TABLE 9.4
Site Variation in Transdermal Delivery

Transdermal	Body Site	Reason
Nitroglycerin	Chest	Psychological: the patch is placed over the heart
Scopolamine	Postauricular	Scientific: behind the ear was found to be the best absorbing area
Estradiol	Trunk	Convenience: easy to place and out of view
Testosterone	Scrotum	Scientific: highest skin-absorbing area
Testosterone	Trunk	Scientific/convenience: removal from trunk skin is easier than scrotal skin

delivery. The transdermal nitroglycerin patch is placed on the chest more for psychological reasons than that related to scientific regional variation skin absorption. Some transdermal systems take advantage of regional variations in skin absorption and some do not (Table 9.4).

Shriner and Maibach (8) studied skin contact irritation and showed that areas of significant response were neck > perioral > forehead. The volar forearm was the least sensitive of eight areas tested. This is in contrast to the commonly held belief that the forearm is one of the best locations to test for immediate contact irritation.

9.1.3 Individual Variation

It is well understood that chemical trials are designed with multiple volunteers to account for individual subject variation. This extends to *in vivo* percutaneous absorption where individual subject variability has been demonstrated. This subject variation also extends to *in vitro* human skin samples (9). Table 9.5 shows the in vitro percutaneous absorption of vitamin E acetate through human skin *in vitro*. Percent doses absorbed for two formulations, A and B, are shown for 24-hour receptor fluid accumulation and for skin content (skin digested and assayed at 24-hour time point). Assay of skin surface soap and water wash at the end of the 24-hour period gives dose accountability.

TABLE 9.5
***In Vitro* Percutaneous Absorption of Vitamin E Acetate into and through Human Skin**

	Percent Dose Absorbed		
	Receptor Fluid	**Skin Content**	**Surface Wash**
Formula A:			
Skin source 1	0.34	0.58	74.9
Skin source 2	0.39	0.66	75.6
Skin source 3	0.47	4.08	89.1
Skin source 4	1.30	0.96	110.0
Mean ± SD	0.63 ± 0.45[a]	1.56 ± 1.69[a]	87.4 ± 16.4
Formula B:			
Skin source 1	0.24	0.38	–
Skin source 2	0.40	0.64	107.1
Skin source 3	0.41	4.80	98.1
Skin source 4	2.09	1.16	106.2
Mean ± SD	0.78 ± 0.87[a]	1.74 ± 2.06[b]	103.8 ± 5.0

[a] $p = 0.53$ (nonsignificant; paired t-test).