



# Researcher Examines the World of Fake Injectable Products

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In the world of aesthetics, manufacturers of quality products have taken considerable time and effort, as well as investing much money, to get their products to market. Now, the dubious world of fake facial injectables has arrived. Counterfeit products are out there and easily found. You don't have to look too far on the Internet before you find them. My hunt began on a prominent search engine, through a sponsored link that took me straight to the supplier's website, based apparently in New Zealand. What I found was a complete do-it-yourself (DIY) kit for patients to self-inject at home.

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So what are these products? Where do they come from? What about their quality? Do they even work?

We used to call these products either counterfeits (illegal copies of the original branded products), or look-alike, sound-alike products (the same type of product but with a different name; always unlicensed and of unknown origin). Now we simply call them fakes.

There is a growing concern that unlicensed, cheap botulinum toxin (BoNT) products and dermal fillers of unknown origin and certainly unknown quality are readily available worldwide through the Internet. Many clinicians are aware of these products through direct advertising that they regularly receive. While few actually try them – even though they are guaranteed effective and of high quality – because they would be responsible if any serious adverse effects occurred, selling even small quantities of these can yield significant profits, which is why they exist.

Nothing was heard or known about these products until 2006, when reports began surfacing of a single patient case after use of an illegal product<sup>1</sup> and then the famous Florida incident<sup>2</sup>, which actually occurred in 2004. Both of these reports were of the same incident. The effects on the patients involved were exceptionally serious and continued, in one case, for several years afterwards.<sup>3</sup>

In March 2008, scientists Terry Hunt and Ken Clarke at Allergan, Inc. (Irvine, California, U.S.), described the BoNT product Nanfeng CNBTX-A and the quality and potency issues with this fake product.<sup>4</sup> Coincidentally, our team had prepared a report for the Toxins 2008 meeting on a number of illegal BoNT products that had been sent to us.<sup>5</sup> These two reports came out virtually together and the main issue in both was that some products labeled with a certain BoNT potency actually contained significantly more than what was shown. This inaccuracy represented a serious danger; over-dosing could easily occur. More importantly, the big unknown was the quality. There was no way of knowing if they were even sterile.

**Table 1. Potencies of Fake Botulinum Toxin Type A Products**

	Country where product identified	Likely country of origin	Labeled Potency	Actual Measured Potency [u/vial]	Comments
<b>Counterfeit Products</b>					
Dysport counterfeit [called SpainTox]	Brazil	Unknown	500	~1.5	
Dysport counterfeit	Iran	China	500	No toxin detected [ $<20$ u/vial]	Poor quality replica [Cap, seal, stopper, dark particles, incorrect excipients]
Dysport counterfeit	Russia	China	500	71	Contains excipients known in toxins of Chinese origin
<b>Look-A-Like Products</b>					
Lanzhou CBTX-A [Prosigne in Brazil, Quick Star in U.S.]	Hong Kong	China	100	145	Rebranded as other products
Estetox-A	Iran	China	100	No toxin detected [ $<20$ u/vial]	From Lanzhou
Refinex/Amazing	Iran	China	100	~125	May be rebranded as other products
Novotox Ultra	Iran	China	150	~35	Indicated of Canadian origin
Canitox	Iran	China	100	~98	Indicated of Canadian origin
Linurase	Iran	China	50	~233	Indicated of Canadian origin

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A number of actual counterfeit toxins have appeared in various countries across the world, but especially in Russia and Latin America. They are generally available from anonymous suppliers through just a mobile phone number. Others, look-alikes, are more visible through their advertising on the Internet, although there has been a trend recently for these to disappear and then reappear under a different name – same vial, same colors, same writing style, just a name change. At last count, there are over 40 sources for these products on the Internet, across the world, including Europe, Canada and the U.S.

In 2009 we reported our initial findings on these fake toxins.<sup>6</sup> We found that several of these products contained no detectable toxin while others had much lower quantities than what appeared on the label (Table 1). Our greatest concern was that some had up to five times more toxin per vial than what was shown on the label.

One product called Linurase, apparently supplied by a Canadian company, had 50 units listed on the vial, yet contained almost 250 units. The company stated that the product was only in clinical trials (hence selling is illegal). However; today, the product is still available from Internet sources and the company continues to claim it is still in clinical trials. There is a real possibility that any patient treated with these super-potent BoNT products will be harmed unknowingly. This is a significant issue and cannot be overstated. If such products are used in higher, therapeutic doses for medical indications (which many of these products are also being advertised for), the risks are even higher.

Without doubt, the biggest concern with these products is their quality. In fact, with unlicensed, illegal products, there may be no quality standards applied at all. They could be made anywhere and certainly the standards of packaging (for example, crooked flip tops – Figure 1) and labeling are often terrible, indicating poor quality standards.

The vial of toxin in the DIY kit I found (Figure 2) was hand labeled with a transparent label and now surprisingly has an expiration date. However, the first time I bought this same product the date wasn't there. Furthermore, the company

listed on the label, Peptide Protein Pharma, is registered to an apartment in Hong Kong.

