March 2, 2020

Division of Dockets Management
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Valisure Citizen Petition on Metformin

Dear Sir or Madam:

The undersigned, on behalf of Valisure LLC and ValisureRX LLC (collectively, "Valisure" or "Petitioner"), submits this Citizen Petition ("Petition") pursuant to Sections 301(21 U.S.C. § 331), 501 (21 U.S.C. § 351), 502 (21 U.S.C. § 352), 505 (21 U.S.C. § 355), 702 (21 U.S.C. § 372), 704 (21 U.S.C. § 374), and 705 (21 U.S.C. § 375) of the Federal Food, Drug and Cosmetic Act (the "FDCA"), in accordance with 21 C.F.R. 10.20 and 10.30, to request the Commissioner of Food and Drugs ("Commissioner") to issue a regulation, request recalls, revise industry guidance, and take such other actions set forth below.

A. Action Requested

Valisure has tested and detected high levels of N-Nitrosodimethylamine ("NDMA") in specific batches of prescription drug products containing metformin, a drug used to control high blood sugar in patients with type 2 diabetes. The World Health Organization ("WHO") and the International Agency for Research on Cancer ("IARC") have classified NDMA as a Group 2A compound thereby defining it as "probably carcinogenic to humans."[1] The carcinogenic nature of nitrosamines in general, and NDMA specifically, has been well documented in the scientific community since the 1960s.[2] FDA currently recognizes the danger of this compound and, as a result, has set strict daily acceptable intake limits on NDMA in pharmaceuticals of 96 nanograms ("ng").[3] Furthermore, the presence of this probable carcinogen in a medication that is taken daily by adults and adolescents for a chronic condition like diabetes, makes this finding particularly troubling.

[1] International Agency for Research on Cancer and World Health Organization, *IARC Monographs on the Identification of Carcinogenic Hazards to Humans,* Volume 17, Supp. 7 (1987) (https://monographs.iarc.fr/list-of-classifications-volumes/) and *Preamble to IARC Monographs on the Identification of Carcinogenic Hazards to Humans* (2019) (https://monographs.iarc.fr/wp-content/uploads/2019/01/Preamble-2019.pdf).

[2] *E.g.,* Argus, M.F. and Hoch-Ligeti, C., *Comparative Study of the Carcinogenic Activity of Nitrosamines,* JNCI: Journal of the National Cancer Institute 27: 695 (September 1961) (https://academic.oup.com/jnci/article-abstract/27/3/695/958026).

[3] Food and Drug Administration, *FDA updates table of interim limits for nitrosamine impurities in ARBs,* (February 28, 2019) (https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-angiotensin-ii-receptor-blocker-arb-recalls-valsartan-losartan).

This Petition requests that the Commissioner take the following actions:

1) request a recall of identified batches of metformin on the basis that, due to contamination with a probable human carcinogen, these drugs are adulterated under Section 501 of the FDCA (21 U.S.C. § 351) and misbranded under Section 502 of the FDCA (21 U.S.C. § 352);

2) conduct examinations and investigation under Section 702 (a) of the FDCA (21 U.S.C. § 372(a)) regarding these products, their manufacturing processes, and the manufacturer submissions made for FDA approval under 704 (a)of the FDCA (21 U.S.C. § 374(a)), and effect labeling revisions as needed;

3) provide information to the public regarding these products under Section 705(b) of the FDCA (21 U.S.C. § 375(b));

4) update and revise FDA guidance document FY20-058-DPA-S, to include the analytical methodology outlined in this petition and in Attachment A for improved quantitation of NDMA in metformin and to avoid underestimation of NDMA levels; and

5) promulgate regulations requiring robust independent chemical batch-level testing and verification of the chemical content of batches of pharmaceuticals of drugs and, while these regulations are pending, issue guidance requesting such testing and verification.

Background on Petitioner

Valisure is an online pharmacy currently licensed in 38 states and an analytical laboratory that is ISO 17025 accredited by the International Organization for Standardization ("ISO"). Valisure is registered with the Drug Enforcement Administration (Pharmacy: FV7431137, Laboratory: RV0484814) and FDA (FEI #: 3012063246). Valisure's mission is to help ensure the safety, quality and consistency of medications and supplements in the market. In response to rising concerns about counterfeit medications, generics, and overseas manufacturing, Valisure developed proprietary analytical technologies that it uses in addition to FDA standard assays to test every batch of every medication it dispenses.

