Latest Developments in Human Subject Protections: DSMBs/DMCs, Secondary Research Issues, and Patient Access to Experimental Drugs under *Amgen* and *Abigail Alliance*

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Other “hot topics” covered in other sessions of this conference

Billing third party payors for services related to clinical trials

Time and effort reporting and grant activities – OIG investigations and settlements

International sponsored research projects: not covered here, but a true “hot topic”
Data and Safety Monitoring Boards
Or Data Monitoring Committees:
New FDA Guidance
Overview of DMCs

**Definition.** Data Monitoring Committees (DMCs) – often also known as Data and Safety Monitoring Boards – are charged with conducting regular reviews of interim trial data and are distinct from the sponsor, IRBs and other trial oversight bodies.

**Purpose.** DMCs advise sponsors regarding subject safety and the continuing validity and scientific merit of the trial.
1998 – NIH Policy for Data and Safety Monitoring

Purpose. To ensure the safety of participants and the validity and integrity of the data

Monitoring Policy. Each NIH Institute and Center should have a system for the appropriate oversight and monitoring of the conduct of clinical trials.

DSMB Policy. DSMB must be established for all NIH supported or conducted multi-site clinical trials involving interventions entailing potential risks to participants. Monitoring should be commensurate with risks to participants as well as size and complexity of trial...
Pre-existing Guidance


**DSMB Composition.**
- Independent clinical trial experts, one or more biostatistician, and clinicians
- Medical ethicists and medical specialists, as appropriate

**DSMB Responsibilities**
- Evaluate research protocol and monitoring plans
- Regularly review data
- Make recommendations to sponsor, IRB, and investigators regarding the continuation or conclusion of trial
- Maintain confidentiality of data
Pre-existing Guidance

1999 – NIH Guidance on Reporting Adverse Events to Institutional Review Boards for NIH-Supported Multi-Center Clinical Trials

- **Purpose.** To promote the effective, streamlined reporting of adverse events (AEs) to the appropriate IRBs.

- **Policy.** All multi-site trials with DSMBs are expected to submit summary reports of AEs to all participating IRBs by way of the investigator.

- **Protocol.** Protocols should identify the DSMBs and describe the monitoring plan and procedures for transmitting DSMBs reports to all participating IRBs.
2000 – NIH Further Guidance on Data and Safety Monitoring for Phase I and Phase II Trials

Phase III Trials - DSMBs required

Phase I & II Trials - DSMBs may be appropriate

Monitoring in Phase I or Phase II

– Plan must be included in protocol and IRB approved
– Plan must provide for reporting of adverse events to IRB, FDA, and NIH
– Plan will vary by risks, nature and complexity of trial
Pre-existing Guidance

2001 – National Cancer Institute Essential Elements of a Data & Safety Monitoring (DSM) Plan for Clinical Trials Funded by NCI

Guiding investigators and institutions in the formulation of DSM plans in accordance with NIH requirements

- Applies to all phases of cancer trials

DSM Plan
- Must be in place before grants can be awarded

DSMBs
- Generally required for Phase III trials
- DSMB constitution depends on anticipated level of risk to participants
Pre-March 2006 FDA Guideline for the Monitoring of Clinical Investigations

- Proper monitoring necessary
- Sponsor responsible to ensure proper monitoring (21 CFR 312.50)
- Monitoring function may be delegated to a CRO (21 CFR 312.3)
- Monitoring plan elements
- 26 FDA warning letters charging sponsor with failure to monitor

DMCs. FDA regulations impose no requirements for the use of DMCs in trials, except for research studies in emergency settings in which the informed consent requirement is excepted. (21 CFR 50.24(a)(7)(iv))
FDA Guidance
March 2006

Generally similar to draft guidance released for comments in November, 2001

States FDA’s position on the need for and structure and function of DMCs

“Contains Nonbinding Recommendations”
Determining the Need for a DMC

DMCs may be required for large, randomized, multi-site trials.

DMCs generally recommended if:
– trial compares rates of mortality or major morbidity, or
– trial population is at elevated risk of severe outcomes

DMCs may be appropriate in other instances.

DMCs generally unnecessary for trials at early stages of product development and trials addressing lesser outcomes
Determining the Need for a DMC

Safety and ethics considerations may require review of interim data for highly favorable results, highly unfavorable results, or evidence of futility, any of which may require early termination.

