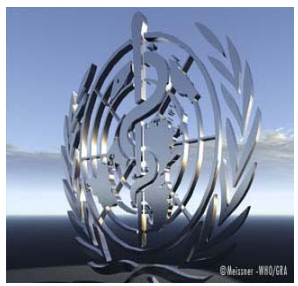
Regional Biosecurity Workshop
Singapore, May 28-30, 2007

WHO Perspectives on Life Science Research and Global Health Security



Tikki Pang, Ottorino Cosivi, Emmanuelle Tuerlings
World Health Organization,
Geneva, Switzerland

Dangerous research ▪ *By* John D. Steinbruner and Elisa D. Harris

When science breeds nightmares

COLLEGE PARK, Maryland

The announcement that an American biologist has tried to create more deadly types of pox viruses in order to develop countermeasures against them raises serious concerns about the lack of control over research involving dangerous pathogens.

The explosion in this type of research after the terrorist and anthrax attacks of 2001 underscores the importance of developing sound oversight mechanisms to ensure that efforts designed to protect the United States against biological attacks do not themselves create new dangers.

The research results announced by Mark Buller of the University of St. Louis at a recent biosecurity conference in Geneva fall squarely in this category. In his work, which was funded by the U.S. government, Buller used biotechnology to deliberately create a more lethal type of mousepox virus, a pathogen affecting mice, and a modified form of the cowpox virus, which can affect humans.

created by Buller fits all three categories, having reportedly killed all of the mice exposed to the disease, including those that had been vaccinated or given the antiviral drug cidofovir.

The National Academy of Sciences committee recommended that these and other experiments of concern be added to the existing oversight process used by the National Institutes of Health, or NIH, to ensure that biotechnology research is conducted safely.

Unfortunately, only institutions that receive National Institutes of Health funding for biotechnology research are required to follow the institutes' oversight rules. This means that most of the relevant research in private industry, or in government biodefense laboratories, which the National Academy of Sciences singled out as posing particular dual-use problems, would not be covered by the new oversight rules. It also means that experiments of concern in other countries would be exempt from oversight unless their work was being funded by the institutes.

The institutes' rules, moreover, are in the form of

International Herald Tribune, Dec 3, 2003

CELLULAR IMMUNOLOGY 26, 153–159 (1976)

Cooperation between Mouse T-Cell Subpopulations in the Cell-Mediated Response to a Natural Poxvirus Pathogen

T. PANG, I. F. C. MCKENZIE,[1] AND R. V. BLANDEN

Department of Microbiology, John Curtin School of Medical Research, Australian National University, Canberra, A.C.T. 2601, Australia

Received April 26, 1976

T-cells involved in primary and secondary cell-mediated immune responses to ectromelia virus infection were characterized on the basis of complement-mediated lysis after treatment with antisera against Ly surface antigens. Three cell populations were studied: (a) Cytotoxic T-cells from the spleen taken at the peak (5 days after infection) of the primary response *in vivo*; (b) memory T-cells from the spleens of animals primed 5–6 weeks previously; these cells gave secondary responses *in vitro* when cultured with virus-infected, syngeneic, "stimulator" cells; (c) cytotoxic T-cells from the secondary response *in vitro*.

commentary

Is science dangerous?

Does society need protecting from scientific advances? Most emphatically not, so long as scientists themselves and their employers are committed to full disclosure of what they know.

Lewis Wolpert

The idea that knowledge is dangerous is deeply embedded in our culture. Adam and Eve were forbidden to eat from the bibli Tree of Knowledge, and in Milton's *Parad Lost* the serpent addresses the Tree as t "Mother of Science". The archangel Raph advises Adam to be "lowly wise" when tries to question him about the nature of t Universe. Indeed, western literature is fill with images of scientists meddling w nature, with disastrous results. Scientists portrayed as a soulless group, unconcern with ethical issues.

But is science in fact dangerous, and scientists have special social responsibiliti It is essential to recognize that reliable scie tific knowledge has no moral or ethical val Science tells us how the world is: that we not at the centre of the Universe is neith

Nature
March 25, 1999

M'sia raises concern over misuse of science

KUALA LUMPUR: Malaysia is among the countries which have raised concerns over new scientific research and inventions which could be misused or be detrimental to human interests.

Science, Technology and Environment Minister Datuk Law Hieng Ding said the countries had urged world organisations to come up with appropriate measures to deal with ethical issues for scientists.

entific and Cultural Organisation (Unesco) and the International Council for Science.

The conference, attended by over 2,500 participants from 160 nations adopted a declaration, which among other things stipulated that scientific research and knowledge should respect human rights and the dignity of human beings.

