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Process Equipment Cost, Biotechnology and Pharmaceutical

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Process Equipment Cost, Biotechnology and Pharmaceutical

Discoveries and advances in biotechnology have created a challenge for biotechnology companies: how to estimate costs for commerical ventures.* Companies are now moving from the development process to commercial production. To make ballpark cost estimates for a new plant or for a new piece of equipment, engineers often use the 0.6 power factor model. This method bases the cost estimate of new equipment on a known cost for that type of equipment and the ratio of their capacities raised to a factor *R*. This

*These costs can be updated using the latest cost indexes found in the frontmatter of this encyclopedia.

method was first applied to equipment cost estimates by Williams in 1947 [1] and was later applied to plant costs by Chilton in 1950 [2]. Two recent articles by Remer and Chai provide *R* values for several hundred types of processes and process plants [3] and for engineering equipment [4]. However, they included no autoclaves, fermenters, freeze driers, homogenizers, or other bioprocess equipment. This article lists exponential scaling factors for 58 types and sizes of equipment commonly used in biotechnology. We obtained the data from two sources: a search of the literature on *R* factors and the *R* values we developed while doing cost estimates for several prospective bioprocess plants for recombinant proteins. These bioprocess equipment costs were obtained from vendor quotations.

The Model

The relationship between cost and capacity can be written as

$$\frac{\text{cost}_2}{\text{cost}_1} = \left(\frac{\text{size}_2}{\text{size}_1}\right)^R \tag{1}$$

where cost_1 is the known cost and cost_2 is the unknown cost, and size_1 and size_2 are the corresponding capacities for a given plant or piece of equipment.

R values can be determined by plotting cost estimates for several different operating capacities or sizes (see Figs. 1 through 5). *R* is the slope of the best line through the points, as determined by a least-squares regression analysis. When only two points are known, *R* can be calculated from Eq. (2), which is obtained by taking logarithms of both sides of Eq. (1) and solving for *R*:

$$R = \frac{\ln(\text{cost}_2/\text{cost}_1)}{\ln(\text{size}_2/\text{size}_1)} \tag{2}$$

Different types of equipment have different *R* factors. Most types and sizes of equipment used in bioprocesses have *R* factors that are less than 1. This means that if we double the equipment capacity, the price increases by a factor of less than 2. Those very few types of bioprocess equipment with an *R* factor greater than 1 have diseconomies of scale. That is, doubling the equipment capacity increases equipment cost by a factor greater than 2.

Once *R* is known, it is possible to determine the cost to scale up equipment or a plant using Eq. (1). Table 1 shows the cost ratios for increasing the equipment size by factors of 2, 3, 4, 5, 10, and 20. It shows, for example, that when $R = 0.6$, increasing the equipment size by a factor of 2 gives a cost ratio of 1.52, a cost increase of about 50%. It also shows that increasing the size by a factor of 3 increases the cost by almost 100%, and increasing the size by a factor of 10 increases the cost by about 300%.

TABLE 1 Cost Ratios for Increasing the Size of a Plant as a Function of the Cost Scaling Exponent *R*

	Cost Ratio					
R Value	2 X Size	3 X Size	4 X Size	5 X Size	10 X Size	20 X Size
0.2	1.15	1.25	1.32	1.38	1.58	1.82
0.3	1.23	1.39	1.52	1.62	2.00	2.46
0.4	1.32	1.55	1.74	1.90	2.51	3.31
0.5	1.41	1.73	2.00	2.24	3.16	4.47
0.6	1.52	1.93	2.30	2.45	3.98	6.03
0.7	1.62	2.16	2.64	3.09	5.01	8.14
0.8	1.74	2.41	3.03	3.62	6.31	11.0
0.9	1.86	2.69	3.48	4.26	7.94	14.8
1.0	2.00	3.00	4.00	5.00	10.0	20.0
1.1	2.14	3.35	4.59	5.87	12.6	27.0

Equation (1) can be modified to take inflationary effects into account. This is done by multiplying the size ratio by the cost indices, as shown in Eq. (3):

$$\frac{\text{cost}_2}{\text{cost}_1} = \left(\frac{\text{size}_2}{\text{size}_1}\right)^R \frac{\text{index}_2}{\text{index}_1} \tag{3}$$

Here, index_1 is the cost index for the year in which equipment of size_1 was purchased. Similarly, index_2 is the cost index for the year in which equipment of size_2 was purchased. A number of different indices are available for adjusting equipment cost, including the Marshall and Swift (Stevens) Equipment Cost Index (M&S), the Chemical Engineering Plant Cost Index (CE), the Nelson Refinery Index, the Engineering News Record Index (ENR), and the Consumer Price Index (CPI). Other cost indices are available for other countries [5].

