CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

217469Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

IND 128163

MEETING MINUTES

Novaliq GmbH
c/o Strategic Drug Development Services, LLC
Attention: Scott Oglesby, PhD
US Resident Agent for Novaliq GmbH
6518 Green Rise Road
Hillsborough, NC 27278

Dear Dr. Oglesby:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for CyclASol (cyclosporine A ophthalmic solution). We also refer to the telecon between representatives of your firm and the FDA on March 29, 2022. The purpose of the meeting was to discuss the structure and content of the proposed New Drug Application (NDA).

A copy of the official minutes of the telecon is enclosed for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes. If you have any questions, please call Crystal Bland, MSHA, Regulatory Project Manager at 301-837-7672.

Sincerely,

{See appended electronic signature page}

Wiley A. Chambers, MD
Director
Division of Ophthalmology
Office of Specialty Medicine
Center for Drug Evaluation and Research

Enclosure:

- Meeting Minutes

U.S. FOOD & DRUG ADMINISTRATION

MEMORANDUM OF MEETING MINUTES

Meeting Type: Type B
Meeting Category: Pre-NDA

Meeting Date and Time: March 29, 2022; 1:00 PM – 2:00 PM (EST)
Meeting Location: Teleconference

Application Number: 128163
Product Name: CyclASol (cyclosporine A ophthalmic solution)

Indication: treatment of dry eye disease

Sponsor Name: Novaliq GmbH
Regulatory Pathway: 505(b)(2) of the Federal Food, Drug, and Cosmetic Act

Meeting Chair: Wiley A. Chambers, MD
Meeting Recorder: Crystal Bland, MSHA

FDA ATTENDEES

Alex Gorovets, MD	Deputy Director, Office of New Drugs/Office of Specialty Medicine (OSM)
Wiley Chambers, MD	Director, Division of Ophthalmology (DO)/OSM
William Boyd, MD	Deputy Director, DO/OSM
Rhea Lloyd, MD	Clinical Team Leader, DO/OSM
Martin Nevitt, MD	Clinical Reviewer, DO/OSM
David Summer, MD	Clinical Reviewer, DO/OSM
Erin Ruhland, PhD	Pharmacology/Toxicology Reviewer, Division of Pharmacology and Toxicology of Rare Diseases, Pediatrics, Urologic & Reproductive Medicine/Specialty Medicine
Guoxing Soon, PhD	Statistics Team Leader, Office of Biometrics/Division of Biometrics IV (OB/DBIV)
Solomon Chefo, PhD	Statistics Reviewer, OB/DBIV
Ping Ji, PhD	Clinical Pharmacology Team Leader, Office of Clinical Pharmacology (OCP)/Division of Inflammation and Immune Pharmacology (DIIP)
Nisha Kwatra, PhD	Clinical Pharmacology Reviewer, OCP/DIIP
Chunchun Zhang, PhD	Acting Product Quality Team Leader, Office of Pharmaceutical Quality (OPQ)/Division of New Drug Products/New Drug Products Branch III
Anne Marie Russell, PhD	Product Quality Reviewer, OPQ/ Office of New Drug Products

Vidya Pai, PhD	Branch Chief, OPQ/Office of Pharmaceutical Manufacturing Assessment (OPMA)/Division of Pharmaceutical Manufacturing Assessment (DPMAIV)/ Pharmaceutical Manufacturing Branch (PMB12)
Sateesh Sathigari, PhD	Senior Pharmaceutical Quality Assessor OPQ/OPMA/DPMAIV/PMB12
Aschalew Bekele, PhD	Product Quality Reviewer, Office of Process, and Facilities/Division of Microbiology Assessment/Microbiology Branch III
Patricia Love, MD	Deputy Director, Office of Combination Products/Office of Clinical Policy and Programs/Office of the Commissioner
Oyinlola Fashina, PharmD	Senior Regulatory Project Manager, Office of Surveillance and Epidemiology (OSE) / Project Management Staff
Sofanit Getahun, PharmD, BCPS	Safety Evaluator, OSE/Division of Medication Error Prevention and Analysis 1
Diana Willard	Chief, Project Management Staff, Office of Regulatory Operations/Division of Regulatory Operations for Specialty Medicine (ORO/DROSM)
Crystal Bland, MSHA	Regulatory Project Manager, ORO/DROSM
Milalynn Victorino, FNP-C	Regulatory Project Manager, ORO/DROSM
Ahmed Ayodeji, PharmD	Regulatory Health Project Manager, ORO/DROSM