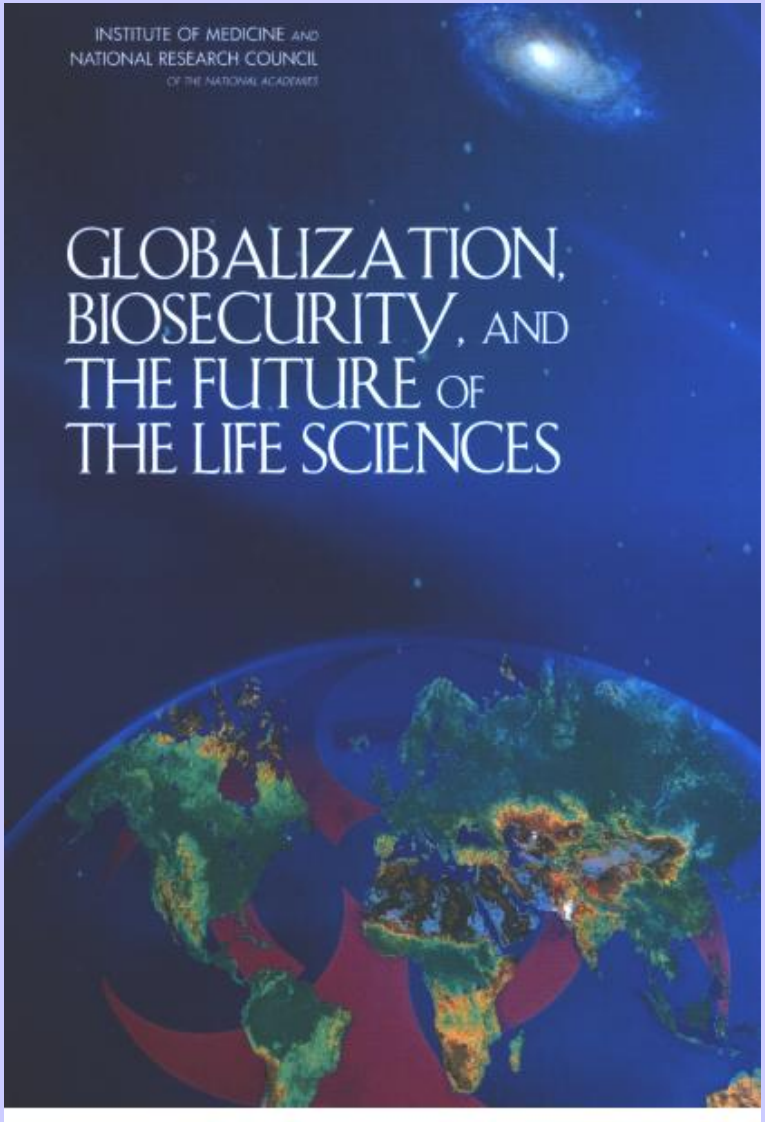
The declaration also acknowledged that some ap-

would be follow-up action relating to the ethical issue.

"Each country should establish suitable measures to address ethical issues on the practice of science and use of scientific knowledge," he said.

On whether the Department of Environment (DOE) would release the conditions attached to the Environmental Impact Assessment report relating to the Selangor Dam project,

The Star
July 8, 1999



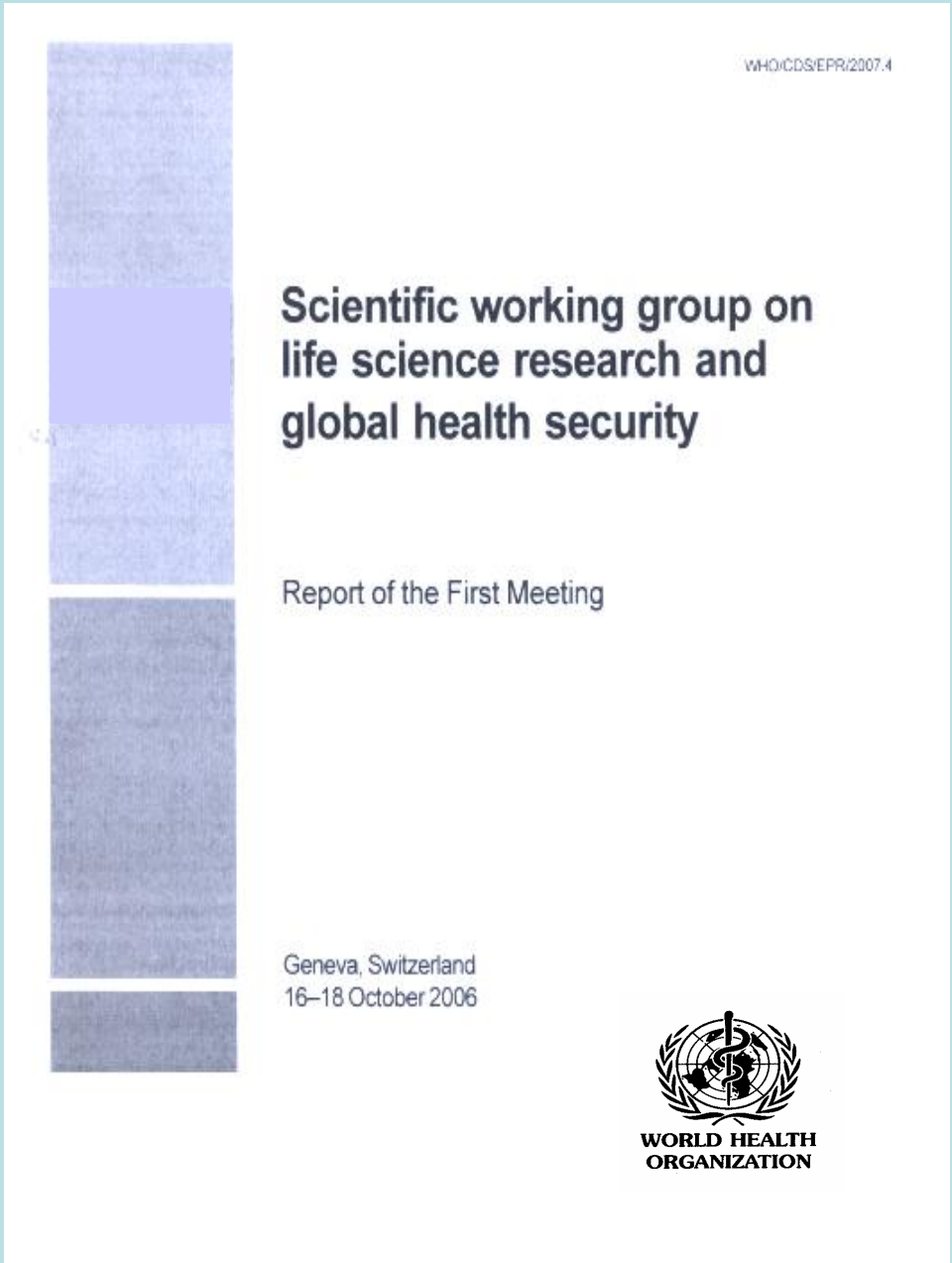
BIODEFENSE

Proposed Biosecurity Review Plan Endorses Self-Regulation

A federal advisory group has come up with a long-awaited blueprint for how the U.S. government should oversee biological research known as "dual use," or experiments that could potentially be used by bioterrorists to cause harm. The voluntary plan would let scientists themselves decide whether their project raises concerns, which would then trigger a higher-level review—a process some critics think is woefully inadequate.

