John R. Senior, M.D.
Associate Director for Science (Hepatology)
Office of Pharmacovigilance and Epidemiology,
Center for Drug Evaluation and Research, FDA

Click to view Biosketch and Presentation Abstract
or page down to review presentation
Ideas Building Upon Ideas ---

*but do it correctly, if possible*

John R. Senior, MD
Associate Director for Science (Hepatology)
Office of Pharmacovigilance & Epidemiology
Center for Drug Evaluation and Research
Food and Drug Administration

18 March 2015 – DILI Conference XV
University of Maryland, College Park Marriott
The theme of this conference is ---

“The Importance of Getting It Right”

--- not just numerical variables and methods for measuring them, and the definitions of diseases and terms ---
--- but also communication of ideas --- do we make ourselves clear, express concepts well and do others understand us?
An old idea (*paraphrased by many)*...

"Those who cannot remember the past are condemned to repeat it."

The Life of Reason, vol. 1; 1905
George Santayana (1863 – 1952)

"Those that fail to learn from history are doomed to repeat it."

House of Commons, 16 November 1948
Winston Churchill (1874 – 1965)
To test this point, I did a little exercise, a little experiment on communication of written ideas in the literature...

About two years ago, I was asked to write a chapter for the second edition of a book on “Anti-Targets II,” to focus on development of ideas concerning drug-induced liver injury, I was not inclined to accept but finally did when they promised to make my chapter publicly available at no cost ...
I drafted a chapter entitled “DRUG-INDUCED LIVER INJURY: CLINICAL AND DIAGNOSTIC ASPECTS”

--- In it I cited 52 references published from 1763 to 2014, many of whose authors were no longer living, but for 19 of the papers with a total of 92 listed authors, I searched out their e-mail addresses;

--- I also ferreted out pdf copies of those papers, aided by the FDA medical librarians;

--- to the authors whose email addresses I could find, I sent, about two months ago, an unapproved proof copy of my paper and a full copy of their published paper.
They were asked the following two months ago:

I should like to conduct a little experiment, and request your assistance. --- I attach a corrected proof copy of a chapter that I wrote recently, and in it I cited your paper [nn] and enclose a copy. Please see if I have correctly captured what you and your co-authors wrote. --- Also, you and I may have both cited some of the same references; I ask if you think I cited them correctly.

This experiment is aimed at understanding each other in what we write. The medical literature builds ideas upon ideas over time, and I think we should strive to get it right in what we write. I shall comment upon the results of this experiment on 18 March (see program).
Scoring Scale for Responses

0) No response
1) Right on; you got it right, understood what we meant
2) No objection; close enough
3) Not quite right; you didn’t fully grasp what we meant
4) Wrong! You missed the point, misquoted us
5) Perhaps we should have explained it more clearly
6) Other comment or non-answer
RESULTS – 1 (to January mailing)

0) 10 no response at all – grade 0
1) 4 right on, you got it right – grade 1
2) 1 close enough, about right – grade 2
3) 2 not quite right, you missed a fine point – grade 3
4) 0 wrong, you misquoted us – grade 4
5) 0 I (we) should have explained better – grade 5
6) 2 other comment – grade 6

7) 19 total
The response rate was rather poor, as indicated above. Appreciating that people are busy, and may be disinclined to respond to survey-like questions,

.... I tried again a month ago in February, giving the partial results, more specific request (please use the rating scale), and found 10 more email addresses...
RESULTS – 2 (to February mailing)

0) 14  no response at all – grade 0
1) 9 right on, you got it right – grade 1
2) 1 close enough, about right – grade 2
3) 2 not quite right, you missed a fine point – grade 3
4) 0 wrong, you misquoted us – grade 4
5) 0 I (we) should have explained better – grade 5
6) 3 other comment – grade 6

29 total
CONCLUSION

So my little experiment was a bust. It really didn’t work. But I learned a lot from doing it --- the careful review of what others had written, the close attention and effort to summarize that and then to try to express it clearly and in logical sequence.

I don’t think ‘ll do it again that way, but maybe in some other way. But I learned that:
1) it was good to get in the habit of obtaining full copies of papers others had written and published,
2) and read them carefully before citing them.
“I have not failed. I’ve just found 10,000 ways that don’t work.”
Thomas A. Edison (1847-1931),

“Brilliant Blunders: Colossal Mistakes by Great Scientists That Changed Our Understanding of Life and the Universe.”
(... Darwin, Kelvin, Pauling, Hoyle, Einstein)
Mario Livio, 2013
The messages of this exercise I take as: Even though we keep trying to learn from and remember, and to avoid, mistakes made by others in the past . . .

... *that may not be enough.*

It is almost certain, at least very likely, that we shall make *new* mistakes and have to learn *new lessons.* We should not expect necessarily to get everything right the first time, or the second, ... or the nth...

There is to be lots of room for humility in the broken path to new, better scientific understanding, as we stumble forward and keep trying.
I close with an example of patient, repeated effort to seek the truth, to keep asking, about the challenging question of what processes are the most frequent causes of acute liver failure, at least in adults in the United States ... from Dr. Will Lee, of Dallas, who today is on service and unable to be here with us.
Etiology of Acute Liver Failure in the USA
Adult Registry (n = 2,224)

ALF Study Group, Jan 2015