



(February 18, 1997)

All NDA, ANDA, and AADA Holders

Dear Sponsors:

On November 30, 1995, the Scale-up and Post-Approval Changes Guidance for Immediate Release Products (SUPAC-IR) was published. Since then a number of questions have arisen in interpreting the Guidance as it applies to specific situations encountered or that could be encountered in the pharmaceutical industry. The purpose of this letter is primarily to share with you the questions that have been asked most frequently or that we consider the most significant. Also included are the Center's responses to these questions. The responses were developed and concurred with by the Office of New Drug Chemistry and Office of Generic Drugs, Center for Drug Evaluation and Research (CDER). We believe the sharing of the information will result in furthering the use of the Guidance to increase regulatory flexibility for industry.

In addition, the Center's Chemistry and Manufacturing Controls Coordinating Committee (CMC CC) has met and reconsidered two SUPAC-IR issues which have been of great concern and interest to industry. The following information on stand alone packaging operation site changes and stand alone analytical site changes represents a re-assessment of how SUPAC-IR should be interpreted on these issues.

#### **STAND ALONE PACKAGING OPERATIONS SITE CHANGES**

For immediate release solid oral dosage forms, a stand alone packaging operations site change, utilizing container(s)/closure(s) in the approved application, may be submitted as a Changes Being Effected supplement. The facility should also have a current and satisfactory cGMP compliance profile with FDA for the type of packaging operation in question before submitting the supplement. The supplement should contain written certification from the packaging facility stating that it is in conformance with cGMP's. If the facility has not received a satisfactory cGMP inspection within the previous two years for the type of packaging operation involved, a prior-approval supplement with the same commitment for stability is recommended.

The supplement should also contain a commitment to place the first production batch of the product on long-term stability studies using the approved protocol in the application and to submit the resulting data in annual reports. Where the product is available in more than one strength, size, or container/closure system, one batch of each combination should be placed on long-term stability studies. Bracketing or matrixing is allowed only if it has been approved previously by FDA. Any changes to an approved stability protocol should have a supplemental approval prior to the initiation of the stability study. Batches should be tested annually as per the stability commitments in the approved application.

#### **STAND ALONE ANALYTICAL TESTING LAB SITE CHANGES**

For immediate release solid oral dosage forms, a stand alone analytical testing laboratory site change may be submitted as a Changes Being Effected supplement, if the new facility has a current and satisfactory cGMP compliance profile with FDA for the type of testing operation in question. The supplement should contain a commitment to use the same SOP's and test methods employed in the approved application, written certification from the testing laboratory stating that they are in

conformance with cGMP's, and a full description of the testing to be performed by the testing lab. If the facility has not received a satisfactory GMP inspection within the previous 2 years for the type of testing involved, a prior-approval supplement is recommended.

The CMC CC and the Center intend that the SUPAC-IR Guidance will be revised to further clarify and update its recommendations and to assure good correspondence between these recommendations and those of other SUPAC documents in preparation. In the meantime, we hope these questions and answers will help clarify the application of the Guidance.

Sincerely yours,

/s /

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Enclosure

## **SUPAC-IR: QUESTIONS AND ANSWERS**

(To the extent these questions and answers provide guidance, that guidance was prepared by the Chemistry, Manufacturing, and Controls Coordinating Committee in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration. Although this guidance does not create or confer any rights for or on any person and does not operate to bind the FDA or the industry, it does represent the Agency's current thinking on questions related to the Scale-Up and Post-Approval Changes Guidance for Immediate Release Products (SUPAC-IR). An electronic version of these questions and answers are also available via Internet using the World Wide Web (WWW). To access the document on the WWW, connect to the CDER Home Page at <http://www.fda.gov/cder> and go to the "[Regulatory Guidance](#)" section.)

### **COMPONENT AND COMPOSITION CHANGES**

1. Q: May one color be replaced with another by placing the batch on concurrent stability and reporting it in the annual report?

A: A change from one color to another should be submitted as a prior approval supplement.

2. Q: Can color be changed under SUPAC-IR?

A: Yes. A change in color, either in amount or from one color to another, is a level 3 component and composition change which calls for a prior approval supplement. However, if the color is merely being removed, it is a level 1 change and can be reported in the next annual report.

3. Q: What is the full definition of a change in "technical grade" of an excipient? Does this only mean a change in excipient specifications that may impact functionality or does it include a change in supplier even if all applicable specifications remain the same?

