**Rare Cancer Treatments, Cleared by F.D.A. but Not Subject to Scrutiny**

**By** [**BARRY MEIER**](http://topics.nytimes.com/top/reference/timestopics/people/m/barry_meier/index.html)

When federal regulators permitted the sale of an unproved device that uses intense heat to combat cancer, they did so for a compelling reason, to give hope to some women desperately ill with cervical cancer.

Over the next two years, however, the few hospitals that purchased the $500,000 device did not take part in a study of patients that the manufacturer agreed to perform as a part of the machine’s approval. Cancer experts also said they were surprised that the Food and Drug Administration had approved the machine in the first place.

The reason: The group of woman for whom the F.D.A. approved the treatment — those with advanced cervical cancer who are too ill for chemotherapy — is so small. “I see, like, one patient like this a year,” said Dr. Junzo P. Chino, a cancer expert at Duke University.

A look at the F.D.A.’s [decision to approve](http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/Recently-ApprovedDevices/ucm286404.htm) the device, which is called the BSD-2000, opens a window onto a little-known regulation known as the humanitarian device exemption.

The program, even its critics agree, is based on the best intentions. Because companies have little incentive to run costly trials for products used by small groups of patients, the exemption requires a producer only to show that a device is safe and has a “probable” benefit, rather than prove its effectiveness, the usual standard.

The rule, which is similar to one governing drugs for extremely rare diseases, also does not require the F.D.A., companies or doctors to collect the kind of data that could later show that an exempted device works. As a result, critics say, ineffective products approved under the exemption can be sold for years while potentially lifesaving ones may never prove their worth.

Moreover, an exempted device can be employed by doctors in any way they want, a practice that is known as off-label use. Since the BSD-2000 got its exemption in 2011, the for-profit Cancer Treatment Centers of America has purchased two of the machines. The company declined to respond to written questions about the numbers and types of cancer patients it treated as well as what it charged for treatments.

“The provision is a good one, but the structure to get good effectiveness data is weak,” said Larry Kessler, a former F.D.A. official who is now a professor at the University of Washington in Seattle.

In an interview two months ago with The New York Times, Dr. William Maisel, the chief scientist at the F.D.A.’s device unit, defended the BSD study ordered by the agency. But in mid-November, the agency and the machine’s producer agreed to kill it in favor of a study intended to capture more patients, including some cancer patients on whom the device is expected to be used off-label.

The new study is intended to capture only safety information rather than data about the treatment’s effectiveness. “There is no requirement that the device ever show more than a probable benefit,” said Dr. Maisel.

The BSD-2000 uses microwave energy to raise the body’s temperature to as high as 113 degrees Fahrenheit (45 Celsius). The treatment, which is known as hyperthermia, is based on the concept that high temperatures can damage and kill cancer cells, usually with minimal injury to normal tissues. Studies have shown that raising cell temperature increases the effectiveness of radiation and chemotherapy, and hyperthermia is typically used alongside one or both of those treatments.

BSD Medical, a small firm based in Salt Lake City, makes another hyperthermia machine called the BSD-500 that the F.D.A. approved in 1983 for the treatment of breast cancer and tumors that lie just below the skin. But while studies have pointed to the potential effectiveness of the BSD-2000, which was developed in the 1980s to treat deep-seated tumors like those in the pelvis, that device has failed for three decades to win medical acceptance amid changing cancer treatment strategies and unsuccessful clinical trials.

Dr. Elizabeth Repasky, a hyperthermia expert at the Roswell Park Cancer Institute in Buffalo, said that she worried that the F.D.A.’s decision to approve the BSD-2000 without better data collection could set back the technology rather than advance it.

“It is not helpful to hyperthermia to have yet another uncontrolled study,” said Dr. Repasky.

Since 1997, when the device exemption program started, about 50 products — heart pumps, orthopedic implants, optical aids — have been approved through it.

There is no question that patients have benefited; one recently exempted device enhances vision in the nearly blind. To qualify, products must be intended for conditions that affect fewer than 4,000 patients annually. But the exemption has also served as a loophole to market devices to far larger groups.

In 2006, the F.D.A. moved to withdraw exemptions issued to two companies that sold implanted devices used to close a tiny opening in the heart based on data suggesting that doing so might reduce the risk of stroke.

The exemption covered patients only with the condition known as a patent foramen ovale, or P.F.O., who had had two strokes despite taking drugs intended to prevent them. But P.F.O. patients who had a single stroke or never had one soon demanded the device.

“It was like taking the genie out of the bottle because there was a presumption” that the devices worked, said Dr. John D. Carroll, a cardiologist at the University of Colorado in Denver.

Facing F.D.A. action, the companies voluntarily withdrew the devices from the exemption program and ran clinical trials aimed at winning full approval. But by then, doctors were using other devices off-label to close P.F.O.’s. Recruiting patients for the clinical studies was difficult, said Dr. Carroll, who headed one trial.

Three studies, including the one headed by Dr. Carroll, subsequently failed to find evidence that the devices were better than drugs in preventing strokes.

Under another exemption, doctors are also now using an implanted electrical brain stimulator made by Medtronic to treat patients with severe obsessive-compulsive disorder who have not responded to drugs.

But Dr. Joseph J. Fins, a professor at Weill Cornell Medical College in Manhattan, said the development represented an uncontrolled medical experiment because doctors were not collecting uniform data about what happens to patients.

“People use it and it begins to become part of the medical environment,” said Dr. Fins, who has been critical of the F.D.A.’s decision to issue the Medtronic exemption. A spokesman for Medtronic said that the company was running a study in Europe to gain data about the treatment’s safety and effectiveness.

In 2007, the F.D.A. rejected giving a full approval to the BSD-2000 for the treatment of deeper-seated tumors after determining that the results of a company-sponsored clinical trial performed at two hospitals in Holland were inadequate to show that it was safe and effective.

One group followed in the study, however — women with advanced cervical cancer unable to tolerate chemotherapy — survived longer if treated with radiation and hyperthermia than with radiation alone. As a result, F.D.A. officials urged BSD Medical to seek an exemption for that patient group, and the company did so.

For BSD Medical, which has struggled financially for years, getting the exemption has meant an increase in BSD-2000 sales here and abroad. And some longtime advocates of hyperthermia say they believe that the exemption will lead to other trials that can shed light on the treatment’s value.

Dr. I-Chow Hsu, a professor at the University of California, San Francisco, said that institution was buying a BSD-2000 to run such trials. One study may involve the use of hyperthermia in the treatment of soft-tissue sarcomas, an area where it appears to have benefit, he said.

“People who have this machine are going to have to come up with other protocols,” other than the cervical cancer one, said Dr. Hsu. “Otherwise, it would be very hard to justify these machines.”

Dr. Repasky, the hyperthermia expert in Buffalo, said she remained concerned that justifying the machine’s cost could lead facilities to use the BSD-2000 in differing ways on different kinds of cancers. And the results of that, she said, will very likely be of little value to anyone.

“The one thing cancer patients want to know is whether a treatment might help someone else in their family some day,” said Dr. Repasky.