

# Regulatory Framework for Approval of Clinical Studies in Brazil

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# Clinical Study Approval System in Brazil

- 💣 Multi-institutional ✓ Well documented
- 💣 Multi-step ✓ Well controlled
- 💣 Multi pain-in-the-neck process ✓ ICH-GCP compliant

# Evolution of the clinical study approval process in Brazil

- 1976 – Law # 6360 – Public Health System Act
- 1988 – 1st Bylaw (#01/88)
  - required Medical Ethics approval of all clinical studies
- 1996 – National Council of Health: Resol. #196
  - Created a new system for CS review and approval
- 1999 – Creation of ANVISA: independent regulatory agency

# Evolution of the clinical study approval process in Brazil - II

- Resolutions from the National Council of Health:
  - #251/99 : Defined groups of studies/review
  - #292/99 : International studies must go to CONEP
  - #301/00 : Best comparator should be used
  - #346/05 : “Umbrella approval” for multicentric studies
- Resolutions from ANVISA
  - # 911/98, # 219/05 : Composition of dossier

# CEP (Brazilian IRB)

- At least 7 members
- Accredited by CONEP after review of written procedures
- Composition of dossier:
  - Protocol, IC, IB...(in Portuguese), CVs, plus:
  - Study budget, insurance, list of participating countries and Brazilian sites
  - Copy of IRB approval in other countries
  - Declarations of responsibility

# CONEP - “National Ethics Committee”

- 13 + 13 members, 3-yr mandate
- Executive staff is permanent
- Monthly meetings (2 days)
- Strong political hues (*social control organism*)
- Short of resources
- Difficult communication



# CONEP – Modus operandi

- CEP submits study dossier, plus:
  - Approval letter and a detailed report
- CONEP will send to 1- 2 referees
- Report issued after monthly meeting
- Communication only with CEPs
- Inquiries or pending issues restart the process (*79% related to inf. consent*)

# CONEP – Modus operandi



Resolution 346 (March 05) on international multicentric studies:

- Only *1st site* will be reviewed
- Approval will be good for all sites  
(if accepted by local ethics committees)
- Communication between CONEP/1st site during the whole study  
(periodic reports, SAE, etc)

# ANVISA – What does it approve in clinical studies ?

- Studies with new drugs/devices
- Importation of supplies
- Exportation of biological samples

# ANVISA – Approval of CS



Sponsor or investigator submit new dossier:

- Copy of dossier submitted to CEP
- Copy of approval letter from CONEP
- Payment of fee
- ANVISA authorizes importation of supplies and study initiation  
(CE=“Special Communication”)

# ANVISA – Approval of importation of supplies



Importer files an import license (on-line), based on exporter's proforma invoice

- Hardcopy of IL sent to ANVISA, together with importation plan
- ANVISA approves IL on-line
- Supplies may be shipped

