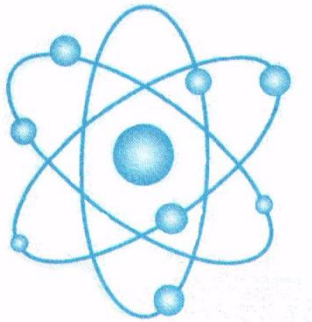


1

Klinisch onderzoek beter mogelijk met een EPD



Prof. Dr. H. Pieterse
Profess Medical Consultancy
Voorzitter NVMA
3 juni 2010

Agenda

2

- Aan welke wettelijke eisen moet mensgebonden onderzoek in Nederland voldoen?
- Hoe test je de betrouwbaarheid van de resultaten?
- Hoe kan ik daarbij het EPD als brondocument gebruiken?
- Aan welke eisen moet het EPD dan voldoen?

Soorten onderzoek

3

- Interventie onderzoek
- Observationeel onderzoek (niet-WMO plichtig)
- Bevolkingsonderzoek
- Onderzoek met embryo's, foetussen, geslachtscellen

Soorten interventie onderzoek

4

- Geneesmiddelen
- Medische hulpmiddelen
- Voedingssupplementen
- Chirurgische technieken
- Gedrags- en psychologisch onderzoek
 - Waarbij handeling wordt verricht of gedragswijze beïnvloed
- Interviews en enquêtes
 - Waarbij handeling wordt verricht of gedragswijze beïnvloed

Regelgeving relaties bij Onderzoek

5



Wettelijke eisen voor onderzoek

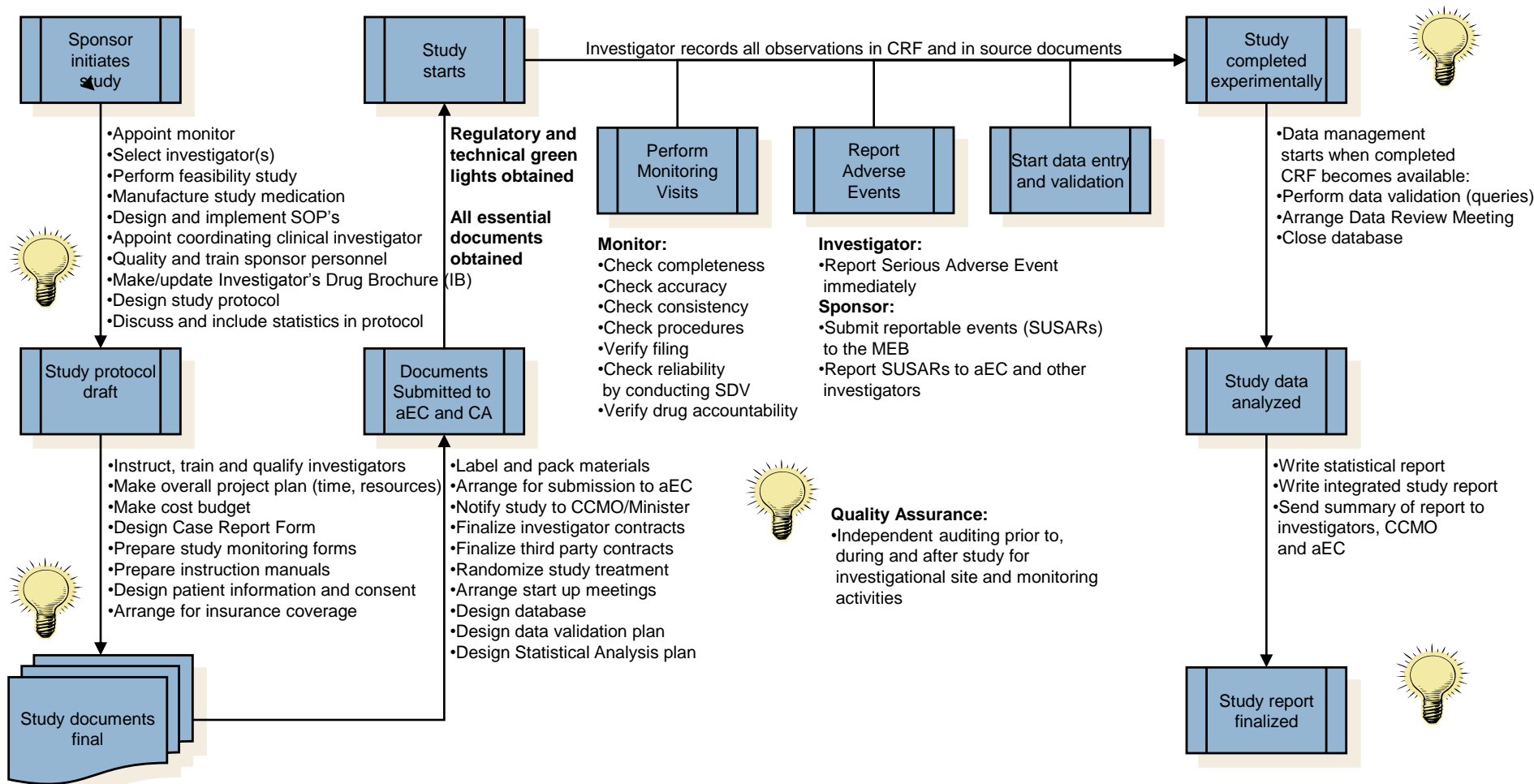
6

- Wet Medisch Wetenschappelijk Onderzoek met Mensen
- Geneesmiddelenwet
- ICH Good Clinical Practice Guideline
- WGBO
- WBP