Considerations of scientific integrity may require independent data review.

The study must present a practical and meaningful opportunity for DMC involvement and effect.
DMCs & Other Oversight Groups

Sponsors, CROs, & Steering Committees
- Monitor trial for overall quality

Endpoint Assessment Committees
- Primary duty to protect participants’ rights and welfare
- Key differences between DMCs and IRBs

FDA
DMC Composition

DMC members appointed by sponsor

Considerations for inclusion on DMC:

- Relevant substantive expertise
- Clinical research and DMC experience
- Absence of significant conflicts of interest
- Inclusion of clinicians and at least one biostatistician
- Appropriateness of medical specialists and/or ethicist
- Diversity
DMC Composition

Trial investigators should be excluded

Conflict of interest procedures should be established to:

- Assess
- Prevent
- Disclose
  - Potential conflicts not impeding objectivity
  - Member service on related DMCs
DMC Confidentiality

Only DMC members should have access to unblinded interim data

– Firewall and sponsor employee access

– Exceptions

• Open-label trials with special safety concerns
• Trials in which severe toxicity or other morbidity is expected
• Pursuant to written trial procedures
DMC Responsibilities

Monitoring during trial and through planned follow-up period of:

– Trial effectiveness
– Participant safety
– Study conduct
– External data relevant to trial
DMC Responsibilities

Making Recommendations to Sponsor

– Termination or continuation of trial
– Minimal data

Maintaining Written Records
– Confidentiality
FDA Guidance
March 2006

Regulatory Reporting Requirements

Sponsors must report all serious and unexpected adverse events to the FDA.

Sponsors are advised to inform the FDA about all recommendations related to the safety of the investigational product whether or not the adverse event in question meets the definition of “serious”.
DMC Independence

“Independence of a [DMC] depends on the relationships of its members to those sponsoring, organizing, conducting, and regulating the trial. Independence is greatest when members have no involvement in the design and conduct of the trial . . . and have no financial or other important connections to the sponsor . . . or other trial organizers. Independence is defined on a continuum . . . .” (FDA Guidance, p. 26)
Benefits of an Independent DMC:

– Enhanced objectivity
– Enhanced scientific credibility and validity of data
– Ability to modify an ongoing trial without raising questions of bias or jeopardizing scientific integrity
– Protection of sponsors from securities law issues that may arise when a party has unique and material information
DMC Independence

DMC Members
– No ongoing financial relationships with a sponsor other than payment for DMC service
– No role in trial other than DMC service
– DMC statistician conducting interim analyses should not have involvement in trial management
FDA Guidance  
March 2006  

Changes from 2001 Draft  
Additional Emphasis Added  

FDA does not require DMCs for all trials  
Design of DMCs (and their relationships with other groups) must be appropriately tailored for each trial  
IRBs may ask whether a DMC has been established and, if so, about its scope and composition  
DMCs must evaluate and adopt necessary measures to protect the confidentiality of data, thereby enhancing data integrity and facilitating interim protocol changes.
Changes from 2001 Draft

FDA Approach to Independence

“Independence is defined on a continuum”

DMC members may be paid

Benefits derived from sponsor interaction with DMCs recognized

The DMC statistician may be the study’s primary statistician but, as such, should be removed from study management
Implementation Issues

- New or revised SOPs and study designs
  - Delineated oversight responsibilities among groups
  - Criteria for determining whether DMC is necessary and appropriate
  - Criteria for selecting DMC members
  - Reporting procedures
  - Procedures for maintaining data confidentiality
  - Firewalls
- DMC charter
- DMC Member Agreements
Consequences of Noncompliance?

- FDA warning letter
- Rejection of IND/IDE
- Suspension or termination of trial
- Tort liability (including failure to adhere to standard of care)
  - Sword or shield?
Secondary Research Uses of Human Data and Tissues: The Catalona case and April 2006 FDA Device Study Guidance
Databases and Tissue Banks

Use of patient information and materials maintained in databases and tissue banks raises patient privacy and property rights concerns. Specific concern is secondary uses of patient information and materials by:

- Researchers who collected the data/tissues in primary study
- Colleagues of the primary researchers, either at the same or other institutions/hospitals
- Commercial or other research sponsors to which data/tissues have been given during the course of primary research
What Might Govern?

