SUPAC

How to Leverage Change in a Heavily Regulated Environment

Russ Somma, Ph.D.

Novartis Pharmaceuticals

Summit,NJ

Somma Tech

Ideas that speed pharma products to market

SUPAC

SUPAC is the most significant guidance made available by FDA to industry in recent history.

Companies may make changes to existing filings with a greatly reduced approval time.

In <u>many cases</u> changes may be made using an annual report. This offers significant advantages with regard to planning and resource allocation.

Somma Tech
Ideas that speed pharma products to market

SUPAC

- **Filing methods available and associated timing.**
- **Annual Report Update (AR)**

  No delay, allows immediate implementation
- **Changes Being Effected (CBE)**

  Generally a 60 day wait for FDA review
- **Prior Approval (PA)**

  Implementation only after FDA approval may be as long as 18 months

SommaTech
Ideas that speed pharma products to market

SUPAC

- **Dosage Forms Covered At Present**
- **IR-Immediate Release Solid Oral Dosage Forms**

  Tablets, capsules, soft gelatin capsules
- **MR-Modified Release Solid Oral Dosage Forms**

  Delayed Release (such as enteric)

  Extended Release (such as time release)
- **SS-Topical Semi-Solid Dosage Forms**

  Creams, ointments, suspensions, emulsions, gels

Somma Tech
Ideas that speed pharma products to market

SUPAC

- **All current SUPACs have associated equipment guidance addenda. These define the aspects of ”same design and operating principle” as required within the parent SUPAC guidance.**

- **These must be used with the guidance documents when considering equipment changes.**

SommaTech
Ideas that speed pharma products to market

SUPAC

- **How do you get the documents?**

- **Guidance documents are available on the FDA website.**

- **www.fda.gov/cder/guidance/index.htm**

SUPAC

- **SUPAC is only a guidance and NOT a regulation.**
- **A company may make changes by filing a supplement using the existing regulations under 21 CFR 314.70(b)(2).**
- **The are many advantages to using SUPAC !!**
- **SUPAC relates to filings in place with FDA.**
- **SUPAC may present challenges when dealing with loosely structured NDAs!!**
- **What is suitable equipment anyway??**

Somma Tech
Ideas that speed pharma products to market

SUPAC

- What is covered?
- Components/ composition
- manufacturing sites
- packaging sites
- analytical testing sites
- scale-up/scale down
- manufacturing equipment
- manufacturing process

Note: drug product only!!!

- What is not covered?
- Drug substance
- multiple changes submitted at one time or in a short period of time
- multiple changes require contact with FDA/CDER

SommaTech
Ideas that speed pharma products to market

SUPAC

- **What are the EU equivalents to the FDA aspects we are discussing?**

  In the case of 21 CFR 314.70(b)(2) we would look to EEC#541/95 and #542/95 as covering the same issues of filing supplements.

  In the case of SUPAC a similar change route is available through documents for Type I and Type II post approval changes.

Somma Tech
Ideas that speed pharma products to market

SUPAC

- **Who can use SUPAC?**
- **Manufacturing**

  We are provided with minimum requirements.

  This allows evaluation of the resources needed before proceeding with the project.

  “How much will it cost for what we will get.”
- **Regulatory**

  Defines the filing mechanism clearly such as AR,CBE or PA.

Somma Tech
Ideas that speed pharma products to market

SUPAC

- **What are FDA's expectations from a company using SUPAC?**
- **A successful general GMP inspection within the last 2 years.**
- **Filing is clearly noted as a SUPAC filing in the cover letter to FDA.**
- **Communicate the type of change and the level of the change (1 ,2 or 3).**
- **Product history pre change and data after the change.**

Somma Tech
Ideas that speed pharma products to market

SUPAC

- **What are FDA's expectations from a company using SUPAC?**
- **A copy of the executed batch record.**
- **Summary of the validation data.**
- **Communication with FDA/CDER if there are any points which are unclear or if multiple changes are anticipated.**
- **In all cases validation of the change is mandated under cGMP.**

Somma Tech
Ideas that speed pharma products to market

SUPAC

- **What are the levels of change?**
- **Level 1**

  Unlikely to have impact on the product. Filed as an annual report update, normal testing as filed in NDA.
- **Level 2**

  Moderate changes such as technical grade of inert, filed as CBE or PA, accelerated stability and dissolution profile testing in addition to filed NDA.
- **Level 3**

  Likely to have impact, filed PA, stability and testing as above in addition a biostudy or IVIV correlation.

