This has been quite a year for pre-approval access and for CUPA. We are pleased to share with you our second annual report. As always, we appreciate your feedback. Please let us know about any contributions you have made to this area — we’re interested in hearing from others who are working on pre-approval access.

**Scholarly Contributions**

Our members authored a variety of academic papers this year. If you don’t have access and would like a copy of something, drop us a note and we’ll send it your way.


In March, in the same publication, Laura Kimberly, Alison Bateman-House, and Art Caplan, along with Marc Beutller and Michael Shen, issued a call for consistency in the expanded access lexicon in “Pre-Approval Access Terminology: A Cause for Confusion and a Danger to Patients.”

Jennifer Miller, Kenneth Moch, and Art Caplan joined Yale’s Joseph Ross in exploring the characteristics of expanded access and compassionate use programs that are listed on ClinicalTrials.gov, and what percentage ultimately receive FDA approval, in “Characterizing Expanded Access and Compassionate Use Programs for Experimental Drugs.” STAT senior writer and Pharmalot columnist Ed Silverman wrote about the article, as did PR Newswire.

Lisa Kearns and Art Caplan responded to a case report in the American Journal of Bioethics on how to allocate scarce doses of nusinersen to a pediatric population. Their commentary, “Hard Choices for Vulnerable Patients: Some Lessons Learned That May Apply,” proposed the CompAC (Compassionate Use Advisory Committees) model guide to this, and all, allocation decisions.

Art Caplan and NYU Division of Medical Ethics research associate Kelly McBride Folkers’ essay “Charlie Gard and the Limits of Parental Authority,” in the September/October Hastings Center Report, discussed limits on parental authority in cases in which continued medical treatment is deemed futile.

Kenneth Moch evaluated the ethical dilemmas that pharmaceutical companies face when deciding whether to grant single-patient use of experimental compounds outside of clinical trials in “Ethical Crossroads: Expanded Access, Patient Advocacy, and the #SaveJosh Social Media Campaign.” Moch was CEO of Chimerix at the time of the extensive media campaign for Josh.
Hardy, a seven-year-old boy whose family sought access to an experimental antiviral being developed by the company.

**Education Outreach and Resources**

We continually update our [website](#) with all things related to pre-approval access, and this year the FAQ section underwent several major updates to keep it current and accurate. We welcome feedback, so please send us your comments. Feel free to use all or portions of the [FAQ](#) for your own websites or other work.

Our education and resource work was certainly not limited to our website! Some of the year’s highlights:

The NYU Division of Medical Ethics partnered with Johnson & Johnson’s Office of the Chief Medical Officer for two Pre-Approval Access Patient Advocacy webinars. June’s event featured presentations from Reagan-Udall Foundation for the FDA’s Executive Director June Wasser, MA, and Johnson & Johnson’s Senior Director, Americas Head, Global Regulatory Policy and Intelligence, as well as Art Caplan. The November webinar consisted of presentations from patient advocates, including two CUPA members: Pat Furlong, of Parent Project Muscular Dystrophy, spoke about patient-focused tools and resources and Andrew McFadyen, of the Isaac Foundation, discussed communication with physicians. They were joined by Mark Fleury, PhD, Principal, Policy Development – Emerging Science, American Cancer Society Cancer Action Network, and Elena Gerasimov, MA, MPH, Director of Programs, Compassionate Use Navigator, Kids v Cancer, who spoke about advocacy groups’ perspective on the current state of pre-approval access.

In April, Art Caplan, Lisa Kearns, Christopher Robertson, and Andrew McFadyen presented a webinar asking “Should Congress Enact a Federal ‘Right to Try’ Law?” (Short answer: no.)

Alison Bateman-House wrote two primers on compassionate use and pre-approval access. These general audience articles detailed how patients and physicians can apply for use of an investigational drug:

- “Our Guide to Pre-Approval Access to Drugs For Both Doctors and Patients” in the Health Care Blog
- “How To Try An Experimental Drug When You Don’t Qualify For A Clinical Trial” in Forbes

Kelly McBride Folkers, Alison Bateman-House, and Lisa Kearns reviewed the pre-approval access landscape, including right to try (RTT) legislation, in “Senate Passes a ‘Right to Try’ Bill: Harm to Patients Comes Next” for the August 4th Cancer Letter (subscription required).

