Proposals of the Advisory Committee on Administrative Reform：Lessons Learned from Drug-Induced Hepatitis

June 5,2010

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The Advisory Committee on Administrative Reform :Lessons Learned from Drug-Induced Hepatitis

- Established by the MHLW, based on a basic agreement between national plaintiffs, their lawyers' groups and the MHLW, concerning the drug-induced hepatitis C litigation.
- **Purpose**:
  To verify the Drug-Induced Hepatitis Disaster
  Make practical proposals on administrative reform
- 20members, including 5 victims ※ my position

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The Advisory Committee on Administrative Reform：Lessons Learned from Drug-Induced

- Two years' deliberations(May 08-Apr 09)
  2008: Interim draft, first proposal
  2009: Final proposal
- Research group for verification
- Survey for victims, company staff hearings
- Questionnaire survey
  For PMDA/MHLW personnel

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The monument of oath

We keep the value of life to heart.
We hereby swear that we will make the utmost effort to ensure the safety and efficacy of drugs, to prevent a recurrence of drug-induced disasters, such as Thalidomide, SMON, drug-induced Creutzfeldt-Jakob, and drug-induced AIDS.
More than 1000 patients were infected by tainted blood products in the HIV scandal. We have established this monument as a token of our reflection on this history.

August 1999 Ministry of Health, Labor and Welfare

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Recurrence of drug-induced disasters and pharmaceutical class actions in Japan

- Thalidomide
- SMON
- Dura mater infected with Creutzfeldt-Jakob disease
- HIV-tainted blood products

"Form-policy-function" of pharmaceutical class actions in Japan

The litigations' purposes are

- Not only for compensation
- But also to…
  clarify the government's responsibility
  establish permanent measures for victims
  find out the truth
  develop preventive measures

Basic agreement
between plaintiffs and the MHLW

Pharmaceutical Class Actions and Administrative Reforms

- Thalidomide (1967)
  ADR report system, drug re-evaluation system, GMP
- SMON (1979) Reform of drug affairs law
  Emergency order, relief system
- Drug-induced AIDS(1997)
  Division of regulation bureau and promotion
  Crisis management system
- Drug-induced Creutzfeldt-Jakob Disease(2004)
  Relief system for biological products
  Education on drug-induced disasters
- **Drug-induced Hepatitis C(2010)**

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A milestone for pharmaceutical class actions

This is the first time the MHLW has established an advisory committee for verification purposes and administrative reform

cf. Negotiations by victims and lawyers

What's possible?

- Verification beyond the lawsuit in question
- Verification of present system
- Wide range of reform measures proposed
- NGOs and victims' opinions reflected

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Contents of the report

Questionnaire survey to PMDA/MHLW personnel

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Fundamental viewpoints based on verification

Problem exists in decision making

True information has not reached doctors and patients,

but has reached drug companies and the MHLW

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"a precautionary principle" is essential

"drastic reform measures" needed for the whole system including the PMDA and MHLW, human resource development, and education

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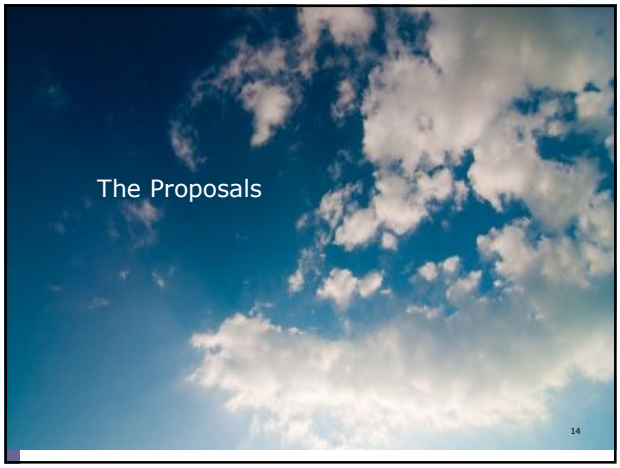

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Systematic reform proposals

1 Basic View
2 Clinical Trials
3 Approval Review
4 Post Marketing Safety Measures
5 Relief System for ADR
6 Medical institutions
7 Societies
8 Pharmaceutical companies
9 Regulatory bureau

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Clinical Trials

Transparency/foundation independent from the influence of drug companies

- Clinical trial registration system should be compulsory
- Broad items for registration and disclosure
- Examinees' rights should be legally defined
- Unified legal system through clinical trials and other clinical research

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Approval Review

Safety and quick examinations

Transparency

- PMDA reviewers' qualifications and quality should be enhanced
- Conditions of approval and evaluations of performances and conditions should be checked thoroughly
- Transparency, such as disclosure of the review process before approval, should be improved.
- MHLW's responsibility for package inserts in drugs should be clarified.