Dennis Kasper of Harvard Medical School in Boston, has now done that. In a 50-page draft report released last week, it says scientists should report annually whether their research is potentially "dual use of concern," perhaps starting with a check box on their grant proposal. A committee, perhaps an expanded version of the institutional biosafety committees (IBC) that now oversee genetic engineering experiments, would

Science, April 27, 2007



Workshops in

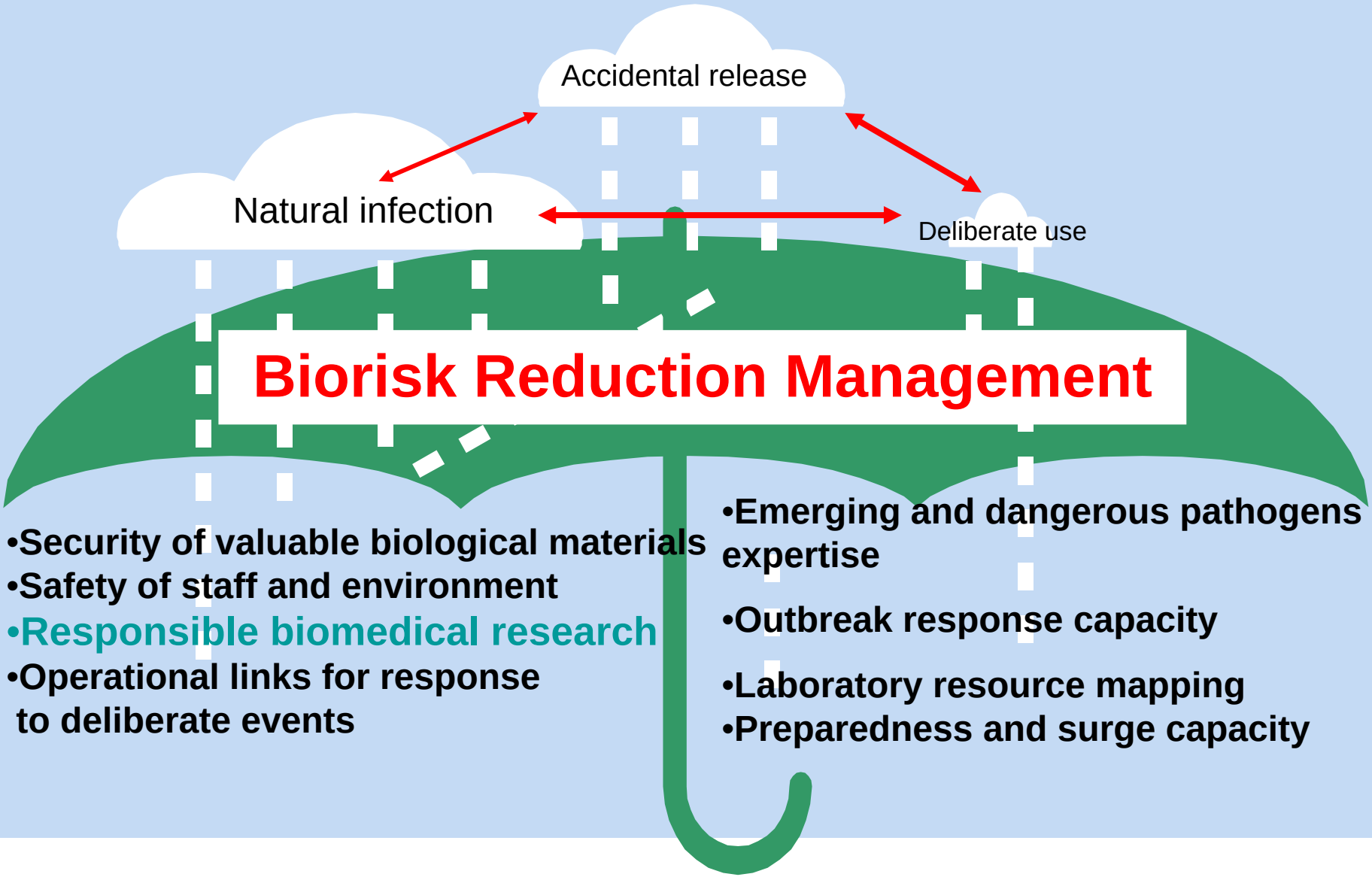
Teresepolis, Brazil
(December, 2006)

Matrahaza, Hungary
(May, 2006)

EMRO Regional Workshop
(Teheran, October 2006)

Dual use Conference
(Berlin, Dec, 2006)

International Roundtable on Dual Use of Life Science Research
(Bethesda, Feb, 2007)


Accidental release
Natural infection
Deliberate use
Biorisk Reduction Management
•Security of valuable biological materials
•Safety of staff and environment
•Responsible biomedical research
•Operational links for response to deliberate events
•Emerging and dangerous pathogens expertise
•Outbreak response capacity
•Laboratory resource mapping
•Preparedness and surge capacity