Lisa Kearns held a weeklong “Ask the Expert” webchat on compassionate use and expanded access for the Smart Patients online community.

Alison Bateman-House led a webinar on expanded access and RTT at the Rare Disease Legislative Advocates’ May meeting.
Art Caplan authored a piece for the Cancer Knowledge Network entitled “‘Right to Try’ Is a Lie!”

CUPA tried to run an “Ask Me Anything” session on Reddit, but we were hobbled by our lack of familiarity with how to use the site. (We remain eager to do this, if anyone wants to guide us in this endeavor!)

CUPA had no hand in this, but it’s big news to those who work in the access to medicines space: In June, the Reagan-Udall Foundation for the FDA launched an Expanded Access Navigator to help walk patients and physicians through the compassionate use (single patient) access process. Initially covering just oncology agents, the navigator was expanded late in the year to include rare disease agents. We’d love to hear feedback from any of you who have used this resource.

Another non-CUPA enterprise that we want to highlight is the WCG Foundation’s pro-bono institutional review board (IRB) service for pre-approval access protocols. According to the WIRB-Copernicus Group’s 2017 annual report: “In 2017, WCG IRBs reviewed 94 requests for expanded access, most of which were in oncology. We perform these IRB reviews pro bono, through the WCG Foundation, to alleviate any financial burden on patients looking to access investigational products.”

**Legislation Watch**

At the end of 2016, President Obama signed the 21st Century Cures Act, which mandated that companies must make publicly available information about their pre-approval access policies once an asset moves into Phase 2 testing. In March, Avalere released a study of 100 publicly traded pharmaceutical and biotechnology companies of various sizes showing that the number of these companies posting their pre-approval access policies had doubled, to 49%, in the month since the Act went into effect. In December, Emily Jung, Patricia Zettler, and Aaron Kesselheim published an article, “Prevalence of Publicly Available Expanded Access Programs,” in Clinical Pharmacology & Therapeutics that reviewed a sample of these policies to see what information has been posted.

Six states passed RTT laws this year — Iowa, Ohio, Kentucky, Maryland, Pennsylvania, and Washington — bringing the total to date to 38. To the best of our knowledge, there has been no substantiated evidence of the laws being used to obtain investigational medical products that couldn’t have been obtained through the FDA’s Expanded Access Program. (A radiation oncologist in Texas is the only physician we know of to have claimed to have used his state’s law; however, the company that manufacturers the product that he appears to have been using has an expanded access program in place.)

The 115th Congress brought the introduction of three federal RTT bills. Rep. Andy Biggs (R-AZ-5) introduced H.R.878, the Right to Try Act of 2017, on February 6. (It is similar, but not identical, to a bill introduced by former Rep. Matt Salmon [R-AZ-5] in 2015.) H.R.1020, the Compassionate Freedom of Choice Act, was introduced by Rep. Morgan Griffith (R-VA-9) in early February. There’s been little to no movement on these bills since their introduction. And, in
late January, Sen. Ron Johnson (R-WI) introduced S.204, the Trickett Wendler Right to Try Act. (It was later renamed the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017.) In April, CUPA started hearing that Johnson may seek to attach S.204’s language to must-pass FDA funding legislation. Very generally, this legislation establishes funding for FDA’s reviews and is renegotiated every five years, and if it didn’t pass, thousands of employees’ jobs would have been in jeopardy.

Right to try was ultimately not added to this bill, but language related to expanded access was. In May, Sen. Orrin Hatch (R-UT) had introduced S.1048, the Enhanced Clinical Trial Design Act of 2017. The bipartisan bill called for a public meeting, including the FDA and the National Institutes of Health, to address potential barriers for patients wishing to participate in clinical trials. It also would have allowed the FDA commissioner to review and revise regulations governing institutional review board (IRB) review for single-patient expanded access protocols. These two provisions were added to the FDA funding legislation via an amendment ("the Hatch amendment").

