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drugs discovered outside of the country, so as to avoid becoming 'guinea-pigs'. Furthermore, there are not enough regulators in the country to decide which Phase I trials are appropriate. However, Piramal emphasized that this law must change if India is to progress.

In an enlightening keynote, Walan provided a frank description of the problems of setting up a base in either China or India. AstraZeneca decided in Jan 2002 to explore the potential for accessing new clinical investigators and patient populations in Asia. Some of the key business considerations involved in this decision included the fact that AstraZeneca sales in China are higher than in India and have the fastest growth rate. Another significant factor was that patent protection is present in China, whereas progress in IPR in India has been slow and importantly, there is also no data protection in India.

However, India does have the advantage that many facilities work in English, but China is more developed in terms of health and welfare indications, has lower infant mortality, and higher life expectancy. The final decision was made to set up a clinical research unit in Shanghai but to investigate the possibilities in India for off-shoring biostatistics and data management.

After moving to China, AstraZeneca discovered several other areas that should be considered when making such a decision, for example: (i) the long time required for clinical trial approval in China precludes participation in many global trials (by comparison, approval can be between 2 weeks and 3 months in USA; 2 weeks guaranteed including approval by the ethical committee in Singapore; but up to 12 months in China); and (ii) the level of information the Chinese SFDA require exceeds EU and US requirements: submissions must be translated into Chinese and the government laboratories recheck the quality of all study drugs. Furthermore, strict regulations on export of genetic material (such as blood, biopsy specimens) can prove a big problem and there are concerns about quality assurance during courier delivery of study drugs. Also, in some therapeutic areas, the number of centres with government approval to conduct clinical trials can be very limited. However, Walan commented that it proved easy to attract highly competent medical professionals to the pharma industry in China and they have an impressive knowledge and facility in English. The staff and investigators have proved very hardworking and motivated, and it is possible to obtain reasonably rapid

approval (e.g. 2 months) for clinical trials in China once the NDA has been filed. There is also a sign of willingness of the drug regulators in China to change the situation of slow approval times, although realistically this is likely to take a couple of years before it matches the US.

Conclusion

The general feeling is that although there are still many outstanding issues that must be addressed (especially by countries such as India and China) to be able to attract substantial western investment and partners, significant progress in this direction has already been made. There appears to be a strong commitment by both governments and the companies within these countries to ensure that rapid progress is made on the key issues such as patent law and regulation, language barriers, broad scientific expertise, business expertise and good partnering skills. The key problem areas that were raised by some of the western multinational companies that have already taken a step to work in Asia were fully embraced by the respective countries and there is a real energy to ensure that investment and partnerships with western multinationals and investors are forthcoming and prove successful.

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Chemical Grues and Little Willies

A grue is simply a comically sadistic and grisly little poem of four lines. The term was originally coined by Robert Louis Stevenson (1850–1894), the author of the well-known romantic adventure stories *Treasure Island* and *Kidnapped*. Stevenson was also a poet whose poems, although not showing the highest poetic genius, were skilful and original, often written with children in mind. The word 'grue' is a Scottish word with roots

in old Swedish ('grua') and Danish ('grue') meaning to feel horror or fear, hence the more common derivative 'gruesome'.

A contemporary of Stevenson, Harry Jocelyn Clive Graham (1874–1930), wrote a collection of grues under the pseudonym Colonel D. Streamer entitled *Ruthless Rhymes for Heartless Homes* [1]. Originally published in 1899, this book was an immediate success and has been reprinted several times over the intervening

A thought-provoking tonic on the lighter side

Column by Raymond C. Rowe, AstraZeneca, UK



Please note that these are the personal opinions of the author and do not necessarily represent those of AstraZeneca.

years. An example from Graham's collection illustrates the basic structure of the grue:

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Billy, in one of his nice new sashes,
Fell into the fire and was burned to ashes.
Now, although the room grows chilly,
I haven't the heart to poke poor Billy.

