NYU School of Medicine Working Group on Compassionate Use and Pre-Approval Access

We’ve come quite a way from our humble beginning in 2014, when several NYU ethicists decided compassionate use was worthy of serious academic study! Over the course of 2016, CUPA (as we have christened ourselves) has sought to advance knowledge about the ethical issues surrounding pre-approval access, as well as to identify best practices and issues that need further attention. We have benefited from hearing from you and look forward to continuing to engage with and learn from you.

We hope the following, our first-ever annual report, will be of interest to you.

Resources

CUPA created a diverse assortment of resources this year. Thank you to the partners who joined us in these endeavors.

Our fall 2015 colloquium, “Pre-Approval Access: Can Compassion, Business, and Medicine Coexist?,” presented in partnership with the New York Academy of Sciences, with funding from Johnson & Johnson, resulted in a wealth of material, available for free online. The two-day event brought together stakeholders from patient groups, industry, the FDA, bioethics, and academia to discuss current issues in pre-approval access. These conversations live on online, both as videos and in a write-up commissioned by the New York Academy of Sciences. Also freely available on the NYAS website is a podcast: “Bioethics Meets R&D: The Ethics of Pre-Approval Access.” Although this podcast was created from the colloquium, it is a stand-alone piece that would be great for teaching.

This year our website underwent a major update. On it you can find links to publications, resources, and a list of frequently asked questions (FAQs). We also added an educational module on pre-approval access (part of our High School Bioethics initiative), which was created by intern Sam Scheer.

In 2016, CUPA members began working with patient groups to help demystify pre-approval access and create community-specific resources. Lisa Kearns and research assistant Kelly McBride Folkers authored “A Primer on Compassionate Use” for the Cancer Knowledge Network (CKN). This was followed by another CKN piece, written by Kelly with Arthur Caplan, entitled “Compassionate Use: Fix What Is Broken.” If you work with a patient-oriented publication/website/platform of some type and would like to collaborate with CUPA to create an FAQ section or host a webinar or an Ask the Expert event concerning pre-approval access, please let us know!

In September, CUPA joined with Johnson & Johnson to host a patient advocacy summit on the topic of pre-approval access. This day-long event included conversations about the evolving landscape of pre-approval access; an update about the NYU School of Medicine’s Division of Medical Ethics’/Janssen Pharmaceuticals’ Compassionate Use Advisory Committee (CompAC) pilot project; and a town hall discussion.
Lisa Kearns served as a “right to try” content expert for the Temple University Law Atlas Project’s Policy Surveillance Program, which debuted in October.

Finally, we wish to remind you of a non-CUPA resource that debuted: Kids v Cancer rolled out a “Compassionate Use Navigator” intended to help pediatric oncologists apply for access to experimental drugs for their patients.

**FDA and Other Federal Entities**

*During the year there was a lot of conversation about the FDA and what it could or should do in the area of pre-approval access (or, as the FDA calls it, “expanded access”).*

In June, the agency unveiled a new, streamlined application form for individual expanded access, Form 3926, in response to complaints that the old one, Form 1571, was too confusing and took too long to complete. Although the older form is still required when submitting an initial IND, the new form for individual compassionate use requests was greeted with widespread approval. The FDA also released three guidance documents: Individual Patient Expanded Access Applications: Form 3926 (guidance for industry), Expanded Access to Investigational Drugs for Treatment Use – Questions and Answers, and Charging for Investigational Drugs Under an IND – Questions and Answers. All three documents can be found on the FDA’s Expanded Access (Compassionate Use) page, under “FDA Resources on Expanded Access.”