Rode draad

7

- Zorgvuldig handelen
- Geloofwaardig handelen
- Verantwoording afleggen
- Transparantie
- Consistentie



- Study documents:**
- IB, study protocol
 - CV's investigators
 - List centres
 - aEC approval
 - CCMO notification
 - Investigator agreement
 - Insurance certificate
 - Patient info, consent
 - CRF
 - Forms AE, ADE
 - Monitor contact info

- Sponsor responsibilities:**
- Sign approved study protocol
 - Ensure that all deviations from protocol are reported and accounted for
 - Ensure that all AE's are reported as required
 - Inform all investigators about all SAE's
 - Inform investigator when study is terminated prematurely or suspended
 - Inform investigators on development status drug
 - Review and approve deviations from study protocol
 - Collect, store, keep secured and ensure completion of essential documents

- Monitor responsibilities:**
- Verify if compliance with protocol is maintained
 - Verify if drug is used according to plan
 - Verify qualification of investigational staff
 - Verify if investigator has access to adequate number of subjects
 - Verify if informed consents are properly signed and dated
 - Verify if AE have been recorded and reported adequately
 - Verify drug accountability and traceability
 - Verify maintenance and calibration equipment
 - Verify recording subject withdrawal, non-compliance
 - Report monitoring visits

- Investigator responsibilities:**
- Have resources to conduct study
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 - Knows the drug and its properties
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 - Protects health and welfare of subjects
 - Communicates with the aEC on SAE's, submission amendments
 - Endeavors to ensure adequate recruitment
 - Ensures that informed consent is obtained and documented
 - Reports any deviation due to emergency
 - Ensures drug accountability

Initiatiefase-1

9

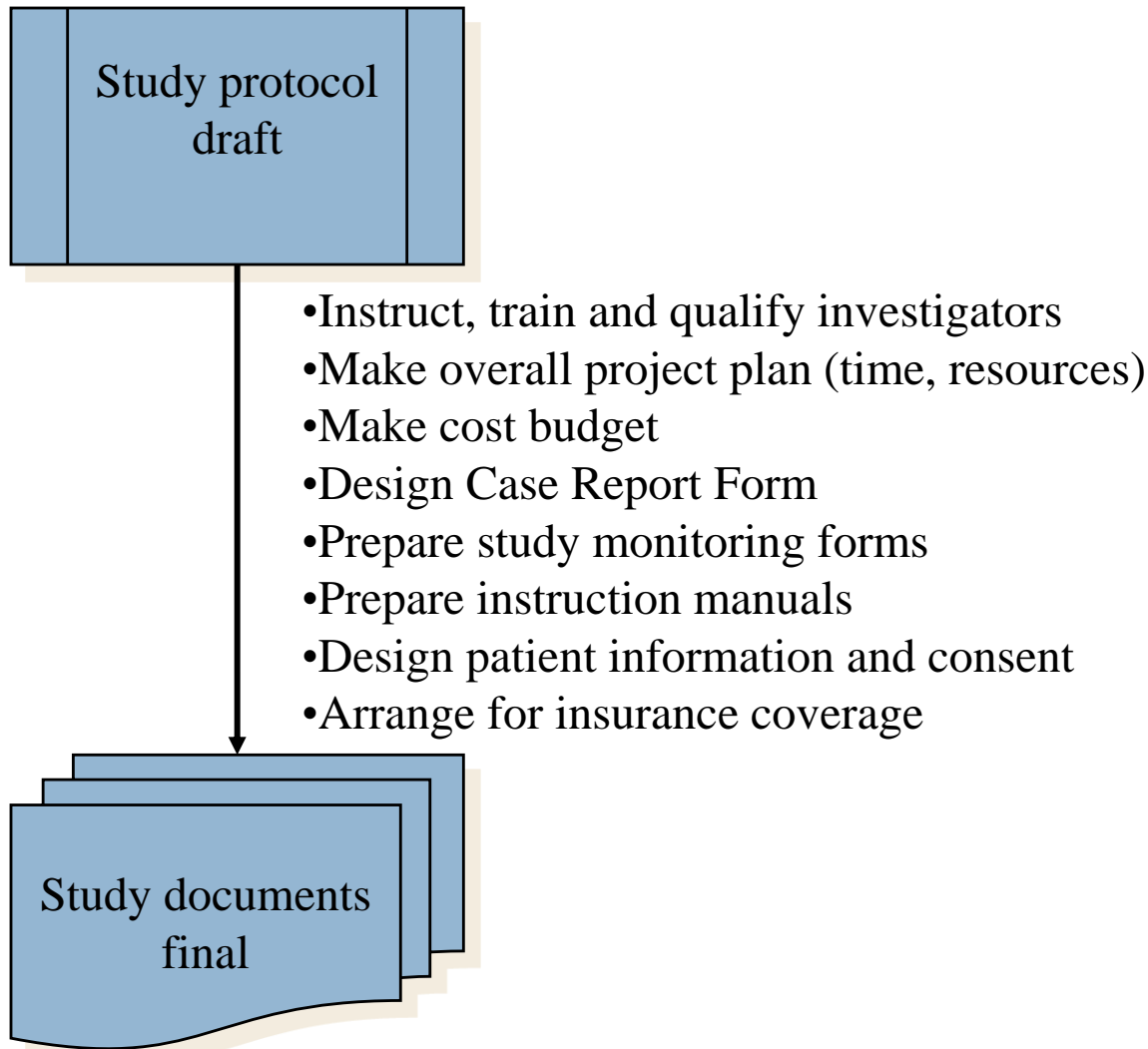


- Appoint monitor
- Select investigator(s)
- Perform feasibility study
- Manufacture study medication
- Design and implement SOP's
- Appoint coordinating clinical investigator
- Qualify and train sponsor personnel
- Make/update Investigator's Drug Brochure (IB)
- Make/update Investigational Medicinal Product Dossier (IMPD)
- Design study protocol
- Discuss and include statistics in protocol

