ESMO Public Policy Webinar:
Clinical Trials Regulation

Rationalising the bureaucratic burden in clinical trials

ESMO Clinical Research Observatory – ESMO Public Policy Group

GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

European Society for Medical Oncology

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October 28th 2021

Rationalising the bureaucratic burden in clinical trials

- Excessive burden of bureaucracy
  - Overinterpretation of regulations
  - Complex procedures
- Patient welfare: Clinical interference
- Conclusions

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Overinterpretation of regulations: Superfluous documents

Guideline for good clinical practice E6(R2)

Step 5

EUROPEAN MEDICINES AGENCY
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1.28. Informed consent

A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed and dated informed consent form.

... Yet , investigators are constantly required to duplicate the documentation process in the medical records (which are not signed by the patient)

Overinterpretation of regulations: Superfluous documents (II)

Request from a study monitor regarding documentation of informed consent in the medical records:

- *"Please (…) **add to the medical records** of patient # 3106002 an addendum to the visit of November 25:*
  - *the version of the informed consent signed by the patient (in our case, **version 8.1** of August 30, 2016).*
  - *That he read it and signed it before performing any procedure of the corresponding visit.*
  - *That he was given enough time to read with confidence the information contained in the patient information sheet*
  - *That he was given the opportunity to ask and all the doubts that had arisen were resolved (or that the patient did not raise any questions or questions, as the case may be).*
  - *That he decided to sign the consent freely and voluntarily.*
  - *That he was given a copy of it."*

Overinterpretation of regulations:
Complex documents templates and procedures

Guideline for good clinical practice E6(R2)

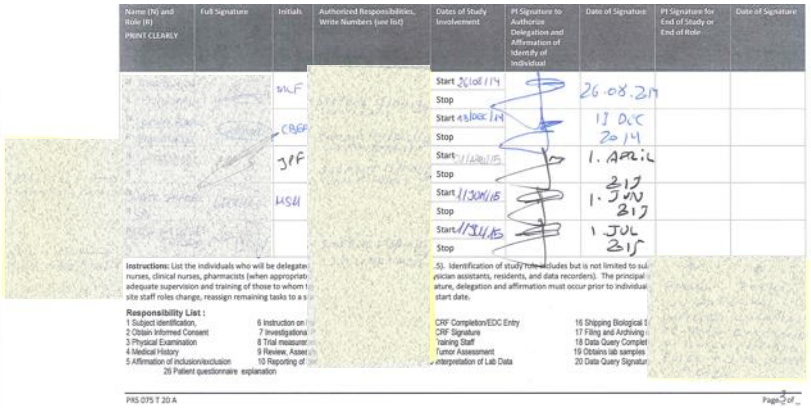
Step 5

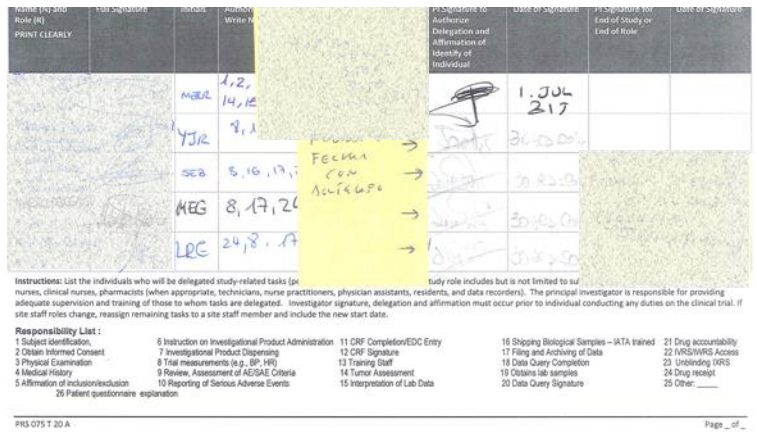
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