Furthermore, Jonathan Jarow and his colleagues at the FDA published “Expanded Access of Investigational Drugs: The Experience of the Center for Drug Evaluation and Research Over a 10-Year Period” in *Therapeutic Innovation & Regulatory Science*. The authors concluded that the FDA expanded access program has approved more than 99% of applications the agency received over the study period (2005–2014). Equally important, this article reported that just two clinical holds due to adverse events were placed on products given to patients on a compassionate use basis. This is important: It may help calm industry fears that if a drug that is given on a compassionate use basis causes a serious adverse event (in patients who are seriously ill and unable to enroll in a clinical trial), development of that drug could be doomed by an FDA clinical hold. Still unanswered is the question of whether investigational drugs that cause serious adverse events in an expanded access setting face heightened scrutiny when the FDA considers them for approval. We have requested that the FDA investigate this and report its findings.

The FDA asked the Regan-Udall Foundation (RUF), the agency’s nonprofit support organization, to study the idea of creating a “navigator” as a way to make the process of seeking pre-approval access easier for patients and healthcare providers. CUPA members participated in several FDA/RUF-sponsored meetings and other conversations on a navigator. Alison Bateman-House’s thoughts about the proposed RUF navigator were reported in the following publications this year:

- Ed Silverman/STAT Pharmalot, “Why an FDA Plan to Find Compassionate-Use Drugs May Be a Band-Aid,” May 12
- Zachary Brennan/RAPS Regulatory Focus, “Expedited Compassionate Use for
Investigational Drugs Coming Soon, FDA Says,” May 16
• Gail Zyla/CenterWatch Weekly, “FDA’s Proposed Expanded Access Navigator Points to Progress, Not Panacea,” May 23

Finally, the U.S. Government Accountability Office is conducting a study of the FDA’s expanded access program. Arthur Caplan and Alison Bateman-House both spoke with GAO researchers, and the GAO report is expected to be released in early 2017.

Also of note, in September 2016, the Department of Health & Human Services released new rules on clinical trials. These rules require that information about pre-approval access for a drug in development be made available on ClinicalTrials.gov.

21st Century Cures
Arthur Caplan and Alison Bateman-House were among the advisers to the legislative staff of Rep. Michael McCaul when that office was working to create the Andrea Sloan Compassionate Use Reform and Enhancement (CURE) Act. A revised version of that bill was incorporated into the 21st Century Cures Act, which was passed by Congress with bipartisan support and signed into law by President Obama on December 13.

These are the sections of the 21st Century Cures Act relevant to pre-approval access:

SEC. 3032. EXPANDED ACCESS POLICY.

Chapter V of the Federal Food, Drug, and Cosmetic Act is amended by inserting after section 561 (21 U.S.C. 360bbb) the following:

“SEC. 561A. EXPANDED ACCESS POLICY REQUIRED FOR INVESTIGATIONAL DRUGS.

“(a) IN GENERAL.—The manufacturer or distributor of one or more investigational drugs for the diagnosis, monitoring, or treatment of one or more serious diseases or conditions shall make available the policy of the manufacturer or distributor on evaluating and responding to requests submitted under section 561(b) for provision of such a drug.

“(b) PUBLIC AVAILABILITY OF EXPANDED ACCESS POLICY.—The policies under subsection (a) shall be made public and readily available, such as by posting such policies on a publicly available Internet website. Such policies may be generally applicable to all investigational drugs of such manufacturer or distributor.

“(c) CONTENT OF POLICY.—A policy described in subsection (a) shall include—

“(1) contact information for the manufacturer or distributor to facilitate communication about requests described in subsection (a);
‘‘(2) procedures for making such requests;

‘‘(3) the general criteria the manufacturer or distributor will use to evaluate such requests for individual patients, and for responses to such requests;

‘‘(4) the length of time the manufacturer or distributor anticipates will be necessary to acknowledge receipt of such requests; and

‘‘(5) a hyperlink or other reference to the clinical trial record containing information about the expanded access for such drug that is required under section 402(j)(2)(A)(ii)(II)(gg) of the Public Health Service Act.

‘‘(d) NO GUARANTEE OF ACCESS.—The posting of policies by manufacturers and distributors under subsection (a) shall not serve as a guarantee of access to any specific investigational drug by any individual patient.

