CSM UPDATE

Review of yellow cards—1986 and 1987

SINCE 1986 MODIFIED versions of the yellow card have been included in both NHS prescription pads and the back of the *British National Formulary*. As a result of their greater accessibility the total number of suspected adverse drug reactions reported on yellow cards in 1986 was much greater than ever before (table I).

TABLE I—Numbers (and percentages) of adverse reaction reports received by CSM in 1986 and 1987

	1986	1987
Yellow cards	10 393 (67)	8 564 (52)
BNF slips	1 874 (12)	3 242 (20)
FP10 slips	1 383 (9)	2 289 (14)
Other (industry, letters, etc)	1 877 (12)	1 955 (12)
Red alert		381 (2)
All reports	15 527	16 431

The increased reporting rate continued in 1987, when 16 431 yellow cards were received. The traditional yellow cards now account for 52% of all reports received by the Committee on Safety of Medicines; the BNF and FP10 cards account for 34%.

During the second half of 1987 the CSM, in collaboration with the Drug Safety Research Unit at Southampton, began an experimental monitoring scheme for new drugs. Under this scheme, known as red alert, every time a new drug is prescribed (as monitored through the Prescription Pricing Bureau) the prescribing doctor is sent a special yellow card with a red triangle on it. This card names the patient and the drug, and the doctor is asked to fill it in and return it if the patient suffers a serious adverse reaction or dies while taking that drug.

In 1986 the CSM also revised its definition of a serious adverse reaction, and such reports now constitute about a third of all those received.

THERE WERE NO major differences between 1986 and 1987 in the pattern of reactions reported. In both years the most common suspected adverse drug reactions were dermatological, followed by reactions affecting the central and autonomic nervous system and gastrointestinal tract (table II). Three hundred and thirty six deaths were attributed to suspected adverse reactions in 1986 and 280 in 1987.

TABLE II—Numbers of suspected adverse drug reactions reported to CSM in 1986 and 1987 according to system affected

Organ/system	Most important reactions*		Serious		Fatal	
	1986	1987	1986	1987	1986	1987
Skin	5 254	4 991	539	524	6	5
Cardiovascular	256	280	246	266	62	57
Central and autonomic nervous system	2 225	2 351	714	736	22	7
Auditory, vestibular and visual	302	323	90	68	0	0
Blood	581	543	505	479	46	28
Collagen and vascular	369	351	193	187	14	18
Endocrine/metabolic	499	500	223	177	5	2
Reproductive (women and men)	311	304	47	31	1	2
Gastrointestinal	2 149	2 471	801	641	97	72
Hepatic	541	573	437	484	27	32
Muscular/skeletal	336	384	37	29	0	0
Psychiatric	786	985	271	332	1	1
Respiratory	501	717	328	415	14	21
Urinary	294	292	142	148	27	23
Others	1 123	1 366	196	432	14	12
Total	15 527	16 431	4 769	4 949	336	280

*Most important reaction in the individual patient.

TABLE III—Numbers of suspected adverse reactions to drugs first marketed during 1986 and 1987

Approved name	Date of marketing	Total reactions	Serious reactions (deaths)
Etodolac	Jan 86	421	80 (1)
Carboplatin	May 86	9	7 (0)
Buserelin	Jun 86	9	3 (0)
Propofol	Jun 86	156	83 (5)
Terodiline	Jul 86	202	41 (2)
Metipranolol (eye drops)	Aug 86	11	4 (0)
Nicardipine	Sept 86	116	29 (5)
Nedocromil	Oct 86	75	12 (1)
Betaxolol (eye drops)	Nov 86	22	15 (0)
Aztreonam	Dec 86	8	2 (0)
Fluvoxamine*	Feb 87	626	92 (5)
Ciprofloxacin†	Mar 87	304	58 (1)
Nabumetone*	Mar 87	402	42 (3)
Goserelin	Apr 87	18	6 (2)
Zidovudine	May 87	8	3 (1)
Terazosin*	Jun 87	25	8 (0)
Human Insulin	Aug 87	18	6 (0)
Nizatidine	Oct 87	8	1 (0)
Famotidine	Oct 87	13	0 (0)

*Includes red alert reports. †All salts.

Ninety seven deaths in 1986 and 72 in 1987 were attributed to gastrointestinal adverse reactions, most of them haemorrhage or perforation.

The group of drugs most frequently associated with serious and life threatening reactions was the non-steroidal anti-inflammatory agents. Reactions included gastrointestinal bleeding or perforation, angioedema, and erythema multiforme.

In 1986 and 1987 serious blood dyscrasias accounted for 505 and 479 reports respectively. Again non-steroidal anti-inflammatory drugs together with mianserin and co-trimoxazole were especially frequently reported in patients with red and white cell dyscrasias.

Desensitising vaccines, muscle relaxants, intravenous anaesthetic agents, and radiological contrast media were the most common suspect causes in patients with anaphylaxis or anaphylactoid reactions. In September 1986 the chairman of the CSM advised all doctors that desensitising vaccines should be given only where facilities for full cardiorespiratory re-suscitation were available and that patients should be kept under observation for two hours after injection.

IT IS TOO EARLY to draw firm conclusions about the adverse reaction profiles of drugs introduced during 1986 and 1987. Serious suspect adverse drug reactions associated with etodolac included gastrointestinal, skin, and pulmonary reactions. At this stage the toxicity of this particular non-steroidal anti-inflammatory drug cannot be distinguished from that of other drugs in the class that are available on prescription. The only other drugs first marketed in 1986 which produced substantial numbers of reports were terodiline, propofol, and nicardipine (table III).

The large numbers of reports related to fluvoxamine and nabumetone reflect the combination of yellow cards and red alert reports received. Drugs more frequently prescribed tend to produce large numbers of reports, while reactions to drugs used mainly under controlled conditions in hospital, such as zidovudine, are relatively infrequently reported.

The yellow card system continues to make a critical contribution to the safety assessment of marketed drugs and the committee is grateful to all those who have reported suspected reactions. Adverse reactions are, however, still grossly underreported and the CSM asks all doctors and dentists to report *all* suspect reactions with *new* drugs (which have an inverted black triangle in the *British National Formulary*, *MIMS*, and the datasheets), and *serious* reactions only with *older* established drugs.—J L BEM, R D MANN, M D RAWLINS (Committee on Safety of Medicines, London SW8 5NQ).