



21 June 1999 5717 '99 JUN 30 P1:44

Jane E. Henney, M.D.
Commissioner
Food and Drug Administration (HF1)
Room 14-71 Parklawn Bldg.
5600 Fishers Lane
Rockville, MD 20857

Dear Dr. Henney:

As your assistant suggested when I called on Friday, 18 June 1999, I am writing to you to express my dismay with the inaccurate "summary" that CDER made of the remarks presented to them in my formal presentation at the FDAMA Stakeholders Meeting held in Philadelphia, PA on 28 April 1999.

In order for you to see my concern, CDER's summary of that presentation, my summary thereof, and a copy of the transcript of said remarks have been included for your review. As you will see when you review the presentation transcript, the presentation parallels the letter I sent to you back in May of 1999.

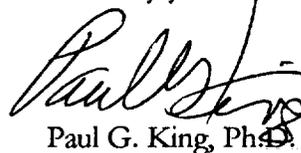
Though I understand that no Agency likes criticism, any summary of any formal criticism should, nonetheless, accurately reflect the comments made.

As you can see from my concerns are also being submitted to the appropriate docket (99N-386). In addition, copies are being sent to my congressman and senators.

Should you wish to discuss any of this matters further with me or need more specifics in any area, then, I would be glad to arrange a time where we could meet (along with any others you felt would be needed) and discuss the issues that have been raised in more detail.

Finally, let me thank you in advance for taking the time to read and reflect upon this letter that I trust you will take.

Sincerely yours

 21 June 1999
Paul G. King, Ph.D.

c.: Congressman Rodney P. Frelinghuysen, Senator Frank R. Lautenberg and Senator Robert G. Torricelli with all enclosures

Enclosures (The CDER Summary, my summary in docket submission form, and a partial transcript of my formal remarks at the CDER FDAMA Stakeholders meeting on 28 April 1999 in Philadelphia, PA)

Dr. King v 33 Hoffman Avenue v Lake Hiawatha, NJ 07034-1022

99N-0386

LET 1

**U.S. Food and Drug Administration Center for Drug Evaluation and Research Conversation with Stakeholders
Temple University School of Pharmacy Philadelphia, April 28, 1999**

Center Director's Report

Center Director Janet Woodcock, M.D., opened the session by reviewing the state of drug regulation and CDER's current level of performance for the 96 attendees. She reported that CDER's core programs, especially in the area of premarket review, are performing efficiently and effectively. She referred the audience to statistical information contained in the CDER 1998 Report to the Nation: Improving Public Health Through Human Drugs (<http://www.fda.gov/cder/reports/rptntn98.pdf>). User fees have resulted in more new drug approvals with the peak in 1996. She noted that approvals for new uses of existing drugs have doubled in the last three years compared with the previous three years, indicating that firms are continuing to conduct studies on drugs once they are marketed. The generic drug program helps improve the affordability of medicines through competition. This program area does not receive support from user fees; but, through streamlining processes, it has reduced approval times from three and a half years to 18 months.

Dr. Woodcock also reviewed the Center's performance in the post-market surveillance programs for prescription drug advertising and promotion, adverse events involving drugs and product quality. Efforts at international harmonization are an important step to setting up a worldwide safety system. Consumers can be assured that drug product quality is very high in United States.

In the area of drug safety, she rejected the notion that shorter approval times have compromised review standards and led to an increase in drug withdrawals. There is evidence that CDER currently performs a higher quality review than previously when it was accused of taking too long to review drugs. For example, the number of patients studied has grown, drug recalls are down, and withdrawals are fewer than in previous decades. In other areas, she reported on the transition to an electronic review environment, noting that the equivalent of 12 million pages of paper were submitted last year electronically. One area for improvement is making better use of regulatory research. The Center met its deadlines related to the FDA Modernization Act of 1997.

Stakeholder Presentations

Paul G. King, Ph.D., a consultant, expressed his views on FDA inspections of current good manufacturing (CGMP) practices. He disagreed with current FDA practices and called for strict enforcement of all CGMP regulations, continual training of FDA inspectors and batch release testing.