‘‘(e) REVISED POLICY.—Nothing in this section shall prevent a manufacturer or distributor from revising a policy required under this section at any time.

‘‘(f) APPLICATION.—This section shall apply to a manufacturer or distributor with respect to an investigational drug beginning on the later of—

‘‘(1) the date that is 60 calendar days after the date of enactment of the 21st Century Cures Act; or

‘‘(2) the first initiation of a phase 2 or phase 3 study (as such terms are defined in section 312.21(b) and (c) of title 21, Code of Federal Regulations (or any successor regulations)) with respect to such investigational drug.’’

IRBs

CUPA members continued to explore the role of IRBs in pre-approval access and will investigate whether it continues to make sense to have IRBs tasked with approving and overseeing pre-approval access to investigational treatments.

In February, Barbara Redman and Alison Bateman-House published a commentary entitled “Institutional Review Boards as Arbiters of Expanded Access to Unapproved Drugs: Time for a Change?” in Therapeutic Innovation & Regulatory Science. This piece has been a topic of discussion for both IRB and regulatory officials, and CUPA will be investigating the topic further.

In September, Alison Bateman-House spoke on “The Ethics of Expanded Access: Is There a Right to Medical Innovation?” for the WIRB-Copernicus Group, and in November Beth Roxland participated on a panel on “Designing and Implementing Expanded Access Programs” at the annual conference of Public Responsibility in Medicine and Research (PRIM&R).
**Right to Try**

Eight more states passed “right to try” laws in 2016, bringing the total to date to 32. Federal right to try legislation was introduced, and right to try was included in the Republican Party platform at the GOP convention in July.

CUPA opposes right to try on the grounds that it has not, and more than likely will not, help patients get access to investigational drugs; that it is more of a political ploy than a genuine effort to help patients; that it creates confusion about how to seek access to investigational drugs; and because it sets patients up for disappointment.

In July, Alison Bateman-House, Kenneth Moch, Arthur Caplan, and Lisa Kearns released their report, “Findings on ‘Right to Try’ Laws and Pre-Approval/Compassionate/Expanded Access to Investigational Medical Products.” You can find it under “Member Articles” on the CUPA website’s Publications and Interviews page.

Outgoing Rep. Matt Salmon (R-AZ) introduced federal right to try legislation in the House of Representatives last year, and Sen. Ron Johnson (R-WI) introduced a companion bill in the Senate in May of this year. Johnson used his position as chair of the Senate Homeland Security and Governmental Affairs Committee to hold two hearings on right to try. At the first hearing, the sole person to speak against the proposed legislation was Nancy Goodman, founder and executive director of Kids v Cancer.

In September, Andrew McFadyen testified against right to try at a second hearing before the same committee. This event was followed by a failed attempt to advance the bill via a unanimous consent vote. Of note, at this September meeting Dr. Ebrahim Delpassand, chief of Clinical Nuclear Medicine at M.D. Anderson Cancer Center, announced via video that he was treating cancer patients with Lutathera under Texas’ right to try law. Since Lutathera was already available via an expanded access program, CUPA does not accept Delpassand’s testimony as evidence that a right to try law has enabled a patient to receive access to a product that otherwise would have been unavailable.

The House of Representatives’ Energy and Commerce Subcommittee on Health was to hold a hearing entitled “Examining Expanded Access to Investigational Therapies” in September, but this event was postponed. At this point, we know of no plans to reschedule.

The federal right to try bills died with the legislative session that just ended and will need to be reintroduced in the new session next year. President-elect Trump’s administration is likely to continue to push right to try. Vice President-elect Mike Pence signed a right to try bill into law when he was governor of Indiana, and he has promised to support federal legislation.