NOVALIQ GMBH ATTENDEES

Christian Roesky, PhD	Managing Director, CEO
Sonja Krösser, PhD	Vice President, Preclinical/Clinical Development
Jörg HaiBer, PhD	Vice President, Supply Chain Management & Analytical Development
[redacted] (b) (4)	
Scott Oglesby, PhD	Regulatory Consultant

BACKGROUND

The purpose of the meeting was to discuss the structure and content of the proposed NDA prior to submission for CyclASol ophthalmic solution for the treatment of signs and symptoms of dry eye disease.

Novaliq GmbH (Novaliq), submitted a Type B meeting request on January 25, 2022. The Meeting Request granted letter was sent to Novaliq on February 4, 2022, and the meeting package was received on February 25, 2022. The Agency sent Novaliq the Meeting Preliminary Comments on March 21, 2022, and in preparation for the

March 29, 2022, teleconference, Novaliq provided responses to the Agency's comments via email to Crystal Bland on March 23, 2022. In addition, Novaliq provided a slide presentation on March 28, 2022, to further clarify and focus the meeting discussion on Questions 1b and 3a.

DISCUSSION

Following, in **bold**, are the questions submitted in the February 25, 2022, meeting package. The FDA responses to these questions are in *italics*. The meeting discussion is in normal font.

CMC

Question 1:

Question 1a: Does the Agency agree that the proposed release and shelf-life specification of perfluorobutylpentane are appropriate to support the CyclASol NDA?

FDA Response to Question 1a: Your perfluorobutylpentane specifications will be an NDA review issue and we cannot advise if they are acceptable at this time. Based on the specifications submitted in your meeting package, we have the following advice for your NDA:

i. *Refractive index – include the attribute of refractive index or provide a scientific justification.*

ii. *Include numerical acceptance criteria for identification tests (e.g. within ± x% of reference standard). Submit labeled GC-FID and IR spectra to support proposed identity specifications.*

iii. *Provide justification for the proposed assay and impurities specifications. We note there is a change from the acceptance criteria in place during development.*

iv. *Submit data from clinical and commercial lots to support the absence of specifications for elemental impurities (e.g.* (b) (4) *) and* (b) (4) (b) (4)

Additional novel excipient CMC comments:

A. Since perfluorobutylpentane is a novel excipient, submit chemistry, manufacturing and controls (CMC) information in your NDA or reference a Drug Master File (DMF) Type IV held by your supplier AGC for this information. In addition to specifications, include properties, synthesis, control of materials, manufacturer, manufacturing process and controls,

structure elucidation, impurities, analytical procedures, release and stability data for clinical and commercial batches and a proposed expiry.

B. Specify if the excipient is manufactured under GMPs.

Meeting Discussion: No discussion was required.

Question 1b: Does the Agency agree with the strategy to introduce (b) (4) (b) (4) as alternative testing site?

FDA Response to Question 1b: No, we do not agree with your strategy to submit (b) (4) as a testing site without finalized analytical transfer at the time of initial NDA submission. At the time of submission, your NDA should provide data to support your proposed commercial product. These data should include release and stability data for batches manufactured, packaged and tested as submitted for your commercial product. Data to demonstrate method transfer and verification at alternate testing sites should be included. Changes, such as testing of perfluorobutylpentane (F4H5) by your drug product manufacturing facility (b) (4) (b) (4) instead of by the excipient manufacturer (b) (4), may be made post approval.

Meeting Discussion: Novaliq clarified that they do not intend to introduce any alternative or additional testing sites for CyclASol NDA and that any potential change to testing, such as sites for incoming testing of the novel excipient or release testing of drug product, may be made post approval. The Agency agreed this is acceptable.

(b) (4)

Meeting Discussion: No discussion was required.

Question 3:

Question 3a: Does the Agency agree that the proposed release and shelf-life specifications of drug product are appropriate to support the CyclASol NDA?

