Agenzia Italiana del Farmaco

AIFA

SUBJECT: New AIFA Information Systems and obligations relating to Clinical Trials

As of 1st January 2013, the Italian Medicines Agency (AIFA) will begin the implementation phase of an innovative new Information System to enable total integration of all AIFA systems via the creation of a Knowledge management which will allow optimal efficiency of all processes to be achieved.

The new system, which is intended to automate all the administrative/accounting and technical/health care flows, will allow simplification of procedures, optimisation of resources and continuation of the process begun by the Agency towards greater administrative transparency.

All the information services the Agency is already using will come together within the new infrastructure. This will allow the highest achievable level of integration, both for internal information sharing and possible interfacing with external systems, particularly those accomplished in accordance with the European Medicines Agency (EMA) standards.

Movement to the new system will require a transition phase for migration and reorganisation of documents, data and services, during which AIFA applications currently in use will not be operational.

In particular, as regards the use of the Osservatorio Nazionale sulla Sperimentazione Clinica [National Monitoring Centre on Clinical Trials], the Register of Observational Studies and the Clinical Research Portal, the movement to the new system will require a transition period of a few months.

To ensure that activities are continued during that phase, detailed instructions are being provided for transmission of documentation, as required by existing law.

In addition, to facilitate users' work, forms of the main appendices to the Minister of Health Decree of 21st December 2007 giving "Directions for submitting the request for authorisation of a clinical trial on a medicinal product for human use to the Competent Authority, for communicating substantial amendments, for declaring the end of the trial and for the request of an opinion to the Ethics Committee" and forms related to the Register of Observational Studies will be published in "word" format on AIFA's Portal.

Please be informed that starting on 1st January 2013, access to the web services of the Osservatorio Nazionale sulla Sperimentazione Clinica dei Medicinali (OsSC) and of the Register of Observational Studies (RSO) will be temporarily suspended for the following users: AIFA, Italian National Health Institute (Istituto Superiore di Sanità), Sponsors, Contract Research Organisations, Service providers other than CROs that use the RSO, Ethics

Committees, Regions and Autonomous Provinces. In addition, also as of 1st January 2013, public content of the Clinical Research Portal will not be available. AIFA will timely publish operational details on how the temporarily suspended services will be restored.

The documentation that must be transmitted during the temporary management period is listed below.

Interventional trials: communications and notices to be sent by Sponsors or delegated CROs

Table 1

Document and legal citation	**Party responsible for sending the document**	**Temporary management**
Clinical trial application (CTA form) Appendix 5 to DM [Ministerial Decree] of 21st December 2007, as amended	Sponsor or CRO delegated by the sponsor (hereinafter "applicant")	Send to AIFA in hard copy and CD ROM format (1 hard copy + 1 CD ROM). *Note: the CD ROM sent to AIFA must also contain the Clinical Trial Application form in "xml" format (see also the following section of this document).* Also send in hard copy and CD ROM format to ISS [National Health Institute] for phase I studies (for information, please contact the phase I Commission: segreteria.commac@iss.it). Send in hard copy format (up to 5 copies) and 1 copy in electronic (e.g. CD ROM) to the Ethics Committees involved.
Documentation attached to the clinical trial application (document list Ia or Ib) Appendix 5 to DM of 21st December 2007, as amended	Applicant	
Withdrawal of the clinical trial	Applicant	Hard copy notification to AIFA and to the Ethics Committees involved. *Note: withdrawal is applicable only in the event that the hard copy application was sent to the Ethics Committee responsible for the single opinion and/or to AIFA and it is still in the initial evaluation phase.*
Substantial amendments to the clinical trial and supporting documentation DM of 21st December	Applicant	Send in hard copy and CD ROM format to AIFA (1 hard copy + 1 CD ROM). *Note: the CD ROM must also contain the Clinical Trial Application*

2007 and Appendix 9 to the DM.		*form in "xml" format, if modified by the amendment (see also the following section of this document).* Also send in hard copy and CD ROM format to ISS, for phase I studies. Send in hard copy format (up to 5 copies) and 1 copy in electronic (e.g. CD ROM) to the Ethics Committees involved.
Declaration as to the trial starting and end in each site DM of 21st December 2007, Appendices 10 and 11	Applicant	Send, only if requested, in hard copy format to AIFA and/or to the Ethics Committee.
Declaration of the end of the trial DM of 21st December 2007, Appendix 12	Applicant	Send in hard copy format to AIFA and to the Ethics Committees involved within 90 (regular end) or 15 days (earlier end)
Results of the clinical trial DM of 21st December 2007, Annex 2, paragraph 6.3	Applicant	Send in hard copy format to AIFA and to the Ethics Committees, within 12 months of the end worldwide.

