Racing with lead shoes

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The enlargement of Europe is a good reason to rejoice, though the new Member States join a dream that is in poor shape: its population is ageing and its number decreasing. In half the EU countries the legal system is so clogged up it is unable to dispense justice, the school system is producing a worsening standard of school-leaver and the social-security system is on the way to bankruptcy. Science in Europe has lost face - appalling business and political mismanagement have driven the GM foods debacle and the BSE scare. There appears to be no decisive action from Brussels to rebuild trust in Science. Instead Europe seems focused on producing paper: On the 18th June, 25 European leaders approved the EU Constitution, its "reader-friendly edition" has 318 pages. The Constitution of the United States has 7 Articles.

The number of regulations having an impact on the European Chemical sector has risen steadily from 19 in 1990 to no less than 527 by February 2003. Chemicals are a cornerstone of EU industry, a major provider of jobs, exports and wealth - a key enabler of endless down-stream industries - and yet the future is bleak. How can any one win a marathon race wearing lead shoes?

REACH (Regulation on Registration, Evaluation and Authorization of Chemicals) is currently being discussed in the European Parliament. The bill is over 1000 pages long. REACH is trying to legislate regionally an industry that is global. Its goals are necessary, but its "how to" approach will further damage Europe's chemical industry.

LEGISLATING THE CHEMICAL INDUSTRY TO DEATH

REACH replaces the current system for new and existing chemicals and extends the requirements for new substances to existing ones. Since 1981 new substances had to be notified before being marketed. Existing substances commercially available between 1 January 1971 and 18 September 1981 were compiled into an Inventory, the so-called EINECS (the European Inventory of Existing Commercial Chemical Substances) that contains 100,116 entries. When EINECS was passed, it grand-fathered existing substances, and for the 23 or so years these EINECS substances were able to continue being produced and sold without having to meet the comprehensive and stringent data requirements demanded from new substances. In other words the notification requirements for new substances affected primarily the companies that were bringing out new products, those that innovated.

REACH has been the object of a great deal of debate - a key point is the uncertainty of the economic impact of the legislation. Industry claims an impending calamity and the Politicians claim to be saving the world. What is certain is that the 20+ years of new substance notification (and the impacts of other disastrous pieces of EU legislation - see box) have had a major impact on the EU fine chemicals industry: in order to avoid the restrictions, the manufacture of R&D products (and commercial Pharma products in general) slowly moved out of the EU - as a result Swiss process chemistry has grown tremendously; many Italian firms moved operations to Spain, Mexico or the USA; kilo-labs and pilot plants mushroomed in the USA and Canada - and India and China became the commodity workhorses of the generics industry in less than a decade. The Orient's success is the West's fine chemicals industry demise.

It is obvious that the European Commission has finally realized that the Golden Goose is moribund and has - half-heartedly- decided to do something about it. Pharma is probably the one industry that will be far better off with REACH - indeed the lower limit hurdle for testing R&D intermediates is no longer set at 10 or 100Kg, it will be 1 ton with multiple waiver opportunities. Furthermore during the commercial phase, if sold to few manufacturers under long term agreements, intermediates may also enjoy substantial relief.

So if the past is any measure of the future, my belief is that more clumsy regulation will add to the long list of handcuffs before common sense prevails. By then it will be too late. REACH will probably be Law in 2007 – then, 30.000 substances (say, most of the Aldrich Catalogue) will either have toxicity data generated (costing from $100.000 to more than a million apiece), or, they will be available in India, China, Japan or America at no extra cost.

Whenever the side-effects of these "save the world laws" are pointed out to the responsible EU Commissioner – Industry does not even get a response (see Wallstrõm letters in **www.http://www.hovione.com/about/default.htm** press room/press releases). The current explosive growth of the chemical industry in the Far East is directly proportional to the hollowing out of the European industrial capacity. Whilst we have high-technology and HSE compliant industrial grave-yards and excellent professionals out of work, China's chemical industry's explosive growth seems to be going hand-in-hand with a horrendous increase in the number of tragic accidents involving fatalities and serious environmental damage.

