

the medication, annual supply requirements of drug substance, assuming no failed batches or recalls, would be 87,600 kg. In addition, supply shortages could not be tolerated, as patients losing access to the medication would present an opportunity for the development of drug-resistant variants of HIV. In February of 1995, more than 1 year before FDA approval and well before final clinical results would be available Merck took the risk of authorizing the construction of production lines capable of meeting the expected high demand for Crixivan<sup>®</sup> (Indinavir).

Of course, the gamble paid off for Merck, as Crixivan<sup>®</sup> (Indinavir) became an exceptionally important drug, but it was not without a great deal of effort on the part of the process and manufacturing teams. More than 400 people were involved in moving the process from the bench to full scale manufacturing, and by November of 1996, less than 9 months after FDA approval, more than 90,000 patients were using Crixivan<sup>®</sup> (Indinavir).<sup>24</sup> It is often the case that the scientist who identify a clinical candidate and the physicians who run the clinical trials are given credit for the launch of new and improved therapies, but the role of process and manufacturing teams such as those involved in the commercialization of Crixivan<sup>®</sup> (Indinavir) should not be overlooked. The clinical efficacy of a novel therapeutic agent is of little real world value if it cannot be commercialized, and this requires a robust manufacturing process. The scientist and staff responsible for establishing a manufacturing process are essential to the drug discovery and development process, as demonstrated by the efforts required to convert the Crixivan<sup>®</sup> (Indinavir) laboratory synthesis to full scale manufacturing.

## NITROFURANTOIN: A SURPRISINGLY SUCCESSFUL DRUG

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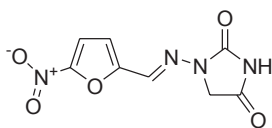


FIGURE 13.11 Nitrofurantoin.

In 1953, nitrofurantoin (Figure 13.11), which is known commercially as Macrobid<sup>®</sup>, Macrochantin<sup>®</sup>, and Furdantin<sup>®</sup>, was introduced for the treatment of urinary tract infections. At the time, no one could have predicted that it would eventually be included in the World Health Organization's List of Essential Medicines. Despite the development of a wide range of modern antibiotics, nitrofurantoin remains a front-line treatment of uncomplicated urinary tract infections. In addition, despite decades of clinical experience, reports of bacterial resistance remain rare. This is