The poems are sometimes called 'Little Willies' after the character who appears in many of them:

Willie poisoned his father's tea;
Father died in agony.
Mother looked extremely vexed;
'Really Will,' she said, 'What next?'

Many grues involve either the administration of chemicals and poisons to individuals, or the use of explosives, both with disastrous consequences. Hence, it is not surprising that grues have been a favourite with chemists to parody their subject. Of course, many are anonymous and not original, but many are very clever in their use of words. Recently, several grues have been collected together as part of a compilation of chemical quotations [2].

'A grisly poem ideal for chemists'

Chemicals and medicines

The oral administration of both chemicals and medicines to animals and humans has been covered in several grues. The physiological effects observed range from those that are scientifically predictable as in:

Little Willie, tried and true,
Fed his sis on methylene blue.
Now sister has a perplexed look
Whene'er she sees a babbling brook.

to those that are extraordinary to say the least, as in:

Little Willie, full of glee,
Put radium in Grandma's tea.
Now Grandpa thinks it a lark
To see her glowing in the dark.

and:

Little Willie, good as pie,
Fed the cat on alkali.
Now the process, with yields first rate,
Produces potassium pussiate.

Methylene blue has a mildly antiseptic action and can be given orally for minor urinary tract infections because it is rapidly absorbed and primarily excreted unchanged in the urine. It does, however, impart a bright blue colouration to the urine and this, combined with the sound of running water increasing the urgency of urinate, could cause distress to anyone taking it.

Sometimes the effect is more extreme as in:

Little Willie, what a spiv,
Fed the cat with laxative.
Now the cat, one year on
Is nothing but a skeleton.

and:

We had a little Willie,
Now Willie is no more,
For what he thought was H_2O
Was H_2SO_4 .

A grue entitled 'Little Willie' from a book of verse entitled *Verse and Worse* [3], published in 1952, is a cautionary tale about the dangers of mercury:

Little Willie from his mirror
Licked the mercury right off,
Thinking, in his childish error,
It would cure the whooping cough.
At the funeral his mother
Brightly said to Mrs Brown,
'Twas a chilly day for Willie
When the mercury went down!'

Acids and explosives

Dissolving bodies in acids is a theme for two well-known grues:

Little Willie, calm and placid,
Boiled his ma in nitric acid.
Now mother dear is just a plastic,
Transparent, clear; but non-elastic.

and:

Little Willie, I hate to tell,
Soaked his dad in HCl.
Now the chemist at his sink
Wonders what made all the stink.

Explosives and their consequences are another theme well represented in this form of poetry. Two examples are:

Willie made some dynamite,
Couldn't understand it quite.
Curiosity never pays;
Willie rained for several days.

and:

Little Willie, hard as rocks,
Put fulminate in Daddy's socks.
Now Daddy really wants to know
How long it takes to grow a toe.

Comment

As many of you know, I have a penchant for doggerel verse notably in the form of limericks and, more recently, clerihews, because I believe that these offer new opportunities for scientists, who generally are not the world's best poets, to express their ideas in a format that is versatile, memorable and, above all, fun. The grue is just another doggerel except that the history of a grue dictates that it should deal with subject matter that is a little more extreme as illustrated in the examples above. The structure of a grue is very easy to copy and many of the grues written are minor modifications of others. In my research, I have not found many alluding to drug discovery and development (apart from those dealing with methylene blue and laxatives), although I hope that this will change when this article is published and I receive examples from you. In the meantime, let me start you off with one of my own:

Little Willie, cool and smug,
Developed a blockbuster drug
That when spread upon the skin,
Allowed the world to see right in!

References

- 1 Streamer, D. (1899) *Ruthless Rhymes for Heartless Homes*, E. Arnold
- 2 Gaither, G.C. and Cavazos-Gaither, A.E. (2002) *Chemically Speaking*, IOP
- 3 Silcock, A. (1952) *Verse and Worse*, Faber and Faber

Raymond C. Rowe

Pharmaceutical and Analytical R&D,
AstraZeneca, Alderley Park,
Macclesfield, Cheshire,
SK10 2NA, UK