

Cautions and Potential Problems with Generic and Compounded Human Growth Hormone (HGH)

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Advances in biotechnology have made it relatively easy to produce recombinant human growth hormone (rHGH) with adequate HGH activity. It is extremely time consuming and expensive, however, to achieve complete safety after it has been extracted, purified and packaged.

At this time there are no generic HGH products that meet all quality control standards required by the FDA. "Somatropin" is merely a generic name for HGH. All FDA licensed and approved HGH products will have an official NDC number on the label (National Drug Code). Without that code, it is a generic, regardless of the trade name assigned.

HGH is large, a complex protein that is made in a cell culture using biotechnology a process that is enormously more complex and different from that used with other generic drugs such as diuretics. HGH is produced in highly temperamental biological cultures that involve living cell replication in complex mixtures of cell nutrients. Scientists are of the opinion that it is virtually impossible to ensure that any two protein cultures produce identical molecules in an identical final product. For that reason, the FDA does not allow the use of "generic" to be applied to HGH and other therapeutic proteins. The FDA uses the term, "follow-on protein product" (FOPP's), instead of "generic." To meet the FDA standards for a so-called "generic" or FOPP, it must be a perfect replica of an approved drug that has lost its patent protection.

Purification and handling of proteins produced in cell cultures can too easily produce variations in folding, unfolding, cross-linkages, and variable aggregates of multiple proteins hooked together as dimers and polymers. These can cause immune responses and allergy to HGH, even endogenously produced HGH. Extraction and purification are very complex. Minuscule residues from the cell culture are inevitable and vary from product to product. It is relatively easy to get hormone activity, but extensive human testing is required for to prove safety for any new FOPP, including so-called "generic" HGH.

Novartis, the Swiss pharmaceutical giant, recently spent \$150 million on very extensive high-tech testing in an attempt to satisfy the FDA that they have a safe and effective FOPP "generic" type of HGH. They documented the structure of the protein molecule, configuration and electrical charge, aggregates, and many other properties as precisely as they could. Despite that effort, they have not been able to obtain FDA approval to market their product in the USA without also conducting human trials to prove safety (*Business Week*, May 9, 2005, page 99). Safety is the foremost consideration.

To be completely safe, dimers, polymers, aggregates, improper folding, glycosylation, broken cross-linkages, pyrogens, and contaminants must be strictly controlled during manufacture and packaging. This molecule is fragile and the freeze drying and packaging process can further alter its structure. Such abnormalities may not block hormone activity, and the product may seem to work quite well in many cases, but the altered molecules may stimulate immune reactions and cause allergy and desensitization to HGH, with subsequent and permanent decrease in hormone response. Such autoimmunity has been reported with as little as one percent of the injected HGH in an altered form, causing the body to neutralize internally produced as well as injected HGH. Adverse reactions may also include anaphylactic shock.

To insure purity and safety, I recommend that you use only FDA approved brand-name HGH that you have personally received in sealed factory packaging, with the manufacturer's holographic logo unaltered. Use only products approved by the FDA, with an FDA approved NDC number (National Drug Code) printed on the side of the package. You can add diluent and load the syringes yourself.

If you prefer not to load the syringes yourself, and if your HGH comes in pre-loaded syringes, I recommend that you insist on also receiving the original manufacturers package from which your prescription was taken, labeled with an approved FDA brand name and NDC code. In this way you can insure that you are not receiving an unsafe or unproven generic. Some clinics dispense the less expensive types of HGH that have not been subjected to all quality control procedures required to insure safety. In my opinion, patient safety should be the foremost consideration.

The ability to rigorously predict autoimmunity and immunogenicity of a protein based solely on laboratory analyses does not yet exist. Lengthy human trials are the only reliable gauge of immunogenicity. Brand name products manufactured in FDA licensed and inspected laboratories have been proven safe in extended human studies over many years. Generic products now appearing on the market, often at much lower prices, have not been tested in that way.

Recombinant human growth hormone is manufactured in cell cultures and is a very large protein with a molecular weight greater than 22,000. It is composed of more than 190 amino acids linked together in a very precise order, then folded and cross linked at strictly defined locations. The result is growth hormone activity identical to that produced in the human pituitary gland. The 3-dimensional shape must be exact for proper effect much like a key that must be in exactly the right shape to open a lock. Molecular variations in HGH may have adequate hormone effect but can stimulate rejection by the immune system.

The reason HGH is so expensive is because of the lengthy clinical trials required to prove safety, and the extreme care required for extraction, purification and packaging. Improper handling or agitation of the HGH molecule during manufacture, separation, purification, freeze drying and packaging can lead to potentially dangerous side effects when injected.

At this time it is not advisable to use any new HGH product without first obtaining thorough documentation about the laboratory in which it was produced, including detailed quality control analysis and human trial to prove safety. If your prescription is an FDA approved product, and if you can be sure that it is not a counterfeit, then that requirement has been satisfied.

Until a new and less expensive source of HGH can satisfy all of those requirements, it is recommended to use only an FDA-licensed, brand-name product that has been obtained from a trusted source.

Counterfeits with unknown ingredients have appeared in the marketplace, with identical packaging including even the manufacturer's hologram. One such product was shown to contain only chorionic gonadotropin.

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