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Interview Questions on ANDA filing

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Abstract

This guidance document provides prominent facts on ANDA filings in FAQ format. It covers aspects like drafting, submission, review, approval of ANDA in question answer format. It is an excellent database for those seeking appointment in large pharmaceutical companies.

Keywords: Drug Master File (DMF), ANDA, NDA, FDA, CDER, OGD

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1. Introduction

The companies like Dr Reddy, Cipla, Biocon, Alembic, Unichem, and Aurobindo offer high profile job to pharma professionals. These companies are known worldwide for filing large number of ANDA. Hence, if you are seeking job in such companies a sound knowledge about ANDA is mandatory. This article is designed to train you to face likely questions during interview. Please try to understand the question before answering. The questions are presented at random.

2. Question Answers on ANDA filing

Table 1. Question Answers on ANDA filing (1-17)

Sr. No.	Question	Answer
1.	What is ANDA?	Authorization to market generic version of New drugs
2.	What is IND?	Authorization to conduct clinical trials on New Drug Substance
3.	What is NDA?	Authorization to market New Drug Product
4.	What is ICH?	ICH is a joint project of Europe, Japan, United States and experts from the pharmaceutical industry to harmonize the quality, safety and efficacy of pharmaceutical product
5.	What are the common Technical features of NDA and ANDA?	Same dosage form Same strength Same contents on the label Same route of administration Same indication/dosage Similar BE pattern
6.	Name the year in which Hatch Watchman Act was enacted? How it influenced market for generic drugs?	Hatch Watchman Act was enacted in 1984. It improved the market share of the generic products to the extent 90%
7.	What is PAI (Preapproval inspection)?	It is an inspection of site prior to approval of ANDA
8.	Describe the objectives of PAI?	Suitability of site layout and space for manufacturing/testing/storage Availability of necessary equipment Availability of necessary test instruments

		Suitability of Man & Material Integrity of key personnel Integrity of QC/QA Labs Environmental Protection Availability and suitability of SOP, QC-QA Manual, SMF, MMFR,BMR
9.	If Module 4 and 5 are applicable to ANDA filing?	Module 4 is not applicable Module 5 is applicable only with respect to BE studies
10.	If 6 months of accelerated and long-term stability data is adequate for ANDA filing?	Yes, provided the applicant signs an undertaking to report the completed studies before marketing the product.
11.	How the drug substance can be solubilized in water?	By derivtazation /inclusion in water soluble matrix/ /pH adjustment/ inclusion of organic solvents
12.	If ANDA for as specific drug covers all its salts/derivatives /polymorphic/chiral forms NDA filing?	ANDA for a specific drug covers only the specified salt form/derivatives/polymorphic forms matching with corresponding NDA.
13.	Why an independent NDA is required for FDC of which individual drugs are already under NDA	The safety and efficacy of FDC may differs from its individual drug components
14.	What is standalone NDA	NDA for a specific drug for its specific derivative FDA section 505(b)(1) is applicable for such NDA
15.	Name the filing required for the new derivative/salt of an approved drug	The extended NDA
16.	Name the filing required for marketing new strength of an approved product	The extended NDA
17.	Name the filing required for marketing two approved drugs as FDC	The extended NDA
18.	Name the filing required for marketing new strength of an approved product	The extended NDA
19.	Name the filing required for introducing new dosage form of an approved drug	The extended NDA
20.	Name the filing required for marketing OTC drug as prescription drug	NDA filing
21.	Name the filing required for changing the origin of the drug in an approved drug product (e.g. natural to synthetic)	The extended NDA
22.	How regulatory applications are aligned for review by FDA?	First in First Review “
23.	If cleaning validation data is mandatory in eCTD?	It may not be a part of filing but FDA can ask it during inspection
24.	How US DMF (for API/Excipients) is incorporated in ANDA?	It is incorporated by quoting DMF No alloted by FDA.
25.	How CEP is incorporated in ANDA?	It cannot be incorporated in any way
26.	Specify the format required for ANDA submission?	eCTD
27.	What is the purpose of “Forced degradation studies”?	To highlight the pH/temperature /environmental conditions by which the drug gets degraded.
28.	What is the purpose of Development History?	To illustrate that the applicant knows the product characteristics, stability, storage conditions adequately
29.	How an applicant shall respond to significant noncompliance or deficiency issued by FDA?	The applicant must explain the probable cause of failure and must correct it
30.	Why intermediate stability studies shall be done?	Intermediate stability data is acceptable incase accelerated data shows deviations
31.	How the drug samples shall be packaged for stability studies?	They shall be packaged in commercially intended containers-closures?
32.	How much shelf life can be proposed for a drug which is stable for 12 months at ambient conditions and 6 months under accelerated studies?	24 months
33.	Explain the minimum batch size required for stability studies of finished products	The batch size shall not be less than $1/10^{th}$ of commercial batch size

