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Editorial

Neglected diseases, neglected technologies, neglected patients?

The much-vaunted era of personalised medicines, in spite of the many advances in drug delivery systems, certainly has not yet arrived. In many situations the idea of individualised medicines is an almost laughable concept. In the developing world, for example, where basic medicines for the diseases that kill in huge numbers are often simply not available at least in affordable forms, it is a rather meaningless concept. A comprehensive report on *Priority Medicines for Europe and the World* by Warren Kaplan and Richard Laing published by the World Health Organisation in November of 2004, highlights many of the issues in the war against *neglected diseases* such as malaria where insufficient research and development effort worldwide leads to loss of life on an unthinkable scale. Short commentaries on the report have been published by Dukes (2005) and by Rawlins (2005), but little has appeared in the pharmaceutical press. Yet, pharmaceutics (as well as pharmacokinetic analysis) has a large part to play in ensuring that appropriate formulations are available for appropriate drugs, and of course in affordable forms. "Innovative" is not a synonym for "expensive".

In a chapter of the report dealing with "cross-cutting themes" there is a reminder of the importance of drug delivery mechanisms, well appreciated by readers of this journal. The authors conclude that "there is a wide range of existing evidence-based, very often off-patent technologies that are heavily under-utilised. Such technologies could be used to improve the "patient-friendly" performance of a number of existing medicines". These, then, one might say are *neglected technologies*, invented but discarded because in many cases funding bodies will not pay for them, or as is sometimes the case, a worthy application has not been found. In all parts of the world, two disparate patient groups for which personalised medicines (or personalised formulations[1]) are sorely needed include children and the elderly, neither of which comprise homogeneous sets, the former because of the rapid changes in metabolism and physiological functions in the progression from neonate through infancy, early and late childhood, and the latter also because of changes in body fat, renal clearance, gastrointestinal function but often because of concomitant pathologies. These then are the *neglected patients*.

We should all be aware of the issues relating to paediatric medicines, discussed comprehensively in a paper by Ernest et al. (2007) and in more general terms by Wong et al. (2003). The issues in relation to paediatric cardiovascular medications have been discussed (Standing and Tuleu, 2005), and general paediatric formulations in practice are discussed by Tuleu (2007) in Paediatric Drug Handling, a recent text (Costello et al., 2007).

One has to say that well into the 21st century we are in a parlous state, where hospital pharmacists work skilfully, but constrained by the lack of appropriate dose forms for the very young and even a lack of helpful information flow between drug firms and pharmacists. Pure drug material is frequently not available from primary manufacturers, so pharmacists use their unique skills to convert adult medicines into formulations for paediatric patient use, but this leads not infrequently to a lack of standardisation and often the use of some unproven formulations. The first publication of the *British National Formulary for Children* in 2005 (the latest edition is the British National Formulary for Children, 2007) will assist to some extent, but will not solve the issue of the lack of formulations for children. This must be of concern and interest to pharmaceutics practitioners.

One of the issues in paediatrics is simply that of dose. Errors occur in practice (Diav-Citrin et al., 2000) often because of the large dilutions that have to be made on wards from adult medicines. It should not be beyond our wit (or will) to produce more flexible dosing systems than are now available. There should be no pride in the industry simply producing scored tablets of adult doses for potent drugs. Solid dose forms are used, but the lack of sustained release medications for children deprives this population and their carers from delivery innovations which benefit the adult population. In the elderly population the usefulness of flexible dosing systems are also obvious: initial titration of, for example, ACE inhibitors are crudely achieved by present tablet formulations (Cohen, 2001).

We develop microfluidic devices, but seem unable to construct systems to provide linear rather than quantal adjustments in dose. With unstable solutions, nanoparticles and micropar-

[1] This phrase will sound strangely familiar to pharmacists of a generation used to preparing medicines extemporaneously for individual patients.

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ticles encapsulating drug can be employed, soluble thin films may be used for buccal administration or films for transdermal administration: both can readily be cut (with appropriate precise devices) to achieve accurate incremental doses. Mini-tablets such as those developed by Knoll might be utilised to provide not only small systems but also fixed dose combinations, another topic raised in the Kaplan–Laing WHO 2004 report. Some of these issues were debated recently at a workshop held in Leiden (Top Institute Pharma Workshop, 2007).

Funding has been a problem in achieving a productive academic-practice interface in formulation development. Research Councils, certainly in the UK, have deemed formulation exercises as trivial and the province of industry, but of course here is the rub: industry by and large has not been keenly interested in being innovative in paediatric and geriatric dose forms. One acknowledges the industrial development of devices such as spacers for paediatric inhalation therapy, and fast melt tablet technologies (Dobetti, 2000) but there does otherwise seem to be a lack of obvious innovation. Academic groups must work more assiduously with those who treat children and the elderly to determine the real needs of the patient population and also to persuade funders and sponsors to accept such patient focussed research in drug formulation and delivery as an important field of activity. It is ironic that much research effort today is directed to the delivery of biologicals by a variety of routes (e.g. oral insulin) when these products may never see the light of day, yet where there is an clear and immediate need, the scientific, professional and industrial machine cannot bring itself to tackle the issues, which primarily focus not only on knowledge of the pharmacokinetics and pharmacodynamics of drugs in individuals gained through new and increasingly sensitive analytical techniques, but the invention of new modes of delivery. Governments must play their part in funding research for what will be genuine personalised medication, otherwise the rhetoric and hype of the post-genomic era will remain hollow.

Clearly it would be good to be proved wrong. We encourage groups who are already in the field of medicines for paediatric and geriatric patients to publish their work in this journal. This might stimulate research by those who have the appropriate technologies to turn their hand to the specialised practical application of their work for these relatively neglected patients, young and old.

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