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Drug lag and shortening of examination period

- Cause of a drug lag is complicated.
  - Drug companies' strategy
- Only limited problems can be resolved by speeding up examinations
- Important to ensure safety
  Lessons Learned from FDA

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Post-marketing safety measures

Construction of fundamental system for review and distribution of information

- Harmonization of approval reviews and post-marketing measures
- More pharmacoepidemiology measures
- Establishment of receipt database
- Regulations for unapproved drugs
- Reform of risk communication system

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Risk Communication

Before marketing approval/post marketing

Adequate collection and provision of information

- Release essential points for PMS at time of approval
- Reform of regulation for package inserts
- Enhance communication with patients
- Reform of advertising regulations
- Early communication

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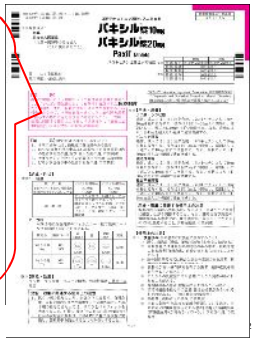
Risk Communication
Package Insert - Paxil

Overseas reports state that following a comparative trial with placebo, Paxil is not effective in patients aged 7 to 18 years old with major depression, and that this drug strengthens the risk of suicidal behavior. Please be careful when prescribing this drug to patients under 18 with major depression.

(Please refer to the following clauses: "precautions concerning the drug's effects", "important fundamental cautions", and "administering to a child."



No warning for pregnant women!

Risk Communication
Package Insert - Paxil

There have been reports that babies born of women who used paroxetine have an increased risk of congenital anomalies. Women who are or may be pregnant should use Paxil only when the therapeutic benefits outweigh the risks. (see Use During Pregnancy, Delivery, or Lactation).

Not noticeable !

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Risk Communication
Provision of Information for Patients

- PMDA website's present condition
  Drug guide for patients
  Manual listing serious side effects
- Whole system needs to be transformed
  ←access, contents, speed

※ secure adequate human resources

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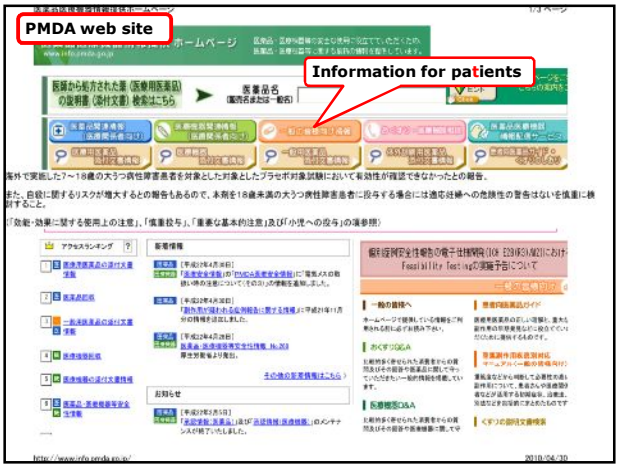
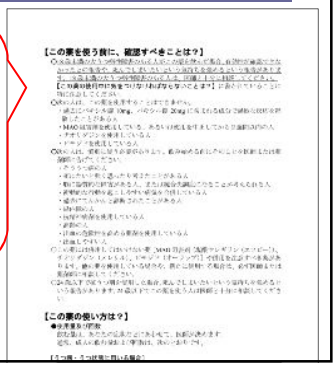


Risk Communication
Drug Guide for Patients

What you should be careful of before using this medicine:

There are reports that this drug has not been effective on patients with major depression and that it strengthens the desire to die. Patients under 18 with major depression must consult a medical practitioner.