Scale-up Factors

Exponential *R* factor values for 58 types and sizes of equipment used in biotechnology and related processes appear in Table 2 in alphabetical order. Because items are usually listed under their generic names, freeze driers are listed under driers and the anion-exchange column under columns. Table 2 shows the ranges over which the *R* factors are applicable and the units for these capacity range values when they were reported in the literature. Guthrie, for example, reported no capacity range values for his *R* factor data [10]. In some cases, the *R* values presented are for a specific size and type of equipment. For example, we included 19 different *R* factors for centrifuges of various capacities and types. For completeness, Table 2 includes some mainstream process equipment that may be required in related process design.

TABLE 2 Exponential *R* Factor Values for Various Types and Sizes of Bioprocess and Related Process Equipment

Equipment	Detailed Description	Size Range		Units	Exponent	Reference
		Minimum	Maximum			
Autoclaves	Single door; gravity unit included; installation and 1 year preventive maintenance included	6,500	32,000	in.^{3}	0.37	Remer and Idrovo
Boilers (steam generators)	Small-package boiler, 150 psi	10	500	hp	0.65	7
	Large-package boiler, 250 psi	6,000	600,000	lb/h	0.77	7
Centrifuges	Disk centrifuges	4,000	60,000	L/h	0.72	8
	General purpose	8	18	hp	0.66	9
	Horizontal basket				1.16	10[a]
	Vertical basket				1.00	10
	Bird solid bowl				0.38	10
	Sharpless super D				0.68	10
	Solid bowl, carbon steel	10	100	hp	0.67	11
	Basket type				1.00	12
					0.80	13
		40	60	in.	0.71	14
	Vertical basket top-drive carbon steel	10	80	in.	1.00	15
	Vertical basket bottom-drive	10	40	ft^2	0.44	15
	Automatic batch horizontal basket carbon steel	7	80	ft^2	0.65	15
	Pusher conveyor carbon steel	10	60	in.	1.00	15
Columns	Anion exchange	5	200	ft^3	0.94	9
	Cation exchange	5	200	ft^3	0.73	9
	Enzyme	Unlimited		ft^3	1.00	9
Crystallizers		10	1,000	ft^3	0.85	9
	Batch vacuum carbon steel	500	10,000	gal	0.68	15
	Conventional forced-circulation carbon steel	10	1,000	tons/day	0.53	15

TABLE 2 *(continued)*

Equipment	Detailed Description	Size Range		Units	Exponent	Reference
		Minimum	Maximum			
	Growth and classifying carbon steel	10	10,000	tons/day	0.62	15
	Mechanical carbon steel	30	150	ft^2	0.55	15
	Growth				0.63	10
	Forced circulation				0.58	10
	Forced batch				0.62	10
	Vacuum batch, carbon steel	500	7,000	ft^3	0.37	11
					0.65	12
Driers, freeze	Chamber, 304L stainless steel shelves and condenser; automatic cycle; includes heat exchanger for rapid cooldown	15	450	L/cycle	0.41	Remer and Idrovo
Dryers, spray		100	10,000	lb/h	0.71	9
Electrodialyzers		8	640	m^2	0.37	9
Evaporator		100	10,000	ft^2	0.50	9
Fermenters	Basic equipment; no computerized control; no biosafety level	200	900	L	0.18	8
		900	14,000	L	0.34	8
		14,000	200,000	L	0.70	8
	Microprocessor controlled; automatic sterilization	20	20,000	L	0.36	Remer and Idrovo
	Manual sterilization	100	20,000	L	0.28	Remer and Idrovo
Filters	Rotary vacuum drum					
	Belt discharge and scraper discharge	40	500	ft^2	0.37	16
	Paper-pulp drums	500	1,500	ft^2	0.50	16
	Single-compartment vacuum drum	10	150	ft^2	0.50	16
	Horizontal table, 316 stainless steel	30	500	ft^2	0.51	16
	Horizontal table, carbon steel	30	500	ft^2	0.41	16

