An EU Regulator's Viewpoint on Why Regulatory Guidelines Should Not Be Followed

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Medicines and Healthcare Products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

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Every Day When I Wake Up

I Thank The Lord I'm Welsh

MHRA
Regulating Medicines and Medical Devices

Medicines and Healthcare products Regulatory Agency (MHRA)

An executive agency of the Department of Health

Medicines and Healthcare Products Regulatory Agency

What is the MHRA?

- The MHRA is:
- an executive agency of the Department of Health
- regulates the safety, quality, effectiveness & performance of medicines and medical devices
- employs over 800 people
- is largely funded by fee income from provision of services to industry
- runs scientific committees which advise Ministers on safety of devices and medicines
- is mainly based in Central London

What are the MHRA Objectives?

- to protect public health
- to provide authoritative information
- to influence international regulation
- to support innovation and the development of medicines and medical devices
- to keep the cost of regulation as low as possible
- to make fact based, decisive judgements which are in the interests of patients and consumers

What does it do?

- ensures that medicines sold in the UK for human use are safe and effective
- ensures that medical devices – from heart valves to walking frames – are safe and meet performance standards
- promotes the safe use of medicines and medical devices
- promotes an understanding that there is an element of risk in all medicines and ensures that the benefits of licensed medicines outweigh the risks
- ensures that labelling and guidance are provided so patients are made aware of any risk and of proper usage

How does the MHRA Carry Out Its Responsibilities?

- operates a system of licensing, classification, monitoring and enforcement to ensure medicines for human use sold in the UK are safe, effective and of a high standard
- manages the system for regulating medical devices to ensure that they are properly tested before being made available to the public
- manages a system for monitoring suspected adverse reactions
- maintains processes to alert doctors and pharmacists if medicines or medical devices do not perform as they should
- takes enforcement action when things go wrong
- represents the UK on international bodies which work to set consistent standards for medicines and medical devices world wide

What Are Its Current Challenges?

- to be **more accessible** in order to meet increasing demands from patients and the public for more information
- to provide even more **timely responses** to health professionals and the industry
- to be more **transparent**, within the limits set by the need for confidentiality
- to be seen to be always **acting in the best interests of patients and consumers**

The MHRA fully supports the NC3Rs. MHRA staff attend the workshops and contribute to many projects.

The MHRA has direct and indirect links with other organisations working in the field of predictive toxicology.

The MHRA welcomes discussions with parties seeking to improve drug development/drug safety procedures.

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MHRA

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Home › **Pharmaceutical industry**

Pharmaceutical industry: A one-stop resource

Printer friendly version (new window)

Welcome to the pharmaceutical industry area of the MHRA website. This section, which has been developed following feedback from users, provides targeted links to information throughout the site, as well as content relevant to the industry.

If you have any feedback on this section and how we can improve it please fill out our feedback form .

There is a link at the top of every page of the MHRA website which links directly to the new section.

News and hot topics

17 Feb 2011 | Best Practice in Reporting of Individual Case Safety Reports (ICSRs)

We have today published guidance for industry that sets the MHRA's position on how to code adverse drug reactions (ADRs) to a high-quality standard for entry into our Sentinel database. This 'Best Practice' guide has been developed combining ideas from both industry trade associations and the MHRA.

16 Feb 2011 | Department of Health announcement about the regulation of herbal practitioners

Contacting the MHRA

This page provides links to information about how to contact the MHRA. It also includes an escalation procedure for industry to resolve any issues informally.

Go to the contacting the MHRA page

Legislation, guidance and policy

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The Role of the Regulator

The Drug Regulator's Tightrope Walk!

Protect public health …

… against negative consequences from unsafe or ineffective medicines.

When in doubt, be negative, "we need more information"

… against negative consequences from failing to meet unmet medical needs.