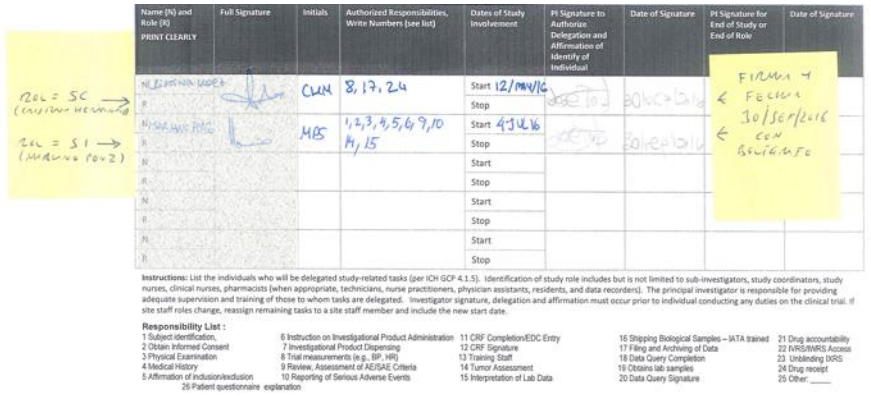
4.1.5.

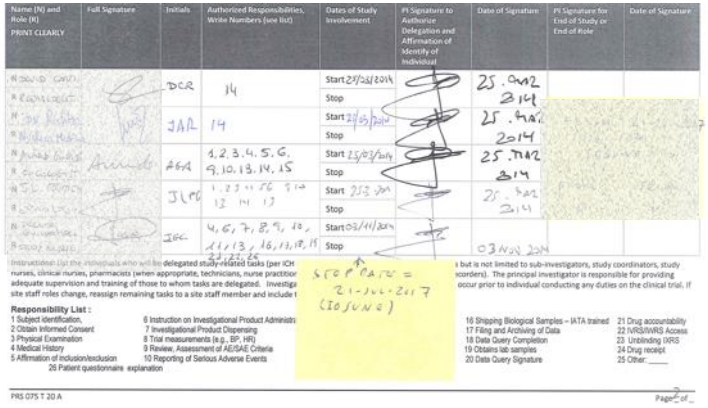
The investigator should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.

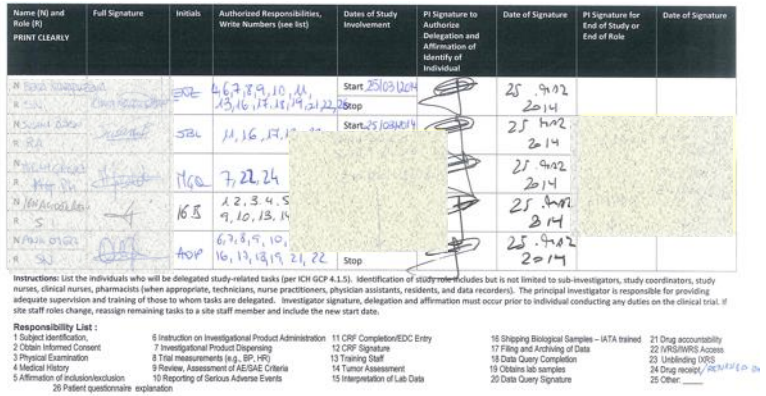
Standard delegation log for a single study