Lorna Totman, Ph.D., director of scientific affairs, Consumer Healthcare Products Association, pointed to the "remarkable success story" of switching about 80 drugs from prescription only sales to over-the-counter sales. The law doesn't say how FDA should make the decision if a drug can be sold over the counter. Consequently, each decision is made on a case-by case-basis, with the FDA demanding more complex data to justify each switch. She called for the Center to identify in advance the kinds of high quality safety studies needed to switch a drug's status. For example, she said that CDER's guidance on hypercholesterolemia effectively blocks OTC switches of cholesterol-lowering drugs. She called on the Center to amend its guidance by identifying specific questions that could be investigated scientifically and would provide evidence for safely switching cholesterol-lowering drugs to OTC status. She encouraged joint workshops with associations and industry with the goal of addressing current problems. Jointly developed meetings help FDA benefit from scientific expertise in industry.

CDER/FDA Panel Discussion

Ways to improve communications about the risks and benefits of drugs were the top issues raised during the audience participation portion. Issues were discussed by a CDER/FDA panel consisting of Dr. Woodcock; Susan Setterberg, Mid-Atlantic Regional Director; Douglas Ellsworth, New Jersey District Director; and Nancy Smith, Ph.D., Director, CDER Office of Training and Communications (OTCOM). Linda Brophy, OTCOM Associate Director, moderated the question and answer session. Issues raised in open discussion included the pros and cons of direct-to-consumer advertising, improving communications for consumers and health care professions about the risks and benefits of drug therapy, and setting priorities for the FDA's limited inspection resources that most effectively meet public health and safety needs.

Paul G. King Consulting

SUPPORT IN CHEMICALS & PHARMACEUTICS

Friday, 18 June 1999

Documents Management Branch [HFA-305]
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

RE: Docket No. 99N-0386

FORMAL COMMENTS TO:

Docket Number : 99N-0386

Comments: Speaker's Response To The Summary Miss-characterization Of My Comments As Made In the FDAMA Stakeholders Meeting Held On 28 April 1999 On The Campus Of Temple University In Philadelphia, Pennsylvania.

On "5/21/99," CDER published a "Summary for CDER" in the FDAMA Docket 99N-0386.

In spite of the fact that both of the "stakeholder" speakers spoke for about the same time, the summary document "summarized" my comments in one-fourth the space given to the comments made by the other presenter, Dr. Lorna Trotman.

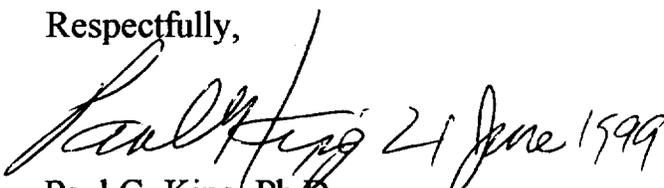
Moreover, while the summary of Dr. Trotman's presentation accurately reflected her comments, the summary of my comments was, to say the least, not accurate.

The following page contains my summary of my comments. In order to be fair, I have restricted them to the same "space" as given to Dr. Trotman's comments.

Please post the following document to the docket with the title "Dr. King's CDER FDAMA Remarks Summary."

Thank you.

Respectfully,


Paul G. King, Ph.D.

Paul G. King Consulting

SUPPORT IN CHEMICALS & PHARMACEUTICS

Dr. King's Summary Of His FDAMA Remarks At PA Meeting

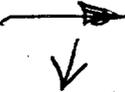
Paul G. King, Ph.D., a consultant, expressed his views on the FDA and the drug industry that it regulates. He began by stating that it is both wrong and illegal for CDER not to comply with the FDC Act's "must" that all drug establishments be inspected by CDER at least biannually. He then noted that an Agency that disregards the law should not be surprised that the drug industry does the same and worse. Next, he observed that CDER lacks any metric-based proof of the competency of its inspection, review and management personnel. He then outlined a training- and assessment- based approach to correcting that deficiency so that their requisite competencies could be established in both the requirements of the statutes and regulations they administer and the basics of inspection science and statistics appertaining thereto. He then suggested that all approved and pending drug applications should be audited and shown to provide scientifically sound proof that they meet the strictures of CGMP regulations because his experience is that this is often not the case.