SOP-Z

Interne voorbereidingsfase-1

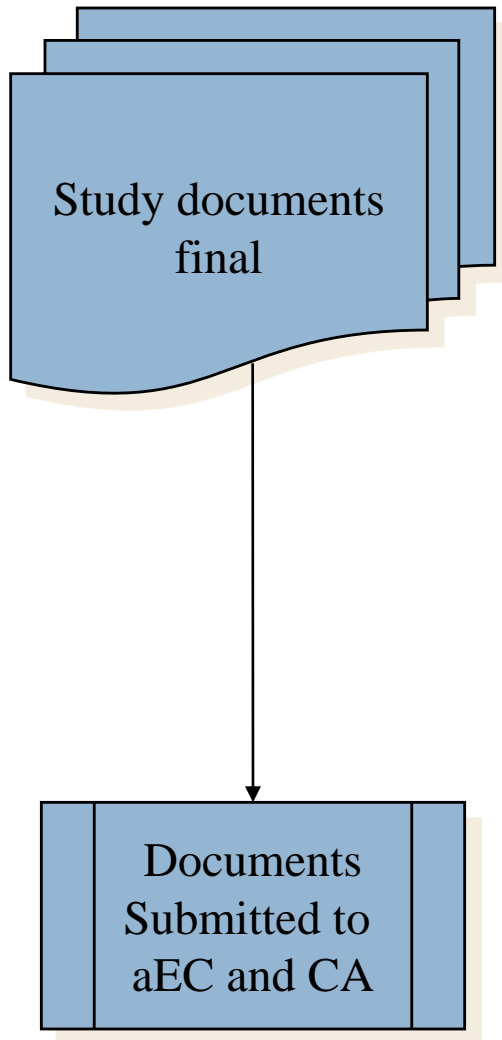
10



SOP-Z

In te dienen documenten-1

11

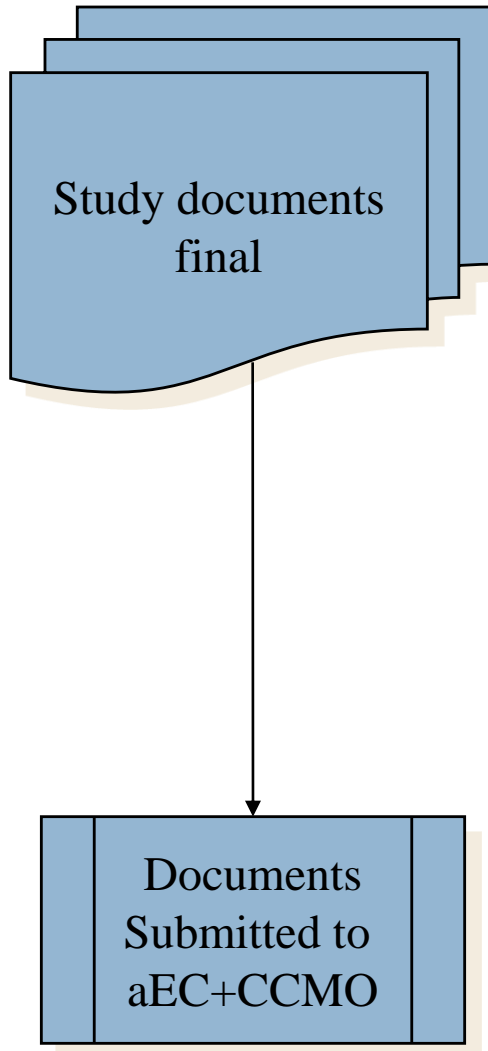


- Essential documents to be submitted
- For details see 2.3
- Prepare other relevant documents like:
 - Study forms
 - Monitoring guidelines
 - SAE form
 - Monitor contact reports

SOP-Z

Externe voorbereidingsfase-1

12

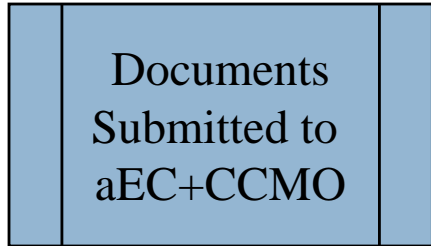


- Label and pack materials
- Arrange for submission to aEC
- Notify study to CCMO/Minister or arrange for approval in case of gene therapy
- Finalize investigator contracts
- Finalize third party contracts
- Randomize study treatment
- Arrange start up meetings
- Design database
- Design data validation plan
- Design Statistical Analysis plan