A: Technical grades of excipients differ in their specifications and intended use. Technical grades may differ in: 1) specifications and/or functionality; 2) impurities; and 3) impurity profiles. If a supplier of an excipient changes but its technical grade AND specifications remain the same, the agency should be notified in an annual report.

4. Q: How does one apply SUPAC-IR to multifunctional excipients, e.g., starch?

A: SUPAC-IR composition changes are based on being able to define the use or action of the particular excipient in the product. This rationale should be included by the applicants as part of their original applications. Not all multifunctional excipients are listed in the guidance. However, if an excipient was utilized to provide multiple functions such as pregelatinized starch as a filler, starch as a disintegrant, starch paste as a binder, then the most conservative recommended change should be followed (e.g., for an excipient that is a filler, disintegrant and binder, the recommended limit for a Level 2 change is " 0.5 percent, see page 7, SUPAC-IR). An applicant may wish to add an explanation of how the change will affect other functions of the excipient in the product. If this information was not included in the original application, the review division should be consulted before filing such a SUPAC change, either through a CBE or annual report.

5. Q: What is the reference source for defining the action of an inactive ingredient, for example, lubricant versus glidant? What if the action is defined differently in two sources?

A: An applicant should be able to justify the choice and the basis for the selection of a particular excipient, i.e., its expected function in the drug product. It may be useful to cite a source. The action may depend on the specific product.

6. Q: Does SUPAC-IR cover changes in granulating solution volume outside the range in an application?

A: Changes in granulating solution volume are not covered under SUPAC-IR. Minor changes are considered as normal operating procedure and should be included in the executed batch record. However, if this represents a permanent change, such a change may be described in the annual report along with the data to justify that the formulation quality and performance (i.e., drug product is within the approved specifications) was not altered.

7. Q: To what category does a change in granulation solvent in a wet granulation process

belong?

A: A change in granulating solvent (e.g., alcohol to water) would alter the composition of the drug product, both qualitatively and quantitatively, even though it may be removed during manufacture of the drug product. Because such a change may have significant impact on formulation quality and performance, it is a level 3 composition change that needs a prior approval supplement.

8. Q: The NDA includes validated/approved ranges for excipients in the formulation. We would like to move the target formula amount of one of the fillers to the upper value in the range. Will this be a level 1 change in composition?

A: All changes are predicated on the target approved in the original application or through a prior approval supplement for a formulation change. For products approved with only a range for an excipient, the target may be assumed to be the mid-point of the approved range. If the new target is within the validated range, the change will be a level 1 or 2 change depending on the specific excipient changed and the percent change (see the SUPAC-IR guidance document). The target originally approved remains the target of record; i.e., Level 1 or Level 2 component changes made under SUPAC-IR do not change the target. If the new target is not within the validated range, the proposed target will need a prior approval supplement.

9. Q: When microcrystalline cellulose is increased by 5%, the tablet weight increases. Can this still be a level 1 change?

A: After the SUPAC-IR change, if the new target weight is still within the range in the approved original application, it is a level 1 change. Otherwise, it is a Level 2 or 3 change, both of which are to be submitted as a prior approval supplement.

10. Q: If one component in a formulation is decreased, must another be increased so that the final weight can remain the same?

A: No. The amount of a single component in the formulation may be changed independent of any other changes. (See 9 above)

11. Q: It is my understanding that the development report should cover ranges of processing parameters. Further, the validation report should cover the target parameters for production. If this is true, when level 1 changes are made, how can the validation cover ranges? For future validation reports, is it acceptable to vary processing parameters to prepare for future SUPAC changes?

A: The validation report should cover the target production parameters; however, it is not restricted to these only. If a range is specific, it needs to be validated. This can involve manufacturing batches of product at the extremes of the desired range(s), with appropriate testing to assure that the extreme range batches continue to meet all quality attributes, including dissolution and possibly in vivo bioequivalence tests. For future validation reports, it is acceptable to vary processing parameters. However, it should be understood that the Center's chemists do not review validation data collected by applicants, post-approval, on the first three production batches, because such information is checked by the Field investigators as part of the cGMP requirements. Thus, a summary of validation data on the test (bioavailability/bioequivalence) batch(es) submitted in the original application for approval is the basis for setting acceptable ranges of processing parameters for

manufacture of the IR dosage form. These data may include parameters such as mixing time, mixing speed, and blend assays. Thus, for future level 1 SUPAC-IR changes, applicants should use the approved validation ranges as described in the application.