The right to try debate on Capitol Hill was matched by debate in the press. Lisa Kearns and Beth Roxland’s “Federal ‘Right to Try’ Bill: Wrong on the Law, and Wrong for Patients” ran in *The Hill* on June 28. On July 14, *The Hill* ran a response by Matthew Bellina, an ALS patient. This, in turn, prompted a response from Beth Roxland. Then, on August 31, *Forbes* ran an article

Right to try has now crossed the border to become an issue in Canada. Andrew McFadyen has created a website, TheTruthAboutRighttoTry.org, to “provide an objective viewpoint on an argument that is emotionally charged.” Alison Bateman-House was quoted in a December 2 Ottawa Citizen article entitled “Fighting for the ‘Right to Try’: Terminally Ill Canadians Want Legal Right to Access to Unproven Treatments.” Andrew view on right to try and his work running the Isaac Foundation were featured in a companion piece, “Medicine’s ‘Wild West’? Why an Advocate for Those with Rare Diseases Opposes Right-to-Try.”

CUPA members (with the help of research assistant Kelly McBride Folkers) further contributed to the right to try discussion this year with these publications and interviews:

- “Medical Ethicist Arthur Caplan Explains Why He Opposes ‘Right-to-Try’ Laws,” January 15, Oncology: Cancer Network
- “Seven Good Reasons to Not Support Right to Try Experimental Drug Legislation in Connecticut” in the Connecticut Post on March 28
- “Is ‘Right to Try’ Bill for New Hampshire?,” New Hampshire Public Radio, April 4
- “‘Right to Try’ Bill in Senate for Terminally Ill Patients,” May 16, Medscape
- “‘Right to Try’ Offers False Hope” in the Providence (RI) Journal on May 20
- “The Senate Should Pass on a Bad Bill that Won’t Help the Terminally Ill: Another View” in the Harrisburg (PA) Patriot-News, June 30
- “‘Right to Try’ Bill Offers False Hope to the Desperately Ill” in the Sacramento Bee on September 22
- CUPA members were quoted in the Washington Examiner in a June 27 article entitled “Dispute Over Helping the Terminally Ill”; in a September 27 article in the Milwaukee Journal Sentinel entitled “Johnson Pushes Right-to-Try Law”; and in September 28’s “‘Right to Try’ Bill Giving Patients Access to Unapproved Drugs May be a Win for Libertarians” by Vice News

and these talks:

- Arthur Caplan spoke about “Is There a Right to Try: Access to Unapproved Drugs” at the June 16 NYU Langone Medical Center’s Pediatrics Ethics symposium.
- Lisa Kearns gave a talk entitled “Variations Among State Right-to-Try Laws Suggest a Political, Not Patient-Centered, Agenda” at American Society for Bioethics & Humanities’ annual meeting.
- Beth Roxland spoke at the MAGI Clinical Research Conference West on October 24 on “How Can We Do Better at Planning for and Responding to ‘Compassionate Use’ and ‘Right to Try’ Requests for Experimental Therapies? Balancing Ethical, Regulatory, and Programmatic Considerations.”
- Beth spoke on “Understanding Federal Compassionate Use Policies and State Right to Try Laws” at the World Stem Cell Summit on December 8.
Publications
The year saw a bumper crop of publications from CUPA members and, occasionally, external co-authors.


The Josh Hardy case and the issues it raised were profiled in Harper’s as the June cover story and in an October 1 story in USA Today that quoted Alison Bateman-House. A similar story from Germany was profiled in Die Zeit, “Wer rettet Klara?” (“Who saves Klara?”), which quoted Kenneth Moch and Arthur Caplan.

Barbara Redman and Arthur Caplan urged IRBs to recognize the problem of reproducibility and its potential impact on patients in “Limited Reproducibility of Research Findings: Implications for the Welfare of Research Participants and Considerations for Institutional Review Boards,” in the July-August issue of IRB.

In November, Avalere released findings showing that only 19% of a sample of pharmaceutical and biotech companies publicly post their pre-approval access policies on their websites. The Avalere study was covered by Pharmalot in STAT, which quoted Arthur Caplan, and by Endpoints News, which hosted a poll asking, “Do you think posting compassionate use policies on your website is a good idea?” 70 percent of readers answered yes, 30 percent no.