Clinical Trial Agreements

HIPAA


FDA Regulations (new April 2006 guidance)

State Laws and Litigation
Device studies often use tissue specimens. FDA device (but not drug) regulations that require informed consent of all subjects includes any “human … on whose specimen a device is used.” Until this guidance, such tissue studies arguably required specific subject informed consent.
New April 2006 guidance recognizes lack of feasibility in requiring such informed consent.

Allows use for device research of leftover specimens that are collected in routine clinical care, specimens from tissue repositories, and specimens collected for other studies.

Specimens must be anonymized or coded, with investigators having no access to code.

Studies cannot be done by same physicians who treated the patient from whom specimen was taken.

Study must be approved by IRB.

This FDA guidance addresses research that would be exempt under the Common Rule.
Commercialization of Data/Materials: Who Has Ownership and Control?

Related to Consent Issue: is it ethical or legal for researchers, research institutions or commercial research sponsors to use the informed consent form as a vehicle for securing a waiver of subjects’ rights in the future commercialization of data/materials collected during a research study (e.g., through the patenting of the results of the research, etc.)
Commercialization of Data/Materials: Who Has Ownership and Control?

1987 Study by Office of Technology Assessment
- Reviewed available legal, ethical and scientific literature
- Concluded no clear answer to questions of who owns/controls this data/materials
- Argument that the value of data/materials is derived from the contributions made by researchers (standing alone, very little commercial value)

FDA, OHRP, and some recent cases have addressed these issues
Commercialization of Data/Materials: Who Has Ownership and Control?

FDA and HHS regulations prohibit the inclusion in the consent form of exculpatory language through which the subject waives, or appears to waive, any of the subject’s legal rights or releases, or appears to release, the investigator, sponsor, or institution from liability for negligence.

– 1996 Guidance (OPRR/OHRP)
– FDA Information Sheet and Q&A
Commercialization of Data/Materials: Who Has Ownership and Control?

1996 OPRR (OHRP) Guidance

– Exculpatory Language (unacceptable):
  • By agreeing to this use, you should understand that you will give up all claim to personal benefit from commercial or other use of these substances.
  • I voluntarily and freely donate any and all blood, urine, and tissue samples to the U.S. Government and hereby relinquish all right, title, and interest to said items.
  • By consent to participate in this research, I give up any property rights I may have in bodily fluids or tissue samples obtained in the course of the research.

– Acceptable Language
  • Tissue obtained from you in this research may be used to establish a cell line that could be patented and licensed. There are no plans to provide financial compensation to you should this occur.
  • By consenting to participate, you authorize the use of your bodily fluids and tissue samples for the research described above.
Q: Is it acceptable for the consent document to say specimens are “donated”?
A: It would be acceptable for the consent to say that specimens are to be used for research purposes. However, the word “donation” implies abandonment of rights to the “property.” 21 C.F.R. 50.20 prohibits requiring subjects to waive or appear to waive any rights as a condition for participation in the study.
1989 Letter from OPRR (OHRP) Director, Division of Compliance to University of California in response to question regarding subject waiver of his/her rights to materials collected in study

- Acknowledges that regulations prohibit inclusion of language in consent form waiving rights
- BUT “regulations are not intended to prohibit the informed subject from making a legitimate donation of his or her” material
- “Therefore, an individual human subject of research may waive his or her rights, if any, in the commercial development of biological materials, or any products of biologic derived using them, taken from the subject in the course of a research activity conducted or supported by the Department of Health and Human Services and approved and conducted in accord with 45 CFR 46.”
Washington University v. Catalona

– Complaint filed by Wash U. (8/4/03) against researcher formerly affiliated with institution

– Alleged improper assertion of ownership rights in a tissue repository maintained at the institution containing specimens collected from patients and research subjects at Wash U.
Catalona (cont.)

– Complaint alleged that Dr. Catalona improperly contacted prior research subjects and patients seeking their consent to transport their samples with him to his new position at Northwestern

– Wash U. sought declaration that any consents given by prior subjects and patients to Dr. Catalona permitting him to take their samples are invalid

– Dr. Catalona argued that patients and subjects retained control over their samples and information even after donating them to the repository and had the right to consent to Dr. Catalona’s taking samples with him to Northwestern

– Some of Catalona’s patients joined the suit on his side
The District Court considered the ICFs, which indicated the research uses, stated that subjects had no “ownership rights” in commercial products derived from their tissues, and often used the words “donate” or “gift.”