When in doubt, be positive, "it might be a patient's only hope"

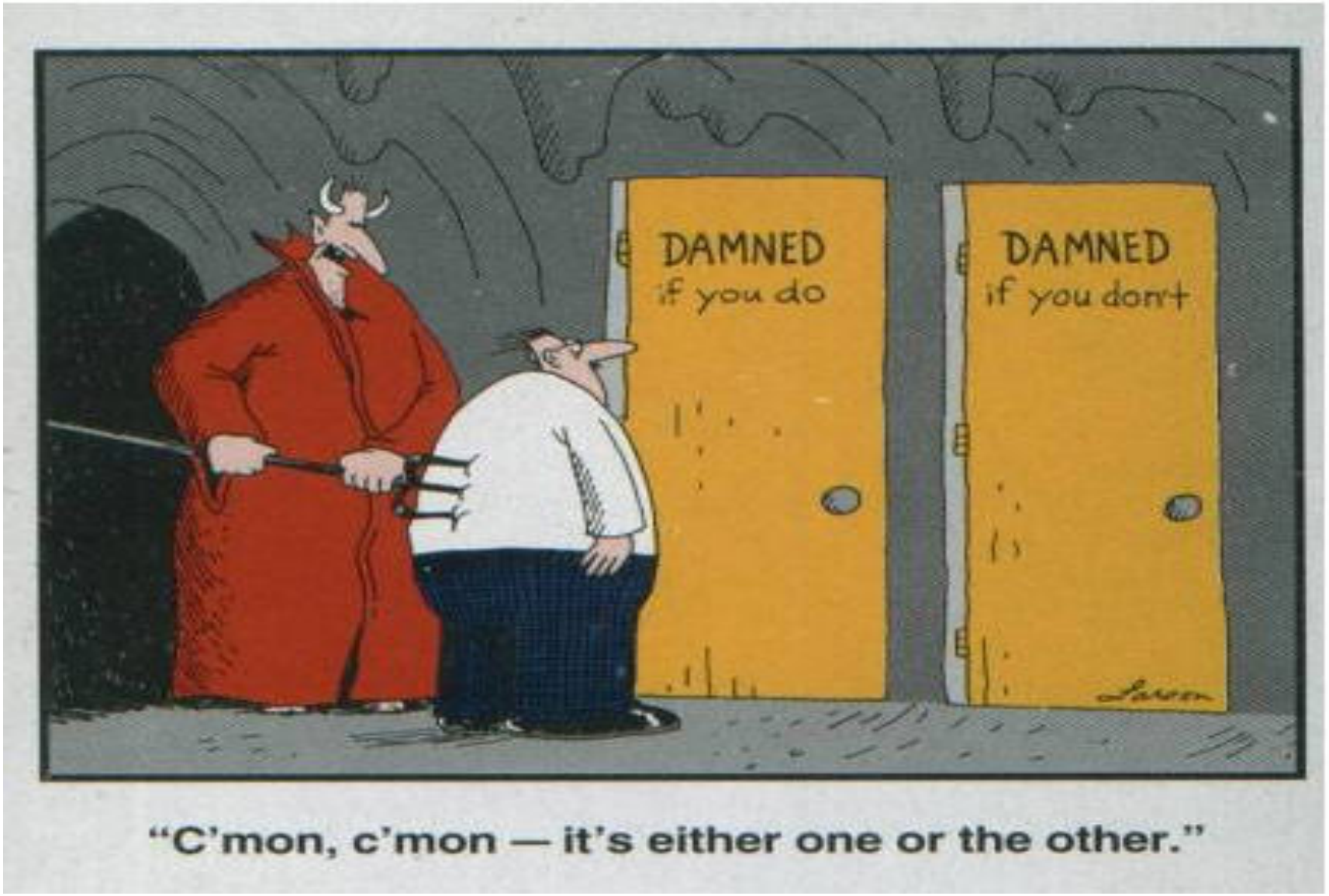
no penalty for being negative!

Are the (dis-)incentives balanced right to influence regulators' behaviour?

What are the consequences?

What are the consequences?

or put another way…..


DAMNED
if you do
DAMNED
if you don't
"C'mon, c'mon — it's either one or the other."

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Enough of my problems….

Let’s turn to yours ☺

Regulatory Guidelines

Regulatory Guidelines are not new!!

The earliest reference to medical regulation in the UK dates from 1421, when physicians petitioned parliament to ask that nobody without appropriate qualifications be allowed to practise medicine. The doctors said that unqualified practitioners caused "great harm and slaughter of many men".

