



December 6, 2013

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

Comments of the Generic Pharmaceutical Association for Docket No. FDA-2012-D-0938-0027: Draft Guidance for Industry; Availability: Abbreviated New Drug Applications; Stability Testing of Drug Substances and Products, Questions and Answers.

The Generic Pharmaceutical Association (GPhA) acknowledges the efforts of the FDA on **Docket Number FDA–2012-D-0938-0027, in response to an FDA call for comments concerning Stability Testing of Drug Substances and Products.** Upon review GPhA and our members crafted several additional questions for consideration following the submission of our initial comments on October 11, 2013. We would also like to thank you for giving us the opportunity to share our thoughts on this important public health issue.

GPhA represents the manufacturers and distributors of finished generic pharmaceutical products, manufacturers and distributors of bulk active pharmaceutical chemicals, and suppliers of other goods and services to the generic pharmaceutical industry. Our members manufacture more than 90% of all generic pharmaceuticals dispensed in the U.S., and their products are used in more than one billion prescriptions every year. Generics represent greater than 84% of all prescriptions dispensed in the U.S., but only 27% of expenditures on prescription drugs. GPhA is the sole association representing America’s generic pharmaceutical sector in the U.S., while this response letter represents the views of the association these comments may not reflect all member company positions.

GPhA has reviewed the questions identified in the above referenced Federal Register Notice and has additional questions to pose to FDA:

- What criteria does OGD use to determine whether the change is deemed to be a “significant” change in the accelerated study samples or not?
- If scoring does not provide minimum dose as required by tablet score guidance, is the comparative dissolution profiling necessary?
- Should a dose dumping study be carried out on half tablets in the case of scored tablets?
- For PEPFAR products do we need to submit the ANDA with three or one batch requirement? “Fixed Dose Combination for PEPFAR” guidance states ANDAs require only one batch with 3 months stability data for submission. Please confirm if this



guidance (one batch with 3 months stability) should be followed when filing PEPFAR ANDAs.

- If bulk packaging product are being shipped, are applicants required to provide accelerated stability data at 0, 3, 6 months? If bulk products are only warehoused for repackaging, is RT stability data at 0, 3, 6 months required?
- If a bulk product is transported to the packaging site different from the manufacturing site, and the product packaged in bulk is not counted toward the 100,000 minimum, is the agency's expectation a stability study on the bulk product at 6 months controlled room temperature?
- In an original ANDA 100,000 units are packed in bottles and accelerated stability is provided. An alternate packaging site is also proposed. Is 3 month RT acceptable to support the proposed 3 month hold time for the future bulk that may be shipped to the alternate packaging site?
- If a drug is on a drug shortage list, can we submit 1 batch with 0, 1, 2 and 3 month accelerated data?
- What are the batch size requirements for extended release tablets and nasal and orally inhaled respiratory products?
- What level of detail on the 356h form is required for description of the type of testing to be performed by a test lab or internal site?
- If a firm finds out early during development that a product will be unstable at accelerated stability and can justify with RLD data will agency consider not doing accelerated stability for submission batches? Will the agency accept 6 months of intermediate and RT data instead? If yes what kind of expiration dating will be granted to the product?
- What are the batch size requirements for orally inhaled products or nasal sprays?
- Do primary batches have to have exactly the same process?
- The guidance states that ANDA submission batch samples should be stored for 1 year after approval of ANDA. Please clarify whether samples of each strength and each pack size should be retained for 1 year or samples sufficient for 5 time analysis will be sufficient which is similar to BE requirements.
- What is the extent of packaging required for parenteral test batches i.e., labeled and the secondary packaging need?
- Can a substantial amount of the primary stability batch be packed in bulk if bulk pack is not going to be a marketed pack?
- Is stability data at multiple orientations for topical solutions and semisolids required?
- What are the tolerances with respect to pull dates, i.e. how many days before or after the time point is it acceptable to pull the samples?
- For injectable products do we need sterility testing stability data at 3 months accelerated or long-term?



- Post June 20, 2014 will an ANDA be refused for receipt if there is an OOS at the 6 month accelerated time point if intermediate data is not submitted in the original ANDA?
- If the product fails stability at 3 month accelerated conditions do firms need to continue accelerated stability testing for 6 months?
- For ANDA products do we need to have the same shelf life as RLD? Can we propose a longer shelf life based on long term stability testing on the three exhibit batches?
- The Guidance states all batches for submission need to be produced at the same site. If there is an alternate site being submitted, does this mean three additional batches from the alternate site also must be submitted?
- Will FDA accept extension of shelf life to 36 months based on satisfactory updated long term data of 3 pilot scale batches submitted in ANDA?
- Is it acceptable to use API from 2 different approved sources in same batch of drug product?
- Is horizontal orientation for stability sufficient for products packaged in syringes?

Finally, we believe the FDA is the only regulatory body qualified to make the public health decisions regarding stability testing, and we support FDA's efforts to work towards the development of a clear and proven Guidance.

Sincerely,

A handwritten signature in black ink, appearing to read "D.R. Gaugh". The signature is written in a cursive, flowing style.

David R. Gaugh, R.Ph.
Senior Vice President for Sciences and Regulatory Affairs