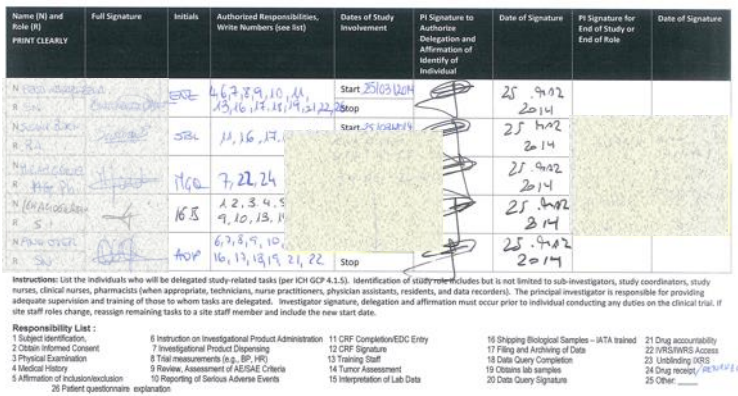




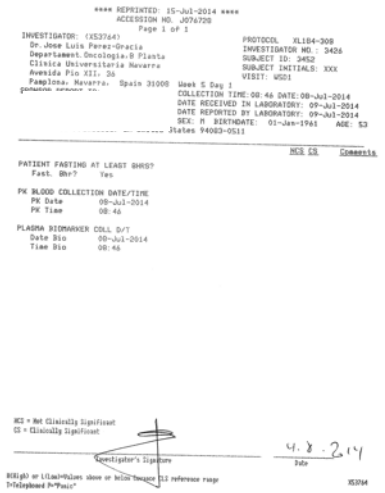


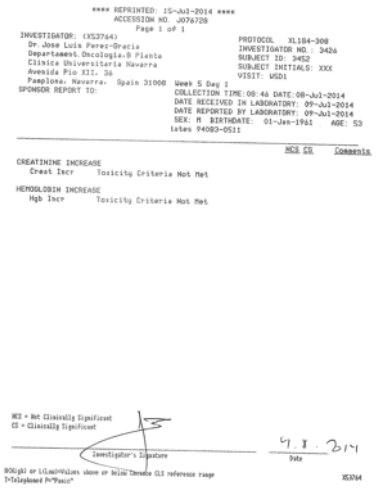


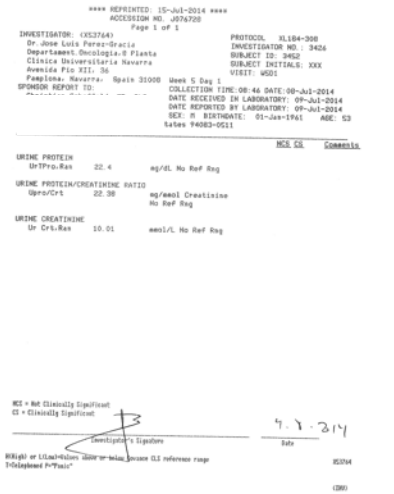


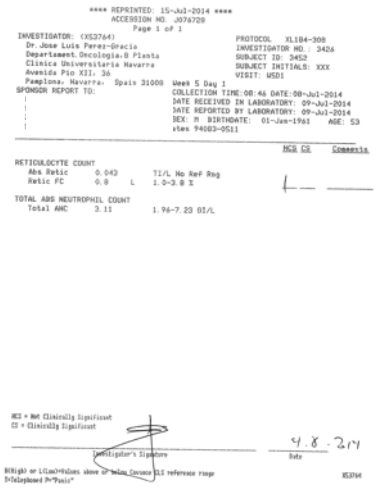


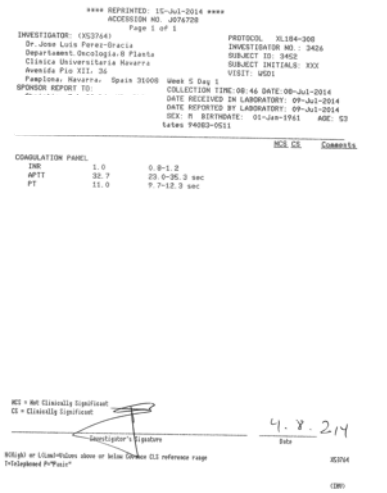
Central lab reports for one single patient and visit

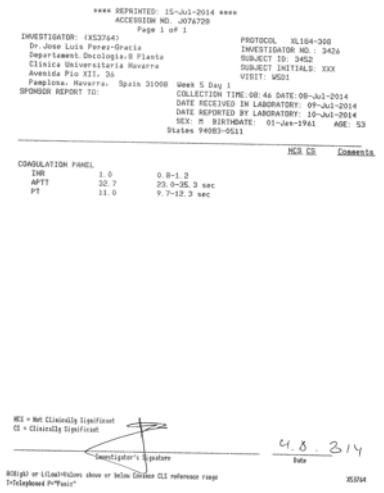












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Investigator Portal

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PAREXEL Safety Information System

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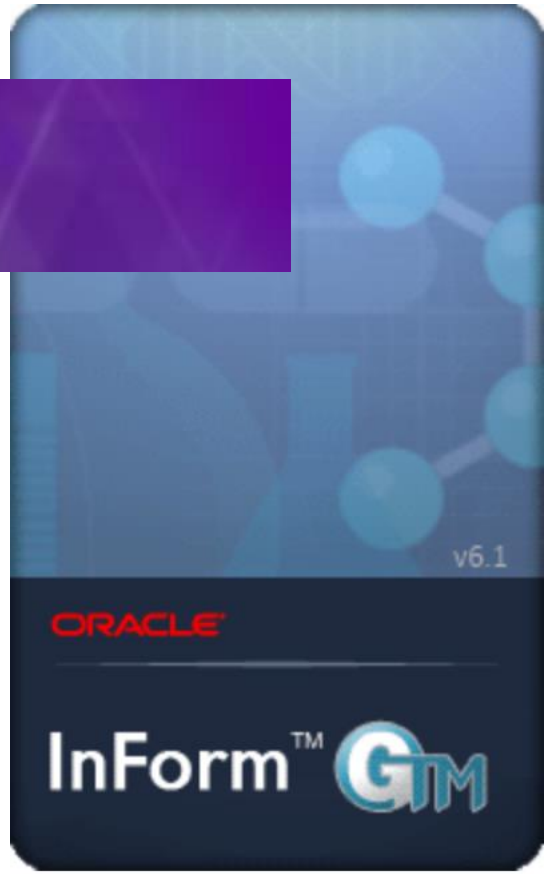