The control of medicines by officials in the United Kingdom dates back to the reign of King Henry VIII (1491-1547). The Royal College of Physicians of London had the power to inspect apothecaries' products in the London area and destroy defective stock.

The Royal Commission, after long deliberation, issued a report in 1912 calling for a minimum set of experiments to be conducted prior to using a new medicine. The proposed Act was due to go before Parliament in 1914, but WW1 intervened!

Sadly, unfortunate events have catalysed the development of medicines regulation throughout the world more than the evolution of a knowledge base!!

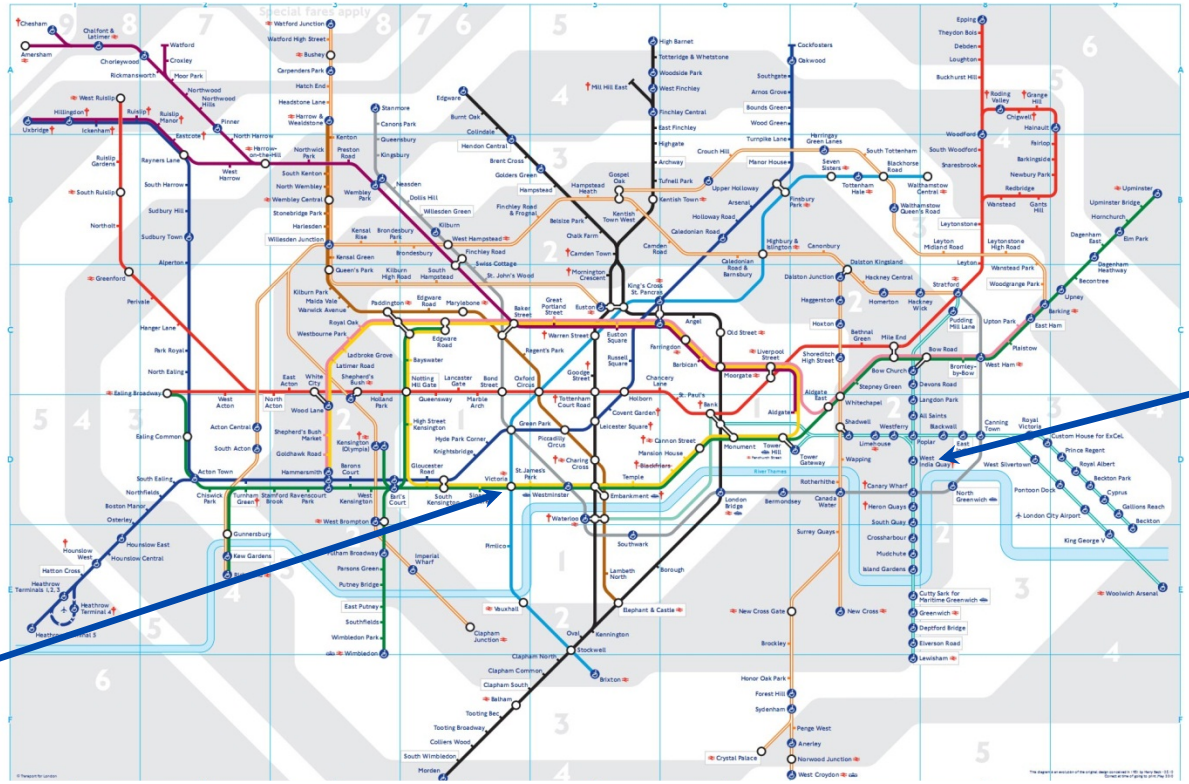
As a result of the Thalidomide tragedy in the late 1950s/early 1960s, the whole regulatory system was reshaped in the UK where a Committee on the Safety of Drugs (CSD) was started in 1963 followed by a voluntary adverse drug reaction reporting system (Yellow Card Scheme) in 1964.

In the United States, The Drug Amendments Act of 1962 was passed by Congress requiring the FDA to approve all new drug applications (NDA) and, for the first time, demanded that a new drug should be proven to be effective and safe.

The need for harmonisation of drug regulations came after preliminary contacts between officials from Japan, EU and US, discussed during the International Conference of Drug Regulatory Authorities in 1989.