Interventional trials: obligations relating to the EudraCT European database

To create the XML file to be sent to AIFA, the applicant is required to access the EudraCT's public website, https://eudract.ema.europa.eu/, click on the link "*Access to EudraCT*" in the vertical menu on the left and then create the file using the link "*Create*", "*clinical trial*" and "*EEA*".
Once all the fields in the CTA are completed, the file can be created and saved in "xml" format using the "Package" command on the horizontal command toolbar. At the end of the process, click the "Create Submission Package for National Competent Authority" button and save the file as a "ZIP" file.

EudraCT contacts and compilation guides in English are available at the address https://eudract.ema.europa.eu/help/Default.htm#eudract/contact_us.htm

Table II

Sending information to EudraCT / EU Clinical Trials Register	**Party responsible for sending the document**	**Temporary management**
Initial Clinical Trial	Applicant	One copy of the information

Application form		relating to the clinical trial in Italy, in English, must be sent to AIFA when the initial application (Clinical Trial Application) is submitted.
Clinical Trial Application form, if modified following an amendment	Applicant	One copy of the information relating to the clinical trial in Italy, in English, must be sent to AIFA when the substantial amendment is submitted.

Interventional trials: communications and notices to be sent by Ethics Committees

Table III

Document and legal citations	**Party responsible for sending the document**	**Temporary management**
Single Opinion Appendix 6 to DM of 21st December 2007, as amended; Legislative Decree no. 211/2003, article 7	Ethics Committee	Send in hard copy format to AIFA, to the other Ethics Committees participating in the clinical trial and to the applicant. Transmission: within 30 days of the receipt of a clinical trial application in the prescribed form. The communication must be sent within 60 days for a mono-centre clinical trial.
Acceptance / Refusal of the Single Opinion Appendix 8 to DM of 21st December 2007	Ethics Committee	Send in hard copy format to the applicant within 30 days of the receipt of the single opinion. Send in hard copy format to AIFA, only upon request.
Ethics Committees' opinions on substantial amendments DM of 21st December 2007, article 8, paragraph 4; Legislative Decree no. 211/2003, article 10.	Ethics Committee	Coordinating Ethics Committee: send in hard copy format to the Applicant and to AIFA* within 20 days. Ethics Committee that gave the single opinion for a mono-centre clinical trial: send in hard copy format to the Applicant and to AIFA* within 35 days.

		**AIFA should not be sent opinions expressed as to matters exclusively relevant to the Ethics Committee: information to subjects, facilities and staff and financial questions, as detailed in list Ia – Appendix 5 to DM of 21st December 2007* Ethics Committee of the collaborating sites: send in hard copy format to the Applicant within 15 days of the coordinating Ethics Committee's opinion. Send, only upon request, in hard copy format to AIFA.

Establishing of a new Ethics Committee

New Ethics Committees must send their resolutions of establishing (in hard copy format) to the relevant Regions/autonomous Provinces (Health Department), which are responsible for validating them and verifying that the information from each new Ethics Committee meets the minimum requirements under current applicable law (DM of 12th May 2006 and law 189/2012 converting decree law 158/2012).
A copy of the form containing the "General data relating to an Ethics Committee established pursuant to DM of 12th May 2006", all parts of which have been completed, as well as all information relating to the members (Forms 1 and 2, attached – in Italian) must be attached to the resolution.

Please note that until Regions/autonomous Provinces do not successfully validate the new Ethics Committees through a formal document, they are unaccredited and thus may not begin evaluating clinical trials.

Following the (positive or negative) outcome of the validation, the relevant Regions/autonomous Provinces must send to the AIFA e-mail address sperimentazione.clinica@aifa.gov.it:

- a copy of the resolutions of establishing
- a copy of the completed form with all data regarding the Ethics Committee, its members and the head of its technical/scientific secretariat
- a copy of the regional/provincial official document validating the Ethics Committee

Already existing Ethics Committees

Any change to the general data of an already existing Ethics Committee, as well as resolutions updating its composition (reappointments, resignations and/or replacement of members, etc.) or an Ethics Committee's ceasing its activity must be sent in hard copy format to the relevant Region/autonomous Province and via e-mail to AIFA, with the related file attached in pdf or image format, to the address: sperimentazione.clinica@aifa.gov.it.

Interventional trials: communications and notices to be sent to the Regions where the clinical trial is conducted by applicants and Ethics Committees

In accordance with the provisions of article 11 of Legislative Decree no. 211 of 24th June 2003, the Regions and autonomous Provinces access, via the Osservatorio, the information about all clinical trials conducted in the region, including data relating to the Ethics committee's opinion, the commencement, any early end and regular end of the clinical trial, as well as data relating to the results obtained and the reasons for any discontinuation of the clinical trial. This method ensures that the sponsors' obligations to transmit the data to the Regions and autonomous Provinces under the above-cited article 11 have been satisfied.