SOP-Z

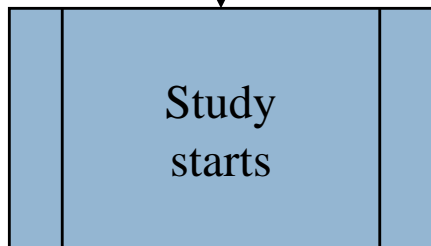
Groen licht-1

13



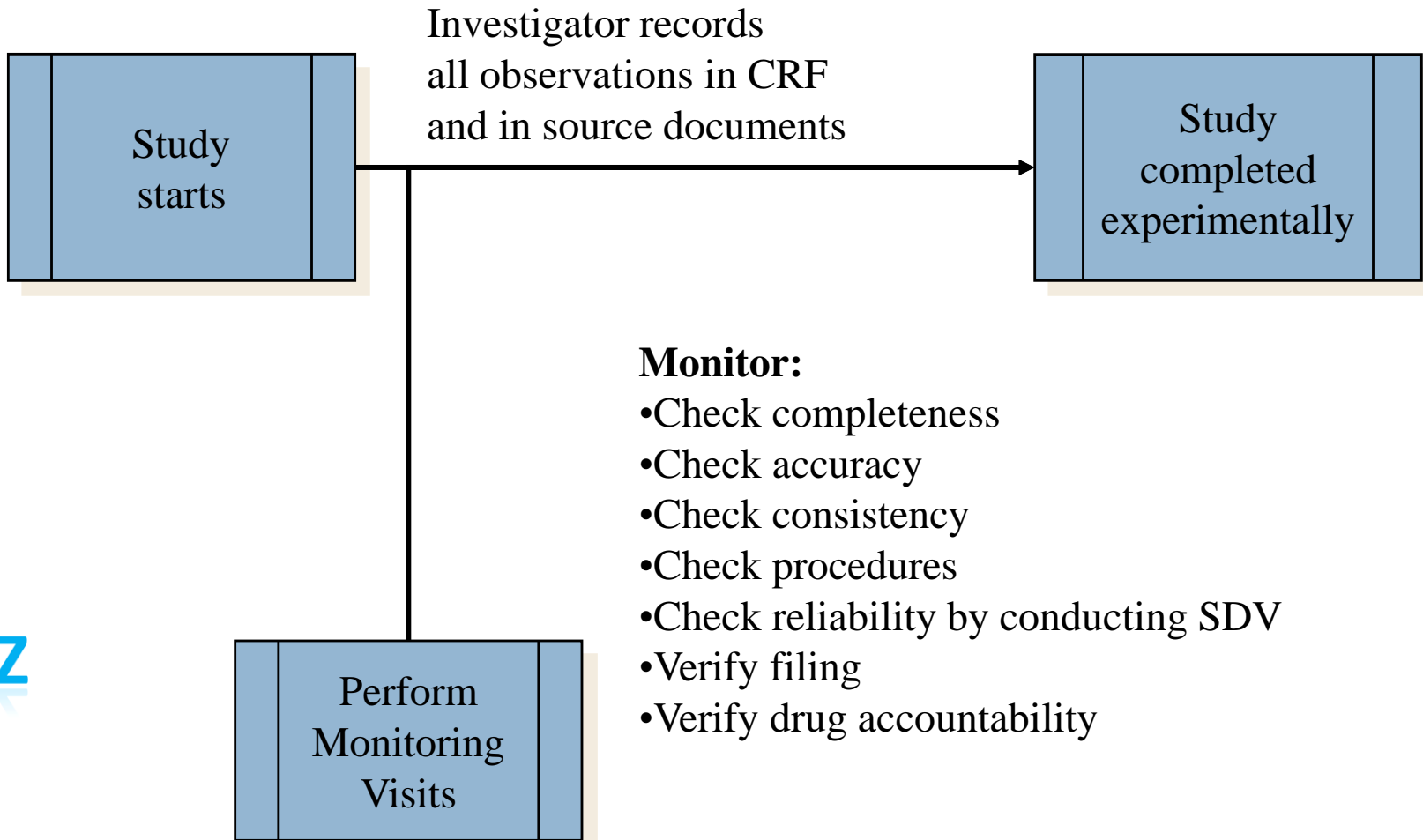
Regulatory and technical green lights obtained

