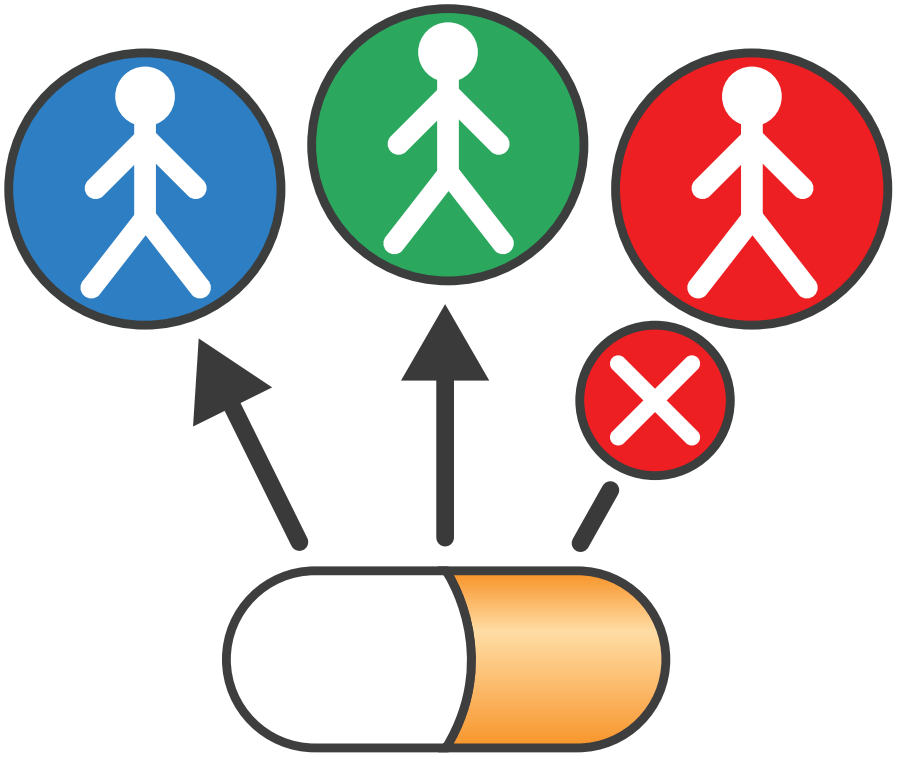
Personalized Medicine and Companion Diagnostics Go Hand-in-Hand

Personalized medicine is an evolving field of medicine in which treatments are tailored to the individual patient. You may have a condition, for example, that is caused by a mutation in your genes. With advances in personalized medicine, you might be prescribed a medication that targets that specific mutation.



Companion diagnostic tests show which patients could be helped by a drug and which patients would not benefit, and could even be harmed.

To learn which patients would benefit from a particular drug therapy or, conversely, which patients should not receive the medication, the Food and Drug Administration works with drug and device manufacturers that are developing certain tests called companion diagnostics.

Companion diagnostics are medical devices that help doctors decide which treatments to offer patients and which dosage to give, tailored specifically to the patient, says Elizabeth A. Mansfield, Ph.D., Deputy Office Director for Personalized Medicine in FDA's Office of In Vitro Diagnostics and Radiological Health. The companion diagnostic is essential to the safe and effective use of the drug. They go together.

Because the companion diagnostic test is designed to be paired with a specific drug, the development of both products requires close collaboration between experts in both FDA's device center, which evaluates the test to determine whether it may be cleared or approved, and FDA's drug center, which evaluates the drug to determine whether it may be approved.

Patricia Keegan, M.D., an oncologist and supervisory medical officer in FDA's Division of Oncology Prod-

There are now 19 cleared/approved companion diagnostic tests for selection of drugs to treat various diseases and conditions, and they are listed at: www.fda.gov/companiondiagnostics

ucts II, part of FDA's drug center, explains that the agency requires a companion diagnostic test if a new drug works on a specific genetic or biological target that is present in some, but not all, patients with a certain cancer or disease. The companion diagnostic test is used to identify who would benefit from the treatment and sometimes to determine if there are patients who not only would not benefit, but could be harmed by use of a certain drug for treatment of their disease.

The process works best when development of the test begins before the drug enters clinical trials, Keegan explains, increasing the likelihood that the participants in the trials are the patients most likely to benefit from the treatment.

FDA's device center is issuing a final guidance on the development, review and approval or clearance of companion diagnostics to help companies identify the need for these tests earlier in the drug development process and to plan for co-development of the drug and companion diagnostic test. The goal is to stimulate early collaborations that will result in faster access to promising new treatments for patients with serious and life-threatening diseases.

"This will give health care providers more confidence in these tests to direct the therapies because the tests and therapies have been developed and evaluated together," Mansfield says.

Most recently, FDA approved a companion diagnostic genetic test to select patients with metastatic colorectal cancer for treatment with the drug Vectibix. The test detects seven mutations in the KRAS gene in colorectal tumor tissue. When the KRAS gene is mutated, those mutations could render Vectibix ineffective in treating the colon cancer.

The patient could be a good candidate for this treatment if he or she does not have a mutation. So in this case, the approved companion test will be used to identify people who would not be helped by the drug.

This is the second time that FDA has approved this test—called the QIAGEN *therascreen* KRAS RGQ PCR Kit—to help colorectal cancer patients and their health care providers determine the potential effectiveness of a drug. In July 2012, FDA approved the test for use with the drug Erbitux, which was also found to be ineffective in patients with a mutated KRAS gene.

It Began With Herceptin

The road to companion diagnostics began in 1998 with FDA approval of the cancer drug Herceptin, which shuts off a protein present in abnormally high amounts in about one-quarter to one-third of breast cancers. These breast cancers are typically very aggressive. The companion diagnostic test looks for excessive levels of a particular protein, called HER2, in a patient's tumor or for extra copies of the HER2 gene in a patient's tumor, indicating that Herceptin could be an effective treatment for that patient's breast cancer.

Multiple companion diagnostics can be approved for a drug—as they have been for Herceptin—as scientific knowledge evolves with practical application of the therapy, enabling the tests to become more sophisticated.

With the advent of more drugs that target particular genetic mutations, there has been increasing acceptance from drug manufacturers that these diagnostic tests can greatly increase the clinical success of certain medications by carefully identifying patients' tumors where the drug may work, says Keegan. There are now 19 cleared/approved companion diagnostic tests for selection of drugs to treat various diseases and conditions, and they are listed at *www.fda.gov/companiondiagnostics*. Most drugs with a companion diagnostic test have been cancer treatments that target specific mutations. FDA

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