FDA Response to Question 3a: Your drug product specifications will be an NDA review issue and we cannot advise if they are acceptable at this time. Based on the specifications submitted in your meeting package, we have the following advice for your NDA:

i. *Add viscosity.*

ii. *Include numerical acceptance criteria for identification tests (e.g. within ± x% of reference standard).*

iii. *Tighten total impurities to NMT (b) (4).*

iv. *Unspecified unknown impurities should have a limit of 0.1% per ICH Q3B(R2).*

Additional drug product CMC comments

C. *Expiry – the stability section of your meeting package reports temperature and humidity effects under accelerated conditions (40 ± 2°C/75 ± 5% RH) and a proposed (b) (4)-month expiry based on 12 month stability data. Refer to Guidance for Industry Q1E Evaluation of Stability Data June 2004 for extrapolation of stability data.*

D. *Please provide data to support the long-term storage condition of 60% RH used in your stability protocol and the absence of water content testing.*

E. *In the NDA submission, please include:*

- *Droplet volume from multiple container batches.*

- *One-time weight loss study on a primary stability batch through expiry and a one-time freeze-thaw study.*

- *Leachables/extractables on the proposed commercial container/closure by using screening analytical methods (such as HPLC, GC etc.) and studies on at least three stability batches through expiry. Refer to USP <1663>, <1664> for recommendations.*

- *Data demonstrating container-closure integrity of the drug product container intended for commercial use.*

Additional Microbiology comments for the future NDA submission
We note that the drug product is packaged in multi-dose containers. Therefore, data from antimicrobial effectiveness studies performed per USP <51> or an equivalent method should be provided with the NDA submission. Also, note that at least one of the primary batches of the drug product should be tested for antimicrobial effectiveness at the end of the proposed shelf life. For additional information refer the Guidance for Industry Q1A(R2) Stability Testing of New Drug Substances and Products. 2003.
https://www.fda.gov/media/71707/download

Regarding the Agency's expectations for filing an NDA submission for aseptically filled products, refer to the following two guidance documents.

- *Guidance for Industry for the Submission Documentation for Sterilization Process Validation in Applications for Human and Veterinary Drug Products. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/submission-documentation-sterilization-process-validation-applications-human-and-veterinary-drug*

- *Guidance for Industry, Sterile Drug Products Produced by Aseptic Processing — Current Good Manufacturing Practice. 2004. https://www.fda.gov/media/71026/download*

Meeting Discussion: Novaliq asked if the Agency agreed that in accordance with ICH Q3B(R2) and based on the total daily intake (TDI) if a limit of 1.0% (Identification Threshold) for unspecified unknown impurities is acceptable. The Agency agreed that 1.0% is acceptable, but not based on the 40 µg TDI per ICHQ3B(R2), but on the basis of the product strength (0.1%). The Agency recommends NMT 1.0% for any unspecified impurity if an ophthalmic drug product strength is ≤ 0.1%.

Question 3b: Does the Agency agree with the strategy to introduce (b) (4) as alternative testing site?

FDA Response to Question 3b: See response to Q1b.

Meeting Discussion: No discussion was required.

Non-Clinical

Question 4: Does the Agency agree with Novaliq's plan to structure the non-clinical module with regards to the references to listed drugs and published literature?

FDA Response to Question 4: We agree.

Meeting Discussion: No discussion was required.

Clinical

Question 5: Does the Agency agree that the results from CYS-003 and CYS-004, two independent adequate and well-controlled, multicenter trials, demonstrate efficacy of CyclASol for the treatment of DED?

FDA Response to Question 5: The question cannot be answered without a review of a submitted application. Studies CYS-003 and CYS-004 both met their primary sign endpoints demonstrating statistical superiority in change from baseline in total corneal fluorescein staining at Day 29. Neither study met its prespecified primary symptom endpoint, change from baseline to Day 29 in OSDI (CYS-003) and Dryness score (CYS-004). Improvement in Schirmer's Score ≥ 10 mm will need to be reviewed in the context of the completed study reports because it was a post hoc analysis.

Meeting Discussion: No discussion was required.

Question 6: Does the Agency agree with Novaliq's proposed amendment of the ISE SAP?

FDA Response to Question 6: Agree.

Meeting Discussion: No discussion was required.

Question 7: Does the Agency agree that the planned safety assessments reporting, with the initial submission package to include the 6-month interim safety report of the ongoing CYS-005 trial is acceptable for the planned NDA of CyclASol, considering the established safety of topical cyclosporine formulations on the ocular surface for the treatment of dry eye disease?