We are eagerly awaiting the consequences of the Hatch amendment, given its similarity to provisions that CUPA called for in the fact sheet and recommendations for improving patient access to investigational medicines we released in April. Some of our recommendations were to: 1) strengthen the FDA’s Expanded Access Program; 2) clarify the FDA’s authority over investigational drugs; 3) explore ways to make expanded access a more appealing prospect to pharmaceutical and biotech companies; 4) commission an expert group to explore whether IRB oversight is needed for single-patient expanded access protocols; and 5) promote awareness of, access to, and equity in clinical trial enrollment. Art Caplan, Alison Bateman-House, and Kelly McBride Folkers expanded upon these recommendations in a Health Affairs blog post entitled “Right to Try Won’t Give Patients Access to Experimental Drugs. Here’s What Will.”

In a deal with Sen. Ron Johnson to get the FDA funding bill passed, the Senate passed his RTT bill, S. 204, with no debate. Despite some patient-friendly amendments by Senate staff — including removing liability protections for providers in instances of gross negligence or willful or reckless misconduct, and easing the ban on FDA’s consideration of adverse events in all instances — CUPA still believes the bill is flawed; the group’s opposition was described in a Clinical Leader article, “Senate Revises Right-To-Try, CUPA Still Gives Thumbs Down.”

Having passed the Senate, the bill went to the House of Representatives, where it currently sits. In October, the House’s Energy & Commerce Committee’s Subcommittee on Health held a hearing called “Examining Patient Access to Investigational Drugs.” Alison Bateman-House and Kenneth Moch were invited to testify, as were Naomi Lopez-Bauman of the Goldwater Institute; Matthew Bellina, an ALS patient and right to try advocate; Ellen Sigal, the chair and founder of Friends of Cancer Research; and FDA Commissioner Scott Gottlieb. Their written testimonies and a video of the hearing can be found through the link above. A briefing packet circulated to subcommittee members prior to the hearing included a Hill op-ed, “The House Should Read The Fine Print On ‘Right to Try’ Bill,” by Alison Bateman-House, Lisa Kearns, and Kelly McBride Folkers. After the hearing, Bateman-House recounted her testimony for Forbes in “What I Told Congress About Patient Access to Experimental Medicines.”
FDA and Other Federal Changes

The long-awaited and eagerly anticipated GAO report on the FDA’s Expanded Access Program was released on July 11. It noted improvements the agency had made to the program and called for the FDA to clarify how data from adverse events that occurred in an expanded access context may affect the drug development and approval process. By the time the GAO report came out, the FDA had already sought to clarify its stance on adverse outcome use in an article. One major finding: “There was no instance in which expanded access [led] to a negative regulatory decision regarding a drug application.” (Another example of the FDA attempting to correct the record in this area is McKee et al.’s article “How Often Are Drugs Made Available Under the Food and Drug Administration's Expanded Access Process Approved?,” which surveyed a variety of legal databases and found no incidences of drug manufacturers being sued in relation to expanded access.)

Reactions to the report were mixed. Some outlets saw it as pro-FDA, while others took a dimmer view. Alison Bateman-House explained and expanded upon the report in “To Speed Access to Compassionate Use, Look Beyond the FDA.”

In early October, FDA Commissioner Gottlieb announced a revision to the IRB requirements for review single-patient expanded access requests. As he stated in an FDA Voice blog post:

Prior to treating a patient under expanded access, the physician must obtain approval from the Institutional Review Board (IRB) at their facility. This is an important step to protect the rights, safety and well-being of human subjects in clinical research — but assembling the full board may cause delays because it may not routinely meet. As part of a plan to simplify the process for physicians seeking access to an investigational product to treat their patient, I’m announcing today that just one IRB member — the chair or another appropriate person — can now approve the treatment. I believe the simplified IRB process will facilitate access while still protecting patients.

Kelly McBride Folkers and Alison Bateman-House asked “Will New FDA Regulation on IRB Review Speed Patient Access to Experimental Drugs?” in a Health Affairs blog post. Their answer: A lack of data on IRB review of expanded access protocols hinders the ability to evaluate such new policy changes.

We will be following this new regulation closely in 2018, as part of our ongoing study the role of IRBs in expanded access.