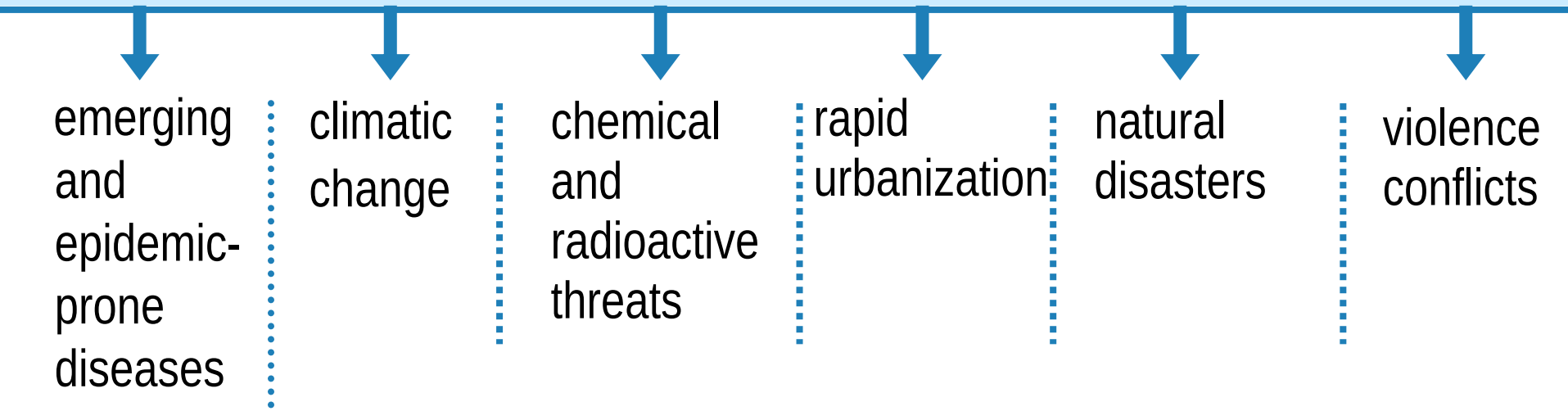
Five priority areas

- Raising awareness
- Preparedness for intentional release
- Develop risk assessment methodologies
- Develop guidelines for research oversight
- Build core capacities in countries

World Health Organization 2007–2011

Health and security

- **Universal vulnerability**
- **Collective action on the continuum of prevention, preparedness, prevention of spread, rapid and appropriate response, recovery and rehabilitation**



"Health security affects individuals and communities and also has an international dimension. All threats to health security at all levels reveal our shared vulnerability, and call for collective action"

Dr Margaret Chan,
WHO Director-General
Address to the 60th WHA
May 15, 2007

World Health Report 2007-Promoting Global Health Security
World Health Report 2008-Primary Health Care

The Six Core Functions of WHO

World Health Organization

LEADERSHIP AND PARTNERSHIP
RESEARCH AGENDA
NORMS AND STANDARDS
POLICIES
TECHNICAL SUPPORT
MONITORING AND ASSESSMENT

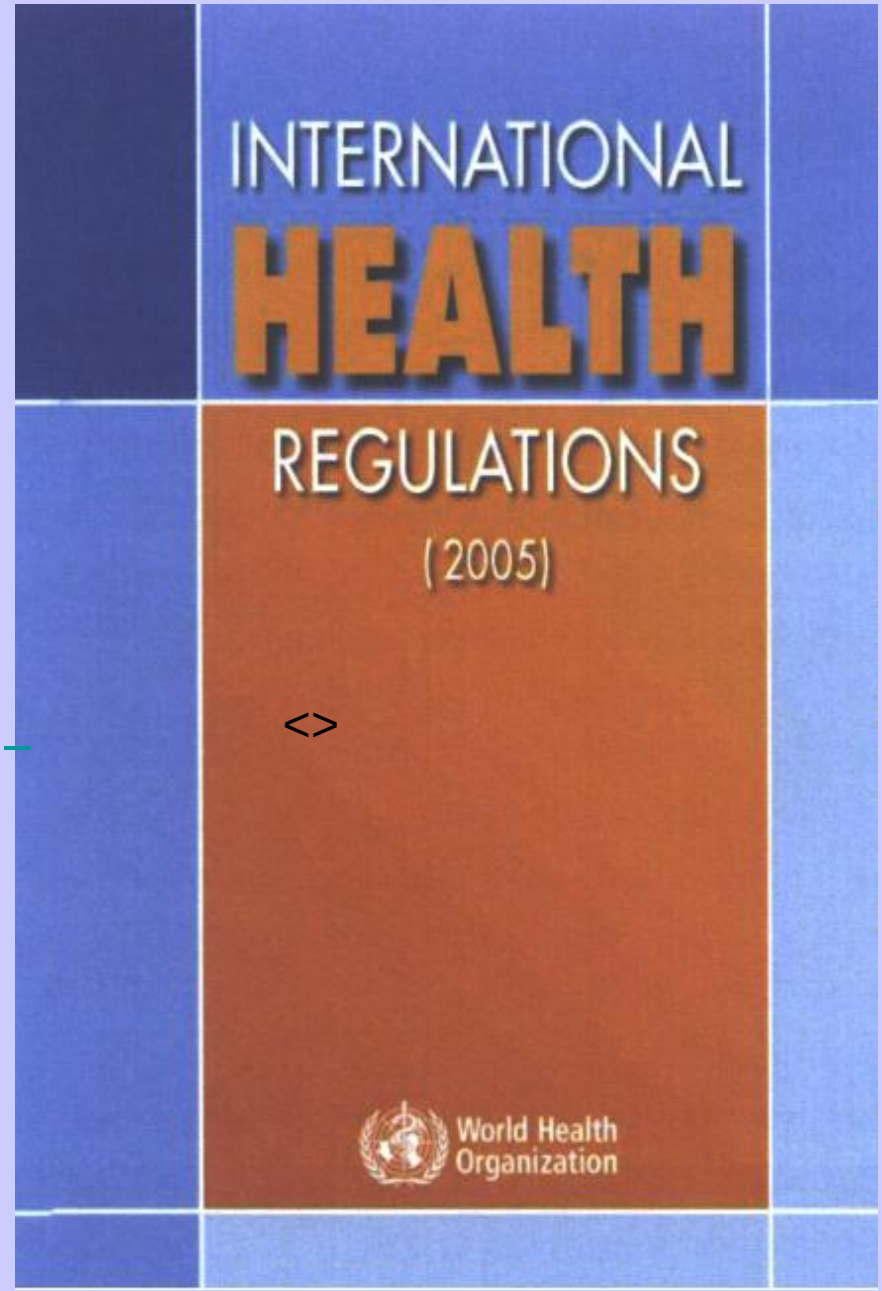
WHO Core Functions

Building on WHO's mandate and its comparative advantage, six core functions have been defined for the Organization.