The Court concluded that patients had surrendered their rights to direct uses of their biologic materials. Patients still have option, presumably, to “drop out” of the tissue repository, but not to direct that Wash U do something specific with the tissues.
Commercialization of Data/Materials: Who Has Ownership and Control?

Holding clarifies rights of institutions that host research, as long as ICFs are consistent with subject donation and institutional ownership.

Institutions should clarify tissue/data ownership in their employment agreements, faculty rules/handbooks, ICFs, and policies and procedures.

Nagging question of the legality of exculpatory clauses in Wash U ICFs.

Catalona has appealed to Circuit Court, appeal pending as of September 2006.
Patient Access to Experimental Drugs under *Amgen* and *Abigail Alliance*
Clinical trial apparently yields reductions in morbidity and/or mortality for at least some subjects who were receiving the experimental agent – an agent not otherwise approved for marketing for other purposes, and thus available ONLY through the trial. Trial ends as planned, or is terminated by sponsor, and subjects are thus deprived of access to the study drug.
The Basic Dilemma

If FDA application is pending, dilemma may be largely resolved when drug is approved and marketed, and thus available once again to the subjects.

BUT problems persist if there are subjects with no other good or equivalent treatment options and:

- Long “lag time” between close of study and FDA approval (e.g., Imclone’s Erbitux experience), and no subject access during that lag; OR
- Mortality, and not just increased morbidity, is at issue for subjects during any “lag time,” however brief; OR
- Sponsor determines not to pursue regulatory approval for drug at all, thus effectively ending any possibility of subjects’ future access to a drug that the subjects think ameliorated their disease condition.
Possible Solutions: Some Better than Others

Subject and his or her physician tolerate the lack of study drug and seek alternate treatments, or return to standard therapy, if any is available. “Compassionate Use” – company makes unapproved drug available consistent with FDA or EEU guidelines for certain subjects, pending marketing approval; and when approval arrives, dilemma is resolved.
Possible Solutions: Some Better than Others

Company makes drug available, also under “compassionate use” rubric, but *without prospect of marketing application or approval*:

– For how long must the agent be made available?
– And at what cost, and who pays?
– Who monitors AEs/SAEs in this context?
– And what are the ethics of such an arrangement when the company considers the drug or device as not meriting ultimate marketing, perhaps for safety or efficacy reasons, but still makes the agent available to certain former research subjects?
– How much of this would/should FDA or EMEA tolerate?
Possible Solutions: Some Better than Others

Subject tries to compel company to continue to provide study drug, and may be joined in that effort by a sympathetic physician/investigator.

Pressure through media, elected representatives, regulatory agencies, or even the courts

Under what legal theories might a subject in this situation proceed, against company
Case Study: Suthers v. Amgen, U.S. District Court, New York, June 6, 2005

Note that case was filed against Amgen on behalf of two subjects who no longer were able to receive study drug, by the same attorney and law firm that sued University of Pennsylvania over death of Jesse Gelsinger and that sued Johns Hopkins over death of Ellen Roche in hexamethonium study.

Evidence that continued access by former research subjects to experimental therapies may become a major issue for controversy and litigation, and a focus for plaintiffs’ attorneys with med mal backgrounds.
Phase II study of glial cell line-derived neurotrophic factor (GDNF) to stimulate production of dopamine, to alleviate or reverse symptoms Amgen’s clinical trial, in interim results, showed some adverse side effects (appearance of neutralizing antibodies), and low efficacy. Data suggested that primates in parallel animal model studies developed brain lesions. Amgen halted the trial, notified FDA and investigators; and apparently abandoned plans to push farther with trials or with any future NDA. But some medical experts disagreed, including some study investigators who had seen significant improvement in some subjects from the study drug.
Two subjects at NYU, supported by the investigator/study physician there, sued Amgen, demanding continued access to the drug.

These two subjects and the NYU PI believed that it had been clinically effective for them; NYU PI took subjects’ side in lawsuit.

Subjects alleged in court documents that Amgen "treated the patients as mere guinea pigs, as material to be discarded," and had violated a legal and moral obligation to continue to supply the drug.
Case Study: Suthers v. Amgen

Injunction sought based on claims: breach of contract, breach of fiduciary duty.

