January 6, 2011

Food and Drug Administration
Division of Dockets Management (HFA-305)
5630 Fishers Lane, Room 1061
Rockville, MD. 20852

Re: **Docket No. FDA-2010-D-0319**
Draft Guidance for Industry and FDA Staff on Dear Health Care Provider Letters: Improving Communication of Important Safety Information

Ladies and Gentlemen:

Reference is made to the Federal Register Notice dated November 12, 2010 (Docket No. 2010-D-0319) requesting comments on the Draft Guidance entitled "Dear Health Care Provider Letters: Improving Communication of Important Safety Information".

In accordance with the above mentioned Federal Register Notice, Hoffmann-La Roche, Inc. / Genentech USA, Inc. (Roche) is herewith providing input/recommendations on the above mentioned Draft Guidance (see attached document).

Roche has collaborated extensively with FDA on reviews of safety information (subsequently leading to health care professional communications) originating from of our development programs and marketed products. We applaud the efforts being made by the Agency to promote a consistent approach to the content and overall formatting principles for US DHCP Letters. Streamlining this communication tool is of great interest to Roche as this provides for consistency and transparency in the information being provided to health care practitioners.

We would like to thank the Agency for the opportunity to provide comments and make ourselves available to clarify any points included in the attached communication.

Sincerely,

Ruben Diaz
Director, Regulatory Affairs
Hoffmann-La Roche Inc.
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RD/tc
Attachments:
HLR No.: N2011-00105

SUBMISSION OF COMMENTS
Dear Health Care Provider Letters:
Improving Communication of Important Safety Information
January 2011

COMMENTS FROM: F. Hoffmann-La Roche / Genentech USA, Inc. ("Roche")

GENERAL COMMENTS

1. FDA Consultation: A concern is raised regarding the time required to obtain feedback from such consultation. The current experience is that it can take months for some DHCPLs to receive feedback. For reactive letters regarding critical safety issues, this would be a problem. Furthermore, it is Roche's policy to issue DHCPLs in certain cases, e.g. when warnings are added to labels, even if a Health Authority says it is not necessary. DHCPLs remain a Company responsibility, and are often time-critical. If consultation with a review decision of FDA is expected, there needs to be a clear guideline regarding the timeline for such review, and an understanding that the company is ultimately responsible for the content of the DHCPL.
2. Expansion of Target Audience beyond Prescribers: Roche supports the principle of considering additional healthcare providers besides prescribers in the potential target audience for a DHCPL.
3. Length Limitation for DHCPLs / potential conflict with Fair Balance guidelines: Roche requests that the potential conflict between the recommended length and the fair balance guideline be explicitly addressed in the Guidance, preferably by keeping the recommendation for DHCPLs of two pages or less, and including a statement to "see enclosed Prescribing Information" in order to cover the fair balance provision.
4. Inclusion of Relative Risk Information (line 222): Absolute risk information is also necessary for understanding the nature of a safety issue. Take the use of human growth hormone (hGH) in childhood cancer survivors for example. Use of hGH raises the risk of a secondary cancer in such patients from 2% to 6%. It also raises the risk of a secondary tumour after bilateral retinoblastoma from 10% to 30% (based on a very small number of cases). Both of these represent a 3x increase in relative risk; however, by some individuals the first risk is considered acceptable while the second is not. Therefore, Roche agrees with the inclusion of relative risk information, if meaningful, and encourages the inclusion of absolute risk information for precise information as well.
5. Follow-up Assessment of DHCPL Impact: Since manufacturers are not responsible for assessing the practice of medicine and physician behavior with regard to other forms of healthcare provider communication such as prescribing information, it is inconsistent and unreasonable to expect a manufacturer to fulfill this role with respect to DHCPLs. This is the role of the local bodies which certify physicians and regulate medical practice (e.g., state licensing authorities and state medical boards). For certain critical issues where prescriber-to-manufacturer communication is necessary to ensure patient safety, the REMS mechanism may be more appropriate.