1. Providing leadership on matters critical to health and engaging in partnerships where joint action is needed;
2. Shaping the research agenda and stimulating the generation, translation and dissemination of valuable knowledge;
3. Setting norms and standards, and promoting and monitoring their implementation;
4. Articulating ethical and evidence-based policy options;
5. Providing technical support, catalysing change, and building sustainable institutional capacity;
6. Monitoring the health situation and assessing health trends.

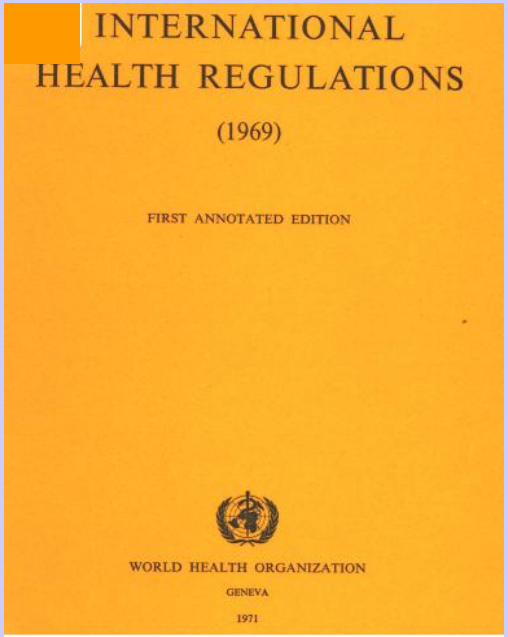
Why WHO?

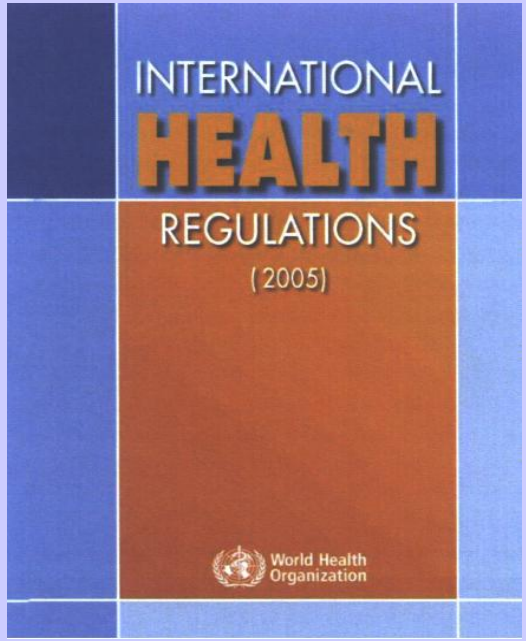
- Political legitimacy-supranational organization
- Direct reach into ministries of health
- Neutrality, independence, technical capacity
- Collective experience in managing public health events
- Decentralized structure & country presence
- Norms and standards function
- Convening capacity
- Global networks and partnerships
- Precedence for legal instruments



IHR is a legally-binding international agreement to prevent the spread of disease

IHR 2005 enters into force on June 15, 2007

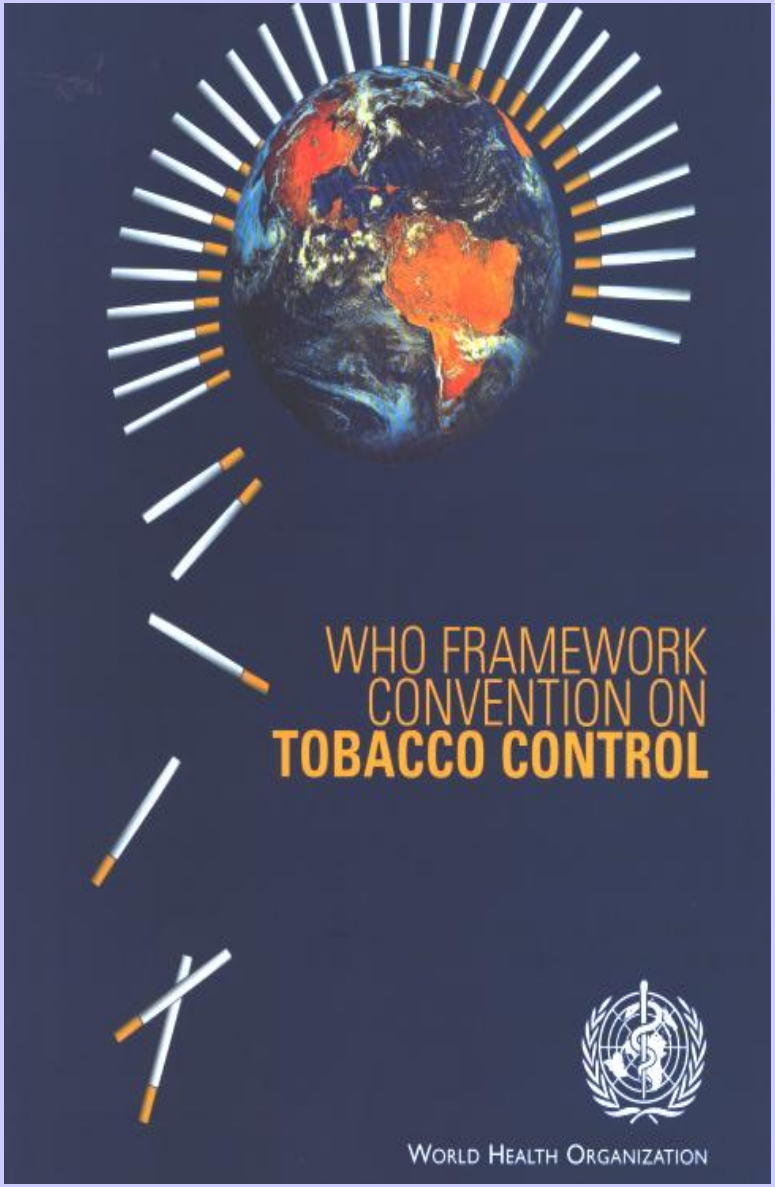


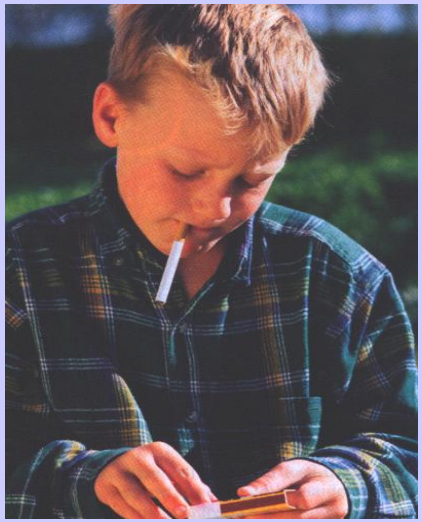


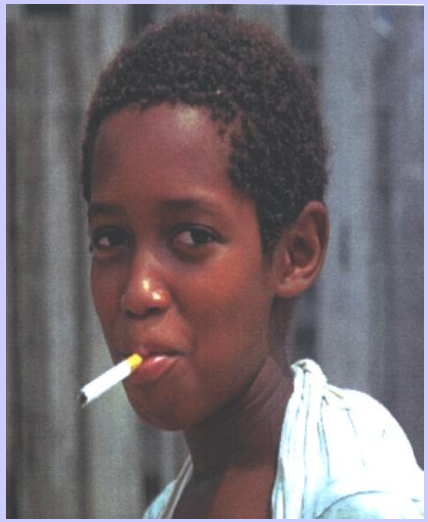
Control of borders → **Containment at source**

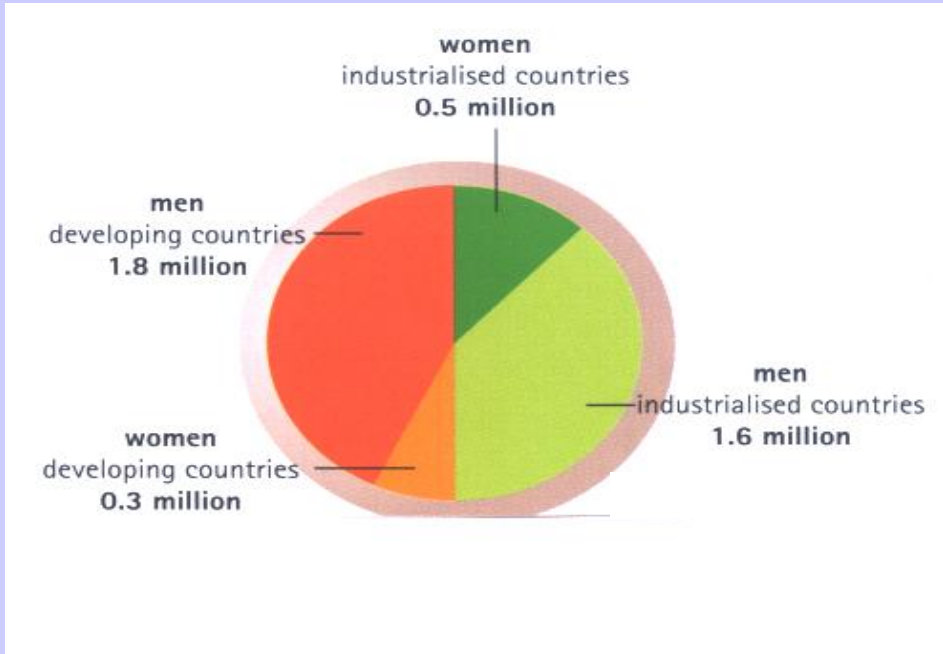
Diseases list → **All public health threats**

Pre-set measures → **Adapted response**


WHO FRAMEWORK
CONVENTION ON
TOBACCO CONTROL
WORLD HEALTH ORGANIZATION






women
industrialised countries
0.5 million
men
developing countries
1.8 million
men
industrialised countries
1.6 million
women
developing countries
0.3 million

ASEAN-Disease-Surveillance.Net :: South East Asian Nations Infectious Diseases Outbreak Surveillance Network

Home

"Promoting Regional Disease-Surveillance Response Capabilities and Cooperation, Through Web-based Information Exchanges"

National Center for Infectious Diseases

International Emerging Infections Program

IEIP Home Contact Us NCID Home

CDC

Department of Health and Human Services

Centers for Disease Control and Prevention

Thoughts on next steps and future directions

- Explore partnerships, enhance synergies, obtain buy-in and ownership
- Continue to raise awareness & visibility-build on current interest, "think out of the box", e.g. use other biosecurity angles
- **Stepwise approach** to develop **global** regulatory oversight mechanisms

  Registration of dual use research

- Inter-regional meeting (Dec, 2007) (WPRO-SEARO)

BBC News, March 15, 2006

TGN 1412 Fiasco

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Last Updated: Wednesday, 15 March 2006, 09:52 GMT

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Six taken ill after drug trials

Six men remain in intensive care after being taken ill during a clinical drugs trial in north-west London.

The six are being treated at Northwick Park hospital

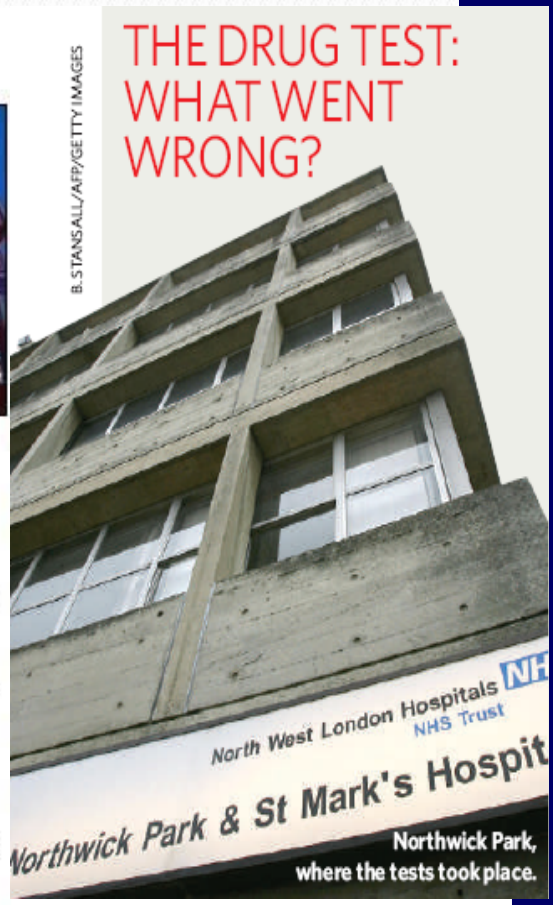
The healthy volunteers were testing an anti-inflammatory drug at a research unit based at Northwick Park Hospital when they suffered a reaction.