SHARED INVESTIGATOR PLATFORM

ORACLE® RDC Onsite

Cumbersome online platforms: Instructions to reset a password

Dear xxxxxxxxxxxxxxxxxxxxxx

The directions below will permit you to use your current CPAC/myLearning password to verify your identity and create a new password to access InForm.

1. Cut and paste the following URL in your Web browser to access the Password Management application for CPAC, myLearning and InForm: https:// com/password_reset

2. Click on 'Site Users' link on Password Management Application menu page.

3. Enter your current CPAC/myLearning User ID and click the 'Continue' button.

4. At the next screen, select one of the three options to authenticate

    a. Current CPAC/myLearning Password or Activation Code you were emailed by the Helpdesk analyst

    b. Answer personal questions (use this option if you have forgotten your password)

    c. Retrieve and Use Email PIN (Clicking on this option will trigger an email to you with a 4-digit PIN.)

5. Enter information in the authentication screen based on the selection you made and click 'Authenticate'.

6. You are now on Home screen with three options. Click on 'Change Password' option.

7. Select CPAC/myLearning or InForm (depending on which password you need to reset)

8. Enter a new password and confirm it following the on-screen instructions to set up a strong password. For security purposes, your InForm password cannot be the same as your CPAC/myLearning password.

9. Click the 'Change Password' button. When the confirmation page displays, you will see a list of the InForm trials to which this new password applies.

10. The next screen is a confirmation that your password was successfully changed. You will also receive an email letting you know that your password was successfully reset.

11. You can now access CPAC, myLearning or InForm via the URLs available on this final confirmation page.

12. As a reminder, when you logon to InForm, you must enter your USER NAME in UPPERCASE.

Your User ID for CPAC/myLearning and InForm trials remains the same. However, your password for InForm trials is different from your password for the CPAC/myLearning applications.

You can access InForm:
a. By clicking on the hyperlink for the trial listed on the password change confirmation screen, or
b. Via CPAC by clicking on the computer icon to the right of Site Name and Site#, or
c. By clicking on or cutting and pasting the following URL in your web browser:

Your Case number is

Recibidos Dr. Pérez García. Movil por XXXXXXX Acabo de ver que has firmado los pacientes!! Muchísimas gracias Jose Luis por tu ayu... 14 may.

Recibidos Last steps before PI signature_URGENTE - Dr. Pérez García - I just called the helpdesk on your behalf. They confirmed they have... 14 may.

Recibidos Dr. Pérez García. Movil por Mauro Filori - Perdona Jose Luis que te haya llamado al móvil. Me salta el contestador con lo que en... 14 may.

Recibidos Last steps before PI signature_URGENTE - Dr. Pérez García - Buenos días Dr. Pérez Gracia, Siento que esté siendo todo tan com... 14 may.

Recibidos Dr. Pérez García. Helpdesk en tu nombre - Perdona Jose Luis todo el tiempo que te están "robando" para poder gestionar lo que... 14 may.

before PI signature_URGENTE - Dr. Pérez García - It is impossible for me to call, I have a lot of patients to visit; and in the evenin... 14 may.

Recibidos Last steps before PI signature_URGENTE - Dr. Pérez García - Dear Dr Gracia, First of all, I'm really sorry for my mistake on your n... 14 may.

before PI signature_URGENTE - Dr. Pérez García - Dear Ervelyne: I have just tried again and it still does not work. In addition, the... 14 may.

Recibidos Last steps before PI signature_URGENTE - Dr. Pérez García - Dear Laura, Credentials have been res-sent to Dr. Perez García yest... 14 may.

Recibidos : Last steps before PI signature_URGENTE - Dr. Pérez Gracía - Dear Dr. Garcia, I apologize for the issues. I have c... 13 may.

before PI signature_URGENTE - Dr. Pérez Gracía - Dear team: I have received the new password and it still does not work. I have... 13 may.