CUPA in the Press

CUPA members published a variety of op-eds this year, including:

- Lisa Kearns in the Hill, “Straightening Out the Set Record on ‘Right to Try’” (in response to an op-ed from Naomi Lopez-Bauman of the Goldwater Institute, “Setting the Record Straight on Right to Try”)
• Kelly McBride Folkers in STAT News: “Adding ‘Right to Try’ to FDA User Fee Bill Would Undermine the Agency’s Work”
• Alison Bateman-House, with Harvard’s Amee Sarpatwari, in the Boston Globe, “Don’t Limit the Powers of the FDA”
• NYU Division of Medical Ethics postdoctoral fellow Carolyn Chapman, Richard Klein, and Andrew McFadyen in the Health Care Blog, “Right to Know: Why the FDA Should Not Be Cut Out of Expanded Access Requests”
• Lisa Kearns in the Hill, “17 Real, Workable Ways to Improve Patient Access to Experimental Drugs”
• Andrew McFadyen, Kelly McBride Folkers, and the Isaac Foundation’s Alexandra Hall in the Health Care Blog, “Vulnerable Patients and Right to Try. Doing More Harm Than Good”
• Alison Bateman-House, with House of Representatives staff member Andy Taylor in the Hill, “Right to Try Misses the Real Issue. There Is Another Solution.”
• Jane Reese-Coulbourne discussed the impact of the passage of the Senate right to try bill in a blog post titled “Expanded Access to Experimental Medicines: Where Is Federal Legislation Taking Us?”
• Andrew McFadyen, Beth Roxland, and the Isaac Foundation’s Alexandra Hall in the Hill: “The Prescription Drug User Fee Act Must Refrain From Adding Right to Try Provisions”
• Jane Reese-Coulbourne in the Nov.-Dec. issue of Pharmaceutical Commerce (see page 19), “Pre-Approval Access and Real-World Evidence: A Win-Win Proposition” and “Right to Try’ Legislation and EAPs”
• Andrew McFadyen with Alexandra Hall in the Hill, “Congress, Put Patients First and Vote Against ‘Right to Try’”
• NYU Division of Medical Ethics postdoctoral fellow Carolyn Chapman on the Health Affairs blog, “Is It Time For The FDA To Consider A Differentiated Approval System?”
• Richard Klein in Healthcare Analytics News, “Dispelling the Myths and Misconceptions Around Expanded Access”
• Pat Furlong and Richard Klein responded to rumors that S.204 would be pursued with renewed vigor early in 2018 in the Hill, “Right to Try’ Is No Magic Wand”
• Alison Bateman-House penned for Forbes a primer on a topic of great interest to many in the compassionate use community: “What You Need To Know About Clinical Trials (Before You Need One).”

CUPA members were quoted and participated in interviews extensively in the press:

• Andrew McFadyen debated “The Ethics of ‘Right to Try’ in California — Exploitation or Hope?” on KPCC, NPR’s Southern California affiliate.
• Alison Bateman-House is quoted extensively in Steve Friess’s “Will Trump Give ‘Right to Try’ a Boost?” for Undark.
• Art Caplan, Lisa Kearns, and Kenneth Moch were interviewed by Ted Roelofs for “This Law Promised Medical Hope for Dying Patients. Was It a Cruel Deception?” in Bridge, a news and analysis publication from the Center for Michigan.
• Art Caplan is quoted in “Push Grows for ‘Right to Try’ Laws that Loosen Access to Experimental Treatment” in the Minneapolis Star Tribune.

• Art Caplan spoke about “Right to Try Legislation and What It Means for Patients” on the Chad Hartman radio show.

• Lisa Kearns was interviewed about S. 204, the federal right to try bill, on the Steele & Ungar Show on SiriusXM POTUS.

• Art Caplan was cited in a July 1 article in Alcalde, “A Cure for Clara.”

• Alison Bateman-House enumerated many of RTT’s patient-hostile provisions in Trudy Lieberman’s “This Solution May Come with Problems”; the article originally appeared in the Watertown Public Opinion and was picked up by several national news outlets.

• Alison Bateman House was quoted by Joan Quigley in “New Hope — and Risk — for People with Terminal Illness” on NJ.com.

• Alison Bateman-House was quoted extensively in “Medical Ethicist: ‘Right to Try’ Bill Will Not Improve Experimental Access to Treatment” in PJ Media.

