

Changing Roles of IRBs

Background

- **Required components of IRB activity**
 - **Review of fundable federal grants (all human research if have Multiple Project Assurance)**
 - **Approval of consent forms**
 - **Monitoring of ongoing studies**
 - **Continuing review (at least annually)**
 - **Serious adverse events (SAEs), deviations amendments**

Changing Roles of IRBs

Background

- **FDA & OHRP administer Federal Regulations governing IRBs**
 - **Function**
 - **Composition**
 - **Includes**
 - **Review of all federally sponsored human studies**
 - **Human studies of drugs and devices regulated by FDA**

Changing Roles of IRBs

Introduction

- **IRB activities increasing**
 - **More research**
 - **Local institutional**
 - **Multicenter trials**
 - **Increasing oversight of IRBs and reinterpretation of regulations by FDA, OHRP**
 - **Increasing oversight by IRBs (continuing review, SAEs/deviations)**
 - **Emphasis on education**



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Objectives

- **Mayo Foundation IRB experience, 1986-2000**
 - **Volumes**
 - **Reorganization**
 - **Cost**
 - **Service**
- **Major issues from local perspective**
 - **Education**
 - **Informed consent**

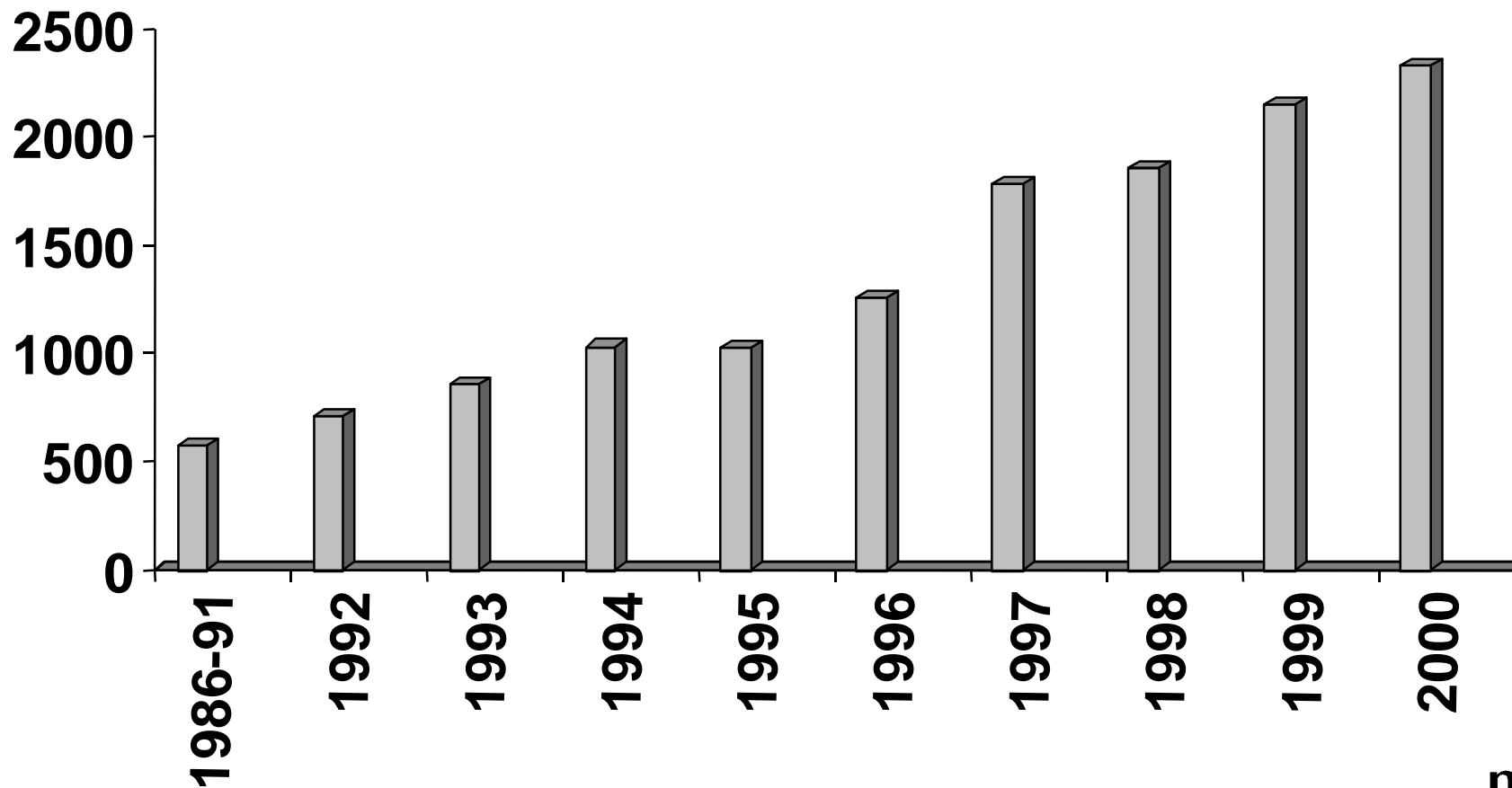


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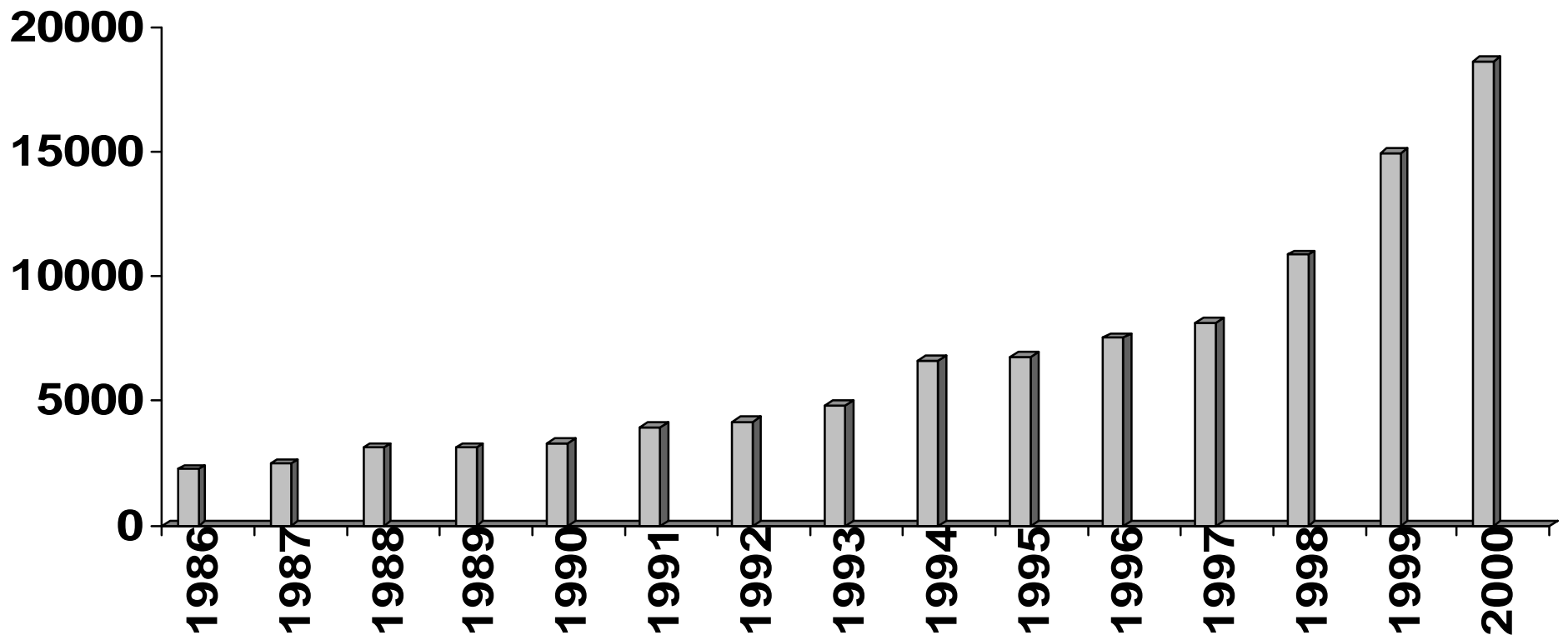
Objectives (2)