In an August 7, 2018, inspection of Valisure's facilities by FDA, it was determined that since Valisure's unique testing facility is not a part of the pharmaceutical manufacturing system and does not perform release testing, stability testing or any related services for pharmaceutical manufacturers, Valisure did not require FDA registration. However, Valisure has elected to maintain voluntary registration status with FDA. Valisure also received guidance that since it operates outside of the manufacturing industry using the appropriate ISO guidelines as opposed to GMPs, any product failures or concerns that Valisure identifies should be reported back to the pharmaceutical industry. Valisure has complied with this guidance and routinely provides reports to applicable parties in the pharmaceutical industry.

Given the high potential risk to public safety, Valisure seeks to utilize this Citizen Petition to bring these concerns directly to the attention of the Commissioner and FDA, and to request that they take prompt action.

B. Statement of Grounds

In addition to the information described above, which is incorporated by reference, Valisure provides the following as its statement of grounds. FDA currently recognizes the danger of NDMA and, as a result, has set a strict daily acceptable intake limit on NDMA in pharmaceuticals of 96 nanograms.[4] There have been a multitude of manufacturer recalls of angiotensin receptor blocker ("ARB") medications, such as valsartan and losartan, due to the detection of NDMA in excess of these limits.[5]

There have also been extensive recalls[6] of Zantac and other ranitidine-containing products following Valisure's finding of NDMA's connection to ranitidine.[7] However, it is important to note that the presence of NDMA in metformin products may be primarily due to contamination during manufacturing as opposed to a fundamental instability of the drug molecule, which is the case with ranitidine.[8] [9] [10] [11] [12]

Valisure's analysis closely followed FDA-recommended LC-MS protocol for metformin drug substances and drug products posted February 4, 2020, designated FY20-058-DPA-S.[13] Valisure's laboratory is ISO 17025 accredited specifically for the analysis and determination of

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[4] *Id.*

[5] Food and Drug Administration. *Search List of Recalled Angiotensin II Receptor Blockers (ARBs) Including Valsartan, Losartan and Irbesartan* (September 23, 2019) (https://www.fda.gov/drugs/drug-safety-and-availability/search-list-recalled-angiotensin-ii-receptor-blockers-arbs-including-valsartan-losartan-and).

[6] Food and Drug Administration. *FDA Updates and Press Announcements on NDMA in Zantac (ranitidine)* (February 3, 2020) (https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-ndma-zantac-ranitidine).

[7] Johnson, Carolyn (November 8, 2019) A tiny pharmacy is identifying big problems with common drugs, including Zantac. *The Washington Post*. https://www.washingtonpost.com/science/a-tiny-pharmacy-is-identifying-big-problems-with-common-drugs-including-zantac/2019/11/08/6dd009ca-eb76-11e9-9c6d-436a0df4f31d_story.html.

[8] Valisure FDA Citizen Petition Requesting to Recall Ranitidine (dated September 9, 2019) (https://www.regulations.gov/docket?D=FDA-2019-P-4281)

[9] Emery Pharma FDA Citizen Petition Requesting to Recall Ranitidine (dated January 2, 2020) (https://www.regulations.gov/docket?D=FDA-2020-P-0042)

[10] Zeng, T. and Mitch, W.A. (2016). Oral intake of ranitidine increases urinary excretion of N-nitrosodimethylamine. *Carcinogenesis*. Vol. 37, p. 625-634 (https://www.ncbi.nlm.nih.gov/pubmed/26992900).

[11] Le Roux, J., et. al. (2012). NDMA Formation by Chloramination of Ranitidine: Kinetics and Mechanism. *Environ. Sci. Technol.* Vol. 46, p. 20 (https://pubs.acs.org/doi/10.1021/es3023094).

[12] Juan Lv, Lin Wang, Yongmei Li (2017). Characterization of N-nitrosodimethylamine formation from the ozonation of ranitidine, *J. Environ. Sci.* Vol. 29, p. 116 (http://www.jesc.ac.cn/jesc_en/ch/reader/view_abstract.aspx?file_no=S1001074216316357&flag=1)

[13] Food and Drug Administration. FDA Guidance Document FY20-058-DPA-S (February 4, 2020). *Liquid Chromatography-High Resolution Mass Spectrometry (LC-HRMS) Method for the Determination of NDMA in Metformin Drug Substance and Drug Product* (https://www.fda.gov/media/134914/download).