In contrast, legal, licensed BoNT products must meet the quality standards of every country in which they are marketed and manufacturers use very significant resources to ensure that their compliance is at the highest levels.

After our initial findings for these unlicensed products, changes in their composition were found. Originally, our research revealed they contained gelatin and a sugar, most likely to provide a physical powder in the vial. However, more recently, mannitol has been detected in quite large quantities of up to 30 milligrams per vial.

Therapeutically, mannitol is used as an osmotic diuretic agent and a renal vasodilator. Typically, illegal drug dealers use mannitol to dilute drugs before sale, thus the product is less potent, but the dealers have an increased supply. Could it be that illegal drug dealers have now moved into the illegal toxin business? Or are illegal suppliers simply learning from other illicit activities?

Until recently there was no knowledge of organized crime being involved in selling illegal BoNT products until a report about illegal toxin products appeared in the U.S. press.<sup>7</sup> From the report, a picture emerged of “an illegal network of fake Botox suppliers that operates largely in the shadows” and a “man with a suitcase of vials” going around salons in St. Petersburg, Russia. As well, a spokesperson for Allergan also confirmed that, “there are organized criminal networks and they act as agents for one another.”

In summer 2010, Ken Coleman and Ray Zilinskas, from the Monterey Institute for International Studies (Monterey, California, U.S.), published an extensive report in *Scientific American* on the issues related to these illegal toxin products.<sup>8</sup> They were very clear about the widespread availability of such products, even if many contained only minuscule amounts of BoNT. Access to considerable amounts of BoNT by illegal groups is clearly a subject of biological terrorism in the making. The U.S. has significant programs relating to bio-terrorism and especially to BoNT, which is a Tier 1 select agent – the highest threat category.



Figure 1. Illegal toxin product (Mexico) showing poor quality control (crooked top) and manufactured in Shanghai, China.



Figure 2. Illegal toxin from DIY kit, 2011



Figure 3. Illegal toxin product claiming to be of Canadian origin. Note poor quality label and appearance of vial.

So where is the source of these counterfeit and look-alike BoNT products? Many seem to have comparable compositions, which are similar to the legal toxin product from Lanzhou in China. Others, however, state on the vial that they are made in Shanghai (Figure 1), for example, so that's a little easier. Another group, claiming to be from Canada, with Canadian flags appearing on their labels (Figure 3) and even Canadian-sounding names (Canitox) are definitely not from that country. These products are not legally available in Canada.



Figure 4. Fake dermal filler claiming to be from a French company that no longer exists. Obtained from Internet source, 2011.

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If it seems there is very little published about these illegal BoNT products, then it is befitting to say there is absolute silence in the literature on illegal dermal fillers. This is strange, considering that they also have a very significant ability to harm patients and even kill them, through anaphylactic shock. Moreover, they are used in far higher quantities than BoNT so purity and contamination are key issues. They are injectables and should also be sterile.

I recently investigated these products in conjunction with the U.K. television company the BBC. They wanted to make a documentary about using facial injectables and illegal products were to be discussed. I was appalled by what I found for dermal fillers. Availability of these products from the Internet is greater and

wider than for fake BoNT products. So-called permanent dermal fillers are readily accessible to the general public, despite all the issues known about their use. We bought two syringes for the program and later I took a closer look at what we had (Figure 4). These findings were published in September this year.<sup>9</sup> Apart from one web commentary<sup>10</sup>, this is the only publication to my knowledge on these illegal dermal filler products.

Once received, we observed that the dermal filler was of an appalling standard, leaking in the sachet, with the label claiming it was a product from a French company that is no longer in business (Figure 4). Furthermore, the packaging displayed Chinese characters along the sachet, as well as incorrect English (Figure 5).

So what do we do about these products? How do we convince patients not to go near them? To begin, the first action has to be to continue gathering information, collecting data through analyses and publishing the findings. This attracts the clinical community's attention, especially if the literature is published in their mainstream journals.



Figure 5. Fake dermal filler with apparent Chinese characters on sachet and incorrect English labeling.

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Simultaneously, opportunities should be taken to present the situation at appropriate congresses around the globe. Since 2008, I

have continued to do this at the *International Master Course in Aging Skin (IMCAS)*, both in Paris and Asia. I also presented the findings to the *World Congress on Biological Products (WCBP 15)*, held in Washington, D.C., U.S., in January 2011, widening community awareness of this problem.

Ideally, we would like to see cooperation between the bigger companies involved in the various business areas, both BoNT and dermal fillers, but regrettably there is no evidence of this happening. This should not be a subject

of competition, but a simple collaboration to achieve a greater effect.

Last, but by no means least, we must use data to inform enforcement authorities in each country that they are found, as they have the power and resources to find and prosecute the perpetrators. This has happened in several cases, but clearly not often enough. Some companies are reluctant to be involved in this grey area, saying they are not going to act as regulators. However, this is not the issue; we need strong cooperation and support to achieve the single goal – no illegal products. ■

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