SPECIFIC COMMENTS	
1. Items could be presented as bullets with link to the respective sections	Section I, Line 27 – 29
2. Header typo: HDCP should be DHCP	Section III
3. Refer to General Comment #1: While consultation with the FDA review division is advisable, in light of the often urgent nature of the communication, the agency should establish a deadline for a response by the division to such proposed letters to ensure that the consultation does not become a cause for undue delay in issuing a letter. If the review division has not commented by the deadline, then the manufacturer should be authorized to proceed to disseminate the letter as submitted.	Section III
4. Ultimate responsibility around decisions to issue a DHCPLs remain with the manufacturers.	Section III, Line 71
5. Clarification is needed what "appropriate review division" of the FDA mean? 6. What is the specific process recommended by the FDA for this Consultation activity 7. What are the timeframes for consultation and issuance of the DHCP letter	Section III, Line 75 – 77:
8. Change in behavior: consider adding the following text "(e.g. discontinuation criteria, special monitoring in special patients groups, certain intake)"	Section IV, line 90
9. Suggest to add bullet points that cover the following: • Manufacturing complaints that may pose a health hazard to the patients • Preventive or mitigation actions added to Warnings	Section IV, A, line 107 - 113
10. Suggest to add bullet points that cover the following: • A change to any variables of an existing dosing algorithm	Section IV, B, line 124 - 127
11. Suggest to add a 2nd bullet as follows: • Source / nature of new information	Section V, A, line 152 - 156
12. Suggest adding the following text "…plus any impact to existing communication tools (e.g., USPI) specifically highlighting the impacted sections	Section V, A, line 153
13. This bullet doesn't seem to come back again in the more detailed description of content	Section V, A, line 154
14. Length Limitation for DHCPLs / potential conflict with Fair Balance guidelines. Please refer to General Comment # 3. The proposed guidance establishes a two page limit and proceeds to prescribe in some detail the format and contents of the DHCP letter, and requires a reference to the full prescribing information (which must be enclosed) and a medication guide or approved Patient Information, if any. Given the page limitation and the requirement to enclose a full PI, the FDA should clearly state that the body of the letter need not also include a customary statement of indication and important safety information or brief summary (fair balance). Save for discussions or references to that material in the body of the letter as the case may be, the enclosed PI should suffice for conveying the fair balance indication and important safety information.	Section V, A, line 159
15. Consider the following content layout: *1. Letter Heading* *2. Date (Month and Year)* *3. Subject Line – identifying DRUG NAME first, followed by the issue* *4. Addressees (Target Audience)* *5. The Body of the Letter* *6. The Interior Paragraphs*	Section V, A, Line 174 - 352

SPECIFIC COMMENTS	
7. The Final Paragraph *8. Types of Information That Should Generally Not Be in a DHCP Letter*	
16. Is the statement that FDA reviewed and agreed to the content important to the audience? As there is not enough clarity to expect a standardized approach, removal of statement is recommended.	Section V, A, Line 190 - 192
17. Replace "heading" with "date line"	Section V, A, Line 216
18. Suggest to add bullet points that cover the following: • Important Changes to the DRUG NAME Prescribing Information – Severe Renal Injury • New DRUG NAME Medication Guide	Section V, A, Line 227 - 233
19. DHCPL Target Audience: Please refer to General Comment # 2. While Roche supports the principle of considering additional healthcare providers besides prescribers in the potential target audience for a DHCPL, emphasis is being placed on the added burden on manufacturers to identify all HCP with prescribing privileges.	Section V.A.2./Lines 199-209:
20. See General Comment # 4: All relative incidences /frequency information should at least be accompanied by absolute numbers (e.g. risk doubled if 1/10,000 to 2 / 10,000), this "misinformation" should be avoided. Absolute numbers should be preferred. Roche agrees with the inclusion of relative risk information, and encourages the inclusion of absolute risk information as well.	Section V, A, line 222
21. Manufacturer agrees with making an effort to identify degree of risk.	Section V, A, line 260-264
22. It should be considered to provide the correct information first and afterwards the text to be corrected. Ideally with strike through of old wrong information and new text	Section V, A, line 300-301
23. Suggest to add bullet points that cover the following: • Reference to Sponsors website and Medial Information Department for further information on product	Section V, A, line 332 - 339
24. Assessment of the DHCP Letter impact: please refer to General Comment # 5. The last line of this paragraph should be deleted as it would in effect impose on manufacturers the responsibility for policing the practice of medicine which is the province of the individual state licensing authorities and state medical boards. The manufacturer's obligation should be limited to assessing whether the communication was received and the recipients were aware of the information.	Section VI. Lines 376-380: