FIGURE 8.9 Automatic balance that weighs product and prints statistics to determine compliance with USP weight variation requirements for tablets. (Courtesy of Mocon Modern Controls.)

Tablet Weight and USP Weight Variation Test

The quantity of fill in the die of a tablet press determines the weight of the tablet. The volume of fill is adjusted with the first few tablets to yield the *desired weight and content*. For example, if a tablet is to contain 20 mg of a drug substance and if 100,000 tablets are to be produced, 2,000 g of drug is included in the formula. After the addition of the pharmaceutical additives, such as the diluent, disintegrant, lubricant, and binder, the formulation may weigh 20 kg, which means that each tablet must weigh 200 mg for 20 mg of drug to be present. Thus, the depth of fill in the tablet die must be adjusted to hold a volume of granulation weighing 200 mg. During production, sample tablets are periodically removed for visual inspection and automated physical measurement (Fig. 8.9).

The USP contains a test for determination of dosage form uniformity by *weight variation* for uncoated tablets (5). In the test, 10 tablets are weighed individually, and the average weight is calculated. The tablets are assayed, and the content of active ingredient in each of the 10 tablets is calculated assuming homogeneous drug distribution.

Content Uniformity

By the USP method, 10 dosage units are individually assayed for their content according to the method described in the individual monograph. Unless otherwise stated in the monograph, the requirements for content uniformity are met if the amount of active ingredient in each dosage unit lies within the range of 85% to 115% of the label claim and the standard deviation is less than 6%. If one or more dosage units do not meet these criteria, additional tests as prescribed in the USP are required (7).

Tablet Thickness

The thickness of a tablet is determined by the diameter of the die, the amount of fill permitted to enter the die, the compaction characteristics of the fill material, and the force or pressure applied during compression.

To produce tablets of uniform thickness during and between batch productions for the same formulation, care must be exercised to employ the same factors of fill, die, and pressure. The degree of pressure affects not only thickness but also hardness of the tablet; hardness is perhaps the more important criterion since it can affect disintegration and dissolution. Thus, for tablets of uniform thickness and hardness, it is doubly important to control pressure. Tablet thickness may be measured by hand gauge during production or by automated equipment (Figs. 8.10 to 8.12).

Tablet Hardness and Friability

It is fairly common for a tablet press to exert as little as 3,000 and as much as 40,000 lb of force in the production of tablets. Generally, the greater the pressure applied, the harder the tablets, although the characteristics of the granulation also have a bearing on hardness. Certain tablets, such as lozenges and buccal tablets, that are intended to dissolve slowly are intentionally made hard; other tablets, such as those for immediate drug release, are made soft. In general, tablets should be sufficiently hard to resist breaking during normal handling and yet soft enough to disintegrate properly after swallowing.

Special dedicated hardness testers (Fig. 8.13) or multifunctional systems (Fig. 8.12) are used to measure the degree of force (in kilograms, pounds, or in arbitrary units) required to break a tablet. A force of about 4 kg is considered the minimum requirement for a satisfactory