Relatives are with the patients, who suffered multiple organ failure. Two men are said to be critically ill.

An investigation has begun at the unit, run by Parexel, which said it followed recommended guidelines in its trial.

The men were being paid to take part in the early stages of a trial for the drug to treat conditions such as rheumatoid arthritis and leukaemia until they were taken ill on Monday within hours of taking it.

Eight volunteers were involved, but two were given a placebo at the unit which is on Northwick Park Hospital's grounds but is run independently.



Nature, March 23, 2006

The NEW ENGLAND JOURNAL of MEDICINE

Perspective

NOVEMBER 23, 2006

Dangerous Deception — Hiding the Evidence of Adverse Drug Effects

Jerry Avorn, M.D.

September 30 is becoming a day of infamy for drug safety. On that date in 2004, Merck announced that rofecoxib (Vioxx) doubled the risk of

authors advised against further use of the drug, since safer, cheaper alternatives are available.

After the study was published,

Observational Studies of Drug Safety — Aprotinin and the Absence of Transparency

William R. Hiatt, M.D.

The full safety profile of a new drug is rarely known at the time of approval by the Food and Drug Administration (FDA). Most drug-development programs designed for treatments of symptomatic indications are under-

The recent discussions of aprotinin (Trasylol, Bayer) by the Cardiovascular and Renal Drugs Advisory Committee of the FDA, which I chair, provide insight into the strengths and weaknesses of using observational data to assess

to determine causation, but they can detect signals that may suggest a safety concern.

In an observational study, decisions to use specific drugs are made by local physicians, according to their perceptions of the

Duplicity on drug safety

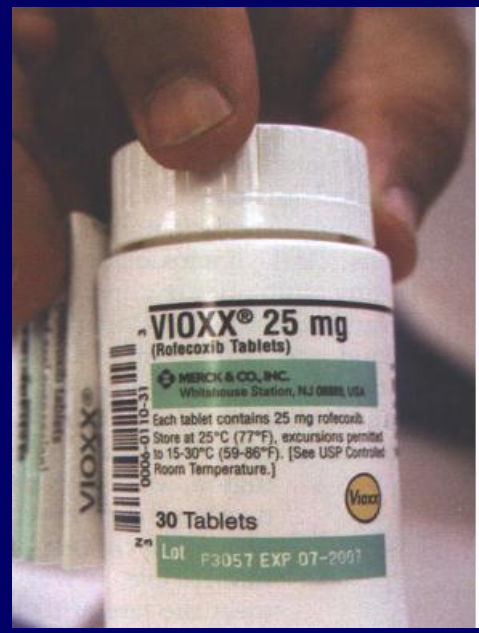
Bayer AG's limp excuse for withholding data suggesting that a heart-surgery drug is dangerous won't wash. The failure by the German pharmaceutical giant to tell the U.S. Food and Drug Administration of the disquieting results of a large observational study cannot be sloughed off as a mere "mistake on the company's part." Rather, the circumstances suggest that Bayer sought to hide the results of a study until some way could be found to discount them. It came clean only when forced to by a whistleblower.

Trasylol has long been used in heart surgery to reduce blood loss and the need for transfusions. Although extensive data seemed to document the drug's effectiveness and safety, two studies published this year found that it increased the risk of kidney failure, heart attack and stroke.

Even so, an FDA advisory committee, after a public meeting on Sept. 21, concluded that Trasylol was still acceptably safe and effective for certain patients. The committee had not been told — because Bayer representatives who participated in the meeting kept mum — about the most recent large study the company had sponsored, which raised even more questions about the drug's safety.

After the fact, a whistleblower, possibly an outside researcher, reportedly called both the FDA and Bayer to force full disclosure. Preliminary results of the suppressed study showed that Trasylol may increase the chance for death, serious kidney disease, congestive heart failure and strokes. This incident underscores the importance of requiring drug companies to publicly register all safety studies.

IHT, Oct 7-8, 2006



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International Clinical Trials Registry Platform (ICTRP)

WHO > WHO sites

International Clinical Trials Registry Platform

New standards for registration of human medical research

19 May 2006 -- WHO is urging research institutions and companies to register all medical studies that test treatments on patients or healthy volunteers. Registration of clinical trials – including preliminary studies – will be fundamental to ensuring transparency and fulfilling ethical responsibilities.

Full text | Related articles in The Lancet

Clinical trials are one of the most important sources of scientific evidence on the safety and effectiveness of health interventions. Access to information about ongoing, completed and published clinical trials is essential for appropriate decision-making. Researchers, research funders, policy-makers, medical practitioners, patients and the general public need such information, to help guide research or to make treatment decisions.

WHO/Stephenie Hollyman

To ensure transparency and to increase public trust in the conduct of clinical research, it is important that all clinical trials be registered at inception and that all results be made publicly available. With the approval of the World Health Assembly in May of 2005, the International Clinical Trials Registry Platform is taking the lead in setting international norms and standards for trial registration and reporting. The Registry Platform consults with relevant stakeholders worldwide to produce consensus-based policies that uphold scientific and ethical principles on clinical trials but that are also practical and feasible.

