ドラッグ・ラグ、ワクチン・ラグの要因

医薬品の臨床試験の実施基準の国際的整合性について

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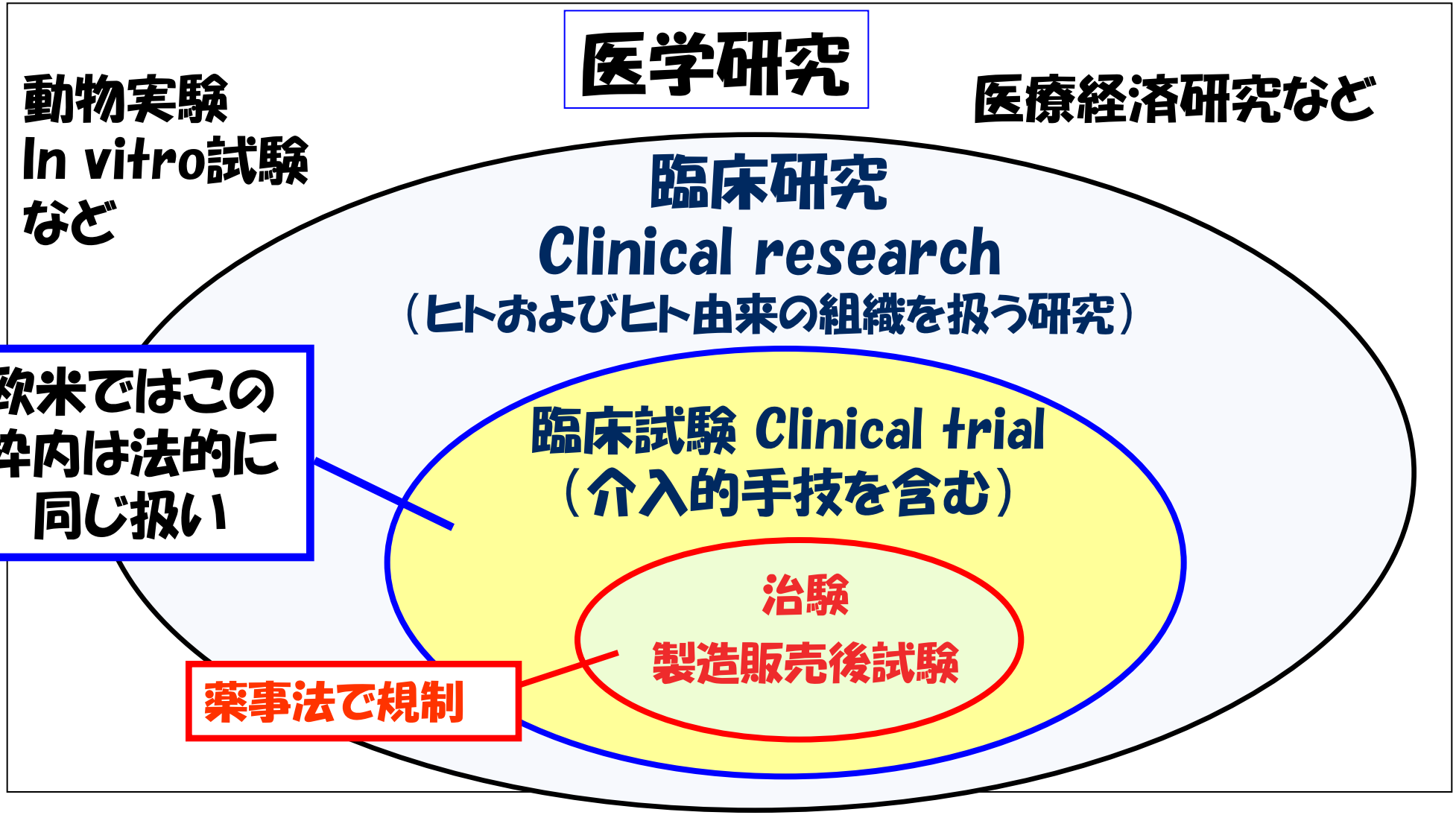
藤原康弘