Paul G. King
2/19/99

**FDAMA Stakeholder Meeting
Wednesday, 28 April 1999 In Philadelphia, PA**

1 with the outside world, we're doing
2 them, but we certainly aren't doing them
3 at a high level. So, I think our report
4 card is mixed but for our core, we're
5 performing very well. We face numerous
6 challenges as the world changes and as
7 our job is somewhat redefined and we
8 invite your suggestions and comments,
9 and that is really one of the purposes
10 of this meeting. So, I thank you for
11 your attention.

12 LINDA BROPHY: Thank you,
13 Janet. She certainly has given us a
14 context to have a conversation.
15 The next section of our
16 discussion this afternoon, we'll hear
17 from two of our stakeholders. We have
18 two stakeholder presentations.
19 The first is Dr. King, who is a
20 consultant from Paul G. King Consulting,
21 and he has come to speak to us for about
22 ten minutes.

 23 PAUL G. KING: Well, I want to
24 thank everyone for letting me have the

**FDAMA Stakeholder Meeting
Wednesday, 28 April 1999 In Philadelphia, PA**

27

1 chance to say a few words. I guess I'm
2 a contrarian in many respects.

3 Let me just start off by saying
4 I'm not speaking for myself, I'm not
5 speaking for industry and I'm not
6 speaking for the agency. I'm speaking
7 for the people who watch their children,
8 parents and friends suffer from the side
9 effects of the agency's failure to
10 protect the public from those in the
11 pharmaceutical industry, whose greed
12 outweighs their concerns for the public
13 health. That's who I'm speaking to.

14 As a consultant, time and time
15 again, I have witnessed FDA-regulated
16 companies, large and small, deliberately
17 not comply with a law or regulation
18 simply so they could make more money.
19 They have done this because their
20 management was, and is, confident that
21 they will get away with their
22 noncompliance — or, if caught, profit
23 more than their overall cost. Though my
24 heart goes out to the FDA in many

**FDAMA Stakeholder Meeting
Wednesday, 28 April 1999 In Philadelphia, PA**

28

1 respects, its decision not to inspect
2 every drug establishment as often as
3 required by law is not only wrong, it's
4 illegal.

5 Beset by priorities, loss of
6 many knowledgeable personnel under REGO,
7 and underfunded, the agency has
8 attempted to balance conflicting
9 priorities instead of holding fast and
10 protecting public health by strictly
11 enforcing all of the current CGMP regulations
12 for drugs.

13 Emboldened by an FDA that holds
14 itself above the law and overlooks the
15 industry's deliberate noncompliance with
16 certain regulations, many firms, under
17 the same cost and manpower pressures
18 imposed on the FDA,
19 have likewise reduced their compliance
20 program.

21 Given their agency's lead, why
22 should anyone be surprised that many of
23 the firms it regulates currently not
24 only ignore applicable laws and

**FDAMA Stakeholder Meeting
Wednesday, 28 April 1999 In Philadelphia, PA**

29

1 regulations, but are also pushing for
2 even more concessions?

3 For example, emboldened by
4 their success in getting the FDA to
5 ignore enforcement of key parts of the
6 drug CGMP's, the industry is now
7 pressuring the agency to allow skip-lot
8 testing, although they know full well
9 that the CGMP regulations explicitly
10 require the testing of each batch.

11 Instead of wasting time
12 considering such initiatives, the agency
13 again needs to begin rigorously
14 enforcing compliance with all of the
15 drug CGMP regulations.

16 This bring the public
17 face-to-face with a major flaw in the
18 science-based questions posed to the
19 stakeholders.

20 As Dr. Henney has recognized,
21 without knowledgeable personnel who
22 understand the true minimum requirements
23 of both the sciences and regulations
24 involved, the agency will continue to

**FDAMA Stakeholder Meeting
Wednesday, 28 April 1999 In Philadelphia, PA**

30

1 accept the pseudo science that some
2 firms submit as "valid science", and the
3 non-compliant or violative practices
4 that some firms are using.