Recibidos Last steps before PI signature_URGENTE - Dr. Pérez García - Thanks Laura, Including Barb and Carolyn in copy to help resolutio... 13 may.

Recibidos Last steps before PI signature_URGENTE - Dr. Pérez García - He is trying to login but system doesn't recognize his passwords a... 13 may.

Recibidos Last steps before PI signature_URGENTE - Dr. Pérez García - Please keep Paco, Barb and Carolyn in copy to help resolution, Tha... 13 may.

Recibidos Last steps before PI signature_URGENTE - Dr. Pérez García - Dear Ervelyne Dr. Perez García is trying to reset the password, sinc... 13 may.

Recibidos Last steps before PI signature_URGENTE - Dr. Pérez García - Hi Leandro What is the issue? Dr Perez Garcia didn't receive new p... 13 may.

Recibidos Last steps before PI signature_URGENTE - Dr. Pérez García - Hi Everlyne Can you hep PI to reset the pssword? BR Leandro Barb... 13 may.

Recibidos ca: INCB54828-201: Last steps before PI signature_URGENTE - Dr. Pérez García - Dear sender, I will be out of office on Monday t... 13 may.

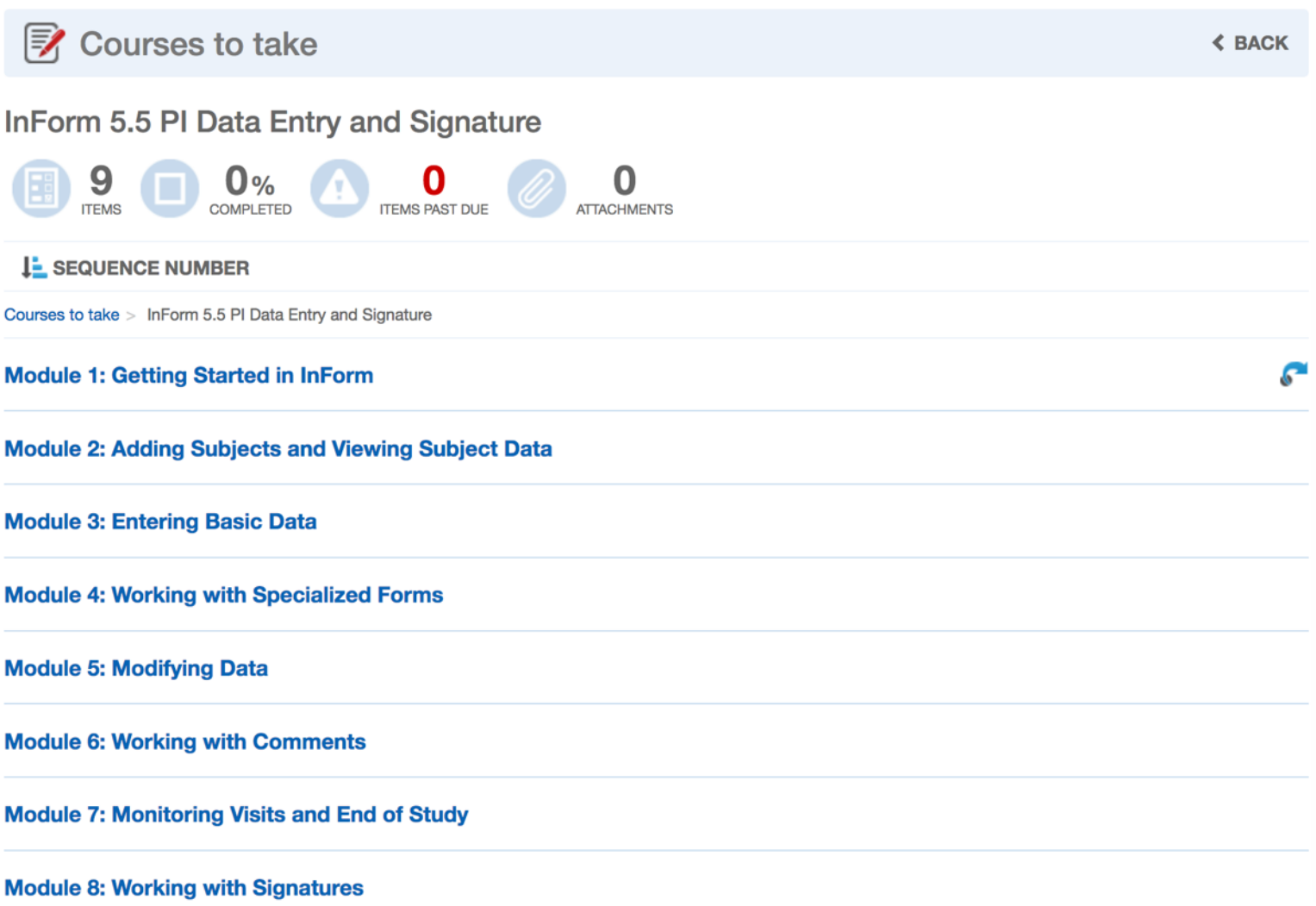
before PI signature_URGENTE - Dr. Pérez García - Estimada Laura: Muchas gracias por tu mensaje. He intentado firmar, pero el ... 13 may.