All essential documents obtained



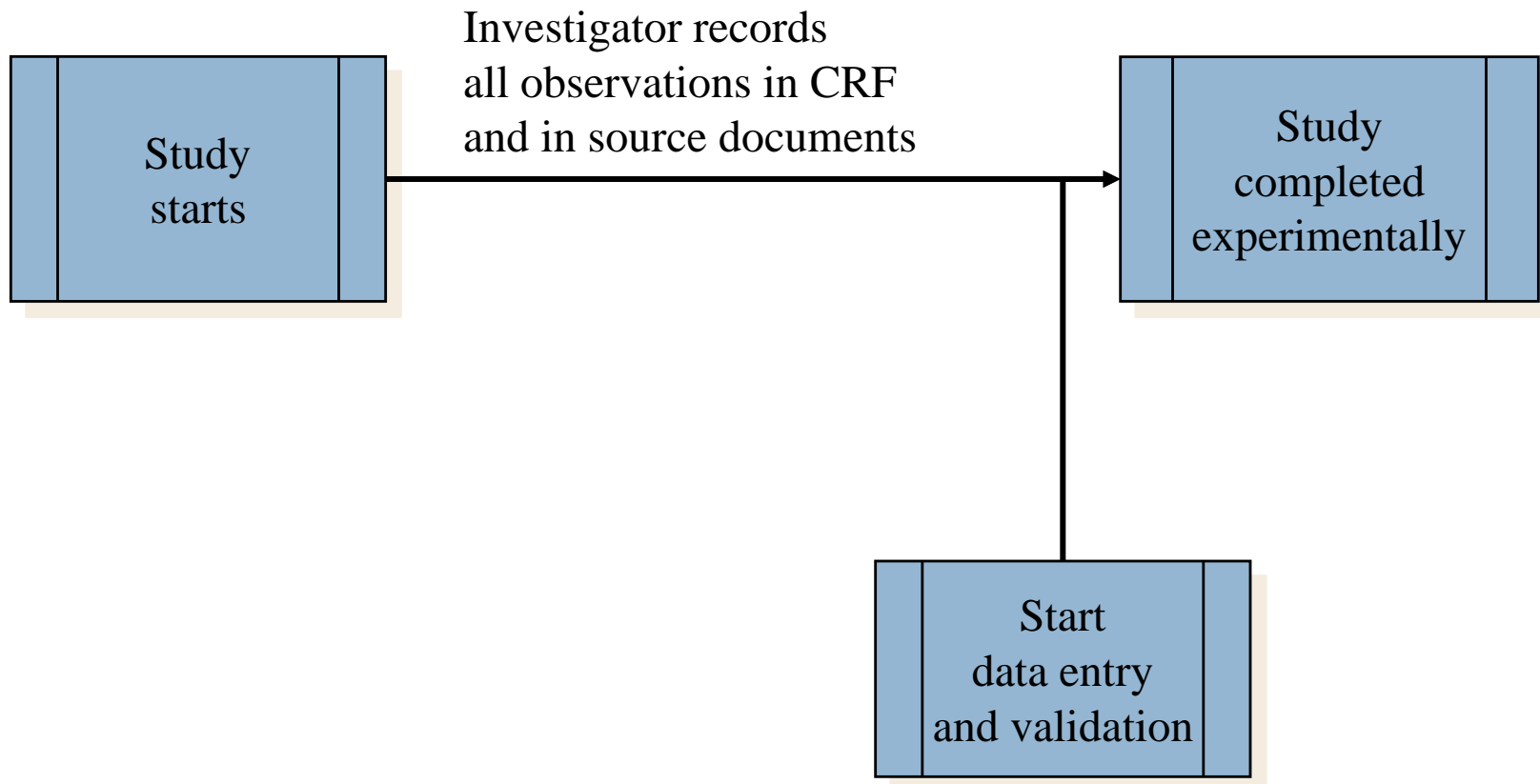
Uitvoeringsfase-2

14



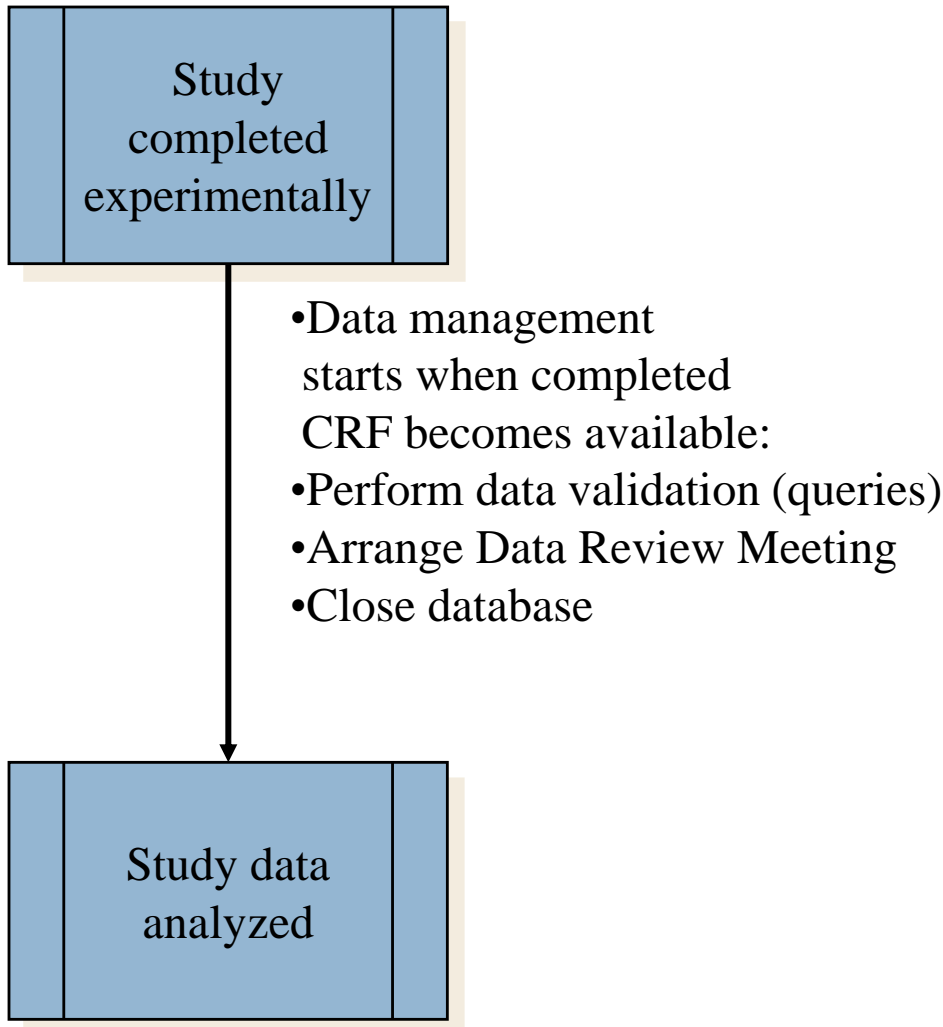
Uitvoeringsfase

15



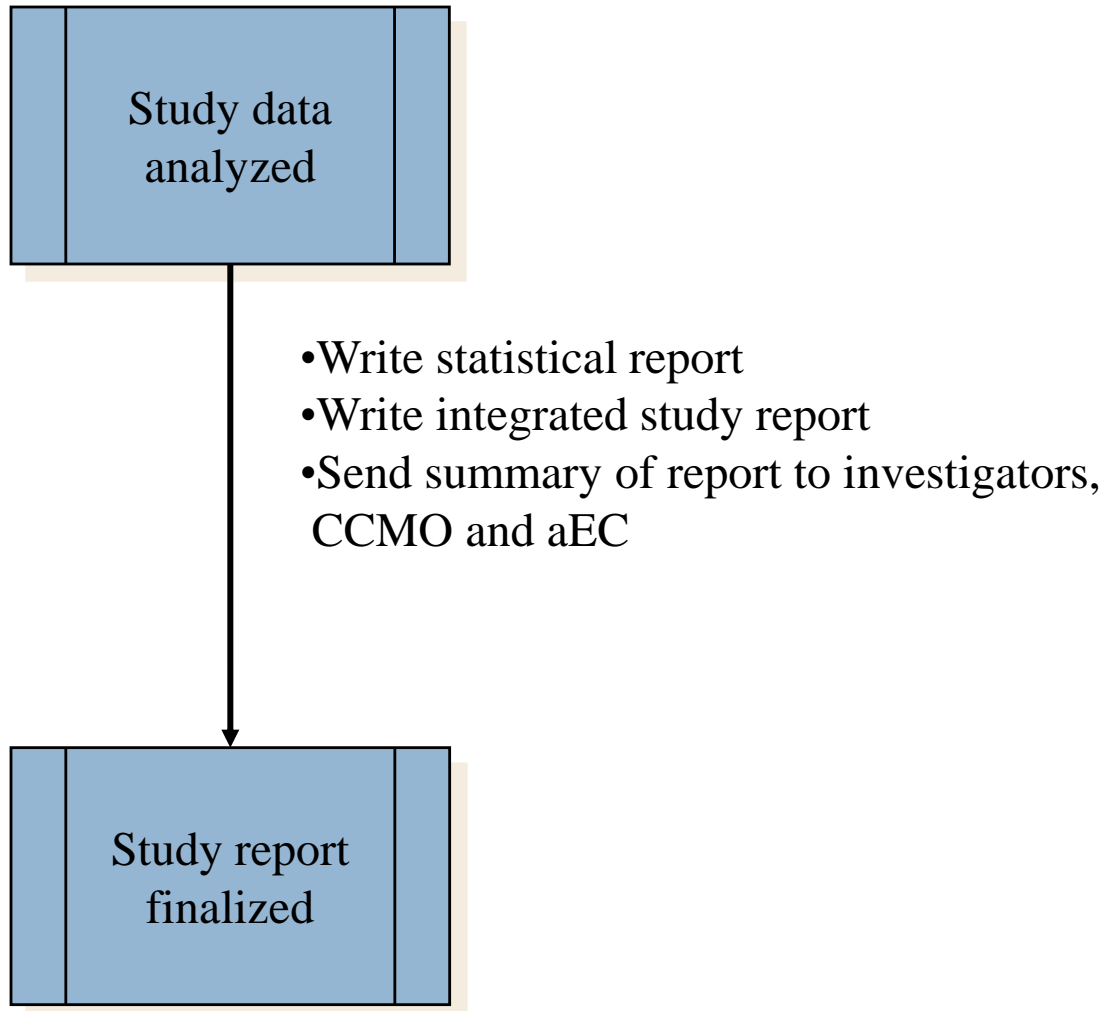
Analyse fase

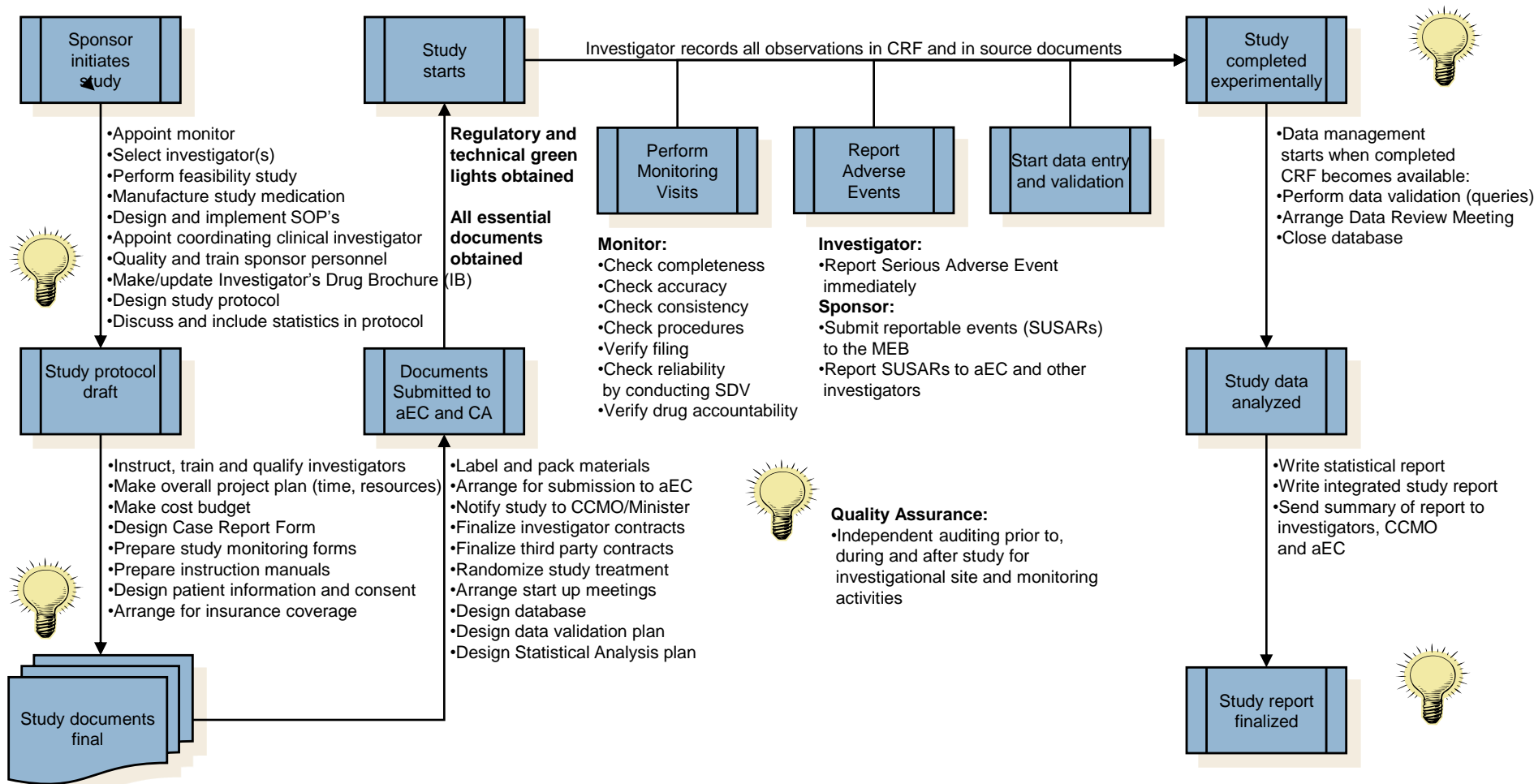
16



Rapportage fase

17