NDMA.[14] Valisure has reviewed the FDA protocol for NDMA detection in metformin and made modifications to the LC-MS protocol that improve the precision of the method. Because FDA recently revised guidance for the analysis of NDMA to an LC-MS approach as opposed to higher-temperature GC-MS methods that were previously recommended,[15] Valisure has maintained the metformin method it uses on an LC-MS instrument.

Petitioner recognizes that FDA has also expressed concern over NDMA contamination in metformin and posted an update[16] and analytical results[17] on February 3, 2020. In this detailed update, FDA states that "to date, no sample of metformin that FDA has tested exceeds the acceptable daily intake for NDMA."[18] FDA's data show seven companies of which 16 batches were tested with nearly all results concluding that no NDMA was detected. It is unclear what methodology FDA used to select the limited scope of batches and companies that were tested; though given Valisure's results, it appears a broader approach may be necessary. To further assure validity, sampling and testing should be performed by independent third parties with direct access to the standard pharmaceutical supply chain.

Valisure acquired metformin batches from all companies reasonably available to it through its pharmacy suppliers. Valisure's analysis of 22 companies selling metformin and a total of 38 batches revealed 16 batches from 11 companies where NDMA levels were detected above the 96 ng daily acceptable intake limit, which was factored using a common number of tablets taken per day. Several batches contained over 10 times the daily acceptable intake limit and there was significant variability from batch to batch, even within a single company; underscoring the importance of batch-level chemical analysis and the necessity of overall increased quality surveillance of medications.

Valisure's results will be of significant concern to medical practitioners who already struggle to prescribe safe medications and who rely on external government and private sector oversight to ensure contaminant-free drugs. Due to the discovery of significant levels of NDMA contamination, Valisure's pharmacy will not sell the affected batches of metformin it has acquired and Valisure cannot obtain a refund for these tainted products because they have not been recalled.

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[14] Certificate of Accreditation, ISO 17025, Valisure, LLC https://www.pjview.com/clients/pjl/viewcert.cfm?certnumber=17468.

[15] Food and Drug Administration. (January 28, 2019). FDA Guidance Document FY19-005-DPA-S. *Combined N-Nitrosodimethlyamine (NDMA) and N-Nitrosodiethylamine (NDEA) Impurity Assay* (https://www.fda.gov/media/117843/download).

[16] Food and Drug Administration. *FDA Updates and Press Announcements on NDMA in Metformin* (February 3, 2020). (https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-ndma-metformin)

[17] Food and Drug Administration. *Laboratory Tests/metformin* (February 3, 2020). (https://www.fda.gov/drugs/drug-safety-and-availability/laboratory-tests-metformin).

[18] *Id.*

Petitioner urges the Commissioner and FDA to expeditiously request recalls on the affected batches of medication so they are removed from the American drug supply, and to take other such actions outlined in this Petition as deemed appropriate.

Analytical Methods

FDA published a method titled "Liquid Chromatography-High Resolution Mass Spectrometry (LC-HRMS) Method for the Determination of NDMA in metformin Drug Substance and Drug Product" (FY20-058-DPA-S). Based on the testing principle of this method, Valisure scientists used LC-HRMS instrumentation but with modified methodology that achieved a lower limit of detection ("LOD"), a lower limit of quantitation ("LOQ"), and a wider reportable range than shown by FDA, and uses isotopically labelled NDMA to measure recovery in the background of each unique medication matrix. Table 1 shows a summary of method performance comparisons, Table 2 explains a few key differences between the methods and a detailed overview of the method is contained in Attachment A to this petition.

Table 1. Testing Scope Validated by FDA and Valisure using LC-HRMS.

NDMA	**FDA**	**Valisure**
LOD (ng/mL)	1.0	0.3
(ppm)	0.01	0.003
LOQ (ng/mL)	3.0	1.0
(ppm)	0.03	0.01
Range (ng/mL)	3.0 - 10	1.0 – 200
(ppm)	0.03 - 0.1	0.01 - 2.0

Table 2. Summary of Method Differences and Assessment of Data Quality.