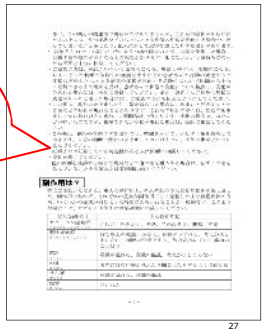
No warnings for pregnant women!



Risk Communication
Drug Guide for Patients

If you are or may be pregnant, please consult your doctor

Any serious risk cannot be understood !



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Risk Communication
Drug Guide for Patients

- Revised in May.2010

  "*There have been reports that babies born of women who used paroxetine have an increased risk of congenital anomalies….*"

- Lag 4 years behind

  Jan.2006 MHLW
  Revision of package insert

  Dec.2005 FDA
  Category D

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Risk Communication
ADR report system from patients

- Establishment of an ADR report system from patients is essential

- Issue raised by SSRI in UK
  Risk of suicidal behavior
  Why does yellow card system not work ?
  BBC program and patients' report
  (65000calls, 1400mails,124000 web accesses)

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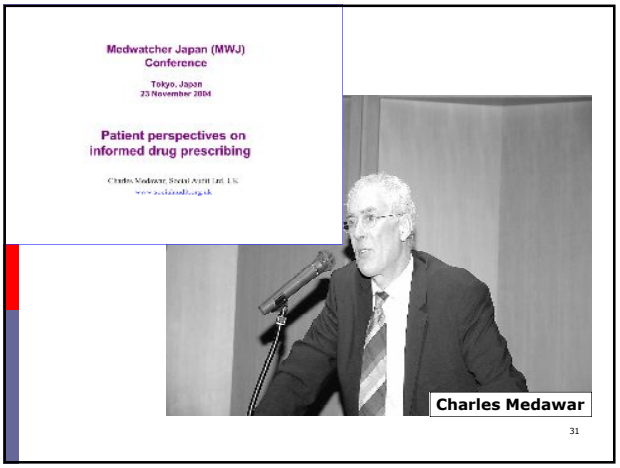

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Risk Communication
Advertising regulations

- Information such as scholarly information/medical practitioners' talks and reports/medical information for patients' associations
- Information for patients' associations raising excessive expectations on effects and efficacy

*definition of advertising

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Relief System for ADR

- Familiarize doctors and patients with the system
- Examine the range of objects for relief
  :anti-cancer drug, fetus

※ Petition

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Regulatory Agency

- Current — PMDA and MHLW
- Unify PMDA and MHLW, or maintain current system ?
  - "Pharmaceutical Bureau" Plan
  - "Act for the Total Number of Civil Servants"

※ Questionnaire survey to PMDA/MHLW personnel

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Regulatory Agency

- The following points are essential regardless of the organization
  - ・Government must take responsibility
  - ・ Harmonization of approval reviews and post-marketing safety measures
  - ・Transparency and specialization
  - ・Reflection of people/patients' opinions
  - ・Adequate funding to remain independent from companies
- . Secure proper personnel
  - ・ Continuous reviews of this organization

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Establishment of a third party organization to watch and evaluate drug regulations

Aims to prevent drug-induced disasters

Watches and evaluates entire drug regulations,

Admonishes and recommends that the MHLW regulate

※ 1997 JFBA statement
※ 2003 Medwatcher Japan proposal
※ 2009 Medwatcher request letter
※ 2010 JFBA opinion letter

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Establishment of a third party organization to watch and evaluate drug regulations

- Authority to inspect, admonish
- Whole administrative issue
- 10 members

(victims, consumers, pharmacoepidemiologists, doctors, pharmacists, lawyers)

- Staff with specialized knowledge who are able to inspect, and support members.

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Establishment of a third party organization to watch and evaluate drug regulations

- Independence, expertise, mobility

  Must be different from existing council
  Position in organization law
  Procedure for selection of members

- Re-review every three years

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Real value will be questioned in future

- Understand what the report proposes
- The establishment of a third party organization is a breakthrough
- Basic Act for Drug Safety

Now, change the culture surrounding drugs!

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