Injunction denied by court June 2005: federal judge found that Amgen had retained the discretion to stop the trial.

“It is not illogical for a participant to assume that a company that has invested hundreds of millions of dollars to acquire the rights to a therapeutic treatment, and then spent millions more to test it, would want to bring the treatment to market if safe and effective. But that is a far cry from establishing a contract by which Amgen bargained away the freedom to terminate the research trials in its sole discretion.”
Case Study: Suthers v. Amgen

Breach of contract claim insufficient because Research Informed Consent had made clear that study could be terminated:
- For safety reasons
- By Investigator and study site (NYU)
- Or by Amgen

The “consent document makes it plain that ‘Amgen . . . may decide to stop the study at any time.’”
Breach of fiduciary duty claim insufficient because Clinical Trial Agreement had made clear that:

• NYU acting as an independent contractor
• No fiduciary relationship between plaintiff/subjects and Amgen

"Clinical Trial Agreement between Amgen and NYU makes clear that [NYU PI Dr.] Hutchinson and NYU performed as independent contractors, and not as agents of Amgen:

In the activities connected with the Study, Institution agrees to act as an independent contractor without the capacity to legally bind Amgen ... and also agrees that it is not acting as an agent or employee of Amgen ..."
Case Study: Suthers v. Amgen

**Key points that protected Amgen:**

Informed consent explicitly gave Amgen option to terminate the study for any reason.

Informed consent was worded in such a way that, at least in this court’s judgment, there was NO legal relationship established between the subject and Amgen.

Clinical Trial Agreement included a clear statement that the investigator/study site was acting as an independent contractor, not an agent of Amgen.

Would NYU have been so lucky as to escape liability if the two subjects had ALSO sued NYU and if NYU PI had made any verbal assurances to subjects of continued access to study drug?
Parallel case to *Suthers v. Amgen*, filed by same attorneys

Sixth Circuit affirmed District Court’s denial of plaintiffs’ motion for injunction to force Amgen to provide GDNF

In doing so, the Sixth Circuit warned about the need for clarity in informed consent on this issue of continued availability of treatment.
bney v. Amgen, Sixth Circuit Court of Appeals, March 2006

... the University, through its Informed Consent Document, did a poor job informing the plaintiffs as to the grounds upon which the study would terminate and their access to GDNF would be denied. We urge [the IRBs in this Circuit] to take additional measures to ensure that patients fully understand that even if they or their physicians believe an experimental treatment to be safe and efficacious[,] there may be circumstances under which they will be denied continued access to treatment. If this had been properly explained to the plaintiffs ... at the outset of the clinical trial ... perhaps the litigation ... could have been avoided.”
Let’s assume that a company in Amgen’s situation WANTED to continue to make such a study drug available:

Or let’s assume that outside of a study, a patient would likely benefit from a study drug even though trial is ongoing:

Or let’s assume that such a patient outside the study would likely benefit from the drug due to emergency or very serious medical condition:

HOW TO MAKE UNAPPROVED DRUG AVAILABLE?

Often referred to as “compassionate use” but the FDA actually has no such term in its guidance or regulations.
"Compassionate Use" under A Regulations is a Misnomer

Instead, FDA Guidance defines two categories of access to unapproved drugs:

• **Emergency Use**
  
  Requires FDA and manufacturer pre-approval and that meets the definition of life-threatening

• **Early or Expanded Access**
  
  Treatment IND and full IRB approval required
  
  Pioneered in AIDS drug context

Emergency Use of Unapproved Drug: DA Regulations

21 C.F.R. § 312.36

Subject must be in a “life-threatening” situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval.

• “Life-threatening” includes “severely debilitating,” i.e., serious danger of “irreversible morbidity”

Standard: No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.
Emergency Use of Unapproved Drug: DA Regulations

Only one emergency use allowed of a test article (drug, biologic) without prospective IRB review

- Theory is that if a physician or hospital recognizes therapeutic value of a study drug in a serious treatment context, let them become a study site or apply for Treatment IND!