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Betrouwbaarheid toetsen

19

- Verificatie tegen de brongegevens (ICH GCP 5.18)
- Representatieve steekproef door monitor
- Check validatie van computersystemen (ICH GCP 5.5.3)
 - Systeem voldoet aan eisen gebruiker (acceptance testing)
 - Ontwikkeling van systeem conform state of the art model (V-model)
 - Procedures zijn beschreven voor alle taken en verantwoordelijkheden

Resultaten registreren

20

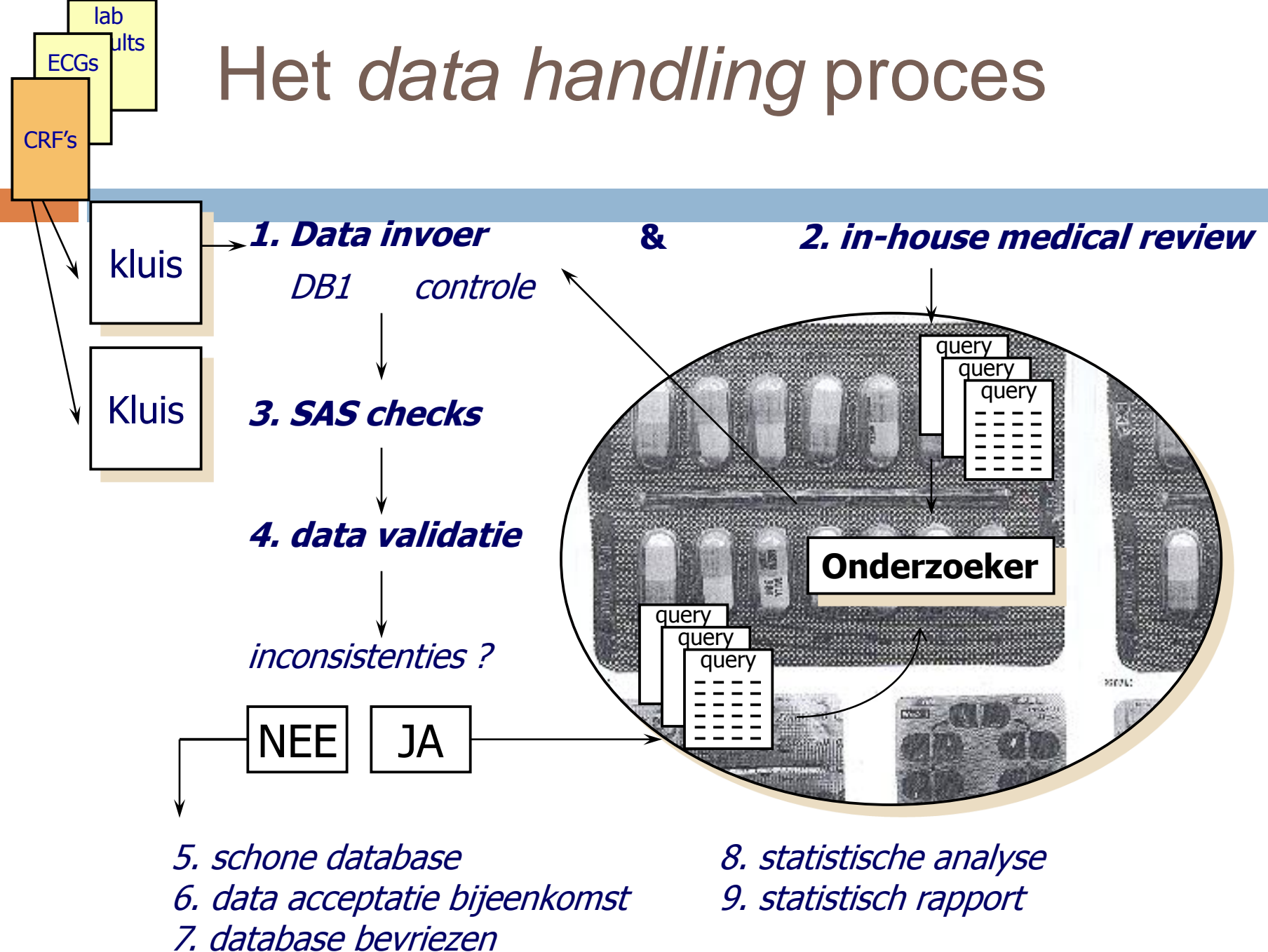
- De onderzoeksgegevens worden op een verzamelformulier vastgelegd
- Case Report Form