2012/03/02

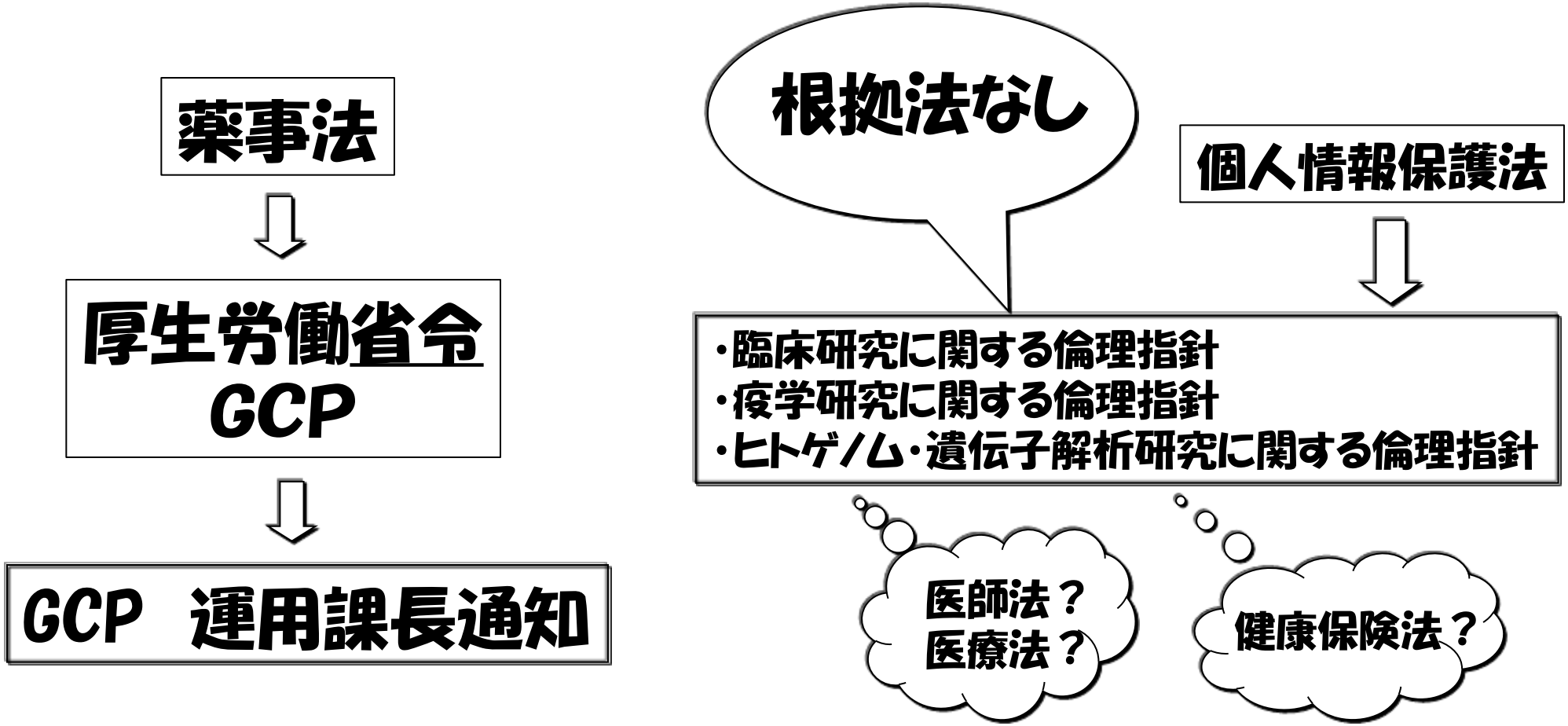
治験と臨床研究・臨床試験



臨床研究・臨床試験を巡る法体系が欧米と比して日本だけ違う

欧米では、
日本の薬事法令のように
医薬品・医療機器の審査・承認ための
法体系とは
別に、
広く臨床研究・臨床試験における
被験者の人権保護や
臨床研究・臨床試験の科学的な質、
データの信頼性を確保するための
法体系が存在。