	Corrosion-resistant horizontal vacuum belt	20	1,000	ft^2	0.49	16
	Continuous vacuum tilting pan, 316 stainless steel	200	600	ft^2	0.5	16
	Rotary vacuum disk					
	Paper-pulp	200	1,000	ft^2	0.55	16
	General industrial and metallurgical services	100	2,000	ft^2	0.40	16
	Vacuum rotary drum carbon steel	10	1,500	ft^2	0.48	15
	Vacuum rotary disk	40	1,000	ft^2	0.68	15
Heat exchangers		100	5,000	ft^2	0.65	9
	Shell-tube, floating head carbon steel	20	20,000	ft^2	0.59	15
	Shell-tube–finned tube floating head	3,000	10,000	ft^2	0.78	15
	Air-cooled, finned	200	20,000	ft^2	0.80	15
	Plate coil carbon steel serpentine type	5	15	ft^2	0.36	15
		15	40	ft^2	0.78	15
	Double pipe, mild steel (tube in tube)	1	100	ft^2	0.68	7
	Plate 316 stainless steel	100	200	ft^2	0.65	15
		200	500	ft^2	0.65	15
		500	1,000	ft^2	0.90	15
	Spiral plate carbon steel	2.5	7.5	ft^2	0.43	15
		7.5	60	ft^2	0.83	15
Homogenizers		40	7,000	L/h	0.50	8
Reverse osmosis		Unlimited		m^2	0.80	9
Ultrafiltration		Unlimited		m^2	1.00	9
		20	800	m^2	0.86	8
Water purification system	Type IV water	10	2,000	L/h	0.27	Remer and Idrovo
				Average *R*	0.63	
				SD of *R*	0.21	

[a]Guthrie reported no range values.

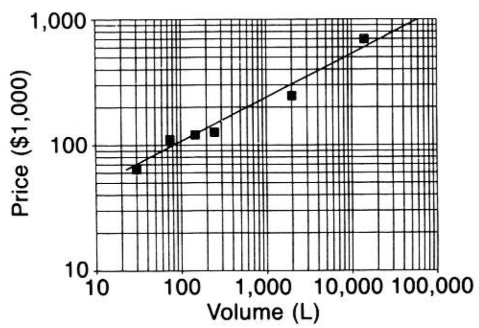

FIG. 1 Cost versus capacity for fermenter with options that include automatic sterilization.

Averaging all the R values in Table 2, we arrived at a value of 0.63, with a standard deviation of 0.21. A study determined that the average R value for 75 types of engineering equipment is 0.68 [4]. Another study of 200 chemical processes determined that the average R value for plants is 0.67 [3]. These values are close to our average R value of 0.63 for bioprocess equipment. Using our average value of 0.63, we see a rule of thumb emerge: Doubling the size of a piece of equipment increases the cost by about 55%; tripling the size increases the cost by about 100%.

Figures 1 through 5 present biotechnology equipment cost charts developed by the authors. R values were calculated by fitting the best line through the data points using the method of least squares. R is the slope of the line. Table 3 summarizes the exponential cost scaling factors R and the coefficients of determination for five different types of biotechnology equipment based on vendor's price quotations. The coefficient of determination values range from 0.91 for autoclaves to 0.99 for freeze driers and manually sterilizable fermenters. This means that 91% of the total variation in autoclave costs is accounted for by a linear relationship with size on a log-log plot (Figs. 1–5). Similarly, 99% of the variation in freeze drier costs is accounted for by a linear relationship with size: the greater the number of cost estimates, the greater the confidence in the resulting R factors. It also helps to get cost estimates from several vendors when developing R factors.

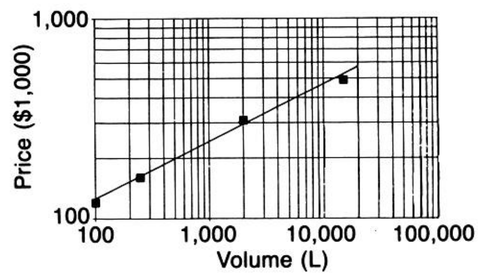

FIG. 2 Cost versus capacity for fermenter with manual sterilization.