- **Relations between IRBs**
 - **Investigators**
 - **OHRP**
 - **FDA**
 - **NIH**
 - **Industry**
- **Data Safety Monitoring Boards (DSMBs), multicenter and unicenter studies**
- **SAEs/deviations**

New Protocols Reviewed by IRB 1986-2000



Total IRB Items (New Protocols, Progress Reports, Adverse Events etc.) 1986-2000



Activity Summary 1995-2000

- **Total protocols reviewed**
 - **1995 - 854**
 - **1999 - 2151**
 - **2000 - 2328**
 - **8% > 1999**
 - **273% > 1995**
- **Overall total IRB items**
 - **1995 - 6774**
 - **1999 - 14945**
 - **2000 - 18640**
 - **25% > 1999**
 - **275% > 1995**

Changing Roles of IRBs

- **Prior to 2000 - one board**
- **August 4th, 2000, a fully convened board began meeting each Friday**
 - **Membership of original Mayo IRB split to form second board**
 - **No new consultants added**
 - **Community members added for all three practice sites**



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Reorganization

Before 2 Boards

- 14 Consultants
- 3 - 4 hr meetings
- Frequent loss of quorum
- Backlog of items remaining after loss of quorum or late hour

After 2 Boards

- 14 Consultants
- 2½ to 3 hr meetings
- No loss of quorum
- No backlog - all complete items submitted by deadline are placed on agenda

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Reorganization

- **Before 2 Boards**

- 1 Executive SC* (4 hr/wk)
- 1 SAE/Deviations SC (1 hr/wk)
- 6 fulltime staff

*Subcommittee

**Conference phones,
electronic projection

- **After 2 Boards**

- 2 Executive SC (8 hr/week)**
- 1 SAEs/Deviations SC (2½ hr/wk)**
- Admin SC (1.5 hr/wk)**
- Mini & annual planning retreats (½-1½ days)
- 13 fulltime staff



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Results of Reorganization

- **Protocols > minimal risk; 10-1 to 12-12-00**
 - **103 studies**
 - **90% (93/103) reviewed within 13 days (mean 10 days, range to 27days)**
 - **1 investigator request to attend meeting**
 - **3 holidays intervened**
 - **4 submitted to Exec but needed Full**
 - **2 unknown reasons**

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Results of Reorganization

- 46% (n=47) approved first review
- 31% (n=31) eventually approved
- 24% (n=25) awaiting investigator response
- Notification after IRB meeting 82% \leq 5 working days (range 1-8 working days)
- Receive contingency responses after approval (n=31) mean 7 days (median 4, range 1-25 days)
- Activation after receiving contingency response 7 days (mean and median, range 1-16 days)

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Results of Reorganization

- **Summary**
 - **Time to approval after IRB submission**
 - 47% within 13 days (no contingencies)
 - If contingencies & investigator responds - mean of ~ 29 days (31% of submissions)
 - 24% of investigators have yet to respond
 - **Conclusions**
 - IRB response time is excellent; ?
improvement
 - Investigators/other cause much of the delay

Changing Roles of IRBs Education (2000)

- **Initiated and conduct biannual ½ - 1 day orientation/education programs for all IRB members and staff**
- **IRB Chair, administrator and legal representative initiated human subject research presentations to**
 - **Divisions/departments (>1500 participants)**
 - **Research & administration leadership (quarterly; Foundation, MCR, MCS and MCJ)**

Changing Roles of IRBs Education (2000)

- **Executive Subcommittee and staff created web-based Mayo Investigator Training Program**
 - **Launched June 2000**
 - **December 2000 - all staff (3500) actively participating in human subject research complete investigator training**
 - **Includes assessment**
 - **Necessary for any new human studies**
 - **Ongoing updating for content and readability**



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Continuing Review

- **“Inadequate continuing review” - failure of once yearly review @ convened meetings (OHRP activities; ohrp.osophs.dhs.gov/references/findings.pdf)**
 - **Previously used expedited review - full review only if deemed necessary by reviewer**
 - **Now full Board review; more time spent without enhancing protection**
 - **Time might be better spent in on site monitoring of informed consent**