日本では、臨床研究・臨床試験に関して<u>承認・申請目的のもの（＝治験）</u>でしか科学性や倫理性の法的担保なし



米国　国家研究法

PL 93-348, 1974 HR 7724
PL 93-348, JULY 12, 1974, 88 Stat 342
(Cite as: 88 Stat 342)

UNITED STATES PUBLIC LAWS
93rd Congress - Second Session
Convening January 21, 1974

PART 46—PROTECTION OF HUMAN SUBJECTS

Subpart A—Basic HHS Policy for Protection of Human Research Subjects

utero, including nonviable fetuses, as subjects.
46.210 Activities involving the dead fetus, fetal material, or the placenta.
46.211 Modification or waiver of specific requirements.

Subpart C—Additional Protections Per...

米国　連邦規則　Title 45CFR Part 46
（"Common Rule"と呼ばれています）
連邦政府から研究資金を得て実施されている
臨床研究の被験者保護を規定

An Act tO ... OF NATIONAL
RESEARCH ... MEDICAL AND
BEHAVIOR ... IAN SUBJECTS
INVOLVED ... ES.

changes in approved research.
46.111 Criteria for IRB approval of research.
46.112 Review by institution.

oners.

Subpart D—Additional Protections for

米国政府は、日本や欧州と異なり
ICH-E6(ICH-GCP)を単一の法令で発出していない

米国 Clinical Research Enhancement Act

公的研究費にもとづく臨床研究環境整備をうたっている

Public Law 106–505
106th Congress

2000年11月

An Act

Nov. 13, 2000
[H.R. 2498]

To amend the Public Health Service Act to provide for recommendations of the Secretary of Health and Human Services regarding the placement of automatic external defibrillators in Federal buildings in order to improve survival rates of individuals who experience cardiac arrest in such buildings, and to establish protections from civil liability arising from the emergency use of the devices.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

Public Health Improvement Act.
42 USC 201 note.

SECTION 1. SHORT TITLE; TABLE OF CONTENTS.

(a) SHORT TITLE.—This Act may be cited as the "Public Health Improvement Act".

(b) TABLE OF CONTENTS.—The table of contents of this Act is as follows:

EU 臨床試験指令
Directive 2001/20/EC

DIRECTIVE 2001/20/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 4 April 2001

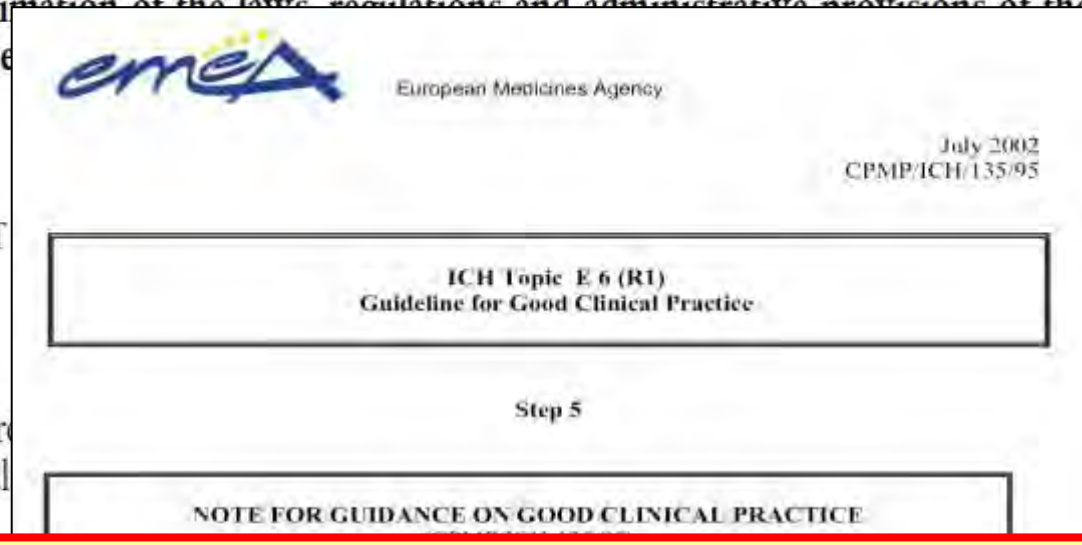
on the approxi[illegible] Member States relating to the [illegible]inical trials on