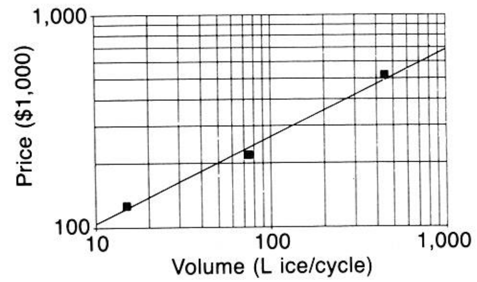

FIG. 3 Cost versus volume for freeze drier with options that include automatic cycle and a heat exchanger for rapid cooling.

Figure 1 shows unit costs for 30–15,000 L fermenters with automatic sterilization and temperature, agitation, airflow, pressure, pH, dissolved oxygen, and antifoam controllers. The exponential factor R is 0.36, and the coefficient of determination is 0.97. Figure 2 shows unit costs for 100–15,000 L fermenters with manual sterilization and temperature, pH, dissolved oxygen, and antifoam controllers. The exponential factor R is 0.28, and the coefficient of determination is 0.99. Figure 3 shows unit costs for freeze driers. The condenser plate volumes range from 15 L ice/cycle to 450 L ice/cycle. The chamber, shelves, and condenser plates of the freeze driers are fabricated of 304L stainless steel. Each unit comes with an automatic freeze-drying cycle, a water-cooled heat exchanger for rapid cool down after sterilization, and an automatic steam cycle. The exponential factor R is 0.41, and the coefficient of determination is 0.99. Figure 4 shows unit costs for type IV water purification systems with capacities from 18 to 980 L/h. The exponential factor R is 0.27, and the coefficient of determination is 0.98.

Figure 5 shows unit costs of freeze driers versus water removal rate. The first three data points, from 0.55 to 15 kg/h (shown in the lower range), were developed by the authors and are based on costs for equipment purchased without such options as automatic freeze drying cycle, water-cooled heat exchanger, and automatic steam cycle. The other three data points, from 450 to 45,000 kg/h, were published by Renshaw et al. [6]. Renshaw's fixed capital costs include installation, piping, insulation, instrumentation, elec-

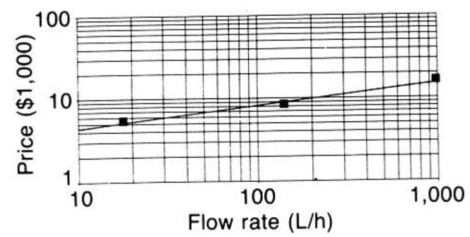

FIG. 4 Cost versus flow rate for a type IV water purification system.

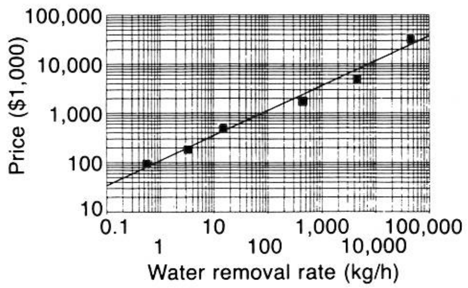

FIG. 5 Freeze drier cost versus water removal rate.

trical auxiliary, engineering, and contingency costs. The exponential factor *R* is 0.49, which is close to the 0.41 value shown for freeze driers in Table 3 for the range 0.55–15 kg/h. The coefficient of determination for the entire range 0.55–45,000 kg/h shown in Fig. 5 is 0.98. Note how well a straight-line approximation works for a range of 5 orders of magnitude.

Limitations

Some types of bioprocess equipment, such as high-performance liquid chromatography (HPLC) systems, are difficult to scale up using the exponential *R* factor method. Several important parameters must be considered when sizing HPLC systems, including loading and resolution of the purification process. Because of these various factors, no *R* values for HPLC systems are reported.

Range of Validity

Ranges, when available, and their calculated *R* factors are shown in Table 2. Care must be taken to avoid extrapolating far outside the range of validity.

Extrapolated outside the maximum capacity shown, cost could become a linear function of capacity. *R* could approach 1 because equipment size may be limited by current fabrication technology, design, or transportation.