12. Q: What is the guidance to determine if a new drug falls into the category of narrow therapeutic range?

A: Appendix A of the SUPAC-IR guidance lists a number of such drugs. In addition, 21 CFR 320.338 describes how to determine if a drug falls into this category.

13. Q: Is a change in gelatin capsule size considered a SUPAC-IR component and composition change?

A: Issues related to empty gelatin capsules are not covered in the SUPAC-IR guidance. Only the component categories discussed in the document are covered. Changes for other components should be submitted in accordance with the provisions of 21 CFR 314.70.

14. Q: When making a component or composition change according to SUPAC-IR, and the approved application has a range and target for a specific component, does the range move when the target changes?

A: No. The range remains the same even when the target changes. Such changes are predicated on the target approved in the original application or through prior approval supplement for a formulation change. Changes to the approved range should be made by prior approval supplements in accordance with the provisions of 21 CFR 314.70.

15. Q: Are wetting agents covered under SUPAC-IR?

A: No. Only components included in categories spelled out in the guidance qualify as SUPAC-IR changes. Thus, wetting agents are not covered.

16. Q: Can inks be changed under SUPAC-IR? If so, how?

A: If the new ink has been used in other approved products the change is allowed under SUPAC-IR as a level one change. Alternatively, if all of the components of the ink have been used in approved drug products, the switch also can be made under SUPAC-IR. A justification should be given; reference should be made to the approved product(s) where the ink and/or the components are already used.

17. Q: Can inks be eliminated under SUPAC-IR?

A: Ink can be eliminated as a level 1 change.

## **MANUFACTURING SITE CHANGES**

1. Q: Must the inspection which is required for a site transfer have been conducted for the same dosage form?

A: Yes.

2. Q: What is the meaning of "same environmental conditions"?

A: "Same environmental conditions" refers to such conditions as the same temperature range, the same humidity control range, and the same lighting intensity.

3. Q: Is moving to/between contract manufacturers covered by SUPAC-IR?

A: Yes. The guidance defines site changes as a change in location of the site of manufacture for both company-owned and contract manufacturing facilities.

4. Q: If a foreign firm moves to a new manufacturing site (new building) how would they initiate the inspection of that facility?

A: The answer is the same whether the new site is foreign or domestic. The submission of a supplement (changes being effected or prior approval) for the site change will trigger an inspection request from the reviewing division. The move to a new manufacturing site may qualify as a level 1 change in which case the proper submission would be an annual report. In either case an applicant could ask the Field to evaluate their facility. Any site change under SUPAC-IR calls for the new site to be in compliance with cGMP regulations. Should the firm wish to schedule an inspection prior to submission of the site change information to the application, a foreign firm should contact the Foreign Inspection Team in the Division of Manufacturing and Product Quality, Office of Compliance, CDER. Domestic firms should contact their local district office.

5. Q: Some investigators have stated that any 483 observations (no matter how minor) means that the inspection is "violative" for the company. Should a firm assume that if they receive a 483 observation that they are "violative"?

A: The districts use three classifications, NAI (no action indicated), VAI (voluntary action indicated), and OAI (official action indicated). Generally, a firm classified NAI has no findings or a few insignificant findings and is considered to be in compliance and therefore not violative. A firm classified VAI usually has several violations that can be significant if they are not corrected as soon as possible. If the corrections and commitments appear adequate the firm is not considered to be violative. Generally, when a firm is classified OAI the findings are significant and should result in some or all of the following: withhold approval of an application, a warning letter, or an injunction, seizure, and/or prosecution. A firm will remain OAI until they have corrected the deficiencies.

6. Q: If a site change described in Section IV includes manufacturing, packaging, and testing together, is it covered?

A: Yes.

7. Q: When packaging (or testing) is the only part of the manufacturing process which is being moved, is this situation covered by SUPAC-IR?

A: Yes. Originally, only packaging (or testing) site changes which were part of a site change for complete manufacturing operation as described in #1 above were covered by SUPAC-IR. However, that position was recently reassessed by FDA. Packaging or testing site changes separate from the rest of the manufacturing operation are acceptable under SUPAC-IR as described in the cover letter.