• Art Caplan discussed the toothlessness of state right to try laws and industry disinterest in the legislation in “Will ’Right to Try’ Bill Actually Help Anyone?” in MedPage Today.

• Alison Bateman-House was quoted, and her and Lisa Kearns’s paper “Who Stands to Benefit? Right to Try Law Provisions and Implications” was referenced, in “Right-to-Try Laws Could Dampen Industry Participation in Expanded Access Programs” in FDA News (both subscription required).

• CUPA’s work was cited in a piece by Carrie Feibel on NPR’s All Things Considered, “Patients Demand The ‘Right to Try’ Experimental Drugs, But Costs Can Be Steep.”

• Art Caplan and Alison Bateman-House participated in an AMA Journal of Ethics discussion forum about compassionate use.

CUPA at the Microphone

CUPA members had a busy year speaking at conferences, seminars, forums, and events.

The June 21–22 NYU/New York Academy of Sciences colloquium, “The Need to Accelerate Therapeutic Development — Must Randomized Controlled Trials Give Way?,” featured several CUPA members as moderators and panelists. Highlights included keynotes by former FDA chief Robert Califf and current CDER (Center for Drug Evaluation and Research) director Janet Woodcock. The panel on the FDA’s decision to approve Sarepta’s Duchenne muscular dystrophy drug Exondys 51 was especially lively, with a STAT News bulletin referring to it as a “Sarepta-flavored Twitter cage match.”

CUPA members spoke at a multitude of events, including:

• 5th Annual Chief Medical Officer Summit (Boston)
• Medical, Ethical, and Legal Aspects of Experimental Therapy Conference (Warsaw, Poland)
• Virginia Tech Carilion School of Medicine (Roanoke, VA)
• New York Genome Center (Manhattan)
• American Cancer Society Cancer Action Network webinar
• Association of Health Care Journalists New York Chapter meeting (Manhattan)
• WideTrial’s 2017 Expanded Access Summit (Cambridge, MA)
• Pre-Approval Access Programs Conference (Philadelphia)
• American Society for Bioethics & Humanities annual conference (Kansas City, MO)
• Early and Managed Access Programmes Europe conference (London)
• Laguna Biotech CEO Forum (Laguna Beach, CA)
• FDA/CMS Summit (Washington, DC)
• Rutgers University Institute for Health, Health Policy, and Aging Research (New Brunswick, NJ)
• World Orphan Drug Congress (Washington, DC)
• Yale University School of Medicine (New Haven, CT)
• Pediatric Grand Rounds YNHCH (Bridgeport, CT)
• 28th International Symposium on ALS/MND (Boston)

Looking Ahead…

On January 24, the NYU Division of Medical Ethics is hosting a guest lecture by Carole-Anne Baud, a visiting scholar from the Department of Civil Law at the University of Geneva. Her talk is titled “Compassionate Use of Drugs in Switzerland — Challenges and Perspectives.” Please email Kelly McBride Folkers if you’d like to attend this talk at our Manhattan campus.

We will continue to urge lawmakers to oppose right to try legislation and instead implement our recommendations to improve patient access to investigational products — including improving the FDA’s existing expanded access system, incentivizing the pharmaceutical and biotechnology industries to make their products more readily available for patients seeking pre-approval access, and working to make clinical trials more easily accessible, and to a more diverse population. We retain as a core belief the idea that clinical trials (be they primarily for drug development purposes or for treatment purposes) ought to be the primary way by which patients access investigational medical products.

Likewise, we will continue to urge all stakeholders worldwide to adopt more uniform terminology so we can move away from the confusion of terms currently in use (e.g., “expanded access,” “early access,” “compassionate use,” “managed access,” “special access,” “single patient,” “named patient,” etc.)

CUPA is beginning to explore the uptake, relevance, and impact of the congressionally mandated use of “real-world evidence.” Data gathered from expanded access protocols may constitute real-world evidence that could be used in future drug approvals; how can this be done in the most just and responsible way? We hope to meaningfully contribute to the conversation about how to handle data collected from sources other than randomized controlled clinical trials — as always, in service of improving patient and research participant access and safety.

Thank you!
Your interest and involvement this year has been invaluable. May the progress continue in 2018.
Sincerely,
The Working Group on Compassionate Use and Pre-Approval Access (CUPA):

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