How the post trial access issue has progressed throughout the world in recent years

Sanitary point of view on post-trial access

Fanny Nascimento Moura Viana
DEVELOPMENT OF A NEW MEDICINE

**DRUG DISCOVERY**
- Synthesis
- Identification of targets

**PRE-CLINICAL**
- In vitro testing
- Pharmaco dynamics
- Pharmaco kinetics
- Toxicology
DEVELOPMENT OF A NEW MEDICINE

Pharmacotechniques

Clinical Trials

Phase I

Phase II

Phase III

Approval/registration

Postmarketing

Phase IV
In Brazil, production, marketing and use of medicines can only be made after granting sanitary registration by the Ministry of Health.

Situations where unproven medical therapies is permitted:

- Clinical Trials
- Compassionate Use
- Expanded Access
- Post trial Access
INSTANCE FOR APPROVAL OF CLINICAL TRIALS IN BRAZIL

- ETHICS
- HEATH SURVEILLANCE
- CEPs/CONEP
- ANVISA
APPROVAL OF CLINICAL TRIALS IN BRAZIL

DOSSIER
- Sponsor
- CRO/ORPC

CEP(IRB)

JUDGEMENT

DOSSIER + IRB JUDGEMENT

CONEP

ANVISA
With the advent of the AIDS epidemic, AIDS activists demanded what they called “expanded access,” arguing that AIDS patients who were not enrolled in a clinical trial should be allowed to take experimental drugs under the supervision of their personal physicians.

(GROOPMAN, J., 2006)

In Brazil, the concept of Expanded Access was defined in 1999: RDC 26 (December 17)
Concept

Sponsored process of providing new product, promising, not yet approved in the National Health Surveillance Agency, which is in phase III development in Brazil or in the country of origin, for patients with serious illnesses and life threatening, in the absence of satisfactory therapeutic alternatives available in the country, without additional cost to the patient.

RDC No. 26, December 17, 1999
In cases of research involving situations for which there is no established treatment ("Humanitarian use" or "compassionate") could be authorized to release the product in an emergency, provided there has been approval by the CEP, CONEP and ratified by the SVS / MS.

Resolution of National Health Council (CNS)
No. 251, August 7, 1997.
The compassionate use is also characterized by the use of unproved medical therapies outside the context of clinical trial to patients with serious illnesses and life threatening that have no therapeutic alternative registered in the country, but the authorization is for each individual patient differently expanded access programs.
Continued use by participants in a survey after the conclusion of clinical trials.

DECLARATION OF HELSINKI

“The protocol should describe arrangements for post-study access by study subjects to interventions identified as beneficial in the study or access to other appropriate care or benefits”.

COUNCIL FOR INTERNATIONAL ORGANIZATIONS OF MEDICAL SCIENCES (CIOMS)

“Additionally, if an investigational drug has been shown to be beneficial, the sponsor should continue to provide it to the subjects after the conclusion of the study, and pending its approval by a drug regulatory authority.”
Continued use by participants in a survey after the conclusion of clinical trials.

RESOLUTION NO. 196/1996 (CNS)
The search should guarantee the return of benefits gained through research to the people and the communities where they are held.

RESOLUTION NO. 251/1997 (CNS)
The sponsor should ensure access for the drug under investigation for patients who have benefited from using.
BENEFITS OF RESEARCH

Several benefits to the community:

- Training of health workers,
- Improvements in the infrastructure,
- Provision of standard treatment available,
- Provision of public health measures, among others.

*The benefit of research not only directly related to the research subjects who participated in the study.*

DAINESI, S. M., 2006
BENEFITS OF RESEARCH

The subjects in the study benefited clinically have the right to continue receiving free medication that brought a good for your health, beyond the benefits that the study has brought to the community.

JÚNIOR, B. R. S., 2007
The responsibilities of the sponsors do not end with the completion of the study, as they should provide conditions of security and monitoring the use of the drug as long as necessary while the research subject is benefiting from the experimental treatment.

JÚNIOR, B. R. S., 2007
RISK MANAGEMENT

- Was the safety properly evaluated in studies in the early stages?

The effects of the drug are monitored for short periods and safety assessment is related to the study period and does not extend the closed.

GOLDIM, J. R., 2008
TOP QUESTIONS

- How long should such access post-study?
- Who is responsible for providing and storing the product in research?
- How to monitor and report adverse events outside the context of a controlled clinical trial?
- Does a single study prove the efficiency of a particular intervention?
- Does the individual benefits correspond to the results obtained in the study as a whole?

The superiority of a new drug must be proven through a statistical analysis of survey data and not from the clinical evaluation of a single patient.

DAINESI, S. M., 2006 / 2009
• For cases where there is patient benefiting from the drug under investigation,
• Best alternative therapy,
• The protocol does not provide an extension of the study

DONATION OF THE DRUG

www.anvisa.gov.br
Criteria and procedures:

- Quantitative;
- Final study report;
- Letter explaining the need to execute the decision recommended by the Resolution CNS 251/97;
- Medical report;
- Notification CEP;
- Declaration by the sponsor:
  - supply of study medication and safety evaluation.
Aprovação de Estudos Clínicos ANVISA

Estudos Submetidos à ANVISA para Aprovação
Estudos Aprovados pela ANVISA
Requests approved by ANVISA to use unregistered drugs outside the context of clinical trial in the period from January 2008 to July 2010.

<table>
<thead>
<tr>
<th>Type of Access</th>
<th>No. of patients included</th>
</tr>
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<tbody>
<tr>
<td>Expanded Access</td>
<td>73</td>
</tr>
<tr>
<td>Compassionate Use</td>
<td>316</td>
</tr>
<tr>
<td>Post Trial Access</td>
<td>109</td>
</tr>
</tbody>
</table>
Therapeutic class of expanded access programs authorized by ANVISA from January 2008 to July 2010.

- **ANTINEOPLASTIC**: 18%
- **ANTIRETROVIRAL**: 82%
Therapeutic class of compassionate use authorized by ANVISA from January 2008 to July 2010.
Status of registration of medicinal products authorized by ANVISA for use in programs of expanded access and compassionate use from January 2008 to July 2010.
- The donation of non-approved drugs may have been under-reported or under-counted,
- The donation post-study can is covered in a program extension, which is nothing more than an extension of the research with the same subjects recruited.

NOTIFICATION OF THE EXTENSION STUDY
- Review of RDC No. 26, December 17, 1999 (EXPANDED ACCESS) include compassionate use and donation after study;

- Procedural donation after study;
  - Medical report;
  - Final study report;
  - Quantitative;
  - Notification IRB;
  - Sponsor: supply of medication, safety evaluation, monitoring.
THANK YOU!

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