A BLEAK FUTURE FOR THE TECHNOLOGIES OF TOMORROW

The negative impact is not only on traditional areas of science (chemicals, fertilizers, polymers, paints, etc..) but also in the knowledge based activities of the future - the same industries that Brussels claims to be promoting and encouraging. The same European fine chemicals industry that is being attacked is also the workhorse of modern biotechnology. Do Brussels politicians and bureaucrats know that whenever a NASDAQ biotech invents a new cancer drug, a new HIV fusion inhibitor, a new peptide or a new oligonucleotide the development and the production of the active ingredient takes place in Europe? Europe has 90% of the world's merchant industrial capacity for all these new technologies - those very jewels of the European Industry that every day face a tougher regulatory environment. This is sad, if not ironic, for the valleys of the rivers Rhine and Rhone are both the cradles of chemistry and of the CECA and the EEC, the precursors of the EU.

As Europe legislates its fine chemicals industry out of business, it also fails to grasp the opportunities that would level the playing field, benefit the European population and support its industry. For example global guidelines on Good Manufacturing Practices (GMPs) – ICH Q7a – have been established for Active Pharmaceutical Ingredients (APIs). These were ratified into national laws and regulations in Europe well after the USA, Japan, Australia and Canada had done so. Unfortunately Europe has no FDA style comprehensive inspection system for enforcing these GMP guidelines. As a result pharmacies in Berlin, Madrid and Athens can dispense medicines made with active pharmaceutical ingredients produced in factories in Inner Mongolia, Hyderabad or Shanghai that were never the object of an inspection by a European official. The loop-holes in the EU's equivalent to the FDA Drug Master File system are also glaring: a Hamburg trader can be the holder of a "certificate of suitability" for an API and use it in the drug approval process.

Europe has the best API plants, and the best talent in API Science and GMP - our compliance record as measured by FDA may well be better than that of US based plants (e.g. FDA warning letters, fines, consent decree situations, etc..). European producers are competitive when supplying the USA, but see their own home market being conquered by cost-competitive Far Eastern firms - these are producers that would for the most part be excluded from the EU market if there was any enforcement of GMP standards in API production.

THE EU NEEDS AN EQUIVALENT TO THE FDA'S FOREIGN INSPECTION SERVICE

When will the EU have an equivalent to the FDA's Foreign Inspection Service? The EU must establish and fund such a service under a central EU agency – the EMEA comes to mind. The member states can continue supervising secondary manufacture, however API plants are far fewer, they are technologically far more complex and must face a level playing field of compliance. Only a centralized, well-funded service drawing on the most experienced inspectors the Member States have to offer could make this possible. API manufacturers whether located inside the EU, or exporting to the EU, must meet the ICH Q7a criteria appropriate to the type of compound (oral, injectable, etc..) and the inspection must be traceable to the specific product's CEP/DMF. Without such an inspection system in place the EU cannot responsibly claim that our pharmacies consistently provide high quality products. With no enforced level-playing field our API industry will be at a systematic disadvantage and will not be able to survive.

Sadly for the moment the only legislation coming out of Brussels seems bent on turning valuable assets into industrial graveyards and squandering know-how and expertise. Mr. José Manuel Barroso, the new President of the EU Commission, tells us he has a Dream: the Lisbon Agenda will make the EU the most competitive economic block in the World by the end of the decade. He could start by taking the lead out of our running shoes.

SPC "The Supplementary Patent Certificate" is probably the one piece of Brussels legislation that has had the most far-reaching and damaging effect to the EU pharmaceutical fine chemicals industry – virtually crippling Italian and French firms.
IPPC – The "Integrated Plan for Pollution Control" deals with very valuable HSE issues, the very same ones that the voluntary Responsible Care® industry program started to address in 1984. The format of this legislation is better suited to continuous process industries (such a refineries and large volume commodities like polymers), indeed for a batch-production industry of very high value, low volume and difficult to forecast products and sales, the IPPC amounts more to a set of hand-cuffs that limits flexibility and hurts speed – key attributes of competitive firms.
More info in *Legislating to Death* in **http://www.hovione.com/h_press/Legislating_to_death.pdf**