	FDA Method	**Valisure Method**	**Assessment of Results**
Mass Spectrometry	Orbi-Trap HRMS with optimized parameters	Q-TOF HRMS with optimized parameters	Both HRMS can achieve desired mass resolution and accuracy for the analytical purpose
HPLC Method	XSelect CSH C18 2.5 µm, 3.0 x 150 mm with optimized flow and gradient	Luna Omega PS C18 HPLC column 3 µm, 4.6 × 100 mm with optimized flow and gradient	Valisure's method generates increased chromatographic resolution and sharper peaks, thus resulting in higher signal to noise ratio at same concentration than FDA method (Figure 1 and Figure 2)
Quantification	Comparing sample peak area with average of six 3 ng/mL standard injections	Isotopic dilution calibration curve with r^2 greater than 0.999, sample concentration is corrected by internal standard (See Attachment A)	Without use of an internal standard, the FDA method has the potential to underestimate the NDMA concentration due to matrix effects.

Figure 1 and Figure 2, on the next page, illustrate the results from FDA's and Valisure's detection method when analyzing the same 20ng/mL NDMA reference sample.

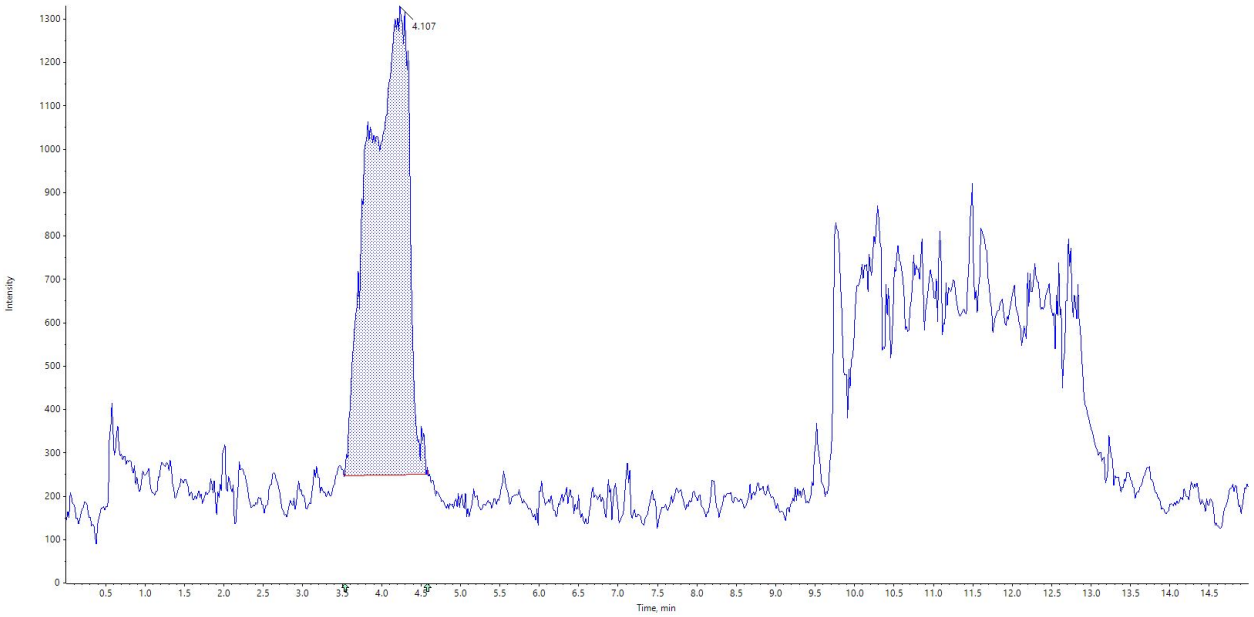

Figure 1. Identified peak of 20 ng/mL NDMA standard solution using FDA method FY20-058-DPA-S, with broadened peak and signal to noise ratio of 106.