These discussions revealed a need for the harmonisation of requirements relating to the new innovative drugs and led to the establishment in 1990 of the International Conference on Harmonisation of Technical Requirements for the Registration of Pharmaceuticals for Human Use (ICH), a collaborative initiative between the EU, Japan and the United States with observers from WHO, EFTA and Canada.

ICH meetings are still held twice a year.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Regulatory guidelines are like the modern map of the London Underground.

They don't completely represent the "real" world.

There's almost always more than one way to reach an objective and the recommended route might not be the one you should follow!

NEVER FOLLOW A REGULATORY GUIDELINE IF THERE IS A GOOD SCIENTIFIC RATIONALE NOT TO!!!

- General points:
  - Guidelines are generally written in order to provide an element of flexibility and not to place undue legislative restraints on scientific progress.

  - All studies should be conducted according to acceptable current protocols. Each study should be planned and designed taking into account the properties and indications of the drug concerned.

Regulator's HATE:

Applications where studies have been conducted "because that's our company's normal strategy"

Applications where it appears little or no thought has been given to the rationale for some studies.

Applications where studies were conducted even though there were strong scientific reasons not to do so.

A Rigid Adherence to Good Science is Far More Important than a Rigid Adherence to Regulatory Guidelines.

Projects should be designed by the Scientists rather than the Regulatory Affairs “Professionals”

Your Regulatory Affairs personnel probably do not know what Regulator’s think!!

Problem Areas and How to Resolve Them

Scientific Advice!!

Risk comes from not knowing what you're doing!

Warren Buffett

The MHRA, and many other EU Member States, have, for many years, provided scientific and regulatory advice to sponsors.

Scientific advice can be requested during any stage of the initial development of the medicinal product (before submission of a marketing authorisation application), and also during the pre-submission period for a variation to an existing marketing authorisation.

Meetings can also be held with the MHRA to discuss pharmacovigilance, advertising, proposal changes to labelling or package leaflets or post-authorisations regulatory advice relating to a product range.

The MHRA prefers to meet face-to-face with companies but in exceptional circumstances, video-conferencing may be arranged.

Telephone and tele-conference meetings are generally not considered satisfactory to discuss complex scientific and regulatory issues.

The MHRA Licensing Division held about 350 Scientific Advice meetings with Companies in 2013.

The MHRA Clinical Trials Unit has held almost 110 meetings with companies, academic institutes or hospital groups over the last 12 months!

The CTU's email helpline fields about 250 queries a month.

Scientific advice can also be obtained from the CHMP.

The Scientific Advice Working Party (SAWP) has been established as a standing working party with the sole remit of providing Scientific Advice and Protocol Assistance to applicants.

It is the SAWP/CHMP responsibility to give Scientific Advice to industry by answering to questions based on the documentation provided by the company in the light of the current scientific knowledge.

In addition, time permitting, the SWP occasionally invites/accepts offers from organisations wishing to discuss new paradigms in drug discovery/development.

SWP members also participate in numerous organisations/ initiatives in the all fields of toxicology.

You don't have to listen to Regulators… but it does help!

We do get fed up making the same comments to the same Sponsors/Applicants!!

We do like it when people take notice of what we've said.

Actually, Regulatory Affairs people do not ALWAYS know how Regulator's think!

However, don't be afraid of standing up for yourselves if you're certain you're right! (just be careful how you tell us that we're wrong).


AND THAT'S MY LAST SLIDE. ANY COMMENTS?
Dilbert.com DilbertCartoonist@gmail.com
YOU STOLE AN HOUR OF MY LIFE. SOMETHING INSIDE ME DIED. I WILL NEVER HAVE ANOTHER GOOD DAY.
zzzz
12-7-11 ©2011 Scott Adams, Inc./Dist. by Universal Uclick
I WENT IN WITH LOW EX-PECTA-TIONS.
AVOIDS THE DELUSION THEY WANT TO LISTEN TO YOU!

Any Questions ?

Don’t be shy!

There’s no such thing as a silly question to a Regulator!

And I promise I won’t take note of your names!!

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Any Further Questions ?

Please Feel Free to Contact the MHRA If You Have Any Further Queries:

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