Making insulin usage safer — the universal colour code

François Bonnici

Today, following a few decades of manufacturing advances, an expanding range of insulin preparations is being used to meet the short-acting and basal requirements of patients with diabetes.

Because of the frequently dangerous confusion caused by innumerable products on the world's markets, with their different concentrations, brand names, haphazard and unmatching colour codes and alternative delivery devices — made worse by the recent availability of a whole family of new insulin analogues — the International Diabetes Federation and the World Health Organisation (WHO) have long advocated a uniform system of international product recognition on a universal scale to minimise therapeutic errors known to happen frequently.[1]

François Bonnici is Professor Emeritus at the University of Cape Town Faculty of Health Sciences and Co-Director of the Diabetes Clinical Trials Unit, President of Diabetes South Africa, Member of the WHO Expert Panel on Diabetes and Chairperson of the Local Organising Committee of the Cape Town 2006 World Diabetes Congress.

As from now South Africa will start to benefit from this initiative in which all players, including all major insulin manufacturers, fulfil a responsible role for the common good of the world's diabetic community. Thankfully we are already a single-strength market following the successful changeover to the U-100 insulins 20 years ago.[2]

For the greater safety of our patients we now have to endorse the universal colour code for the four most frequently prescribed human insulin ranges, namely regular/soluble, NPH isophane, lente and biphasic 30/70 mixtures.[3] This will only apply to the multinational-sourced innovator insulins and not to the possibly less effective generics that may one day

Table I. International colour code for human insulin preparations

Product group	Product	Colour name	Colour*
Short-acting insulin	Regular	Yellow	
Long-acting insulin	NPH Isophane	Light green	
	Lente	Turquoise	
Biphasic insulin	Premixtures 30/70	Brown	

*The colours illustrated here are approximate guidelines only.

reach our market. These four insulin ranges have been assigned international individual colour codes (identified by specific pantone colour numbers) now adhered to by all major manufacturers (Table I). It was also unanimously agreed that insulin manufacturers would not use the colour-coding initiative in their marketing activities, nor would any single company claim ownership of it.

All parties are still actively working together to produce a colour code for insulin analogues, particularly as new long-acting clear solutions — no longer cloudy suspensions — could easily be mistaken for fast- or short-acting similarly clear insulins.

The short-acting clear-looking regular/soluble range is coded yellow, shared by the products Actrapid and Humulin R. Their average time course of action is reasonably reproducible and predictable, with onset in 30 minutes, peak 2 - 5 hours and duration 5 - 8 hours.

The most used intermediate/long-acting cloudy-looking products belong to the NPH isophane range and are coded light green, shared by Protaphane and Humulin N. Their time action is fraught with large intra-individual variations in bio-availability due to inconsistent subcutaneous absorption. On average the onset of action is 1 - 3 hours, peak at 6 - 12 hours, and duration 16 - 24 hours, but these may vary substantially between patients, depending on the site and depth of injection and the ability of patients to accurately re-suspend the cloudy NPH insulin in syringes or pens before injection.

Also intermediate/long-acting and cloudy in appearance, insulin preparations in the lente range, now coded turquoise and comprising Monotard and Humulin L, are much less frequently used nowadays as they suffer even more significant pharmacokinetic limitations and inconsistent bio-availability. Patients would benefit from being switched over to NPH insulins instead, and for safety reasons these preparations should eventually be withdrawn from use.

Biphasic 30/70 mixtures are now all coded brown and the products available in this premixed range are Actraphane 30/70 and Humulin 30/70. These are cloudy fixed mixtures of regular and NPH insulins with an average time course of action, with onset in 30 minutes, peak at 2 - 12 hours and duration 16 - 24 hours. They share with NPH insulins a number of common disadvantages including inconsistent absorption and the need for adequate re-suspension before injection.

The large intra-individual and interpatient variations in bio-availability are one of the most difficult aspects of insulin treatment, making it difficult to plan dosing accurately. Adequate instructions regarding pre-injection re-suspension can make a difference of up to 50% in the effectiveness of cloudy prolonged-action insulins.

The present worldwide strategy of universal colour coding will facilitate product recognition, making it safer for health care professionals and patients alike. The minor pharmacokinetic differences between human insulins of different sources of manufacture (i.e. *Escherichia coli* and yeast), if any, are overshadowed by the large variability in absorption which is shared by all cloudy insulins and is inherent to their state of suspensions. Therapeutic product equivalence, although never absolute, is as close as it has ever been before.

Patients can now be moved safely from one insulin brand to another when circumstances of availability or price compel the prescriber or dispenser to do so, from pens to syringes and vials or *vice versa*, unit for unit, as long as the colour code identification is respected (and the concentration is standardised, which it is in South Africa). Patients for whom it is deemed preferable to use a pen device, viz. those on a multiple injection regimen, those with poor vision, arthritis, the young, the elderly, should not be summarily switched to syringes and vials without due consideration for their personal circumstances. This would be a major retrogressive step which could adversely influence their adherence to treatment and quality of life.

The act of dispensing insulin will thus be made safer and more educative, with opportunities for enhanced pharma-covigilance regarding colour-code recognition, proper re-suspension, recommenddations for storage, and emphasis on dialing or drawing-up and injection techniques with the specific delivery device prescribed.

1. Continued push for universal colour coding. *Diabetes Voice* 1999; **44:** 36-37.
2. Bonnici F. Making the change to U-100 insulins: a patient education guide. *S Afr Med J* 1983; **64:** 201-203.
3. International Diabetes Federation. *Universal Colour Code e-Atlas*. 2003. **www.idf.org** (last accessed 11 February 2004).