8. Q: Does the Center require any communication from the Field when a company reports a

site change in the annual report?

A: The facility should have had a successful cGMP inspection within the past two years and the Center does not expect to hear from the Field at the time of submission of the annual report. A firm may request an assessment of a proposed site change from the appropriate FDA district office.

9. Q: Does Section IV apply to the addition of facilities not previously listed, or is it limited to sites already listed in the location of operations section?

A: SUPAC-IR section IV does include site changes to facilities not already listed in the NDA/ANDA/AADA. For CBE supplements, a new manufacturing site should have an acceptable cGMP status, as previously discussed.

10. Q: Are build-outs (extensions of a building) considered a SUPAC-IR level 1 site change?

A: At the current time, the Center's position is that build-outs qualify as level 1 site changes. The change should be reported in the annual report as long as the facility has had a satisfactory cGMP inspection within the last two years.

11. Q: Is it possible to have a site change covered under SUPAC-IR when the change results in different/revised SOPs?

A: If SOPs are different, the implication is that the manufacturing process has also changed. Thus, this site change is not covered under SUPAC-IR. A prior approval supplement is required under 21 CFR 314.70 (b) (2) (vi).

12. Q: What is meant by "personnel common to both manufacturing sites" under part IV. Manufacturing?

A: This means personnel "already working on the campus who have suitable experience with the manufacturing process."

## **MANUFACTURING PROCESS CHANGES**

1. Q: If no range was established through validation studies for mixing time, is it possible to make a level 1 change in mixing times?

A: This situation does not qualify as a level 1 change.

2. Q: If a parameter is not specified in the application (e.g. mixing speed), and you want to change it, is the change within range or outside?

A: If the approved application does not contain the necessary details (e.g., mixing speed), and one wants to change the method of manufacture of the drug product (i.e., equipment and/or process with associated parameters), a prior approval supplement should be filed.

## MANUFACTURING EQUIPMENT CHANGES

1. Q: When going from equipment of one scale to one which is 2 or 1/10 the scale, the operating parameters will always change (e.g., airflows will decrease, spray rates will decrease). It is unlikely that the parameters will have been previously validated. Therefore, it would appear that any such change will be a level 2 change. Please comment.

A: If a scale-down of the production batch to 2 or 1/10 the size is needed, operating parameters that would fall within the range established for manufacture of the test batch and the first three production batches (i.e., validation batches) will be regarded as a level 1 change. If they fall outside the validation ranges the change would be permitted under SUPAC IR as a level 2 change. Regardless, SUPAC IR does not address scale-down below 100,000 units.

2. Q: Is a change in mill screen size (to improve flow during formulation) a level 1 change?

A: A screen size change to an alternate screen of the same design (holes) and operating principle (sifting) but different diameters to facilitate flow of powder will be regarded as a level 1 change, provided the alternate screen has not altered the particle size distribution of the screened material. Under such conditions, the information can be filed in the annual report.

3. Q: Must the equipment be moved from the old site to the new one when the manufacturing site is changed?

A: A company need not move equipment for a SUPAC-IR site change. However, any equipment should be of the same design and operating principle as the old equipment, and the SOPs and formulation should be the same.

## IN VITRO DISSOLUTION

1. Q: Can the equation for profile dissolution be used for comparing a generic product with the reference listed drug product?

A: Yes. The equation can be used in this situation. However, under SUPAC-IR, dissolution testing is generally conducted on the applicant's product before and after a particular change is made.

2. Q: For Case C testing, specific media are cited. Can other media or other pH's be used?

A: The five media indicated for Case C dissolution testing are presented as examples only. Other media, as appropriate for a particular drug product, if properly justified, may be used. Such a situation could involve using different solution compositions to attain a certain pH, as well as some at different pH conditions.

3. Q: For SUPAC-IR changes which require multi-point dissolution in several media, is this required of AA drug products?

A: For AA drugs (i.e., those drugs identified in the Approved Drug Products With Therapeutic Equivalence Evaluations or the "Orange Book" as not presenting bioequivalence problems) when the original application only required multi-point single medium dissolution testing for approval, then a multi-point single medium dissolution will be satisfactory where Case C is specified in the SUPAC-IR guidance.

4. Q: The inclusion of "n" in the f2 formula implies that the number and time of the pulls is left to the discretion of the FDA investigator. Choosing points late in the curve could insure a high f2. How will this be avoided?