Recibidos Last steps before PI signature_URGENTE - Dr. Pérez García - Estimado equipo investigador, Antes de nada, querría presentarme... 13 may.

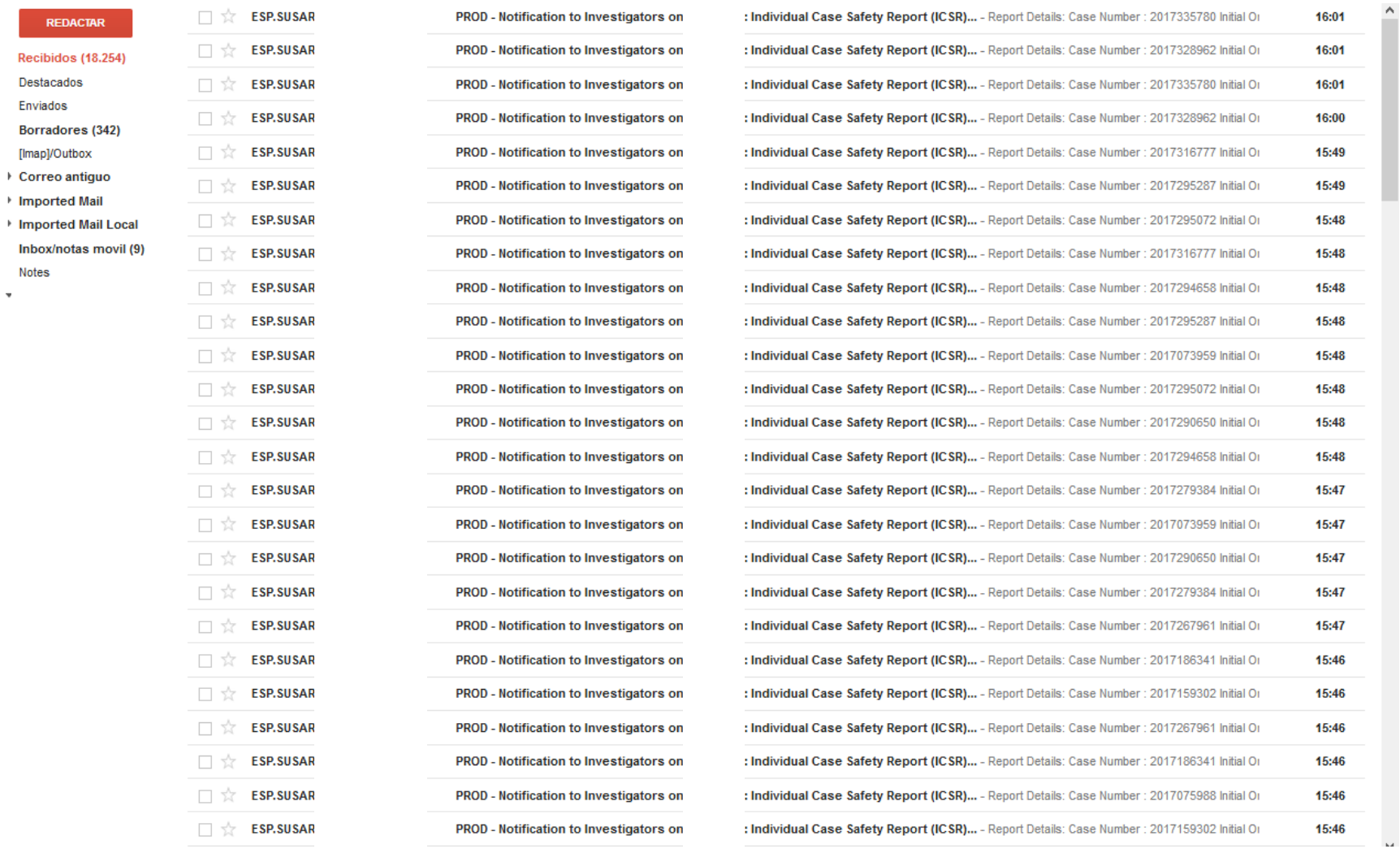
Recibidos Last steps before PI signature_URGENTE - Muchas gracias Silvia, si nos podéis confirmar cuando el PI lo tenga firmado! Y lo in... 13 may.