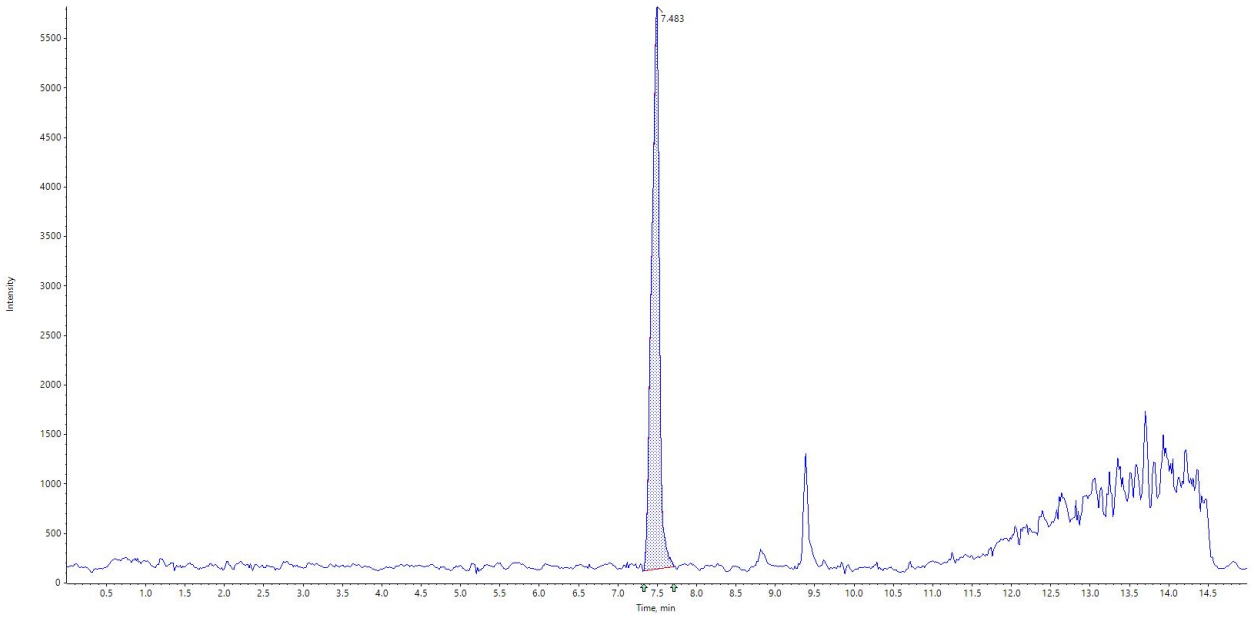

Figure 2. Identified peak of 20 ng/mL NDMA standard solution by Valisure's LC-HRMS method, with greater chromatography resolution and signal to noise ratio of 797.

Petitioner urges FDA to revise their guidance to industry for the analysis of NDMA in metformin to include methods such as those utilized by Valisure that achieve lower LOD, lower LOQ, and a wider reportable range, and are less at risk of underestimating NDMA levels. It is of particularly high importance to precisely quantify NDMA in a drug like metformin, given that tablets are often taken four times a day, yielding an acceptable amount of NDMA per tablet of only 24ng (96ng daily intake limit divided by four tablets per day).

Analytical Findings

Using the LC-HRMS method described above for the determination of NDMA in metformin, Valisure analyzed 38 unique batches from 22 companies with the results detailed below:

Table 3. Detailed results of NDMA analysis on various batches of metformin. Three tablets from each batch were tested individually and the amount of NDMA detected is reported as an average followed by the standard deviation of the results from the three tablets. An asterisk "*" denotes data generated by Emery Pharma from the same batch.

Company	Dose (mg)	Type	Lot	NDMA (ng/tablet)	Common Tablets/Day	Times Over Acceptable Daily Intake Limit of NDMA
ACI Healthcare USA, Inc.	500	Metformin IR	D105061	31 ± 4	4	1.3X
ACI Healthcare USA, Inc.	500	Metformin IR	C105019A	Not Detected	4	
ACI Healthcare USA, Inc.	500	Metformin IR	D105019	Not Detected	4	
Actavis Pharma, Inc.	500	Metformin ER	1376339M	182 ± 2	4	7.6X
Actavis Pharma, Inc.	750	Metformin ER	1354471A	320 ± 25	2	6.7X
AiPing Pharmaceutical, Inc.	500	Metformin ER	190300211	Not Detected	4	
AiPing Pharmaceutical, Inc.	1000	Metformin ER	190200411	Not Detected	2	