SUPAC

- How do these aspects relate to technical operations?

  The following items, while not a complete list, may hold the major value for using SUPAC.

  - Manufacturing Site Change
  - Batch Size Change
  - Manufacturing Process Change
  - Manufacturing Equipment Change
  - Analytical Testing Site Change
  - Packaging Site Change

SUPAC

- **Manufacturing Site Change**
- **Level 1**

  Same facility, filed as an AR, normal testing
- **Level 2**

  Same campus, different building, filed as CBE, accelerated stability, dissolution profile testing
- **Level 3**

  Different campus, international transfers for example, CBE for IR and PA for MR, testing as above with biostudy or IVIV correlation for MR only.

SUPAC

- **Batch Size Change**
- **Level 1**

  Scale-up to ten times the biobatch, filed AR, long term stability and normal testing as per NDA.
- **Level 2**

  Scale-up beyond ten times the biobatch, filed as a CBE, all the above plus accelerated stability and dissolution profile testing.

SUPAC

- **Manufacturing Process Change**
- **Level 1**

  Within the existing process ranges supported by the current NDA, filed AR, normal testing.
- **Level 2**

  Outside the existing ranges, filed CBE, long term stability and dissolution profile testing.
- **Level 3**

  Different process, filed PA, all the above plus accelerated testing and biostudy or IVIV correlation.

SUPAC

- **Manufacturing Process Change**
- **Older Products**

  These will require careful review to identify critical process parameters, adequate specifications, clear manufacturing directions and a critical review of the product history.

  Although SUPAC offers an opportunity to improve our procedures the cost of dealing with incomplete data must be considered a risk.

  At the least they must be validated within recent process history!!

SUPAC

- **Manufacturing Process Change**
- **New Products**

  These offer the best opportunity for change since past history is clear in development reports and validation.

  Review may be simplified to examination of the related development documentation.

SommaTech
Ideas that speed pharma products to market

SUPAC

- **Manufacturing Equipment Change**
- **Level 1**

  Change to an automated or mechanical material handling system, or equipment of the same design and operating principle, filed AR, long term stability and normal testing.
- **Level 2**

  Change to a different design and operating principle, filed PA, all the above plus accelerated stability and dissolution profile.

SUPAC

- **What is same design and operating principle?**

  The equipment addenda define equipment into “class” “sub class” and “example”.

  The class defines equipment that have the same operating principles, while sub class defines variation in design.

  Equipment changes within a class are defined as the same (level 1),changes to another class are different (level 2).

SommaTech
Ideas that speed pharma products to market

SUPAC

- **What is same design and operating principle?**
- **Example:**

  The class of diffusion mixers contains several sub classes. The mixing action within the class is the same while the sub class defines physical attributes. Therefore V blenders are in one sub class while bin tumblers are in another. They both have the same mixing action but differ in physical design.

  They are considered the same in this case!

Somma Tech
Ideas that speed pharma products to market

SUPAC

- **Analytical Testing Site Change**
- Covers drug product testing ONLY!
- The site must have a recent cGMP certification.
- One batch released from the site must be on long term stability.
- Must use only testing procedures filed in the NDA.
- These changes normally require a 30 day wait for FDA review prior to implementation.
- Offers advantages for third party utilization to deal with large/rapid changes in testing volume.

SUPAC

- **Packaging Site Change**
- The site must have a recent cGMP certification for the specific packaging procedure under consideration.
- Filed as a CBE with the associated 30 day review period.
- First batch must be placed on long term stability.
- Offers advantages for third party utilization in order to deal with rapid growth in product demand. It offers an alternative to capitalization for more equipment.

SUPAC

- **How can we use SUPAC to improve our business practices?**

  It allows us to leverage regulatory changes quickly in a heavily regulated environment.

  Develop products and associated strategies which will provide greater flexibility in the future.

  With the right strategy we will move faster than our competitors.

SommaTech
Ideas that speed pharma products to market

SUPAC

- **Will SUPAC have associated cost savings?**

- The value of SUPAC is reduced regulatory burden and this equates to time savings.
- The cost of assembling good data packages will not be reduced since all changes require associated validation and documentation.
- SUPAC is regulatory relief and NOT validation relief.
- Rapid implementation of changes and subsequent entry into the market will yield the benefits!

Somma Tech
Ideas that speed pharma products to market