34.	If stability data can be expressed in terms of weeks i.e. 24 weeks in place of 6 months	No. It need to be expressed only in months
35.	If expiry of API can be based on stability studies performed on Pilot batches	The stability of API must be performed on samples picked up from commercial batches
36.	If expiry of dosage form can be based on stability studies performed on Pilot batches	Yes. It is accepted by FDA
37.	State the data required under stability studies of drug products to be stored at ambient conditions?	Accelerated stability data over six months Ambient stability data over alloted expiry date
38.	How the samples of liquid orals, semi-solids, and suspensions shall be positioned for the stability studies?	The sample shall be positioned in an inverted, horizontal and an upright position.
39.	If pilot and commercial batches can differ in product composition?	No
40.	State the Application fee to be paid under GUDFA for ANDA filing"?	Initial Application fee FY 2020 is $ 176,237.
41.	What is GUDFA?	Generic Drug User Fees Act.
42.	If ANDA holders have to pay annual fees to maintain their filing	It is mandatory
43.	What does data exclusivity means?	The properirory data cannot be copied or incorporated by reference in any other data. NDA holders have data exclusivity right for 5 -7 years
44.	What does Market Exclusivity means	Exclusive Marketing rights. NDA holders have exclusive market right for 5 -7 years
45.	State the Market exclusivity period for "First to File" ANDA"	6 months
46.	Explain Paeditric Exclusivity	Exclusive market right for 6 months It is granted to NDA holder to conduct paediatric studies under FDA directives
47.	How the Patent exclusivity (granted by US PTO) and Market exclusivity granted by FDA differ from each other?	Patents exclusivity comes into force from the date patent is filed whereas market exclusivity begins after the drug has been approved by FDA
48.	State the "Paten exclusivity period "´for New Drugs	20 years from the date of filing
49.	State the Market Exclusivity period for New Drug Products	5 to 7 years
50.	Explain Market Exclusivity period for the first to file Generic Drug	6 months
51.	Can a drug have both Patent and Marketing exclusivity granted by FDA	Yes.
52.	Explain Market Exclusivity period for NCE	5 -7 years
53.	Explain Market Exclusivity period for New Orphan drug	7 years
54.	What happens when NDA holder files infringement suit against an ANDA applicant under para iv?	ANDA applicant is put on Hold for 30 moths
55.	How FDA reacts to falsification of BA/BE/Clinical data	The falsifier is debarred for participating in BE studies for life time
56.	What is debarment certificate	It's a declaration stating " We have not employed any debarred persons in clinical trials/BE studies
57.	How the noncompliance under GMP affects ANDA certification?	The applicant gets showcase notice and ANDA is kept on hold until the deficiencies are met
58.	Explain the term "Import Alert"	It's a notification issued to port officials in USA to hold the shipments of drugs restricted for imports by FDA
59.	Explain "Orange Book"	It is a web based downloadable database published by US FDA to identify/detail Approved New and Generic Drugs
60.	Name the CTD modules designated to hold BA/ BE Report	Module 5
61.	What is SPL (Structured Product labelling)?	It's a structures and well defined format for labelling the products under ANDA/NDA.

