



# Ethical Principles in Oncology Research in Turkey

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# Why do we need ethical principles at global level?

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Research contributes to

- Development of appropriate treatments
- Disease prevention measures

Lack of resources & weak infrastructure;

- Researchers in developing countries have limited capacity to conduct their own clinical research
- Undertake research in partnership with groups from developed countries



# “GUIDELINES OF MEDICAL DEONTOLOGY” (Tibbi Deontoloji Nizamnamesi) 13.01.1960

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- **This is the first regulation of investigational drugs in Turkey**
- Item 10: A physician or dentist can not recommend and apply a diagnostic method or treatment unless he had results supporting that they are effective and harmless. But, a new discovery could be recommended by informing the relevant parties that they are at the experimental step.
- Item 11: Any surgical intervention, chemical, physical and biological treatments can not be applied in human for experimental purposes. In cases where there is no benefit with classical methods, a new treatment based on previous classical animal experiments can be used. ....
- Item 12: An official permission must be obtained.....



# CONSTITUTION, 1982

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- “Consent” is mentioned for the first time.
- Item 17: Other than medical obligations and written regulations, anybody can not be included in any scientific and medical experiment without getting his/her consent.



## HEALTH SERVICES FUNDAMENTAL LAW, 1987 (Sağlık Hizmetleri Temel Kanunu)

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- Item 34: Drugs cannot be used on humans with the purpose of scientific research without consent of subject and MoH.

# THE OFFICIAL REGULATIONS OF INVESTIGATIONAL DRUGS

(İlaç Araştırmaları Hakkında Yönetmelik )  
January 1993, Turkish Official Gazette

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## Derived from:

- Helsinki Declaration
  - 1964, 1975, 1983, 1989
- Turkish Medical Deontology Regulation
  - 1960
- States that the researchers must obey these rules.

# THE OFFICIAL REGULATIONS OF INVESTIGATIONAL DRUGS

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- 12 pages
- It was the rules for regulation of investigational drugs between 1993-2008
- This is the first law bringing the local & central ethic committees\*
- There was no regulation for non-medicinical research
- After these regulations, local ethic committees were involved more and more in other research areas
- It was cancelled with the new regulation being effective in December 2008

- The first local ethics committees were established in Hacettepe University
- and GATA in 1986 before this regulation

# THE OFFICIAL REGULATIONS OF INVESTIGATIONAL DRUGS

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Defines:

- stages of the drug research,
- qualifications of the researchers,
- the duties of the local and central ethics committees,
- qualifications for membership of these committees,
- the necessary procedures for working on new drugs,
- specifications for protocols of clinical research,
- the procedures for admission,
- sanctions.



# TURKISH GOOD CLINICAL PRACTICE GUIDELINES (İyi Klinik Uygulamalar Kılavuzu) & GOOD CLINICAL LABORATORY PRACTICE GUIDELINES (İyi Laboratuvar Uygulamaları Kılavuzu )

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- was published in December 1995 in “Turkish official gazette”
- 39 pages
- GCP was adapted from ICH GCP guidelines
- With more detailed descriptions, improvements in research settings became possible in Turkey
- Local ethic committees became more common in different institutions and started to work more efficiently



# THE NEW REGULATIONS REGARDING CLINICAL TRIALS IN TURKEY

## December 2008

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- **EU directive**

Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use

- **The new regulation in December 2008**

It has been discussed intensively within different groups how to combine the regulations of 1993 with this EU directive between 2001-2008 and finally it was published in December 2008 in "Turkish Official Gazette"

# THE NEW REGULATIONS REGARDING CLINICAL TRIALS IN TURKEY

## What is new?: New ethic committees

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- Regional ethic committees instead of local ethic committees will be established (80 local ethic committees will be dissolved within 3 months)
- Central Ethic Committee was dissolved. Advisory Board is going to be established
- MoH, will coordinate the training programs for people who is going to involve in regional ethic committees
- Local ethic committees vs Institutional Review Board in University Research Centers: A discussion point!
- Non-commercial clinical trial was described

# THE NEW REGULATION OF INVESTIGATIONAL DRUGS IN TURKEY

## What is new?: Courses

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- GCP courses was started for potential ethics committee members and will be repeated
- 4 Courses in 2009: “Ethics in Clinical Research”
- “The guidelines for non-commercial clinical trials” are also prepared by Ministry of Health. It will be active following “the new regulations”.

# THE NEW REGULATIONS REGARDING CLINICAL TRIALS IN TURKEY

What is new?: More than drug research

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## Item 2: These Regulations comprise

- clinical drug trials,
- non-drug clinical trials,
- trials conducted with medical devices,
- clinical trials by using a new surgical method, trial sites, real persons or legal entities to conduct these trials,
- bioavailability studies
- bioequivalence studies
- therapeutic trials

# THE NEW REGULATIONS REGARDING CLINICAL TRIALS IN TURKEY

What is new?: Harmonization with EU law

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Item 3: This Regulation has been prepared on the basis of:

- Decree Law Regarding the Organization and Duties of the Ministry of Health
- Fundamental Law Regarding Healthcare Services and in parallel with the Directives:
  - 2001/20/EC
  - 2005/20/EC for the purpose of achieving harmonization with the EU legislation concerning drugs in the conduct of clinical drug trials.