American Health Packaging/(Zydus)	1000	Metformin IR	184759	Not Detected	2	
Amneal Pharmaceuticals LLC	750	Metformin ER	AM180770A	450 ± 100	2	9.4X
Amneal Pharmaceuticals LLC	500	Metformin ER	AM190107AA	395 ± 53 (623 ± 28)*	4	16.5X
Amneal Pharmaceuticals of New York LLC	500	Metformin ER	HD03319A	283 ± 27	4	11.8X
Amneal Pharmaceuticals of New York LLC	500	Metformin ER	HM02918A	282 ± 67	4	11.8X
Amneal Pharmaceuticals of New York LLC	850	Metformin IR	AM180405A	235 ± 17	2	4.9X
Apotex Corp.	500	Metformin ER	NE5801	90 ± 3	4	3.8X
Apotex Corp.	750	Metformin ER	NG2595	Not Detected	2	
Ascend Laboratories, LLC	1000	Metformin IR	4200061B	529 ± 107	2	11.0X
Ascend Laboratories, LLC	500	Metformin IR	4980028B	Not Detected	4	
Ascend Laboratories, LLC	1000	Metformin IR	4200024C	Not Detected	2	
Aurobindo Pharma Limited	500	Metformin IR	MTSA19016-B	30 ± 7	4	1.3X
Aurobindo Pharma Limited	500	Metformin IR	MTSA19070-C	Not Detected	4	

EPIC PHARMA, LLC	500	Metformin ER	190101111	Not Detected	4	
Granules Pharmaceuticals Inc.	500	Metformin ER	4910134A	41 ± 5	4	1.7X
Heritage Pharmaceuticals Inc.	850	Metformin IR	4510157A	254 ± 12	2	5.3X
Heritage Pharmaceuticals Inc	500	Metformin IR	4500753A	206 ± 20	4	8.6X
Heritage Pharmaceuticals Inc.	1000	Metformin IR	4521630A	Not Detected	2	
Ingenus Pharmaceuticals, LLC	1000	Metformin ER	19388005	Not Detected	2	
Lupin Pharmaceuticals, Inc.	500	Metformin ER	G901203	122 ± 11	4	5.1X
Megalith Pharmaceuticals Inc	1000	Metformin IR	442180318	Not Detected	2	
Mylan Pharmaceuticals Inc.	1000	Metformin ER	3090719	Not Detected	2	
Nostrum Laboratories, Inc.	1000	Metformin ER	MEF290206	Not Detected	2	
Oceanside Pharmaceuticals	500	Metformin ER	19D125P	Not Detected	4	
Sun Pharmaceutical Industries, Inc.	750	Metformin ER	JKU0880A	Not Detected	2	
Sun Pharmaceutical Industries, Inc.	500	Metformin ER	JKU2539A	Not Detected	4	

TAGI Pharma, Inc.	500	Metformin ER	5841910035	Not Detected	4	
TAGI Pharma, Inc.	500	Metformin ER	5841905129	Not Detected	4	
TIME CAP LABORATORIES, INC	500	Metformin ER	XP9004	53 ± 12	4	2.2X
Westminster Pharmaceuticals, LLC	500	Metformin IR	B105067B	Not Detected	4	
Westminster Pharmaceuticals, LLC	1000	Metformin IR	B107261B	Not Detected	2	

To further cement the robustness of Valisure's findings, samples from batch AM190107AA were sent to Emery Pharma, an FDA registered/inspected, cGMP/GLP compliant analytical laboratory[19] which performed NDMA analysis on three tablets. Although the methodologies of analysis between Emery and Valisure have small differences, Emery's data came to the same conclusion of finding many times the acceptable daily intake limit of NDMA in samples of metformin taken from batch AM190107AA.

Recall Request and Other Actions

This Petition seeks to have the Commissioner and FDA request recalls for the identified batches of metformin, consistent with FDA's mandate to ensure the safety of the drug supply in America. Table 4 lists the batches of metformin that contained levels of NDMA in excess of the daily acceptable intake limit.

Table 4. All medication batches analyzed by Valisure which exceeded the daily acceptable intake limit of 96ng for NDMA.

Company	Dose (mg)	Type	Lot	NDC	Exp Date
ACI Healthcare USA, Inc.	500	Metformin IR	D105061	71093-132-06	Aug-22
Actavis Pharma, Inc.	500	Metformin ER	1376339M	62037-571-01	Sep-21
Actavis Pharma, Inc.	750	Metformin ER	1354471A	62037-577-10	Feb-21

[19] Emery Pharma (February 28, 2020). (https://emerypharma.com/)

