Written Testimony of
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Ohio General Assembly

Regarding HB 101 - An act relating to substitution of epinephrine auto-injector devices

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Chairman Huffman, Vice Chair Gavarone, Ranking Member Antonio, and members of the Committee, thank you for the opportunity to provide comments on HB 101 on behalf of Mylan Specialty L.P., the distributor of EpiPen® and EpiPen Jr® Auto-Injectors and the authorized generic versions of those products. Unfortunately, we believe HB 101, although well-intentioned, poses significant patient safety risks, creates confusion for both patients and pharmacists, and undermines key provisions of existing law that support the dispensing of epinephrine auto-injectors and their safe and effective use. Accordingly, for the reasons discussed more fully below, we respectfully urge the Committee to reject HB 101 as currently drafted.

We cannot overstate the potential for confusion or the risk to patients that HB101 creates. Epinephrine auto-injectors are a unique class of products. They are prescribed for patients who may be at risk of anaphylaxis from any number of triggers, notably including certain foods, insect stings, and medications. Anaphylaxis, which is an extreme allergic reaction, can proceed to life-threatening effects in a matter of minutes. Moreover, the vast majority of epinephrine auto-injectors are used by patients – including children – or caregivers, not medical professionals, in extremely high-stress situations.

For that reason, epinephrine auto-injectors must be easy to use, and patients and caregivers must be trained in their use. This is reflected in how the EpiPen® and EpiPen Jr® Auto-Injectors and our authorized generic versions of them are made available to consumers.

The FDA-approved labeling instructs healthcare providers to train patients and caregivers when prescribing the drug, and the product is packaged with a free trainer device for repetitive practicing. The goal is for the user, which may include the patient and many others in his or her daily network, to be so familiar and comfortable with the product that he or she can use it in an emergency quickly, safely and effectively.

These imperatives are also relevant to how generic epinephrine products are approved by the FDA. As a general proposition, generic drugs are approved upon demonstrating to FDA's satisfaction that they are therapeutically equivalent to the reference product for which they will be substituted. Therapeutic equivalence means that the generic product can be expected to have the same safety and effectiveness as the reference product when used under the same conditions. FDA has recognized that, with products that are a combination of a drug and a medical device by which the drug is delivered (such as epinephrine auto-injectors), the therapeutic equivalence analysis must take into account the design and operation of the proposed generic auto-injector, how similar or different it is to the already-approved delivery device in the reference product, and the potential implications of any differences.

As FDA has explained, the key consideration is whether, despite the differences between the two devices, patients and caregivers who are trained on and familiar with the reference product auto-injector will, without any additional training or instruction on the new device, be able to safely and effectively use the proposed generic injector in an emergency. A "yes" answer to that question is necessary before FDA will approve a generic version of an epinephrine auto-injector. Accordingly, approval of a generic epinephrine auto-injector – and the associated Orange Book "A" rating of therapeutic equivalence that goes with it – reflects FDA's view that the generic product, if substituted for the reference product, will have the same safety and effectiveness profile. FDA assigns "B" ratings to products that the agency considers not to be therapeutically equivalent, because of actual or potential bioequivalence problems that have not been resolved.

Many states rely on "A" ratings assigned by FDA as the basis for substitution. Ohio law takes a different approach, however, and, rather than requiring products to have been found by FDA to be therapeutically equivalent (*i.e.*, to be "A-rated" to each other in the Orange Book), Ohio permits substitution of "generically equivalent" products, which are products approved by FDA that contain "identical amounts of the identical active ingredients, . . . that meets the

identical compendial or other applicable standard of identity, strength, quality, and purity, including potency, and where applicable, content uniformity, disintegration times, or dissolution rates, as the prescribed brand name drug," so long as the product has not been "listed by the federal food and drug administration as having proven bioequivalence problems." Ohio Rev. Code Ann. § 3715.01(15) (2017). As noted above, FDA generally communicates such determinations through its "B" ratings, but it is clear that not every B-rating in the Orange Book translates to a "proven bioequivalence" problem.

In terms of the currently available epinephrine auto-injectors, there are three FDA-approved epinephrine auto-injectors currently marketed – EpiPen®, Auvi-Q®, and Adrenaclick®. This makes for a competitive epinephrine auto-injector market, even though these products are not rated as therapeutically equivalent to each other. Rather, the three approved epinephrine auto-injectors are listed in the Orange Book with a "BX" therapeutic equivalence code, which according to the FDA means the products are "presumed to be therapeutically *in*equivalent" to each other. This is consistent with the fact that these are three products that do not look the same, feel the same, or work the same way. And because this is a product that a patient or caregiver has to be able to successfully deploy immediately and while under great stress, in a life-threatening situation, there is little room for error, and these differences could matter.