THE EUROPEAN PARLIAMENT [illegible]e of giving legal consent to EUROPEAN UNION, [illegible]given special protection. It is [illegible]r States to lay down rules to

Having regard to the Tr[illegible] [illegible]ay not be included in clinical Community, and in particul[illegible] [illegible]an be obtained using persons [illegible]nt. Normally these persons [illegible]ical trials only when there are

Having regard to [illegible]istering of the [illegible] benefit to the [illegible]owever, there is

Having regard to [illegible]ren to improve Committee (2), [illegible]en represent a [illegible]l, physiological [illegible]s which make


emea European Medicines Agency

July 2002
CPMP/ICH/135/95

ICH Topic E 6 (R1)
Guideline for Good Clinical Practice

Step 5

NOTE FOR GUIDANCE ON GOOD CLINICAL PRACTICE

EUでは
Note for Guidance
(CPMP/ICH/135/95)
としてICH-GCPを法令に組み込んでいる

EUでは
臨床試験指令 DIRECTIVE 2001/20/EC (April 2001)という法律（法令）が存在し。その中で、添付文書の内容を外れる医薬品を使用をするような（介入を伴う）臨床研究（＝臨床試験　clinical trial）については、GCP（ICH-GCP）に従うことを求めている。

EUでは、日本で“治験”と呼ばれている、主に企業が主体となっておこなう臨床試験に加え、医師・研究者が主体となって行う臨床試験もすべてGCP対応を求められている。

規制のやり過ぎには要注意！

EDITORIAL

nature medicine

Safeguarding clinical trials

Efforts are underway to modernize clinical trial standards and normalize regulations to facilitate international collaboration. But as the European Union's Clinical Trials Directive shows, a one-size-fits-all regulatory strategy may be easier to conceive than to implement.

http://www.nature.com/naturemedicine

Nature Medicine　Feb, 2007

NEWS

Tied up in red tape, European trials shut down

The chemotherapy drug doxorubicin has been used to treat soft-tissue cancers in children for more than 20 years, but doctors don't know the most effective dose, nor how it interacts with other drugs.

In 2005, European researchers set out to find these answers in a large, multi-center trial.

Two years on, fewer than half of the 600 participants needed have been recruited. Only 2 of the 16 countries originally involved—Italy and France—began on time. Denmark has yet to start, and Poland, Austria, Sweden and Germany—the last expected to provide 25% of study subjects—dropped out. Trial coordinators canceled plans to analyze data part way through the study. The trial's 2010 end date is likely to be pushed back by at least two years.

Scientists say the study is merely the latest victim of the Clinical Trials Directive, for the Research and Treatment of Cancer estimates that expenses have risen by 85% and says the number of trials it supports has dropped by 63%. The Save European Research campaign, which represents more than 3,000 scientists, says academic drug trials have dropped by 70% in Ireland and 25% in Sweden. The number of Finnish academic drug trials shrunk by 75%.