Amneal Pharmaceuticals LLC	750	Metformin ER	AM180770A	65162-179-10	May-20
Amneal Pharmaceuticals LLC	500	Metformin ER	AM190107AA	65162-178-10	Dec-20
Amneal Pharmaceuticals of New York LLC	500	Metformin ER	HD03319A	53746-178-90	Apr-21
Amneal Pharmaceuticals of New York LLC	500	Metformin ER	HM02918A	53746-178-01	Jan-21
Amneal Pharmaceuticals of New York LLC	850	Metformin IR	AM180405A	53746-219-05	Mar-20
Apotex Corp.	500	Metformin ER	NE5801	60505-0260-1	Apr-21
Ascend Laboratories, LLC	1000	Metformin IR	4200061B	67877-563-01	May-22
Aurobindo Pharma Limited	500	Metformin IR	MTSA19016-B	65862-008-01	Jan-23
Granules Pharmaceuticals Inc.	500	Metformin ER	4910134A	70010-491-01	Jun-22
Heritage Pharmaceuticals Inc.	850	Metformin IR	4510157A	23155-103-10	Apr-22
Heritage Pharmaceuticals Inc	500	Metformin IR	4500753A	23155-102-01	Apr-22
Lupin Pharmaceuticals, Inc.	500	Metformin ER	G901203	68180-336-07	Dec-20
TIME CAP LABORATORIES, INC	500	Metformin ER	XP9004	49483-623-01	Dec-20

Such recalls are important for public safety. As indicated in Table 3, there is significant batch-to-batch variation in NDMA content but many batches of metformin contain no detectable NDMA and thus recalls should not overly burden the U.S. healthcare system.

In addition, for the reasons stated above, FDA should conduct examinations and investigation under Section 702 (a) of the FDCA (21 U.S.C. § 372(a)) regarding these products, their manufacturing processes, and the manufacturer submissions made for FDA approval under 704 (a)of the FDCA (21 U.S.C. § 374(a)) and effect labeling revisions as needed. Further, FDA

should provide information to the public regarding these medications under Section 705(b) of the FDCA (21 U.S.C. § 375(b)).

Batch-level Testing and Verification of Drug Products in the United States

Petitioner is also requesting that FDA promulgate regulations requiring robust independent chemical batch-level testing and verification of medications. In the interim, while these regulations are pending, FDA should issue formal guidance recommending such testing and verification.

This is necessary in order to serve public health and help protect Americans from adulterated drug products, an issue of growing concern. Grounds for this request are also rooted in strong support from the medical community, as evidenced by a recent resolution from the American College of Cardiology ("ACC"), calling for the American Medical Association to advocate for legislation requiring independent testing and verification of the chemical content of batches of pharmaceuticals. The resolution is at Attachment B.

Figure 3 below shows a comparison of testing results from FDA, recent metformin recall announcements from Canada[20] and Valisure's results. This data highlights the vital importance for batch-level testing to be performed by independent entities in an objective manner direct from the pharmaceutical supply chain that delivers medications to the American public.

[20] Health Canada. *Certain Metformin diabetes drugs recalled due to the presence of NDMA* (February 26, 2020). (https://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2020/72287a-eng.php)

