

## **Web pharmacies: A field study of ciprofloxacin and atorvastatin**

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### **Abstract**

244 treatment packs of the broad spectrum antibiotic ciprofloxacin and 198 treatments of cholesterol controlling atorvastatin were sampled from a stratified sample of 61 web pharmacies. Each sample was analyzed for active pharmaceutical ingredient content (API) and 18 of 442 (4%) were found to be grossly (less than 80%) under content (11 cipro and 7 atorvastatin). Most of the 18 came from non-certified sites, but two came from certified sites. None of the failures appeared to be a falsified medicine (packaging appeared correct and contained over 50% API). All failures were made by Asian manufacturers (12 Indian and 6 Chinese). All the failures regardless of source are a risk to patient health. For Cipro they could also accelerate population level resistance to this crucial antibiotic.

### **Background**

In previous work on internet sourced medicines (Bate et al 2010 and Bate et al 2013) my colleagues and I analyzed five well-known branded medicines and used a precise raman handheld spectrometer to assess deviations in quality. In this new effort we assess the active ingredient content of the broad spectrum antibiotic ciprofloxacin. One reason for this technique is that it allows measurement of generic products, which was not possible given earlier assessment techniques. A drawback is that only major failings of the medicine are measured, which means this will likely underestimate the number of substandard medicines.

In different earlier research (Bate et al 2015 and Bate et al 2016) we found that ciprofloxacin lost its patent protection in countries around the world over the last 15 years and so most patients buy generic versions. We bought ciprofloxacin in several dozen cities over the past decade, 9 per cent of the roughly 2,500 samples failed basic quality tests (about 100 samples were patented innovator products and none failed). Seven per cent of which were substandard, products made by legal manufacturers, and two per cent were fake, products made by criminal groups. When a subset was subjected to more stringent tests we found three per cent more substandard medicines (no more fakes), so roughly ten per cent of the ciprofloxacin was substandard. We have not done research on atorvastatin before and there are no sizeable field studies.

### **Methods**

Following the protocol established in Bate et al 2010 we procured from three types of online pharmacies: tier 1 are US-based and certified by the National Association of Boards of Pharmacy (NABP)

or LegitScript.com, tier 2 are certified by PharmacyChecker.com or the Canadian International Pharmacy Association (CIPA) but not by NABP or LegitScript, tier 3 are not certified by any of the four agencies. Most tier 2 and tier 3 websites are foreign. For Cipro, we bought 28 samples from 7 tier 1 pharmacies, 88 samples from 22 tier 2 pharmacies and 128 samples from 32 tier 3 pharmacies. For atorvastatin we bought 22 samples from 7 tier 1 pharmacies, 80 samples from 22 tier 2 pharmacies and 96 samples from 32 tier 3 pharmacies.

We tested the samples with the protocol outlined in Bate et al 2015. All medicines were assessed following the Global Pharma Health Fund (GPHF) e.V. Minilab® protocol to identify substandard or falsified medicines (Jahnke 2001).

## Results

The table below shows the data from our Cipro samples.

	Where made	Tier 1 pass	Tier 1 fail	Tier 2 pass	Tier 2 fail	Tier 3 pass	Tier 3 fail	Total pass	Total fail
	US	21	0	35	0	4	0	60	0
	India	4	1	39	1	60	5	103	7
	China	0	0	6	0	30	4	36	4
	ROW	2	0	7	0	18	0	27	0
	Unknown	0	0	0	0	7	0	7	0
<b>Total</b>		<b>27</b>	<b>1</b>	<b>87</b>	<b>1</b>	<b>119</b>	<b>9</b>	<b>233</b>	<b>11</b>

The table below shows the data from our atorvastatin samples.

	Where made	Tier 1 pass	Tier 1 fail	Tier 2 pass	Tier 2 fail	Tier 3 pass	Tier 3 fail	Total pass	Total fail
	US	14	0	30	0	4	0	48	0
	India	4	0	31	0	53	5	88	5
	China	0	0	6	0	12	2	18	2
	ROW	4	0	13	0	22	0	39	0
	Unknown	0	0	0	0	5	0	5	0
<b>Total</b>		<b>22</b>	<b>0</b>	<b>80</b>	<b>0</b>	<b>96</b>	<b>7</b>	<b>198</b>	<b>7</b>

The results for this study closely echo previous studies, with one worrying change. Even the credentialed sites (tiers 1 and 2), which in prior studies only sold high quality medicines, sold a couple of medicines with insufficient ingredients. Both of these samples were Indian made cipro approved by FDA. Of course far larger samples would be required to make a proper assessment of any problems with these medicines and the sites selling them. As expected the tier 3 sites had the largest problems. And as in previous studies, the source of the problem was once again Asian (Indian and Chinese) made medicines.

## Conclusion

With a rise in antimicrobial resistance it is essential that all medicines are of the highest quality and when it comes to ciprofloxacin that is simply not the case. It is especially concerning that if people buy medicines from non-credentialed (tier 3) sites, that they risk their own lives and could encourage population level resistance to an important antibiotic. Those people buying atorvastatin online should be able to ensure good quality by buying from credentialed sites. But that assumes further investigations find no problems. The entire content of these medicines should be assessed to ensure no impurities or other problems (such as solubility) exist.

## References

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