TABLE 3 Exponential Scaling Factors and Coefficients of Determination for Selected Bioprocess Equipment

Equipment Type	Exponential Scaling Factor *R*	Coefficient of Determination
Autoclaves	0.37	0.91
Fermenters (automatic sterilization)	0.36	0.97
Fermenters (manual sterilization)	0.28	0.99
Freeze driers	0.41	0.99
Water purification systems	0.27	0.98

In many instances, manufacturers build specific pieces of equipment in a limited number of sizes. For needs exceeding such sizes, products are duplicated rather than enlarged. Thus, doubling the size doubles the cost.

Extrapolated outside the minimum capacity shown, cost could become insensitive to size variations. Most of the cost might come from instrumentation and peripherals that support the equipment, not from the equipment itself. In these cases, *R* can approach 0. For instance, the cost of a 10 L fermenter and that of a 20 L fermenter would be about the same because most of the cost comes from instrumentation and control systems rather than the material cost of the fermenter.

A Changing Industry

Some references for *R* factors predate the approval and large-scale production of many biopharmaceuticals. Furthermore, biopharmaceutical equipment technology changes rapidly, and governments have imposed new environmental, sanitary control, and safety regulations. Therefore, some *R* factors may have changed, and others will change. Despite these caveats, we believe that the exponential *R* factor method is simple and often the best choice for ballpark calculations of equipment cost. This method is useful when looking at the effect of equipment size on profitability and when doing economic sensitivity analyses for a large number of variables.

Potential Errors

When a specific value is unknown, an *R* value of 0.6 is often used for equipment, 0.7 for biological or chemical processes. Errors arise if the actual *R* value is significantly different from 0.6 or 0.7. Figures 6 and 7 show the

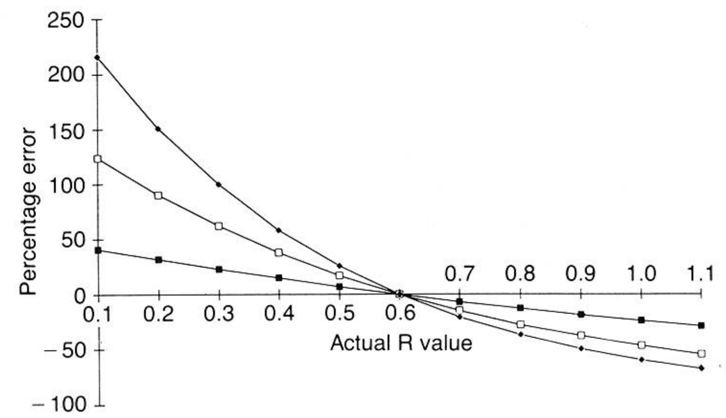

FIG. 6 Potential errors from using the 0.6 cost capacity factor for cost estimates. Scale-up factors: 10 times (diamonds), 5 times (open squares), and 2 times (solid squares).

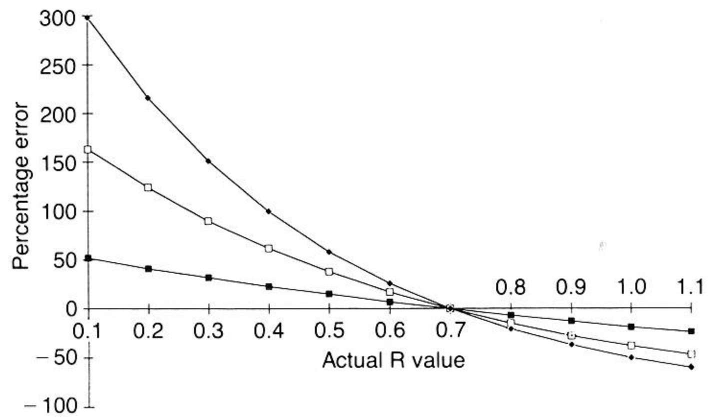

FIG. 7 Potential errors from using the 0.7 cost capacity factor for cost estimates. Scale-up factors as in Fig. 6.

errors that occur when the 0.6 and 0.7 values are used instead of actual values. For example, scaling up by a factor of 5 using an R value of 0.6 when the actual value is 0.8 would throw estimates off by 28% (Fig. 6). In another situation, if you assume an R value of 0.7 and the actual value is 0.3, estimates are off by almost 100% (Fig. 7). Because we found an average R value of 0.63 for bioprocess equipment, it may be better to use that value when no published R factor values are available.