Gegevens verwerking

21

- Data verifiëren met medisch dossier/EPD
- Data invoeren in gevalideerde software systeem (data management plan)
- Data schonen (data validatie plan)
- Data analyseren (statistisch analyse plan)
- Data rapporteren (studie rapport en publicatie)

Het *data handling* proces



the **CANCER BLOG**

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Note: The contents of this blog are for informational purposes only and should not be construed as medical advice or substitute for professional care. For medical emergencies, dial 911!

Jon Sudbo admits to more cheating

Posted Jan 23rd 2006 6:51PM by [Jeri Kemple](#)

This just angers me. What a fraud. What was he thinking? Why did he do it? I may never get the answers, but for what it is worth, he is attempting honesty now. He claims it was not all about the money. Yet he faked two other reports, not just the one he was caught faking. A total of three articles were tampered with by Sudbo. One of them for an article in the New England Journal of Medicine in April of 2004, another in the Journal of Clinical Oncology in March 2005 and the one in the Lancet in October 2005. Sudbo has been on sick leave since Radium Hospitalet accused him of cheating. He has not commented publicly yet, and I can't wait until he does.

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Supporting your

Betrouwbaarheid toetsen

24

- Check validatie van computersystemen (ICH GCP 5.5.3)
 - ▣ Logging procedure (audit trail)
 - ▣ Beveiligingssysteem
 - ▣ Lijst met bevoegden
 - ▣ Backup en restoring faciliteiten

EPD als betrouwbare bron

25

- EPD wordt robuust gebouwd (V-model)
- In EPD is een logging procedure vereist
 - ▣ Geen ongeoorloofde wijzigingen
 - ▣ Geen misbruik van gegevens
 - ▣ Geen wijziging door onbevoegden
- Voor WMO plichtig onderzoek (interventie onderzoek)
 - ▣ Toegang tot EPD (inzage) voor derden geregeld met toestemming van patiënt

EPD als betrouwbare bron

26

- Voor niet-WMO plichtig onderzoek (observationeel onderzoek)
 - ▣ toestemming voor inzage door derden als gegevens herleidbaar zijn tot de natuurlijke persoon
- Inzage voor derden procedure vastleggen conform procedures beveiliging

Validatie van het EPD

27

- Acceptatiecriteria voor opdrachtgevers van onderzoek
 - ▣ Zijn de procedures beschreven?
 - ▣ Is het systeem volgens V-model ontwikkeld?
 - ▣ Is de beveiliging van het systeem geregeld?
 - ▣ Is er een logging procedure die werkt?
 - ▣ Is de backup en restoring geregeld?
 - ▣ Is de elektronische handtekening gevalideerd?

Personal Health Center

POWERED BY |  Microsoft HealthVault[refresh site data](#) | [log off](#)

Summary

My Data

My Meds

News & Articles














User Profile

Health data details

Welcome Sean Smithton

Blood Pressure data details - 30 days and beyond

Period Start End [Get results](#)[record blood pressure](#) [health incident](#)

source	date	activity	bp	notes
	Sep 12, Wed		 120 / 80 	edit
	Sep 5, Wed		 130 / 88 	getting better... edit
	Sep 2, Sun	wonder if this is related?		symptoms: dizziness, coughing edit
	Sep 1, Sat		 140 / 88 	edit
	Aug 26, Sun		 120 / 70 	edit
Fabrikam	May 25, Fri		 104 / 84 	edit
Fabrikam	May 24, Thu		 110 / 80 	edit
Fabrikam	May 23, Wed		 98 / 77 	edit

Toekomst

29

- Een zorgvuldig en betrouwbaar EPD is essentieel voor mensgebonden onderzoek om te zorgen dat

Toekomst

30

- Kosten kunnen worden bespaard op data management (voorkomen van dubbele invoer en de vele controles die plaatsvinden)
- Human factors worden gunstig beïnvloed (velen hebben een pesthekel aan alle bureaucratie!)
- Kwaliteit zal met sprongen stijgen, want alle gegevens worden goed vastgelegd aan de basis en kunnen voor vele doeleinden worden ingezet

V r a g e n ?