Changing Roles of IRBs Multicenter Trials & DSMB

- **Role of local IRBs “more detailed review of research performed solely within that institution”** (*Burman et al; Ann Intern Med 2001; 134: 152*)
 - **Rely upon central IRBs**
 - **Review of multicenter studies**
 - **Common consent form**
 - **Safety and outcome analyses by DSMB**
 - **Essentially no role for local IRBs**

Changing Roles of IRBs

Serious Adverse Events (Safety)

- Prevailing opinions of analysis of safety reports for multicenter trials
 - “This function is critical but...not responsibility of the local IRB” (*Burman et al; Ann Intern Med 2001; 134: 152*)
 - “The NIH/OPRR and FDA should work with IRBs and others in identifying the specific Federal requirements to be eliminated or modified” (*Office of Inspector General 1998;I-90. Publication No. 97-00197*)



Changing Roles of IRBs Multicenter Trials, DSMB & Serious Adverse Events (Safety)

- Proponents of prevailing views claim
 - Concern that reviews, etc. prolong process without enhancing protection
 - Local IRBs cannot “critically review safety reports from multicenter trials because they lack the data elements; the denominator and the study assignment”

(Burman et al; Ann Intern Med 2001; 134: 152)



Changing Roles of IRBs Multicenter Trials, DSMB & Serious Adverse Events (Safety)

- **Views may be shortsighted, ? self-serving**
 - **Do not consider that**
 - **Local IRB reviews can be speedy**
 - **Sponsors conducting reviews and constructing consent forms (NIH review bodies, commercial IRBs)**
 - **May have biases (unintentional or otherwise)**
 - **Are not independent and have interests other than protection of the research participant**
 - **SAE review also method to provide local oversight of ongoing studies**

Changing Roles of IRBs Multicenter Trials, DSMB & Serious Adverse Events (Safety)

- Agree that IRBs cannot evaluate safety without proper information, but is available if persist
 - Solution is for DSMB to provide the information!!
 - DSMB reports inadequate
 - Can be given and maintain blind for investigators participants
 - Information (denominator) required even if only evaluating SAEs at local institution
 - DSMB prospectively must have defined stopping rules (safety, efficacy)
 - Local oversight should be maintained and strengthened

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Summary

- **To decrease workload on IRB members and increase efficiency of review by full board**
 - **Increase number of boards**
 - **Requires more support**
 - **Financial**
 - **Staff**
- **Need new regulations for oversight activities**
 - **Continuing review of research studies**
 - **Serious adverse events**

Changing Roles of IRBs

Summary (1)

- **Continuing review of research studies**
 - **OHRP should relax apparent requirement of full board review of ongoing > minimal risk research** (*Levine; Ann Intern Med 2001; 134: 161*)
 - **Continuing review overlaps with review of SAEs (at local level SAE review is an ongoing process of reviewing ongoing research)**
 - **Allow review by subcommittee with mandate to refer problems to full board**

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Summary (2)

- **Multicenter studies, DSMBs and IRBs**
 - **Suggested role of monitoring of serious adverse events (safety) for multicenter studies should be responsibility of DSMB & local IRB only review SAEs at their institution**
(Burman et al; Ann Inter Med 2001; 134: 152)
 - **Unsatisfactory**
 - **Local IRB cannot judge what action to take unless knows denominator of event (incidence)**

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Summary (3)

- DSMB reports give no useful information**
- To gain appropriate information IRB makes multiple calls**
 - Investigator**
 - NIH**
 - Pharmaceutical/device company**
- Local monitor (usually chair) should have the same information available to DSMB or at least enough to make informed decision (information kept confidential)**

Changing Roles of IRBs

Summary (4)

- **Nurture mission to provide service and guidance to conduct research while honoring & upholding institution's values** (*after Levine; Ann Intern Med 2001; 134: 161*)
 - **Education**
 - **Openness - foster dialogues with**
 - **Investigators**
 - **Institutional committees, Federal regulatory agencies and sponsors**