62.	What is the difference in Generics and Biogenerics?	Generics refer to the synthetic or natural drug under ANDA. Biogenerics refers to biological drug under ANDA
63.	Name the liquid preparations for which BE studies are mandatory?	Oral suspensions/emulsions for systemic effects
64.	What is Drug Price Competition and Patent Term Restoration Act, 1984 (Hatch-Waxman Act)?	It's an act to restrict the monopoly of New drugs and to facilitate launching of their generic version
65.	What is 180 days exclusivity granted to First File ANDA?	It's an exclusive marketing right granted to the "first-to-file" ANDA holder
66.	How confidentiality of critical information in US DMF is secured by applicant?	The applicant issues specific LOA to restrict review the entire DMF.
67.	How many vendors can be used for sourcing API?	Normally, just one vendor is considered adequate. If API is sourced from two different vendors the development studies shall be performed using 3 pilot batched from each vendor
68.	How many API batches shall be used for the development of product under ANDA	Minimum tow API batches from the same vendor shall be used for the product development.
69.	What is common mistake in sampling API?	Sampling 2-3 lots having same batch No in place of sampling 2-3 distinct batches
70.	What is the minimum pilot batch size	$1/10^{th}$ of commercial batch size. However, in some cases one pilot batch can be less than$1/10^{th}$ of commercial batch
71.	List the variations permitted in labelling of the products under ANDA	Pack Size and Shape Color scheme for label
72.	Name the category where variation in packaging is not allowed	The products having fixed treatment cycle
73.	How many Batch records" are required for ANDA filing?	Three Executed Pilot scale batch records + One unexecuted Commercial Scale Batch Record
74.	What is an Exhibit Batch with respect to ANDA	It's a pilot batch marked for BE studies
75.	What are Bio-analytical methods?	The method used for analyzing the drug from bio samples such as blood, urine and faecal matter. It requires validation
76.	Why GUDFA enhances ANDA Review Fees periodically?	To meet the increasing expenses of the agency
77.	Name the functions involved in ANDA filing?	RLD management Product Development Process/Analytical method validation Stability Studies Impurity Profiling BE studies Label Review Form 356h FDA Inspection Management FDA 483 resolutions
78.	Explain the CTD Modules applicable/not applicable for ANDA filing	Module 1 : Administrative Information Module 2 :Overview and summary Module 3 : Quality Please note that Module 4 : Not Applicable Module 5 : Not applicable except BE data
79.	Why it is prudent to conduct intermediate stability studies along with accelerated and long term stability studies?	In case accelerated stability fails, intermediate stability data is considered by FDA
80.	Name the guidelines for "Bracketing and Matrixing Designs for Stability Testing	ICH Guidelines (Q1D)
81.	What is US DMF?	It is a submission that may be used to provide confidential detailed information about API, Excipients, Packaging materials under NDA/ANDA
82.	How reference to a particular US DMF (Type 2,3,4) helps in filing NDA/ANDA applications	The applicant can incorporate it in ANDA/NDA just by reference

83.	What is the object of pre-approval inspection for approving ANDA	To verify cGMP Compliances
84.	SUPAC?	It stands for Scale up and Post approval changes in product under ANDA
85.	SUPAC IR?	It stands for Scale up and Post approval changes in Immediate Release products
86.	SUPAC MR?	It stands for Scale up and Post approval changes in Modified Release Products.
87.	How ANDA filings are numbered in eCTD format? If the same number is valid over the lifecycle of the product?	ANDA filings are numbered by assigning six digit numbers (issued by FDA) prior to submission. Once activated, it remains valid over the life cycle of the product.
88.	What is meant by "Refuse to Receive" with respect to ANDA filing	It is a refusal to accept ANDA Application. This happens when the file structure or its contents are highly deficits
89.	What are the objectives of Hatch-Waxman Act	To facilitate the approval and marketing of generic drugs without conducting detailed safety and clinical studies To control drug prices by provoking competition with new drugs
90.	What is Patent Certificate	It's a self-certified document to state " The applicant has not violated any patent corresponding to NDA listed Orange Book "
91.	What is the aim of BE Studies in ANDA	To establish that the rate and extent of absorption of the generic drug against Reference Listed Drug specified by FDA
92.	Explain historical development of ANDA filings	Prior to 1978, generic drug applications were required to have complete quality. safety and efficacy data During 1978,generic applications were required to have complete quality + published data on safety and efficacy In 1984 generic applications were required to have complete quality data + safety and clinical data incorporated by reference to the specific NDA
93.	Explain the woes of ANDA Holder before Wax Hatchman Act?	Cumbersome regulatory procedures High investment Lengthy time for review and approval High Production cost
94.	What is PARA(1) with respect to ANDA filing	No patent has been filed. ANDA can be filed immediately
95.	What is PARA(2)with respect to ANDA filing	Patent has expired (ANDA can be filed immediately
96.	Explain the PARA (3) with respect to ANDA filing	Patent is near to expiry. ANDA can be filed in advance
97.	What is PARA(4) with respect to ANDA filing	Patent is invalid or irrelevant. ANDA can be filed any time prior to its expiry
98.	Why ANDA filing under Para 4 is often risky?	This Para often involves Litigations/law suits from the Patent Holder
99.	State the time allowed to NDA holder to respond to challenge petition filed by a prospective ANDA applicant under Para 4?	45 days
100.	State the market exclusivity provided to the NDA holder under Para (iv)	30 months

3. Conclusion

The article provides prominent facts on ANDA filings and general queries about ANDA, aspects like drafting, submission, review, and approval of ANDA are the major questions that are generally asked during the Regulatory Affairs Interview from Pharma companies. It is an excellent database for those seeking appointment in large pharmaceutical companies

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Conflict of Interest

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