

AMERICAN ACADEMY OF CHILD & ADOLESCENT PSYCHIATRY

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April 10, 2017

Ms. Leslie Kux

Associate Commissioner for Policy

Division of Dockets Management

Food and Drug Administration

5630 Fishers Lane

Room 1061

Rockville, MD 20852

Re: Docket No FDA-2016-N-1149 Manufacturer Communications
Regarding Unapproved Uses of Approved or Cleared Medical Products;
Request for Comments

Dear Ms. Kux:

The American Academy of Child and Adolescent Psychiatry (AACAP) very much appreciates the opportunity to provide comments pursuant to your call for public input relating to manufacturer communications about unapproved uses of approved medical products, including Food and Drug Administration (FDA)-regulated medications. AACAP represents the interests of 9,200 child and adolescent psychiatrists (CAPs) who frequently make prescribing decisions in treating the pediatric patients they serve. We therefore have a strong interest in this topic and welcome the opportunity to share our perspectives.

As you know, CAPs are specialists who treat children with mental illness, but are first board certified in general psychiatry. All CAPs must then complete an additional fellowship to better serve children and adolescents. All CAPs are eligible or certified in adult psychiatry through the American Board of Psychiatry and Neurology/American Board of Medical Specialists, and many CAPs are board certified in both adult and child and adolescent psychiatry, and therefore treat both adults and children.

CAPs therefore find themselves in a challenging position as they navigate FDA regulations that prohibit pharmaceutical companies from proactively sharing useful information about adult medications with those who have additional specialty training in child and adolescent psychiatry. Given the prohibition on information sharing, CAPs have been excluded from receiving relevant information and learning opportunities that could be useful in their practice. In addition, CAPs experience long response times

when they reach out to drug manufacturers about specific products, due to their reluctance to share information that has frequently been labeled as “off-label promotion.”

Nevertheless, to effectively treat children and adolescents, CAPs must prescribe off-label pharmaceuticals, and some AACAP members have gone into the field of research after noting how few approved medications exist to treat their child and adolescent patients. CAPs are interested in expanding the knowledge-base concerning pediatric psychotropic medications to better understand whether adult medications work in children, whether the dosing profile is the same, whether the side-effect profile is the same, and whether early treatment can convert a life-long mental illness into a more limited one. When additional off-label information about a medication becomes available through trials, and even trials that do not result in labeling, prescribers gain valuable information about safety and dosing that would otherwise not be available.

For example, a National Institutes of Health-sponsored trial of Risperidone, published in the *New England Journal of Medicine* in 2002¹ led to clinicians using Risperidone at study doses for irritability and aggression in patients with autism and other developmental disabilities long before the FDA approval for the indication was given in 2007. Given the prevalence of autism in the United States, patients with autism gained the benefit of improved functioning five years sooner through use of this crucial off-label scientific knowledge than those not so treated. This off-label prescribing changed children’s and family’s lives for the better, and knowledge of this type has the potential to advance an improved standard of care for patients.

CAPs are in a predicament when treating children in which limited FDA-approved coverage exists such as for younger children, children with depression, and children with depression in bipolar disorder, and others. In some cases, there may be no appropriate medication available to prescribe, as with very young children with bipolar disorder. In other cases, there may be only two approved medications, and if neither work, the clinician should be aided in using compounds with efficacy and/or tolerability information, despite a lack of FDA approval. Children with physical illness and mental illness, and children with multiple psychiatric comorbidities, also present special challenges to the clinician. Knowledge of the potential broad coverage of a single medication, and/or information about medication combinations that are potentially useful would be in the best interest of such children.

With respect to the increased availability of information about unapproved uses of approved drugs from sources such as scientific journals, and professional societies such as AACAP, we believe that this is a positive development. The free flow of information about unapproved drugs is essential to both clinicians and family members who are trying to make the best treatment decisions for young patients. Blocking information that is not associated with an FDA-approved indication may hamper high-quality care, and may harm patients by limiting their treatment options. AACAP has created a guide, available on the members-only page of our website, entitled *AACAP’s Medication Tables*² that could be helpful to clinicians when judging the validity and utility of communications regarding unapproved uses for multiple categories of

¹ McCracken, J.T., McGough, J., Shah, B., Cronin, P., Hong, D., Aman, M.G....McMahon, D., (2002). Risperidone in Children with Autism and Serious Behavioral Problems. *New England Journal of Medicine*, 347:314-321.

² American Academy of Child and Adolescent Psychiatry. <http://www.aacap.org/>

medications. The guide includes information about the FDA approval process, scientific evidence, and uses of these medications, both approved and unapproved.

The request for comments also asks for input regarding the factors the agency should consider when determining whether communications about unapproved uses are truthful and non-misleading. AACAP believes the best way to ensure the veracity of such communications would be to have them include objective data such as the level of scientific evidence and the outcomes, demonstrable through rating scales and tables regarding side effects. In cases where the communication about an unapproved use is based on information or data that is not publicly available, AACAP believes that the supportive scientific data should be made publicly available so that it can be carefully evaluated before prescribing decisions are made. Transparency of the information should be monitored based on the files submitted as part of the Investigational New Drug application, which includes a compilation of the study report to FDA, and main outcome tables. This information could be made available on the clinicaltrials.gov website as part of mandated study reporting.

AACAP encourages FDA to review its policies regarding the sharing of information from pharmaceutical companies concerning unapproved uses of approved medications and develop standards for the appropriate sharing of this information. These standards should ensure that pharmaceutical companies share accurate, objective, and non-misleading scientific data about their medications. FDA should work with the pharmaceutical industry to keep a repository of studies completed with their medications and make information on those studies easily available to clinicians on a regular basis.

Once again, we thank you for the opportunity to share our views. AACAP stands ready to offer additional assistance or information to the agency on this important topic. Please do not hesitate to contact Karen Ferguson, at kferguson@aacap.org, with questions you may have.

Sincerely,

A handwritten signature in black ink that reads "Gregory K. Fritz". The signature is written in a cursive, flowing style.

Gregory K. Fritz, MD
President