Therefore, the sponsors, the delegated CROs and the Ethics Committees are required to transmit a single copy of the same information under Tables I and III above to the Regions where the clinical trial is conducted.

Register of Observational Studies

The Register of Observational Studies (RSO) will be temporarily inaccessible as of 1st January 2013; applicants and Ethics Committees continue to operate according to the Guidelines for the classification and conduct of observational studies with drugs (AIFA Determination of 20th March 2008).

The following table lists the information, contained in the RSO web site, to be sent to AIFA by the e-mail address info_rso@aifa.gov.it. To facilitate the users' work, a "word" format version of the required forms will be published on AIFA's Portal.

Observational studies with drugs: communications and notices to be sent by Sponsors or Applicants (CROs or service providers other than CROs self-certified pursuant to DM of 15th November 2011)

Table IV

Information to be sent	**Party responsible for sending the document**	**Temporary management**
Initial registration of the study	Sponsor or CRO or service provider other than a CRO (hereinafter "applicant")	Send to the AIFA e-mail address info_rso@aifa.gov.it
Starting of the study	Applicant	Send, only upon request,

		to the AIFA e-mail address info_rso@aifa.gov.it
End of the study	Applicant	Send to the AIFA e-mail address info_rso@aifa.gov.it
Results and publication	Applicant	Send, only upon request, to the AIFA e-mail address info_rso@aifa.gov.it

Observational studies on drugs: communications and notices to be sent to AIFA by Ethics Committees

Information to be sent	**Party responsible for sending the document**	**Temporary management**
Opinion of the Ethics Committee where the coordinating investigator works (only for prospective cohort studies)	Ethics Committee	Send, only upon request, to the AIFA e-mail address info_rso@aifa.gov.it

Clinical Research Portal

The contents of the Clinical Research Portal (http://ricerca-clinica.agenziafarmaco.it/it/node/1) will be temporarily unavailable as of 1st January 2013.

Access to clinical trials being performed in Italy

Public access to clinical trials on-going in Italy (http://ricerca-clinica.agenziafarmaco.it/it/node/331) will be temporarily suspended as of 1st January 2013.

National Register of Ethics Committees

Public access to the National Register of Ethics Committees (http://ricerca-clinica.agenziafarmaco.it/it/node/47) will be temporarily suspended as of 1st January 2013.

National Register of self-certified CROs

Public access (http://ricerca-clinica.agenziafarmaco.it/it/node/50) is temporarily suspended as of 1st January 2013. Self-certification via the Osservatorio (http://ricerca-clinica.agenziafarmaco.it/it/node/12) is replaced by hard-copy certification only, in the following manner:

New self-certification

Send to the Ufficio Attività Ispettive GCP [GCP Inspectorate], Agenzia Italiana del Farmaco, Via del Tritone 181, 00187 Roma (Italia) a hard copy of Annex 1 to DM of 15th November 2011, "Definition of the minimum requirements which Contract Research Organisations

(CROs) shall satisfy in order to work within clinical trials on medicinal products" for CROs headquartered in Italy and Annex 2 to that DM for CROs headquartered outside Italy.

Change of company name and/or notification of change of business

Send to the Ufficio Attività Ispettive GCP [GCP Inspectorate] and Ricerca e Sperimentazione Clinica [Research and Clinical Trials], Agenzia Italiana del Farmaco, Via del Tritone 181, 00187 Roma (Italia) a hard copy of the information required in the Form 3 attached (in English).

Registers of private centres and private laboratories

As of 1st January 2013, the registers of private centres and laboratories that may conduct clinical trials in Italy will be temporarily inaccessible on-line.

http://ricerca-clinica.agenziafarmaco.it/it/node/48
http://ricerca-clinica.agenziafarmaco.it/it/node/49

Private centres and laboratories are required to continue to send hard copies of eligibility verifications and renewals thereof to AIFA, pursuant to DM of 19th March 1998.

Users' registrations

Registration of new users and changes to users who are already registered (http://ricerca-clinica.agenziafarmaco.it/it/node/12) is temporarily suspended as of 1st January 2013.

For any additional information or requests for clarification, please refer to the Italian Medicines Agency dedicated Help Desk available for users via the e-mail address: helpdesk@aifa.gov.it.

AIFA's address

Please use the following address to send all documentation referenced above when required in hard copy/electronic format:

Agenzia Italiana del Farmaco
Ufficio Ricerca e Sperimentazione Clinica
Via del Tritone, 181
00187 - Roma