Examples

Two examples of estimating costs by this method are shown here. The first uses the R factor to determine the cost of a piece of equipment when the cost of a similar but smaller piece of equipment is known. The second uses the R factor to calculate the cost of a new piece of equipment given the cost of an older piece of equipment.

A Fermenter. A 250 L fermenter with automatic sterilization and temperature, agitation, airflow, pressure, pH, dissolved oxygen, and antifoam controllers was purchased several months ago for $126,000. A cost estimate is sought for a 2,000 L fermenter with similar features. The R value for fermenters with automatic sterilization is 0.36 (Table 2). We can estimate the cost by using Eq. (1):

$$\text{Cost}_2 = \$126{,}000\left(\frac{2{,}000}{250}\right)^{0.36}$$

$$\text{Cost}_2 \cong \$266{,}000$$

A Water Purification System. In 1986, the purchase price for a type IV water purification system capable of handling 20 L/h was $5,000. We wish to determine the cost of a similar system capable of handling 1,000 L/h. The Chemical Engineering Cost Index for 1986 is 318.4 and for May 1990 is 355.6. The R value for a type IV water purification system is 0.27 (Table 2). We can estimate the cost by using Eq. (3):

$$\text{Cost}_2 = \$5{,}000\left(\frac{1{,}000}{20}\right)^{0.27}\frac{355.6}{318.4}$$

$$\text{Cost}_2 \cong \$16{,}100$$

In the Ballpark

Actual vendor quotations are always first choice, of course, but for quick estimates, the R factor and inflation index method usually give good results. The R factors presented here for 58 types and sizes of equipment can help you make ballpark cost estimates in the design and predesign phases for biotechnology or related processes. The Chemical Engineering Index can be found in *Chemical Engineering* ("Economic Indicators"). To adjust the costs in Figs. 1 through 5 for inflation, use January 1990 as the base.

We calculated an average R value of 0.63 with a standard deviation of 0.21. We continue to collect data from our own research. We also hope readers send us any R values they develop so we can periodically update the table of R factors.

Acknowledgment

The results reported in this paper are an outgrowth of research on R factors. These R factors were used to do process economics for producing several recombinant DNA products in *Pichia pastoris* for the Salk Institute Biotechnology/Industrial Associates, Inc. (SIBIA), La Jolla, California. The authors thanks Dr. Robert Siegel of SIBIA for his helpful comments.

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Process Equipment, Cost Scale-up

Obtaining corporate approval for new equipment or estimating detailed costs for a new plant often require that ball-park costs be calculated quickly for different types of hardware during both predesign and design phases. One easy method of developing such estimates is to base them on a known cost for the type of equipment and the ratio of the capacities for the known equipment and the desired equipment, raised to a factor R. This method, often referred to as the 0.6 power factor model, was first applied to equipment cost estimates by Williams in 1947 and then to plant costs by Chilton in 1950.

Determination of *R* Values

The relationship between cost and capacity is given by the equation

$$\frac{\text{cost}_2}{\text{cost}_1} = \left(\frac{\text{size}_2}{\text{size}_1}\right)^R$$

A plot of the ratios on a log-log scale produces a straight line. R values for equipment have a larger range than for entire process plants, for which the values tend to be averaged out by the large variety of equipment.

R Values

The tables in this article summarize R values for many types of equipment. Individual equipment cost information can be used to generate a more accurate cost estimate for an entire plant rather than using a single R value for the entire facility. The R factor cost-estimating approach is especially useful when doing a "sensitivity analysis," for which a high degree of accuracy is not required.

Through an extensive literature search, R values were found for the different types of equipment listed here:

General equipment, Table 1
Heat exchangers, Table 2
Fluid-moving equipment (blowers, compressors, fans, and pumps), Table 3
Tanks, vessels, and towers, Table 4
Environmental equipment, Table 5
Nonequipment (including catalysts/chemicals, engineering procurement fees, labor, services, and utilities), Table 6

When multiple R values for the same process were found, as was the case for filters, we list them in chronological order. Also shown are the ranges over which the values are applicable and the units for the values when known. When we found that a more recent source obtained all their R values from an earlier source, the original source is cited, if it could be located.

In looking at some of the R cost factors, some discrepancies in published factors are apparent as a result of variations in definition, scope, and size. Technology has also advanced over time, making it cheaper to produce larger machinery now than in years past. In addition, new regulations dictate expenditures for environmental control and safety not included in earlier equipment.