5 Yet the reality today is that
6 agency personnel often lack the
7 education, training and/or experience in
8 the regulations they are supposed to be
9 administering or the fundamental
10 sciences that they're supposed to
11 understand, or both, required for them to
12 properly discharge their duties.

13 Beyond hiring people that have
14 the expertise it lacks and simply
15 "providing training", what should the
16 agency's course of action be today to
17 address these recognized deficiencies?

18 First, the agency needs to
19 initially and continually establish the
20 fundamental metric-based competency of
21 its management, review, inspection and
22 testing personnel in the applicable
23 requirements of the statutes and
24 regulations as well as the fundamentals

**FDAMA Stakeholder Meeting
Wednesday, 28 April 1999 In Philadelphia, PA**

31

1 of all aspects of inspection science and
2 statistics.

3 To do this, the agency needs to
4 provide continual training and
5 metric-based assessments of all such
6 personnel to assure that said personnel,
7 "A", understand the requirements of all
8 applicable regulations, "B", properly
9 assess the science submitted or applied
10 and, "C" determine that the science
11 submitted or applied is valid science
12 that truly meets the minimum
13 requirements of the current good
14 manufacturing practices regulations.

15 Second, before attempting to
16 expand its use of science, the agency
17 needs to ensure that all firms
18 incorporate fundamentally sound science
19 in all areas of their submission.

20 Minimally, all existing and
21 pending drug establishments submissions
22 need to be audited and shown to provide
23 scientific proof that, "A", their
24 in-process and batch-release

**FDAMA Stakeholder Meeting
Wednesday, 28 April 1999 In Philadelphia, PA**

32

1 specifications are such that they
2 assure, with a high level of confidence,
3 that every article in each releasable
4 batch will, if tested, comply with the
5 USP'S lifetime standards, but the law
6 requires that; "(B)" All critical control
7 points in each process step of each
8 batch of every product need to be
9 identified and properly controlled using
10 valid inspection plans; — most of the
11 inspection plans that I see are just
12 nonsense; "C", all samples tested are of
13 appropriate size and representative of
14 the batch from which they were taken;
15 and "D", the number of representative
16 samples tested is sufficient to satisfy
17 the statistical minimums required under
18 21 CFR 211.165(d) for validly
19 predicting the lifetime quality of each
20 batch — not just the present values for the
21 samples tested.

22 Third, until the agency can
23 provide the requisite in-depth ongoing
24 metric-based training of and establish

**FDAMA Stakeholder Meeting
Wednesday, 28 April 1999 In Philadelphia, PA**

33

1 the competency of each such employee,
2 the agency needs to seek out, learn
3 from, and rely upon written advice and
4 instruction but only from those outside
5 the agency who can prove that their
6 advice has applied sound science in
7 determining the true minimum
8 requirements for compliance with a given
9 drug CGMP as based supposedly on science.

10 It's amazing. I understand, as
11 a scientist, why the public in general
12 doesn't trust scientists. It's amazing
13 how cheaply some of us sell science to
14 make a buck.

15 The preceding is but a short
16 overview of some issues that this agency
17 must truly address if it wishes to
18 expand the agency's capability to
19 incorporate state-of-the-art science or
20 any science into its risk-based
21 decision-making and to facilitate the
22 exchange and integration of scientific
23 information to better enable the FDA to
24 meet its public health responsibilities

**FDAMA Stakeholder Meeting
Wednesday, 28 April 1999 In Philadelphia, PA**

34

1 throughout a product's life cycle if it
2 truly wants to protect the public.
3 In closing, let me thank the
4 agency for allowing me to speak to these
5 issues today. For those interested, my
6 formal response to all five stakeholder
7 questions is available on-line in the
8 docket, and also, there are 25 copies of
9 what I presented today, more or less, for
10 anyone who would like to have a written
11 copy. Thank you.