TRIAL AND ERROR

The European Clinical Trials Directive has created bureaucratic nightmares and is shutting down trials. Since the directive's launch:

Increase in the cost of academic cancer trials in the UK	200%
Drop in academic drug trials in Finland	75%
Drop in academic trial submissions in Ireland	70%
Increase in the cost of trials supported by EORTC	85%
New trials supported in 2004 by the group	19
New trials supported in 2005 by the group	7

Sources: Cancer Research UK; *Brit. Med. J.*; EORTC

Because the directive is technically not law, "They're getting overwhelmed with the

EU 臨床試験指令のもたらした利点と弊害について、EU全域から医師研究者を集めて討議

PROJECT FINAL REPORT

Publishable

Grant Agreement number:	HEALTH-F1-2007-201002
Project acronym:	ICREL
Project title:	IMPACT ON CLINICAL RESEARCH OF EUROPEAN LEGISLATION
Funding Scheme:	CSA COORDINATION AND SUPPORT ACTION – SA SUPPORTING ACTION
Period covered:	**from** 01 January 2008 **to** 31 December 2008
Project co-ordinator name, Title and Organisation:	
	Dr Ingrid Klingmann, Project Coordinator, EFGCP
Tel:	+32 2 784 36 93
Fax:	+32 2 784 30 66
E-mail:	ingrid.klingmann@efgcp.be
Project website address:	www.efgcp.be/ICREL

Target groups for whom the report could be relevant: all stakeholders implied in clinical research in the European Union, e.g. medical academic institutions, investigators, pharmaceutical companies, pharmaceutical industry associations, European regulatory authorities, European Commission, ethics committees, patients and patient organisations, insurance companies, medical press, politicians.

STATBITE

Key Findings from the "Impact on Clinical Research of European Legislation" Report

The number of staff working in the area of clinical trial applications and investigational medicinal product dossier preparation within companies **doubled in 2007 in comparison to 2003 (2 people vs. 4 people)**

Ethics committees' mean annual budget **increased by more than 50% (404,000 Euros in 2003 vs. 955,000 in 2007)** d
increase in numbe
and suspected un
adverse reacti

倫理審査委員会の年間コストが
4千万円から9千5百万円へアップ
日本の病院にはこんな予算はないし
診療報酬体系にも組み込まれていない

For multinational trials, on average, the time from finalizing the protocol to enrolling first patient **increased from 115 days to 152 days, or 30%**

The mean timelines for clinical trial application review by the individual competent authorities **decreased from 60 to 49 days, or 18%**