ANNOUNCEMENT

The World Health Organization announces new standards for registration of all human medical research
News release

TRIAL REGISTRATION DATA SET

The WHO Trial Registration Data Set

ICTRP IN THE NEWS

Editorial - The Pan American Journal of Public Health - 30 June 2006 [pdf 58kb]

The Latin American Ongoing Clinical Trial Register (LATINREC) - June 2006 [pdf 72kb]

Archive

NEWSLETTER

Issue 3 - July 2006 [pdf 213kb]

Archive

MEETING REPORTS

WHO Registry Platform Mission

To ensure that a complete view of research is accessible to all those involved in health care decision making

This will improve research transparency and will ultimately strengthen the validity and value of the scientific evidence base, and enhance public confidence in research

Standards & Policy Positions

International Clinical Trials Day, Brussels, May 19, 2006

- Which trials must be registered?

  All interventional clinical trials, including early phase uncontrolled trials in patients or healthy volunteers

- When should registration occur?

  At inception of trial and before recruitment of first participant

- What trial data must be registered?

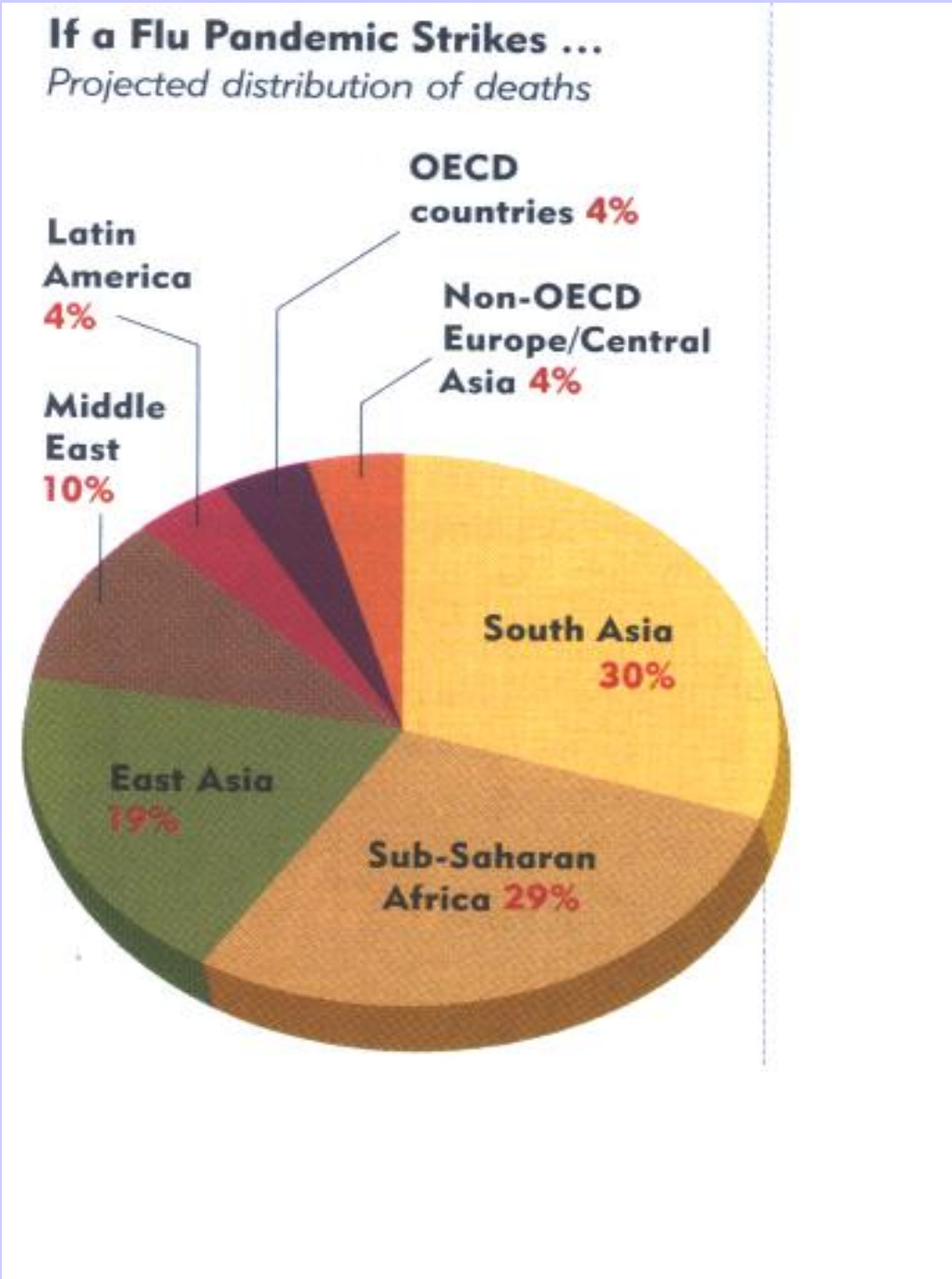
  All 20 items in minimum registration dataset to be publicly disclosed at Registration. WHO does not support any mechanism for delayed disclosure.

WHO Registration Data Set (1)

1. Primary Register and Trial ID# (e.g., ISRCTN number)
2. Date of Registration in Primary Register
3. Secondary ID#s
4. Source(s) of Monetary or Material Support
5. Primary Sponsor
6. Secondary Sponsor(s)
7. Contact for Public Queries
8. Contact for Scientific Queries
9. Public Title
10. Scientific Title

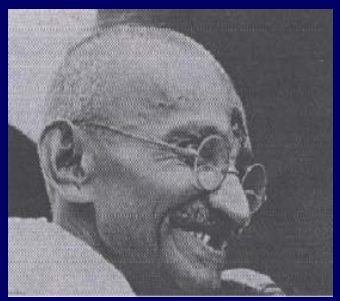
WHO Registration Data Set (2)

11. Countries of Recruitment
12. Health Condition(s) or Problem(s) Studied
13. Intervention(s)
14. Key Inclusion & Exclusion Criteria
15. Study Type
16. Date of First Enrollment
17. Target Sample Size
18. Recruitment Status
19. Primary Outcome(s)
20. Key Secondary Outcome(s)



Murray et al, Lancet 2006, 368, 2211-8

It is not what we do
but what we can do
to make this world a
better and safer place



Gandhi
(1869-1948)