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7 Medicinal Product Safety on the UK Market – A Ten Year Study

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Introduction: Post-marketing product withdrawals and major labelling changes based on new safety signals remain features of advanced healthcare systems.[1-4] We report the results of a ten-year study of the UK market.

Aims: To identify the safety grounds for withdrawal or major labelling change affecting medicinal products in the UK and define the probability of these occurrences.

Methods: All products containing new chemical entities licensed between 1/10/95 – 30/9/05 were included. Exact launch and withdrawal dates were obtained from the licensing authority or the product manufacturer. The first major labelling change dates were determined by triangulation using the same sources, plus 'blue box' British National Formulary warnings and UK Department of Health communications. Data were subjected to Kaplan Meier survival analysis using STATA. Safety data cited in support of each action was classified and stratified according to its strength.[5]

Results: Key data from the Kaplan Meier analyses appear in Table 1.

Kaplan Meier survival probabilities and times for major safety events affecting 518 products licensed in the UK between 1/10/95 and 30/9/95

Product event	Cumulative event survival probability	Median survival time (IQR)	Survival time range
Withdrawal (n=9)	0.978 (therefore probability of a product experiencing an event = 0.022)	5.08 (2.98-7.63) years 264.4 (155.3-396.9) weeks	0.13-10 years 6.9-521.7 weeks
Major labelling change (n=56)	0.862 (therefore probability of a product experiencing an event = 0.138)	4.56 (2.45 – 7.60) years 237.3 (127.4 -396.9) weeks	0.07 – 10.00 years 3.71 – 521.7 weeks

Product withdrawal: 518 eligible products were launched during the study period of which 9 were withdrawn for safety reasons. Spontaneous reports (level IV data) were cited in all cases; higher quality data (level II - randomised controlled trials) were cited for three products. Product labelling changes: changes affected 56 of the 518 products. The highest level of data cited was II, III (Published case series/epidemiological studies), IV, and V (animal or in vitro studies) for 4, 10, 37 and 5 products respectively.

Conclusion: The ten-year probability of adverse drug reactions causing the withdrawal of a NCE-containing product post-marketing is 2.2% (Table 1). This would appear at first glance to be low; but considering the cost of bringing a product to the market in the first place, the investment risk is considerable; two out of every 100 products will fail. Similarly, the risk of at least one licence change being made on safety grounds is 13.8%. Spontaneous reports from healthcare professionals provide the backbone of evidence on which such decisions are made. Higher levels of evidence are rarely cited. Such information informs a review of the decision-making process and assessment of the implications for manufacturers.

Conflicts of interest: None declared.

References

1. Hass AE, Portale DE, Gorssman RE. 1984 New drug introductions, discontinuations and safety issues in the United Sates and the United Kingdom 1960-1982. Office of Planning and Evaluation, FDA, Washington
2. Bakke OM, Wardell WM, Lasagna L. Drug discontinuations in the United Kingdom and the United States, 1964 to 1983: issues of safety. Clin Pharmacol Ther 1984; 35(5): 559-67
3. Hass AE, Portale DE, Gorssman RE. New drugs: their market life and safety. Pharm J 1985 Feb; 23: 235-8
4. Lasser KE, Allen PD, Woolhandler SJ, et al. Timing of new black box warnings and withdrawals for prescription medications. JAMA 2002; 286(17): 2215-20
5. Gray JAM. Evidence based healthcare. Churchill Livingstone, London, 1997: pp72-4