J Natl Cancer Inst March 2010

GCPに関する論点

- 国内単独で治験を実施する際、他国で実施する場合よりも日本で実施する場合の方が手間が著しく増えるような ICH-GCPとJ-GCPとの乖離があれば問題

- 国際共同治験を実施する際、日本でのみ手間が著しく増えるようなICH-GCPとJ-GCPとの乖離があれば問題

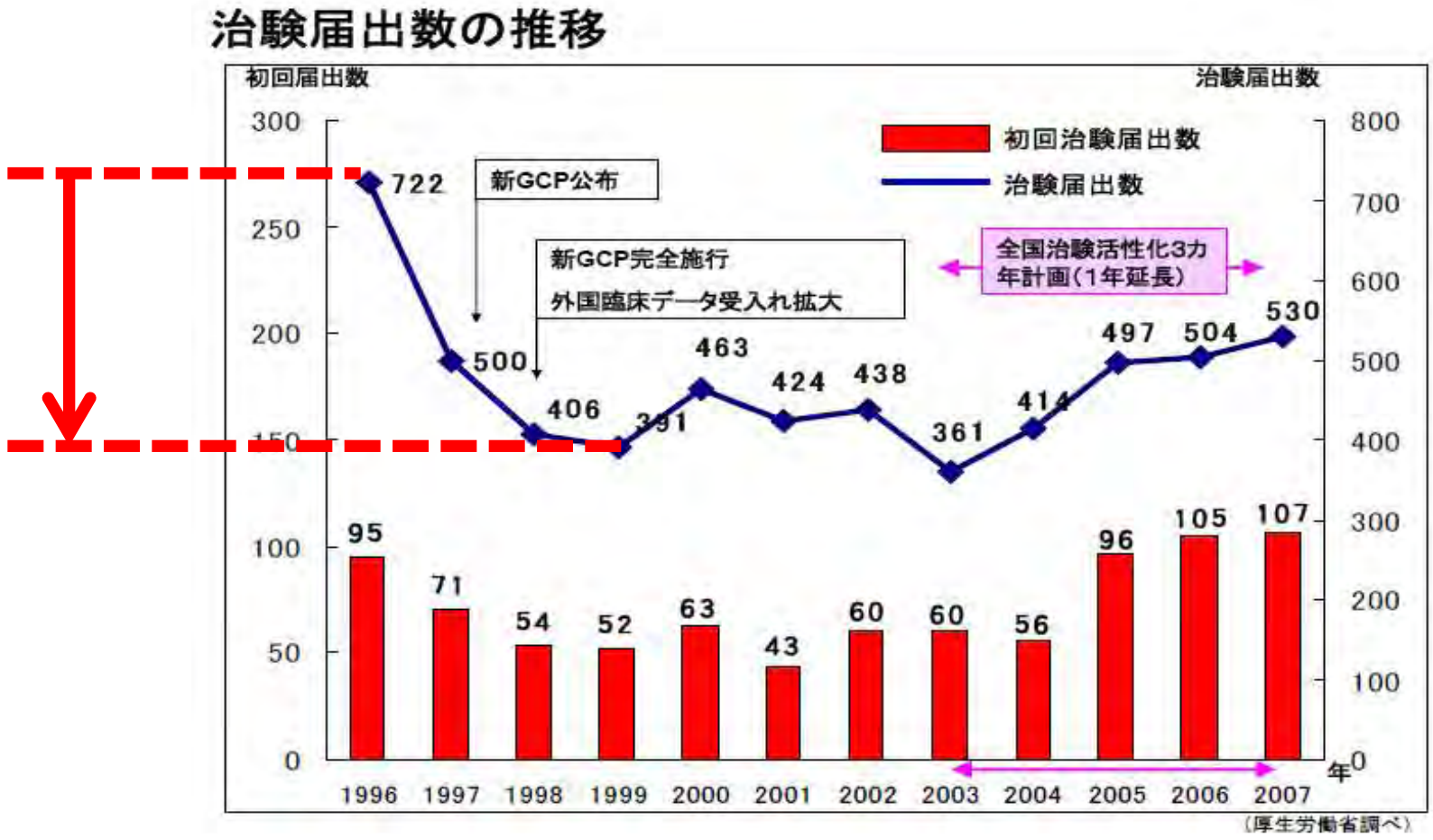
- 厚労省側と企業・医療機関側で意識の差があるために、企業の過度な防衛策としてオーバークオリティが生じているのであれば問題