Here is just one example of a difference that can matter. With the EpiPen® Auto-Injector, when the patient or caregiver has administered the injection and removes the auto-injector from the thigh, the auto-injector automatically sheaths the needle and the product can be disposed of. Adrenaclick®, on the other hand, has an exposed needle when the auto-injector is removed from the thigh. In fact, Adrenaclick® users are told to look for the exposed needle, and if they do not see it, attempt another injection with the same auto-injector. A patient or caregiver trained on the EpiPen® device would not know to look for an exposed needle, would not be surprised with an Adrenaclick® that has no exposed needle (because that is what patients expect from using the EpiPen®), and therefore would not know that the lack of an exposed needle means the patient has received no injection. Such an error can potentially be fatal. Moreover, such an error is easily imaginable, when one recognizes – as FDA explicitly does in its analysis of proposed generic epinephrine auto-injectors – that a patient being dispensed a different product in substitution for his/her prescribed product is not likely to receive instruction or training with the new product.

HB101 does not seem to fully appreciate and accommodate the unique status of epinephrine auto-injectors and the stressful circumstances under which they must be administered and we are concerned about the risks and confusion it can create. To the extent current Ohio law prohibits substitution among B-rated products, HB101 appears to remove that constraint without imposing sufficient protections for patients and creates a distinct standard for drug substitution for emergency-use epinephrine auto-injectors. Alternatively, Ohio law could be seen as currently permitting pharmacists to use their professional judgment to substitute drugs that FDA has not determined to be therapeutically equivalent so long as those products have not been assigned a B-rating that correlates to a proven bioequivalence problem. If this is the case, then HB 101 may operate to modify the professional judgment requirement or increase liability protection for pharmacists with respect to substitutions made for this particular class of emergency use products. In addition, by carving out this class of emergency-use products from the general guidelines governing substitution, HB 101 ignores the possible implications of future developments with regard to epinephrine auto-injectors. For instance, other epinephrine auto injectors which may be even more different than those currently available may enter the market or true A-rated generics may be approved, changing the circumstances under which substitution of a non-A-rated epinephrine auto-injector would be appropriate.

Given the stakes and the uncertainty with regard to the impact of HB101 on patients and pharmacists, we would urge that the legislature refer this issue to the Ohio State Board of Pharmacy for consideration and guidance rather than crafting a substitution law aimed at only epinephrine auto-injectors. If substitutions of distinct epinephrine auto-injectors are to occur, it is critical that the Ohio State Board of Pharmacy create guidelines for such substitution that include ensuring proper training of patients and caregivers in the use of the epinephrine auto-injector dispensed. A key difference between the three marketed epinephrine auto-injectors – a difference that is consistent with the products not being considered therapeutically equivalent – is how each product operates. A patient or caregiver trained on one product likely would not be able to use that training in order to use one of the other products. Notably, HB 101 does not clearly require the pharmacist to conduct the training necessary to ensure that the patient or caregiver will be able to safely and effectively use the new product (with which he or she is not familiar); the proposed statute merely requires that the pharmacist "provide instruction" upon initial dispensing of the distinct device (not subsequent refills), which conceivably could consist of the directions for use in the package insert. Moreover, the statute also does not require that

the pharmacist or pharmacy intern have been adequately trained to train a patient in the use of the dispensed epinephrine auto-injector.

Mylan understands the concerns that have been raised about the cost of epinephrine auto-injectors, and we have taken significant steps to ensure wide access to this life-saving product. Among other things, Mylan has brought to market an authorized generic version of the EpiPen® Auto-Injector that is priced at half the cost of the branded EpiPen® product. Mylan also has established both a coupon program and a patient assistance program, which make the product available to many patients at a significantly reduced cost, and at no cost to uninsured or underinsured patients earning less than 400% of the federal poverty level. For example, a family of four earning less than $97,200 a year can receive EpiPen® Auto-Injectors for free. And finally, Mylan offers a savings card for eligible patients with commercial health insurance, providing up to $300 off the out-of-pocket cost for EpiPen® Auto-Injector and up to $25 off the out-of-pocket cost for the authorized generic.

In January 2017, approximately 87% of consumers who received EpiPen® Auto-Injector or its authorized generic had an out-of-pocket cost of less than $50 and the vast majority paid less than $100. Mylan has also provided EpiPen® Auto-Injectors free of charge to more than 70,000 schools across the country, including 1629 schools in Ohio.

With regard to Sec. 4729.46, Mylan supports the goal of broadening patient access to epinephrine auto-injectors, but does wish to note two concerns related to training and liability protection.

With regard to training, if pharmacists are to be allowed to dispense an epinephrine auto-injector under authority of a protocol but without a prescription as outlined in (B)(1), the pharmacist must be required to provide training to the individual to whom the auto-injector is dispensed, to ensure the patient knows how to recognize signs and symptoms of anaphylaxis, how to properly use the epinephrine auto-injector and what steps to take following administration. These are critical to patient safety, but not required by HB 101 as currently drafted.

With regard to liability protection, we support allowing pharmacists to dispense without a prescription to an individual acting on behalf of a qualified entity, however, we believe this

provision – (B)(2) - should be amended into Sec. 3728.03 rather than Sec.4729.46. We believe that an entity that receives an epinephrine auto-injector under Sec. 4729.46 would not have the liability protections or the requirements of those who acquire epinephrine auto-injectors under Sec. 3728.03 of the Revised Code.

To that end, Mylan would welcome the opportunity to work with the Committee in further developing ways to achieve that goal, because in our view, HB 101 is not the right way to do it.

Thank you for your time and consideration.