE	HU	LV	LT	MT	PL	SK	S
CORE INFORMATION										
Receipt of confirmation of EUDRACT number		Yes	Yes		No	Yes				
Covering letter		Yes		Yes	Yes	Yes				
Application form		Yes	Yes	Yes	Yes	Yes				
Protocol with all current amendments		Yes	Yes	Yes	Yes	Yes				
Investigator's brochure		Yes	Yes	Yes	Yes	Yes				
Investigational Medicinal Product Dossier (IMPD)		Yes	Yes	Yes	No	Yes				
Simplified IMPD for known products. See table 1		Yes	Yes	Yes	No	Yes				
Summary of Product Characteristics (SmPC) (for products with marketing authorisation in the Community)		Yes	Yes	Yes	Yes	Yes				
List of Competent Authorities to which the application has been submitted and details of decisions		Yes	Yes	Yes	Yes A	Yes				
Copy of ethics committee opinion in the MS concerned when available		Yes	Yes	No	Yes	Yes				
ADDITIONAL INFORMATION FOR SPECIAL SITUATIONS										
If the applicant is not the sponsor, a letter of authorisation enabling the applicant to act on behalf of the sponsor		Yes		Yes	Yes					
Copy of authorisation for contained use release of genetically modified organisms (when applicable and available)		No		?						
MS SPECIFIC INFORMATION										
Subject related										
Informed consent form		Yes	Yes	Yes	Yes	Yes				
Subject information leaflet		Yes	Yes	Yes	Yes	Yes				
Arrangements for recruitment of subjects		Yes	No	Yes	No	Yes				
Protocol related										
Summary of the protocol in the national language		Yes	No	No	No	Yes				

Experience in Central Europe

	Poland	Czech Republic	Slovak Republic	Hungary
Submitted	2 none as applicant	4 2 as applicant	3 2 as applicant	2 1 as applicant
Approved	1	2	2	1
Started	1	2	1	1
Finished	1	-	1	-

Experiences with the New Directive (Poland)

- Poland has not finalised guidance documents on the format and extend of the application package.
- Based on verbal information this guidance is just pending signature of the Ministry of Health
- The Polish health authority has adopted a 60 day review period and has complied to this period in our trials

Experiences with the New Directive (Czech Republic)

- SUKL has defined format and content of the application package.
- Guideline KLH-20 replace guidelines KLH-7, KLH-14 and paragraphs 1 and 2 of guidelines KLH-19 as of 1 May 2004 (available in English)
- Regular meetings with Q&A sessions between the authority and parties involved in clinical trials guarantee flow of information

Experiences with the New Directive (Czech Republic)

- The official review period defined by law is 60 days and it was kept in all of our cases
- Internal benchmarks are shorter than the official 60 day review period
- Applicants are given a five day reply period to the deficiency letter
- Informal information is provided to local applicants before submission of the official deficiency letter

Experiences with the New Directive (Hungary)

- Hungary has provided detailed guidance on format and content of the application package
- Verbal information from one of the meetings between the authority and pharmaceutical industry raised expectations about a complete revision of the Hungarian drug law, which involves the clinical trial application as well
- The 60 day review period was kept in all instances

Experiences with the New Directive (Slovak Republic)

- Slovak Republic has not yet implemented detailed guidance on format and content of the application package.
- The Slovak application form has been reviewed and accepted by the European authority
- A written guidance document is under preparation and will basically require a similar amount of information than the Czech guideline

Experiences with the New Directive (Multi-National trials)

- One of the trials performed was a multinational trial involving centres in the UK, Czech Republic, Slovak Republic and Hungary.
- Applications after May 2004 were performed in the UK, Slovak Republic and Hungary.
- After preparing the IMPD for one centre in the UK, compiling of documents for the other centres was rather quick and unproblematic

Experiences with the New Directive (Ethics committees)

- All of the New Member States have implemented a structure of local (single-centre) and multi-center ethics committees
- As in other European member states, no uniform way of operation has been established
- All of the national ethics committees still need their own application forms, which are remarkably different from the EudraCT forms

Other Experiences and Recommendations

- Implementation of the European directive has caused many structural changes in pharmaceutical industry as well
- In some of the companies central departments now take care about EU applications
- Authorities are only obliged to provide information to the official applicant. Consequently the official applicant should be the party, who needs direct access to the authority, I.e. the CRO or Investigator

Other Experiences and Recommendations

- Involve local representatives of CRO or company as early as possible as they are familiar with local requirements not defined in writing
- In some of the countries contracts with the hospitals and the investigators have to be submitted to the authority already together with the CTA. This extends the time period needed to compile the CTA but saves time later on.
- Be aware: often the review period of the authority is not the time limiting factor

Conclusions

- Before May 1, 2004, pharmaceutical industry had to deal with 25 different laws; now we have to deal with 1 law and 25 different interpretations.
- Major achievement of the directive is that competent authorities are now speaking together which they did not in the past.
- Vision: this intensified communication might lead to 1 law and 1 interpretation in a couple of years time