A: It is recommended that only one point past the plateau of the profiles be used.

5. Q: Are the points for dissolution profiles listed in the document just guides, or do you expect to see those specific points? For a quickly dissolving drug, points at 10, 20, 30, and 40 may be more appropriate.

A: The points listed should be considered to be examples. Others points can be used with justification. It is suggested that at least 4 points (other than zero), equally spaced, be utilized.

6. Q: What options are available if f2 fails?

A: If an applicant believes the profiles are similar even if dissolution profiles fail f2, the firm may present a scientific justification as to why the observed difference is not due to the proposed change, and could not have significant impact beyond what is normally seen for batches prepared without the change.

7. Q: For case C testing, if all of the media are not ones typically used, must the dissolution procedure be validated using these media?

A: Yes. All of the methods used should be validated.

8. Q: What methods, other than Dr. Amidon's are acceptable?

A: This is an evolving area of research. "Extent of absorption" may be an appropriate alternative, as indicated in the guidance. Full documentation of permeability may require special clinical testing. Physicochemical and in vitro predictors of permeability are being assessed at the FDA. Pending availability of these methods, firms may rely on literature data from pharmacokinetic/mass balance studies that suggest high extent of absorption of a drug across the gastrointestinal mucosa. Absent this information, firms should assume that a drug substance has low permeability and follow the recommendations *in* the SUPAC-IR guidance accordingly.

9. Q: How exactly is the industry expected to determine or know the permeability of their drug?

A: One source of permeability information is the current research being conducted and sponsored by FDA. This information, for other drugs, could be experimentally determined by an applicant. Other alternative methods, related to permeability, may also be useful.

10. Q: Are we allowed to monitor the metabolites and sum all the components?

A: For determination of extent of absorption related to permeability, it may be appropriate to

consider the sum of all components. As described in the guidance, this is "in the absence of documented instability in the gastro-intestinal tract." In general, it is appropriate to sum all of the components if the formation of the metabolite occurs following permeation through the gastrointestinal mucosa.

11. Q: What constitutes an acceptable in vivo/in vitro correlation? Does "verified" mean validated?

A: Verified may be thought of as synonymous with validated. The Biopharmaceutics Coordinating Committee in CDER is developing guidance that addresses the general question. Pending availability of this guidance, firms should refer to published literature for information on establishing in vitro/in vivo correlations.

## **IN VIVO BIO STUDIES**

1. Q: If the highest strength was the biobatch strength, and waivers were used for the other strengths, does supporting documentation for SUPAC-IR changes refer to all strengths? Does the answer differ depending on whether the strengths are dose/weight proportional?

A: For SUPAC-IR bioequivalence recommendations, the recommended tests apply to all strengths. Regarding bio-requirements, the supporting documentation normally is needed for all strengths. If a bioequivalence study is recommended, then the compositional proportionality of the various strengths may determine if all strengths need to be tested for bioequivalence, or if a strength can be waived. However, this is not the standard comparison that is in the SUPAC-IR Guidance.

2. Q: Will many small changes prompt the Agency to require a biostudy?

A: Generally, a biostudy will not be requested simply because many changes which individually would not normally require a biostudy, are performed.

3. Q: For SUPAC-IR changes which require an in-vivo bioequivalence test, is this requirement also intended for AA drugs which were exempt from bioequivalence testing when originally approved?

A: The Center did not intend for SUPAC-IR to impose additional bioequivalence requirements for AA drugs beyond those in an original application. (AA drugs are those identified in the Orange Book as not presenting bioequivalence problems.) Therefore, if bioequivalence testing was not required originally, it will not be required under SUPAC-IR for AA drugs.

4. Q: Would an in vivo bioequivalence study be needed for an AAA@ or non-bioequivalence problem DESI drug even if it one would be needed according to SUPAC?

A: No, since that would conflict with the agency's current bioequivalence policy.

5. Q: When a bio study is required under SUPAC-IR, to what product should a generic product be compared - the Reference Listed Drug or the generic product approved prior to the SUPAC change.

A: An innovator product should be compared to itself. A generic should be compared to the reference listed drug for that drug product.

## **STABILITY/CHANGE IN BATCH SIZE**

1. Q: When the documentation for a change is one batch on long term stability, is there a time limit between implementation of the change and initiation of the stability study?

A: No. But the stability study should start as soon as possible after the drug product is prepared in the market container.

