

# CURRENT PATENTS GAZETTE



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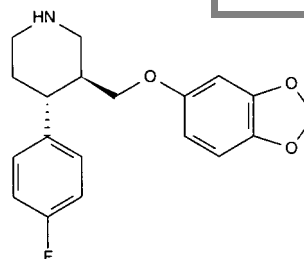
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## DRUG PATENTING IN CONTEXT

Current Patents *Gazette* is the most rapid competitive intelligence service covering innovation in the pharmaceutical industry. Patent applications published during the past week have been classified and analysed, in order to place the inventions in context. For the most crucial innovations, those involving new chemical compounds, additional information is given in the form of front page images. These can be enlarged to show details of chemical structures and inventor teams, for example. Applications filed jointly, representing collaborative research, are highlighted, as are sequences of inter-related documents.

### NEW THIS WEEK



**As paroxetine**, the highly successful antidepressant, begins to lose its basic patent protection, SB continues to build its secondary patent portfolio with 6 applications this week claiming the synthesis of paroxetine hydrochloride and its propan-2-ol solvates ([Page 27](#))

## HIGHLIGHTS THIS WEEK

**Chelating agents** feature in two processes cases, though in one of these the link with pharmaceutical is perhaps a little tenuous. **Schering AG** has claims to a **one-pot synthesis of cyclenes**, and although this is a little-used term it is clear that the intended products are **polyazamacrocycles** of a type which the company has been interested in for some time; one such cascade polymer complex, **gadobutrol**, is a gadolinium-based **contrast agent** which is awaiting regulatory approval. Less obviously pertinent is a synthesis from **Procter & Gamble**, the latest in a series concerned primarily with macrocycles which could form the basis for ionic detergent chelates. However, the P&G ring systems are very similar to Schering's cyclenes, and it may well be that the company's expanding drug discovery activity could in future incorporate the body of expertise built up in the search for novel surfactants. This is a fortuitous but interesting example of the *Gazette's* deliberately broadly-based selection strategy, whereby marginal items will be included if there is the slightest suspicion that there could be some ultimate therapeutic utility. Incidentally, **classical data mining techniques** would also tend to link such patent documents, since they are classed under similar IPC codes, based on the close similarity of the molecules rather than their disparate proposed uses.

**Paroxetine**, the highly successful antidepressant SSRI licensed by **Novo Nordisk** to **SmithKline Beecham**, has begun to lose its basic patent protection, and there has been a considerable amount of so-called "line extension" patenting in consequence. This has covered both new indications (for example obsessive compulsive disorder, social phobia, panic and sexual dysfunction) and novel formulations, such as sustained release dosage forms. However, much of the recent patenting has been concerned with salts and the physical form of the paroxetine active ingredient, and an inter-related series of seven further cases of that type are published, bringing the total patent portfolio for this product to well **over 100 cases**. An interesting aspect of these most recent publications is that they point quite unambiguously to the anhydrate as the preferred species, specifying a polymorph designated as Form A; previously the hydrochloride hemihydrate had seemed to be the preferred physical form.

**Enantiomers of established products** feature in two other chemical process cases which may offer pointers to future brand revitalization efforts. From **Darwin Discovery** in Cambridge UK (the name adopted by **Chiroscience**, now merged with **Celltech**) comes a case focusing on resolution of the optical isomers of **tramadol**, the opioid agonist-type analgesic originated by **Gruenthal** in the 1960s. The German company has itself filed applications on the resolution of tramadol in the past, but with a single exception this seems to be Darwin's first declaration of interest. That exception is a rather curious application WO9840053 with claims to the principle of administering the separate enantiomers of a particular drug separately, in proportions aimed at utilizing to the full the differing activities of the isomers; there tramadol is mentioned as a preferred compound, along with **warfarin**. The other compound covered by enantiomer claims is the antidepressant **venlafaxine**; this seems to be the first time the applicant, **Sepracor**, has worked on its resolution, though the originator, **Wyeth-Ayerst**, shows evidence of interest in the form of metabolic studies of the enantiomer distribution in animals.