議論の在り方に変化が必要

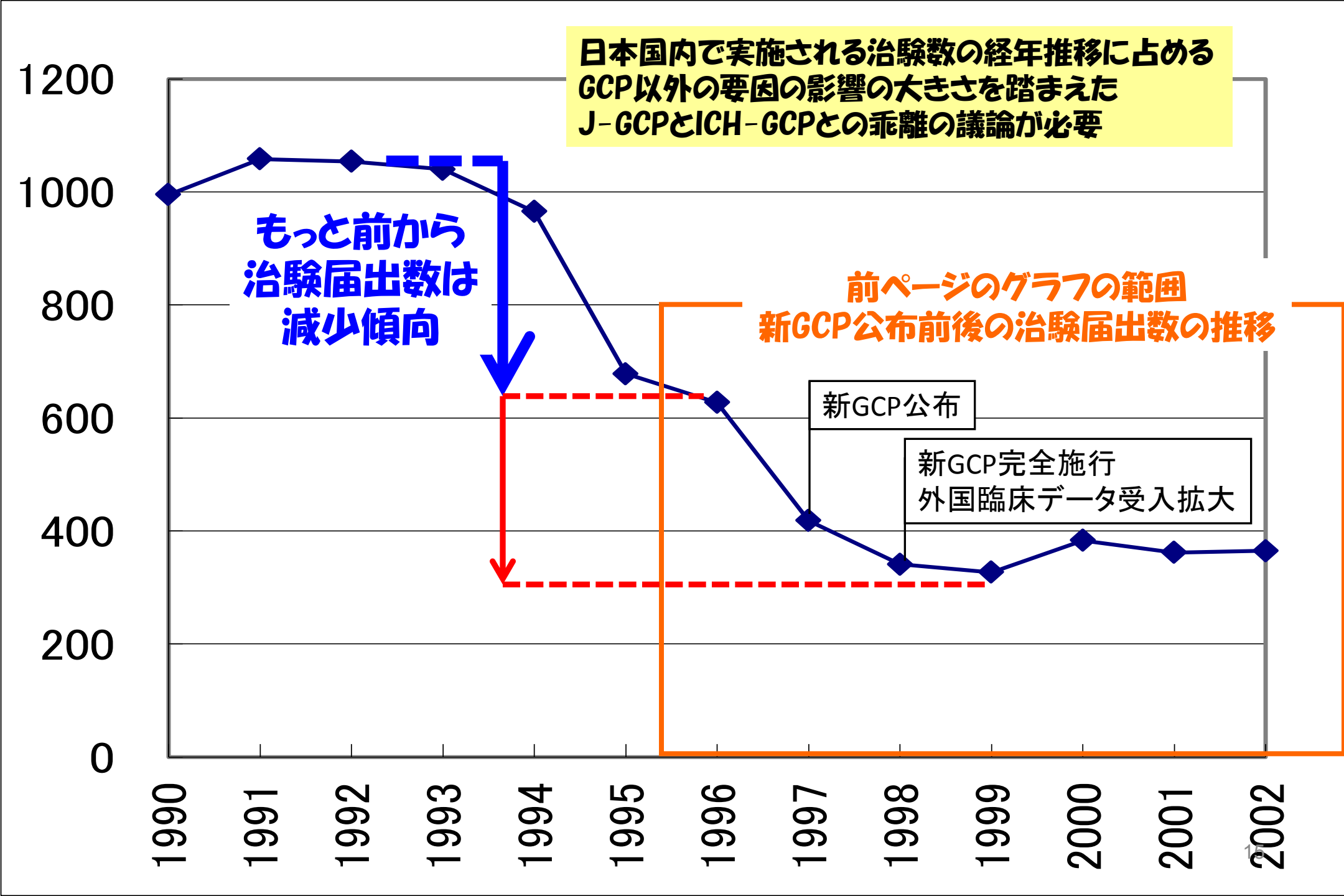
- 「単なるJ-GCPとICH-GCPの乖離」のみを議論していても、
  議論のための議論にしかならない
  - 米国でのGCPとICH-GCPとの間にも乖離は存在
  - J-GCPとICH-GCPの乖離があったとしても、（他国においても同様に乖離はあるのだから）**それだけでは、日本で治験数が減少する理由や治験実施が活性化しない理由にはならない**

- 「実務上問題を引き起こすJ-GCPとICH-GCPの乖離」、「修正することで実務上の大きな効率改善があるJ-GCPとICH-GCPの乖離」を
  議論することが必要
  - 「“オーバークオリティ”なJ-GCPとICH-GCPとの乖離の議論」は
    避ける必要がある

- J-GCPとICH-GCPの乖離に過度にこだわることで、日本で治験実施が活性化しない本来の問題を見落とすことになっては本末転倒である



http://www.mhlw.go.jp/topics/bukyoku/isei/chiken/dl/kasseika_todokede.pdf


日本国内で実施される治験数の経年推移に占める
GCP以外の要因の影響の大きさを踏まえた
J-GCPとICH-GCPとの乖離の議論が必要
もっと前から
治験届出数は
減少傾向
前ページのグラフの範囲
新GCP公布前後の治験届出数の推移
新GCP公布
新GCP完全施行
外国臨床データ受入拡大
1200
1000
800
600
400
200
0
1990
1991
1992
1993
1994
1995
1996
1997
1998
1999
2000
2001
2002