2. Q: What is the stability requirement for a level 3 change involving a product with multiple strengths packaged in bottles and blisters? SUPAC-IR states one batch. Can we bracket?

A: Testing and data collection involving the use of product bracketing are not the subject of SUPAC-IR. Bracketing may be used with prior approval of the Agency. The amount of data required depends on the type of change and whether or not there is a significant body of data available. If an applicant plans to bracket, the proposed protocol should be submitted to the Agency. This plan should include a protocol for each product. It should indicate all of the approved packaging configurations, and what strengths are approved for each of these. It also should include the approved stability test protocol.

3. Q: Who determines how many batches are required for stability when the documentation requests 1-3?

A: The answer will be dependent on the specific drug product and the amount of data already available. The appropriate review division should be contacted for further guidance.

4. Q: When accelerated stability data are required, is that comparative data?

A: Yes. Historical data may be used for comparison.

## **MISCELLANEOUS ISSUES**

1. Q: The recommended documentation for several SUPAC-IR changes indicates that "batch records" or "updated batch records" be submitted. Should copies of batch records be submitted with the appropriate filing? Is batch record defined as the actual blank floor work order or can another manufacturing process description be used? In which cases should the batch records be executed batch records?

A: Wherever "batch record" occurs in the SUPAC-IR guidance, it means executed batch records. These records should be submitted in the designated filing.

2. Q: What does the Agency intend by "notification of change"? Should there be a separate communication to the Agency in addition to the annual report?

A: The Agency should be notified of changes by the appropriate submission as described in the guidance..

3. Q: May a firm make a SUPAC-IR change immediately after approval of the original application, or is there a waiting period?

A: There is no waiting period. SUPAC-IR changes may be made as soon as the application is approved provided the appropriate data are available and filing criteria are addressed.

4. Q: When there is a time lag between when changes are made under SUPAC and the submission of the annual report, what evidence is needed to show that an appropriate change will be submitted in the next annual report? What will the FDA investigator expect to see?

A: The regulations at 21 CFR 314.70 (d) govern the filing of annual reports. Changes are made according to the applicant's change policy/procedures; these are part of the cGMP requirements. Because all changes should be approved by the appropriate quality unit, some set of documentation (e.g., development protocols, validation runs, batch records, etc.) should exist before the change is made. The investigator would expect to see this documentation.

5. Q: Should the information described under "documentation" be submitted in the filing, or does having the appropriate information on site for the inspection satisfy the requirement?

A: The documentation should be included in the designated filing regardless of whether a supplement (prior approval or changes being effected) or annual report is used.

6. Q: Are changes such as tablet shape and size covered under SUPAC-IR?

A: In general, changes involving size and/or geometry of the tablet are not covered under SUPAC-IR, and would need prior approval supplements. However, changes in thickness due to a composition change may be covered under SUPAC-IR

7. Q: What does the Center expect relative to validation for SUPAC-IR changes?

A: A summary of the validation data should be included in submissions describing process changes.

8. Q: What is meant by "validated range"?

A: Validated ranges mean the upper and lower limits are validated for a particular manufacturing process. An example of this is the time required during mixing of bulk powders which supports the minimum and maximum time needed to optimize mixing of the contents

9. Q: Based on the SUPAC video, it appears that a certificate of analysis and dissolution data need not be submitted in annual reports, but should be held on site. Is this correct?

A: These data should be submitted in the annual report.

10. Q: A "significant body of data" is mentioned in several places in the SUPAC-IR guidance. What does this mean?

A: If an applicant for a new molecular entity has at least five years of post-approval manufacturing experience, or if the applicant for a new dosage that is an immediate release solid oral, has at least three years of post-approval manufacturing experience, the Center believes that a "significant body of information" exists for that product.

11. Q: In the SUPAC-IR guidance document, what is meant by a "short period of time"?

A: Because it is difficult to specify a single time frame which could be applied to all situations for drug products, the appropriate chemistry team leader should be consulted. Each situation will be defined on a case by case basis.

12. Q: If a new dosage form of a product that has been marketed for a number of years is accepted for filing as a generic product through the suitability petition process, will it be considered to have a "significant body of information"?

A: No, it would not. As noted in the definition for significant body of information, a significant body of information is likely to exist after three years of commercial experience for new dosage forms.

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*<http://www.fda.gov/cder/guidance/qaletter.htm>*