The occurrence of severe anaphylactic reactions to neuro-muscular blocking agents (NMBAs) during surgery in patients not previously exposed to them has led to much speculation about the environmental exposures which may sensitize individuals to these drugs. In this issue, Stephen Mann reviews the history and literature underpinning the ‘Pholcodine Hypothesis’. This body of work proposes a link between the consumption of pholcodine (an ingredient in many cough medicines for dry cough) and the risk of anaphylactic reactions during surgery when neuro-muscular blocking agents (NMBAs) are used.

Recently, the European Medicines Agency’s Committee for Medicinal Products for Human Use (CHMP) concluded that it found ‘... no firm evidence to substantiate the hypothesis of cross-sensitisation between pholcodine and NMBAs and a subsequent increased risk of anaphylactic reactions during surgery’. However the agency has asked for further case control studies to be undertaken and so it is likely that this story will continue to evolve.

From time to time questions of safety can arise with any drug, but in the case of medicines used in an Over the Counter (OTC) setting, such questions pose particular problems. Some active ingredients that are well established in OTC medicines may rely on an evidence base which is lacking in several ways:

- The evidence of efficacy may be derived from studies performed before current standards of study design became established.
- The safety data from marketed use, although it may be extensive in terms of time and total exposure, may rely largely on consumer reports which generally lack the precision of reports that involve a healthcare professional.

If such an ingredient becomes subject to safety concerns, these factors may mean that it is difficult to provide a comprehensive picture of the benefit to risk ratio for the drug. Nonetheless, drug substances that have stood the ‘test of time’ in widespread use should not be discarded lightly and without considering the unintended consequences that may follow substitution of other drugs.

Older drug substances are major ingredients in many consumer medicines and it is important that the evidence base for these drugs is as comprehensive as possible. In some instances, as with pholcodine, this may be partially achieved by summarising what is known from the literature on a particular safety concern to allow a more informed debate to take place. In other cases it may be helpful to review efficacy data from all sources to act as a resource when questions of benefit to risk balance arise. Such reviews have their natural home in SelfCare and we urge contributors to consider this often neglected group of drugs. The best time to strengthen the evidence base for widely used self-care ingredients is not when they are already under attack.