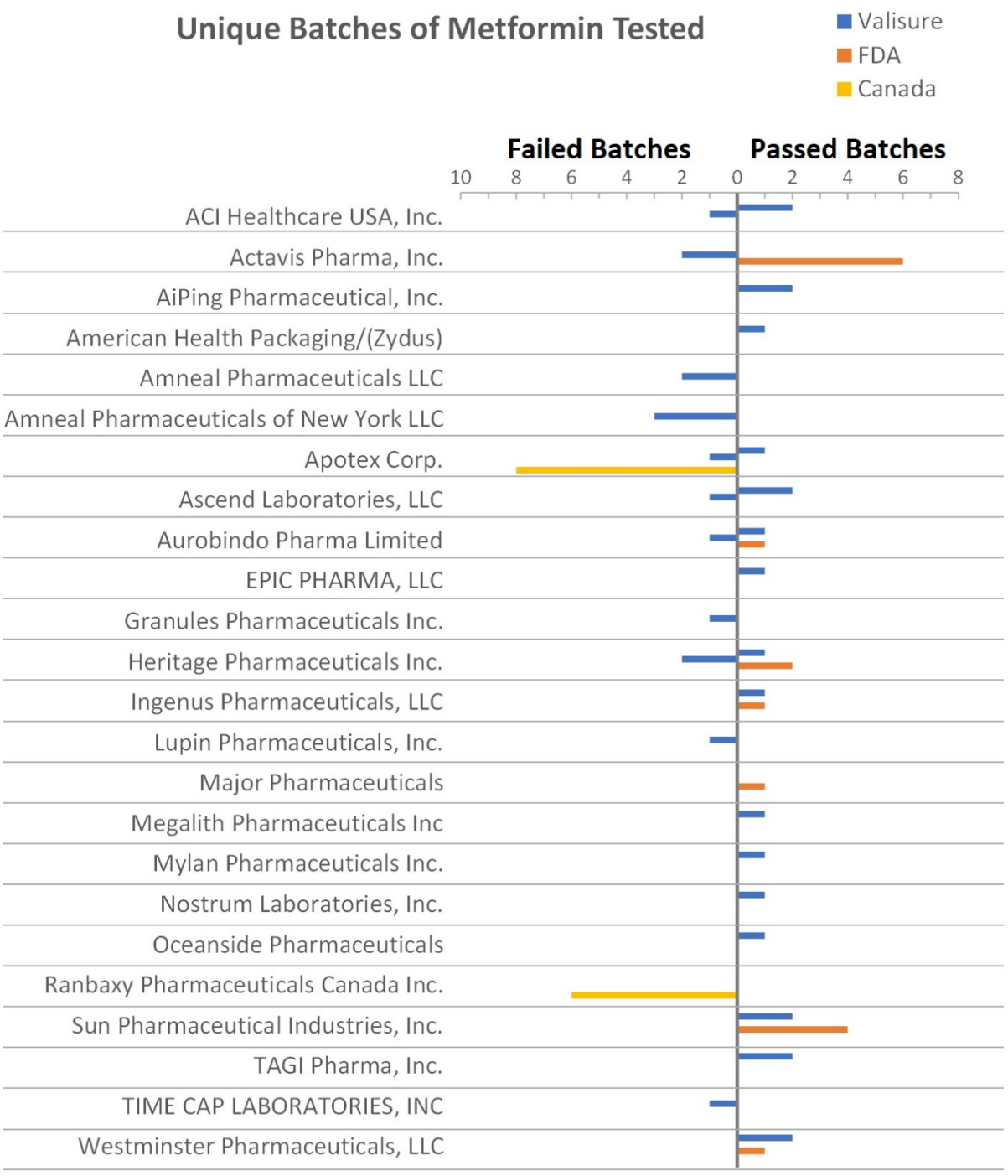

Figure 3. Summary comparison of batch-level data from various companies selling metformin as analyzed and/or reported by FDA, Health Canada, and Valisure.

Valisure's data clearly shows that NDMA contamination above FDA acceptable limits is a pervasive and scattered problem throughout the current American supply chain. FDA has numerous responsibilities and limited resources with which to fulfill them, so it would not be reasonable to expect FDA to itself perform comprehensive batch-level testing. Nevertheless, the absence of such testing exposes the American people to demonstrable risk. For example the limited nature of FDA testing was unable to detect companies that currently have tainted batches in the American and Canadian markets. At least one company that consistently displayed high levels of NDMA in all Valisure-tested batches was a company whose metformin products, to Valisure's knowledge, were not tested by FDA.

As Valisure's results indicate, relying on pharmaceutical companies' self-reporting of analytical results is not sufficient to protect the American pharmaceutical supply from potentially dangerous contamination. Furthermore, even when recalls are voluntarily performed by industry, the lengthy period of time over which such recalls occur is of significant concern to healthcare professionals, including those who have witnessed the over year-long recall process of the ARB medication recalls. It appears that the situation with metformin may be similar and a proactive drive for broad, independent testing should be combined with decisive action on the part of regulators to quickly request recalls and take other actions as appropriate. This is critical so that recalls of metformin do not plague the American healthcare system for years to come.

C. Environmental Impact

Petitioner claims a categorical exclusion under 21 C.F.R. § 25.30, and believes that this Petition qualifies for a categorical exclusion from the requirement to submit an environmental assessment or environmental impact statement. To Petitioner's knowledge, no extraordinary circumstances exist.

D. Economic Impact

Pursuant to 21 C.F.R. § 10.30(b), economic impact information will be submitted by the Petitioner only upon request of the Commissioner following review of this Petition.

E. Certification

The undersigned certifies that, to the best knowledge and belief of the undersigned, this petition includes all the information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Respectfully submitted,

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