Any subsequent use of the investigational product at the institution have prospective IRB review and approval, although FDA permits emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue.
Early or Expanded Access: Options under FDA Regulations

Treatment IND intended to provide early or expanded access to investigational drugs that show some promise of efficacy:

Four Requirements before Treatment IND can be issued by FDA (21 C.F.R. § 312.34):

1) the drug is intended to treat a serious or immediately life-threatening disease;
2) there is no satisfactory alternative treatment available;
3) the drug is already under investigation, or trials have been completed; and
4) the trial sponsor is actively pursuing marketing approval.

Prospective IRB review and informed consent required

Contents of Sponsor’s Treatment Protocol laid out in regulations: 21 C.F.R. § 312.35(a).
Access to investigational drugs for use in a practitioner-initiated Treatment IND may be gained either through a sponsor-initiated treatment protocol, or through separate approval by the FDA. The practitioner must first attempt to obtain the drug from the sponsor. If the sponsor will not establish a treatment protocol, the practitioner may seek to obtain the drug from the sponsor and submit a treatment IND to the FDA requesting authorization to use the investigational drug for treatment use.

Sponsor evaluates requests on a case-by-case basis
No regulatory requirement that the sponsor provide the investigational drug to the practitioner.
Early or Expanded Access: Options under FDA Regulations

Formal “parallel track” recognized by FDA for promising AIDS drugs; most important in mid-1990s with protease inhibitors

“Open label” protocols also available through FDA: still Phase III studies, but to collect additional safety data, and to bridge the gap between the end of case-control trials and marketing application/approval of the study drug
At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study.”

Questions that arise from this new and controversial paragraph:

Is an early termination of a study a “conclusion of the study”?

Is a study drug that appears to have benefit for a few subjects a “best proven” treatment method to which those few subjects therefore should have post-trial access?
Controversial and New Paragraph of the Declaration of Helsinki: Its Footnote

Footnote to Paragraph 30:
“[I]t is necessary during the study planning process to identify post-trial access by study participants to prophylactic, diagnostic and therapeutic procedures identified as beneficial in the study or access to other appropriate care. Post-trial access arrangements or other care must be described in the study protocol so the ethical review committee may consider such arrangements during its review.”
Questions that arise from the footnote:

“Identified as beneficial in the study” is a lower standard than the “best proven” treatment method standard of paragraph 30 and thus might seem to support continued access to study drugs even if positive reaction of subject had been idiosyncratic.

Post-trial access arrangements in these contexts are really not possible to predict, unless company sponsor is willing to commit in CTA and protocol to continued access of subjects to study drug even if marketing is not pursued and/or study is aborted.
The bottom line is that no one knows what the standards of the Declaration’s paragraph 30 and its footnote mean, but they surely point out that this is an issue that should be anticipated, and that limits of supply of study drug or agent should be made very clear in protocol, ICF and IRB review.

The Declaration is not law, and is not a legal standard.
Does the subject have access to care outside the trial?

Where does the subject go for care at the end of trial?

What are treatment options for subjects if a trial is aborted?

Be as explicit as possible in ICF about ability of site, IRB, or sponsor to terminate study before its planned end, and consequential lack of subject access to study drug or agent.

Be explicit in CTA that site and PI are our independent contractors, not agents.
And remember that as compassionate as continued access to study drug may seem to be: If there is to be no marketing application, is the production and access to study drug sustainable? Who will pay for the costs? In perpetuity? Are all former trial subjects eligible or only those in whom unapproved drug seemed to be beneficial? Who will monitor AEs/SAEs? Who bears liability for injury from drug? Is it ethical for a company to support continued, lengthy access to unapproved and even unapprovable therapies?
Circuit Court endorsed Alliance’s view that there are due process rights of terminally ill patients, acting on physician’s advice, to obtain experimental potentially lifesaving medications when alternative FDA-approved treatment is available.

Dissent and commentary: this is a major blow to drug safety regulation in the U.S.
Court acknowledged “compassionate use” access but opined that this was only available for small populations, not all who need such medications.

FDA has asked for rehearing en banc. Some in pharma industry and academic medicine have feared that such broadly expanded access rights ultimately could make it more difficult for pharma and investigators to refuse to provide such access: FDA regs are now a kind of defense against patient/subject demands for access.
Sen. Brownback ACCESS Act introduced for three-tier, expanded access FDA system

ASCO and Nat’l Coalition for Cancer Survivorship filed, in March 2006, a citizen petition to FDA for new guidance on procedures and standards for expanded access to unapproved drugs