24 e-mails in less than 24 hours to solve the access to a signature page

Training courses



Pharmacovigilance:
25 reports on same day … from 15:45 to 16:01



ESMO Open
Cancer Horizons

Check for updates

ESMO Clinical Research Observatory (ECRO): improving the efficiency of clinical research through rationalisation of bureaucracy

ECRO SURVEY

Table 2 Results of the ESMO survey on the administrative and bureaucratic burden in clinical research

Statement	Mean score (0=strongly disagree, 10=strongly agree)	
	Overall score (n=940)	Research experience >5 years (n=690)
The current burden of administrative tasks in clinical research is excessive.	8.3	8.6
Current administrative and bureaucratic procedures in clinical research could be reduced without affecting the safety and rights of the patients and the quality of the data.	8.2	8.5
Current administrative and bureaucratic procedures represent an obstacle for the development of clinical research.	8.1	8.4
It is necessary to incorporate the feedback from physicians about the procedures related with clinical research.	8.6	8.8

ECRO, ESMO Open 2020

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- **Negative impact of the increased administrative burden:**
  - poor use of the limited time physicians have available
  - frustration, loss of motivation and complaints from experienced investigators
  - decreases the interest of young physicians towards developing a clinical research career
  - significantly increases economic costs and contribute to delays in trial implementation
    - Negative impact on drug development and patient access to new drugs
    - Particularly relevant in the setting of independent academic clinical research
  - No evidence that this increased complexity leads to improved patient safety and quality of the data

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“Clinical Interference”

- Situations in which the protocol -or its interpretation by the sponsor/ CRO- impose a decision about patient management which is discordant with the best medical judgement, according to the clinical investigator.

- This may result in harm to the patient, in clear contrast with the main goals of the Declaration of Helsinki and the GCP guidelines.

- Examples:
  - Prohibition of relevant treatments
  - Unilateral decisions to discontinue study treatment
  - Unacceptably prolongued screening periods

"Clinical Interference"

- Example
  - 42 yr-old male NSCLC responding to therapy.
  - We request radiosurgery for a single new CNS lesion, maintaining therapy

- Response:

The patient can continue on XXXXX treatment as long as he is clinically stable.
However, patient can not get surgery or radiation therapy for the brain lesion while he is participating in the study.
Please understand that this is to test the efficacy of XXXXX objectively.

Thanks,

Treatment discontinuation mandated based on independent CT review

Dear Dr. XXXXXXXXXXXX

Attached is the report from Bioclinica on your subject 3106-003 from the Week 80 scans performed on 11-Apr-2016. Bioclinica has confirmed metastasis to left para-aortic lymph nodes.

Based on the development of metastasis, the subject should have an end of treatment (EOT) visit (…) The patient should continue to be followed every 4 months for survival.

Please feel free to contact us if you have any questions.

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Conclusions (I)

1. Urgent need to rationalize the bureaucratic burden associated with clinical research:

   - strict adherence to current legal regulations: **not less ... but not more**
   - respect to the time and expertise of investigators, who should be focused on clinical and research issues.
   - Specific suggestions:

     a. Limiting the administrative documents to those required by GCP and legal regulations
     b. Using simplified document templates
     c. Avoid redundant documentation
     d. Avoid complex electronic resources

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Conclusions (II)

2. Avoid *Clinical Interference* of protocols with best medical practice:
    - Include this concept in GCP
    - Involve IRBs in detecting and preventing it
3. Review and improve Pharmacovigilance procedures.

<u>Regulatory agencies must be aware of these problems and should actively address them</u>

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“The only thing that saves us from bureaucracy is its inefficiency.”

Eugene McCarthy (1916-2005)

European Society for Medical Oncology

Thanks for your time!

jlgracia@unav.es