# THE NEW REGULATIONS REGARDING CLINICAL TRIALS IN TURKEY

What is new?: No inducement

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- Item 5-ğ: No convincing incentive or monetary inducement in order to secure the participation or continued attendance of volunteers in the clinical trial



## THE NEW REGULATIONS REGARDING CLINICAL TRIALS IN TURKEY

What is new?: Seperate application for genetic research

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- Item 6-b: If genetic research will be conducted or germ cells such as sperm and ova will be obtained from the volunteer, a separate consent shall be obtained for each study.

# THE NEW REGULATIONS REGARDING CLINICAL TRIALS IN TURKEY

## What is new?: Children

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- Items 7,8,9: No trial shall be conducted on children, pregnant women, women in maternity period, nursing women or incapacitated persons.

However:

- In cases directly related with the subject matter of the trial
- In clinical conditions that may only be assessed in children
- Data from adults need to be proven also in children, if the trial does not pose a predictable serious risk and it is hoped that the trial may provide a direct benefit for the volunteers, permit may be granted for the conduct of trials on children.

# THE NEW REGULATIONS REGARDING CLINICAL TRIALS IN TURKEY

What is new?: Approvement authority

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- Item 10: Ethics committees shall be established by Ministerial approval in regions to be determined by the Ministry.
- Item 10(14): In subjects within the scope of this Regulation, an Ethics Committee or any other similar Ethics Committee may not be organized by other institutions.

# THE NEW REGULATIONS REGARDING CLINICAL TRIALS IN TURKEY

What is new?: No restriction for Institution

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- Item 15: Clinical trials may be conducted in hospitals that are suitable for ensuring the safety of volunteers and suitable for urgent interventions where necessary and avail of the staff, equipment and laboratory facilities that suit the nature of the trial.
- ~~Research and Training Hospital~~

# THE NEW REGULATION OF INVESTIGATIONAL DRUGS IN TURKEY

## What is new?: Application procedure

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- Item 17(3): Those who would like to conduct a trial within the scope of this Regulation shall apply to the Pharmaceutical General Directorate for any type of trial upon receiving the position opinion of the Ethics Committee, and to the General Directorate of Curative Services for stem cell transplantation, tissue transplantation, genetic trials and the experimentation of new medical devices.

# THE NEW REGULATION OF INVESTIGATIONAL DRUGS IN TURKEY

What is new?: Approval is an obligation

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- Item 17(4): The Ministry shall not grant permit for any trial not approved by the Ethics Committee.
- *Application shall be made directly to the Ministry for trials to be conducted on diseases such as avian flu, severe acute respiratory syndrome (SARS) and Crimean Congo hemorrhagic fever whose treatment is not yet well known and for which it is essential to conduct clinical trials as well as trials on orphan drugs.*

# THE NEW REGULATION OF INVESTIGATIONAL DRUGS IN TURKEY

## What is new?: Multicenter studies

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- Item 17(8): In multi-center studies, the decision to be adopted by the Ethics Committee where the coordinator center is located is enough.
- However, MoH may request for the adoption of a separate Ethics Committee decision for the other centers as well.
- The sponsor shall be obliged to give a copy of the Ethics Committee approval received and the application dossier to the Ethics Committees in the settlement center where each trial center is located, for informative purposes.

# THE NEW REGULATION OF INVESTIGATIONAL DRUGS IN TURKEY

## What is new?: Investigators

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- Item 20(1)-a: Clinical trials shall be conducted by a responsible investigator who is a clinician medical doctor or a dentist, with a team that suits the nature of the trial. Responsible investigator should have completed its specialization or doctorate degree regarding the topic of the trial.
- Phase I clinical drug trials shall be conducted by a medical doctor pharmacologist on healthy volunteers.
- Phase I clinical drug studies related to oncology shall be conducted on patient volunteers by an oncologist and medical doctor pharmacologist.

# THE NEW REGULATION OF INVESTIGATIONAL DRUGS IN TURKEY

## What is new?: Financial responsibilities

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- Item 31(2): The examination and analysis fees of any investigational product used in the trial, as well as the devices and materials utilized in relation with the product shall be covered by the investigator or sponsor and will not be paid by the patient or social security institutes nor will they forced to pay these.
- However, the Ministry, Ministry of Finance and/or Chairmanship of the Social Security Institute may designate different procedures and principles for the drug, examination and analysis fees of the trials encompassed by non-commercial clinical drug trials.

# THE NEW REGULATION OF INVESTIGATIONAL DRUGS IN TURKEY

## What is new?: Violations

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### **Administrative and penalty sanctions**

- Item 33(1): The sponsor, responsible investigator(s) who have conducted trials in violation of the provisions of this Regulation may be banned to conduct trials for a temporary or permanent period of time by MoH.
- Item 33(2): Turkish Penal Code with No. 5237 and the provisions of other legislations shall apply depending on the nature of the deeds, on those who act and conduct activities in violation of the provisions indicated in this Regulation.



# The Questions?

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How this new regulation will effect our reserch practice?

Better use of resources?

Numbers?

Quality?

New questions?

New problems?