Alison Bateman-House published in The Health Care Blog a post detailing how to request access to an investigational drug via the FDA’s expanded access program.

Arthur Caplan and Alison Bateman-House had a short article in Genome entitled “Hope Meets Reality.” Alison also published “Right-to-Try Laws Could Curtail the Development of Innovative New Therapies” in STAT, while Arthur was featured in Endpoints News’ “The Sarepta Dilemma: Bioethics Expert Arthur Caplan Says It’s Time to Rethink How to Regulate Compassion.”

Alison Bateman-House and Arthur Caplan were both featured in the Pink Sheet’s article “Expanded Access Programs Need FDA Policy Changes to Really Expand.”

Arthur Caplan’s was one of three perspectives in an online series called “Why Can’t Dying Patients Bypass FDA Drug Approval?” Notably, this series allows readers to vote for the perspective they agree with most: 7% of voters agree that the FDA has a viable path in place for pre-approval access; 21% agree with Arthur’s perspective, that companies, not the FDA, are the primary decision makers for pre-approval access; and 70% agree with the anti-FDA, pro-patient choice perspective.

And in a non-CUPA project that is nevertheless relevant, Arthur Caplan co-authored an article in the February *Journal of the American Medical Association* (JAMA) on the NYU School of Medicine’s Division of Medical Ethics’/Janssen Pharmaceuticals’ Compassionate Use Advisory Committee (CompAC) project. “The Ethical Challenges of Compassionate Use” was an initial report about the CompAC pilot, in which an NYU-created and -administered independent, international committee reviewed single patient pre-approval requests for a cancer drug and then made recommendations to Janssen about whether to approve each request. The JAMA article was the subject of a *BioCentury* article entitled “Piloting Compassion.” More information about the CompAC pilot was presented in Arthur, Alison, and Joanne Waldstreicher’s “Compassionate Use: A Modest Proposal,” published in the *2016 American Society of Clinical Oncology Educational Book*, and the April *Nature Reviews: Drug Discovery* featured “An Audience with Arthur Caplan.” A *STAT* piece, “Novel System to Get Dying Patients an Experimental Cancer Drug Raises Hopes — and Thorny Questions,” also profiled the CompAC project and quoted Arthur.

**Conferences, Talks, Events**

*CUPA members spoke about issues related to pre-approval access at the following events/to the following audiences:*

- NYU Langone Medical Center Medical Ethics Committee
- National Center for Ethics in Health Care, Veterans’ Administration
- “Healthy Aging Show,” Dr. Radio
- World Orphan Drug Congress
- Chief Medical Officer Roundtable
- ASCO
- BIO
- Rutgers University Institute for Health
- New York City Health and Hospitals Corporation’s annual John Corser Memorial Conference
- DIA
- EveryLife Foundation for Rare Diseases’ 8th Scientific Workshop: Evaluating Early Access Models for Patients: Flashpoints, Frameworks, & Case Studies for Advancement
- 3rd Annual Patient-Centered Clinical Trials Conference
- Public Responsibility in Medicine and Research (PRIM&R) Annual Conference
- 2nd Annual Early Access Programmes meeting
- University of Oxford

And…

In September, CUPA hosted a unique, invitation-only meeting devoted to the issue of pre-approval access to microbiome-based interventions. This meeting will be the basis of a forthcoming project, about which we will share more in 2017.
**Going Forward**
CUPA will continue to work on all the issues mentioned above and on educational efforts to inform patients and physicians about pre-approval access. We hope to remain a valuable resource and an ally for all who seek to make pre-approval access to investigational treatments fairer and more transparent.

Finally, if you have an event or publication related to pre-approval access that you’d like to share with us, please do! We look forward to learning more about what is happening in this dynamic area.

Thank you for your interest and involvement this year, and may the new year be equally productive.

Sincerely,
The Working Group on Compassionate Use and Pre-Approval Access (CUPA)

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