# ANVISA – Approval of exportation of bio samples

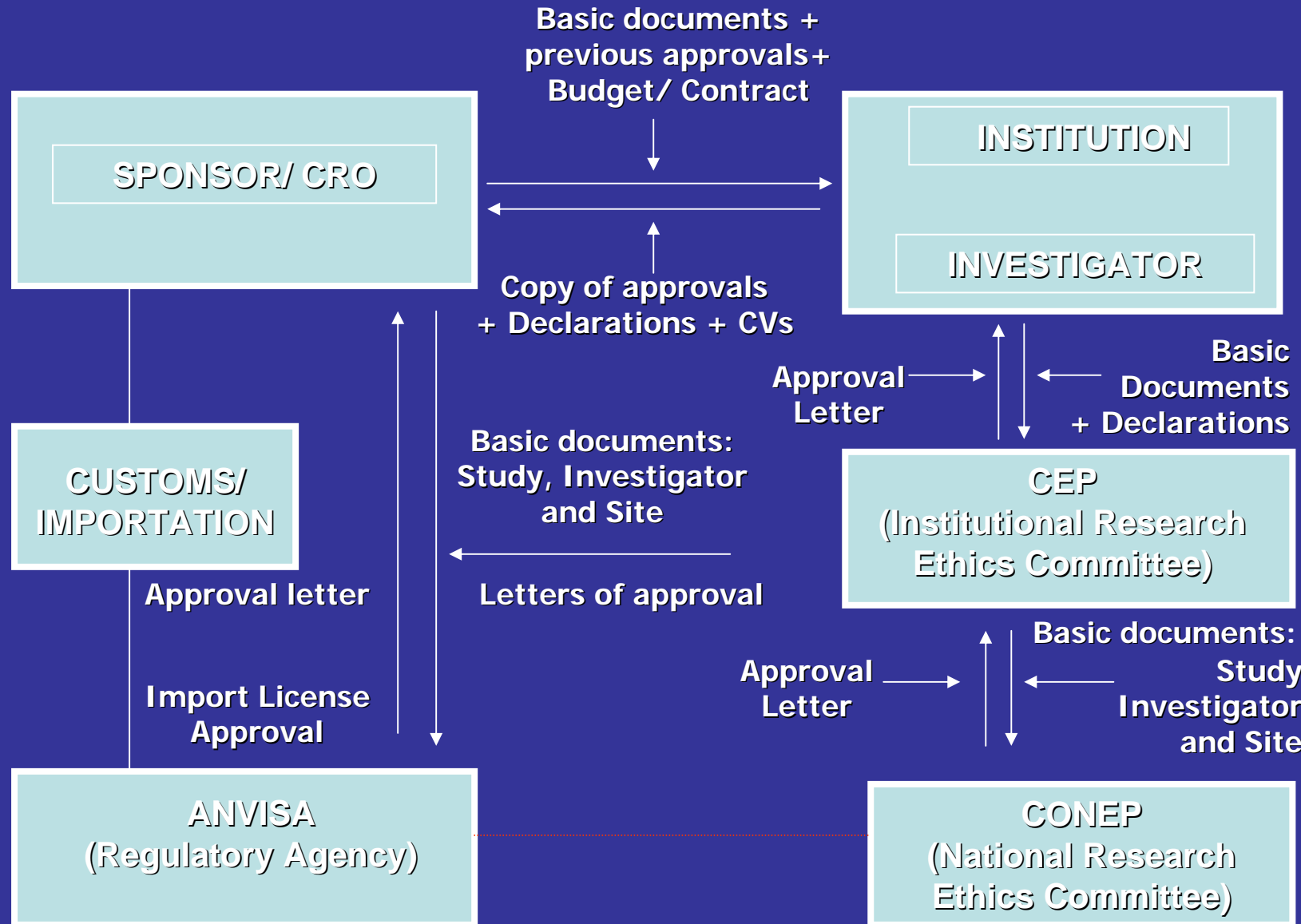


Couriers take care of process:

- Sites must get accreditation number issued by ANVISA
- Project details kept on file: description, type and destiny of samples, patient list.
- Authorization issued for each shipment

# Clinical Study Approval System in Brazil

## In summary



# Clinical Study Approval in Brazil

## *How long does it take ?*



# Clinical Study Approval in Brazil

*How long does it REALLY take*  
?



4 months



6 months

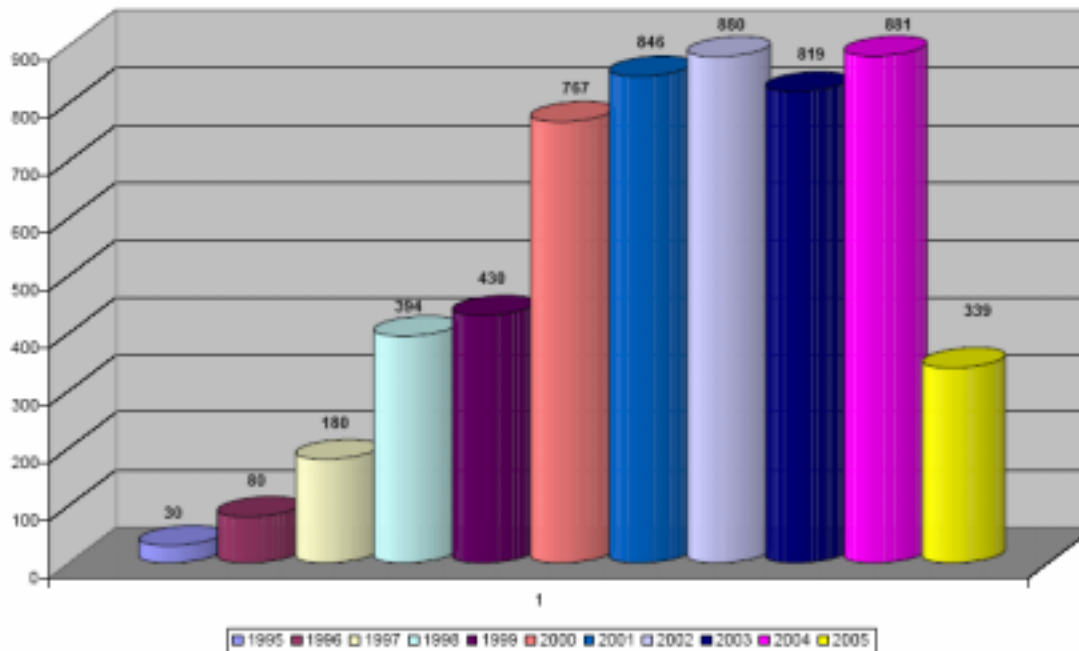


9-12 months

# In spite of that...

## Research activities are growing in Brazil

Número de Comunicados Especiais emitidos de 1995 a 2005 (até abril de 2005)



# And... there is space for more

## 403 accredited ethics committees

### 2667 sites \*

■ North	64	(2.4%)
■ Midwest	261	(9.8%)
■ Northeast	323	(12.1%)
■ South	646	(24.2%)
■ Southeast	1373	(51.4%)



\* Information provided by OCASA, 2005

# Why ?! Positive Prospects

- ☺ Strong patient-doctor relationship
  - ☺ Important recruitment/retention ...
- ☺ Large population underserved by the public health system (“SUS”)
- ☺ ANVISA has doubled # officials in the clinical research office
- ☺ ANVISA and CONEP want to date, but are still very shy, and have angry parents

# Still ... Negative Prospects

- 💣 Timelines are not consistently predictable
- 💣 Placebo studies, very difficult to accept
- 💣 Knowledge of the process still deficient
  - 💣 Investigators
  - 💣 Sponsors/CROs
  - 💣 Authorities !

# Conclusions and Recommendations

- ⇒ If Brazil is in the plans, start early !
- ⇒ Plan big to compensate for high impedance
- ⇒ Work with preferred sites
- ⇒ Be prepared to comply with local uses and procedures
- ⇒ Watch again, things may have changed !

# Thank you

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