A number of entities, largely in China, are manufacturing GS-441524 (GS) and GC374 (GC) for sale mainly to desperate owners of cats with FIP. Some of this synthesis is by non-veterinarians and some with direct or indirect participation of people having veterinary or human health backgrounds. People in China have a great problem with FIP due to their increasing ability to keep and afford pets. There is a particularly high demand for expensive pedigreed kittens, which are at increased risk for FIP. Therefore, the Chinese interest in drugs like GS-441524 (GS) and GC374 (GC) is not entirely financial and opportunistic. Although their first effort was centered around GC, the emphasis of this black market has rapidly shifted to GS. Although this sort of marketing and use of GS and GC is technically illegal, the companies holding patents on GC and GS have no effective means to halt this black market use. Reputable drug companies that are offering GS and GC usually include a disclaimer limiting their use to research purposes only and not for human or veterinary treatments. This disclaimer, when given, has no enforcement power to owners and is being largely ignored. Drugs offered by individuals are often packaged and labelled as dietary supplements, which allows easier entry through customs control of other countries. Fortunately, this mislabeled drug usually contains accurate information on the drug concentration, e.g., 15 or 16.5 mg/ml. The recommended dosage of GS for cats with non-neurological FIP is 4 mg/kg, SC, once a day, for 12 weeks. Cats with neurological FIP may require a progressively higher dosage of 5-10 mg/kg.

Veterinarians, who are under more legal and ethical constraints, may view the black market quite differently from owners of cats suffering from FIP. Some may refuse to participate beyond making the initial diagnosis of FIP, some may help with drug administration and monitoring as long as the owners provide the drug, and some may require signed waivers freeing them of any legal or ethical obligations. I respect whatever course of action veterinarians might take in interpreting their personal oaths to "use their scientific knowledge and skills for the benefit of society through the protection of animal health and welfare, the prevention and relief of animal suffering, the conservation of animal resources, the promotion of public health, and the advancement of medical knowledge."

We already know the problems of involving black market drugs in human medicine. Although the suppliers indicate that they are highly pure, there is no testing for biological activity (i.e., antiviral effect). We already know that GC and GS are being made by an increasing number of individuals and that the quality on a mg/kg or molar dosage may vary. We also know that the price of GC and GS can also vary greatly and that owners can expect to pay many thousands of dollars for enough drug to complete a treatment.

Purchasing sufficient drug, and soon enough to be of help, is only the first step. The drug may be purchased in a powder form, which requires more than average knowledge to successfully convert to a stable and injectable form. In response to this problem, most suppliers are now
offering GC or GS in a pre-diluted form. An oral form of GS-441524 has been recently produced in China and is also beginning to appear on the market. The chemical modifications to allow for oral absorption are well known from HIV/AIDS and HCV drug development. Nonetheless, owners and veterinarians that purchase GS or GC on the black market, usually at a very high price, would normally expect some sort of information from the supplier as to biological (antiviral) activity on a molar basis, diluent used, and information on storage conditions and shelf-life. If the anti-viral activity is the same as the drugs described in research publications, the published information can be directly applied. If they are not, then published information will not apply. Remember, it is very much "buyer beware" in such situations.

Information on where and how to obtain GC376 and GS-441524 is easily found on social websites. These websites have evolved from cat owner groups who have personal experience with FIP and the black market treatment. Although some advice on FIP and how to use these drugs is provided by Chinese sellers, many claiming to have veterinary connections, cat owner groups have been of much greater assistance. We now know that hundreds, if not thousands, of cats around the world are now being successfully treated for FIP using black market obtained drugs. These favorable responses appear to confirm our own published research on both GC376 and GS-441524. Owner groups have become very adept, based on personal experiences, in identifying the most biologically active and economic sources of GC and GS.

It is also critical that the diagnosis of FIP be as strong as possible, as the disease is still frequently mis-diagnosed. Therefore, it is hoped that owners have access to the veterinary expertise required to correctly diagnose FIP and to oversee a treatment with this level of emotional involvement, length, cost, and monitoring. Information on how to administer these drugs have been provided in the form of published scientific publications cited in our supplement on "FIP treatment." There is still a lack of knowledge of how to properly treat cats with the neurological and ocular/neurological forms of FIP. GC and GS penetrate into the brain with some difficulty, which is explained in a second supplement on "Neurological FIP." The only way to increase drug levels in the brain is to increase the blood level by using higher and higher dosage regimens. It does appear that higher dosages, especially with GS, can lead to complete or near complete remission of clinical signs. Nonetheless, it is still uncertain whether every cat with neurological FIP can be cured. Because of these facts, cats with FIP and neurological involvement should be approached with far more caution than other forms of FIP. We are also aware of the potential problem of drug resistance that is either present at the time of initial treatment or that develops during the course of treatment. We observed primary drug resistance in 1 in 20 cats treated with GC376 and 1 in 31 cats treated with GS-441524. Therefore, drug resistance should always be considered in any cat that fails to rapidly respond to initial treatment or that suffers a relapse of clinical signs after a period of positive response. Although it has not been adequately researched, it is reasonable to assume that resistance to one drug will not apply to the other drugs, as their mechanisms of virus inhibition are entirely different.

I will continue to provide as much advice as possible for owners and veterinarians using and contemplating the use of black-market GS and GC to treat cats with FIP. Fortunately, extremely active and knowledgeable owner groups have developed in several countries and are serving as a major conduit between owners and GS and GC suppliers. These groups are active on social
media forums and desperate owners have been able to access them with relative ease and receive timely and critical help.

I must make it clear that I would have preferred these drugs to be approved and commercialized in the normal manner. I am certain that this will happen within the next few years, and as it does, the black market demand for drugs like GS and GC will wane. In the meantime, UC Davis will continue to research new antiviral drugs for diseases like FIP and to share our findings in the conventional manner of peer-reviewed research publications. Our obligations are only to assure owners and veterinarians that our published findings are accurate, reproducible, and applicable.