FDA Response to Question 7: The planned safety assessments reporting for a future NDA submission is acceptable.

Meeting Discussion: No discussion was required.

Regulatory

Question 8: Does the Agency agree that the planned content meets the expectations for filing of the initial NDA?

FDA Response to Question 8: Agree.

Meeting Discussion: No discussion was required.

Question 9: Does the Agency agree that the observed efficacy results in both pivotal trials provide sufficient clinical evidence to support the indication claim: "treatment of signs and symptoms of dry eye disease"?

FDA Response to Question 9: The question cannot be answered at this time, see response to Question 5.

Meeting Discussion: No discussion was required.

Question 10: Does the Agency agree that both Schirmer responder data and corneal staining efficacy data can be summarized in the clinical section of the proposed product label?

FDA Response to Question 10: The question cannot be answered at this time, see response to Question 5.

Meeting Discussion: No discussion was required.

ADDITIONAL COMMENTS

In the Genus decision issued on April 16, 2021, the U.S. Court of Appeals for the District of Columbia Circuit held that articles that meet the device definition in section 201(h) of the FD&C Act must be regulated as devices and not as drugs. In implementing this decision, FDA has determined that the language in 21 CFR 200.50(c) indicating that eye cups, eye droppers, and other ophthalmic dispensers are regulated as drugs when packaged with other drugs is now obsolete, as these articles meet the "device" definition. FDA will be regulating these products, including your product, as drug-led combination products composed of a drug constituent part that provides the primary mode of action (PMOA) and a device constituent part (an eye cup, dropper, or other dispenser). As the drug constituent part provides the PMOA, CDER will have primary jurisdiction over these products, including your product. See 21 CFR Part 3. Should you

disagree with the assessment that your proposed product is a combination product, you may contact the Office of Combination Products (OCP) at combination@fda.gov."

FDA is evaluating how the 21 CFR part 820 requirements as set forth in Part 4 apply to combination products that include such lower risk device constituent parts. Until FDA has further considered the application of these requirements to these combination products, FDA does not intend to take enforcement action with respect to compliance with any applicable 21 CFR part 820 requirements for approved ophthalmic products, including your products if approved. When FDA publishes its current thinking on how the 21 CFR part 820 requirements apply to these combination products, FDA intends to address its timing expectations for application holders and manufacturers of such approved combination products to come into compliance with any applicable 21 CFR part 820 requirements

In your future NDA submission, the Form FDA 356h to your pending application should identify your product as a combination product (see form field 24). Also, identify all facilities involved in the manufacturing of the combination product, including all facilities involved in the manufacturing of each constituent part and all facilities responsible for the disposition (e.g., release) of the combination product.

For location of information on the device constituent part see the FDA eCTD Technical Conformance Guide: Technical Specifications Document: "Guidance for Industry Providing Regulatory Submissions in Electronic Format —Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications" October 2021 accessible at http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/UCM465411.pdf

PREA REQUIREMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Please be advised that under the Food and Drug Administration Safety and Innovation Act (FDASIA), you must submit an Initial Pediatric Study Plan (iPSP) within 60 days of an End-of-Phase-2 (EOP2) meeting. In the absence of an EOP2 meeting, refer to the draft guidance below. The iPSP must contain an outline of the pediatric study or studies that you plan to conduct (including, to the extent practicable study objectives and design, age groups, relevant endpoints, and statistical approach); any request for a deferral, partial waiver, or waiver, if applicable, along with any supporting documentation, and any previously negotiated pediatric plans with other regulatory authorities. The iPSP should be submitted in PDF and Word format. Failure to include an Agreed iPSP with a

marketing application could result in a refuse to file action.

For additional guidance on the timing, content, and submission of the iPSP, including an iPSP Template, please refer to the draft guidance for industry *Pediatric Study Plans: Content of and Process for Submitting Initial Pediatric Study Plans and Amended Pediatric Study Plans*.[1] In addition, you may contact the Division of Pediatric and Maternal Health at 301-796-2200 or email Pedsdrugs@fda.hhs.gov. For further guidance on pediatric product development, please refer to FDA.gov.[2]

PRESCRIBING INFORMATION

In your application, you must submit proposed prescribing information (PI) that conforms to the content and format regulations found at 21 CFR 201.56(a) and (d) and 201.57 including the Pregnancy and Lactation Labeling Rule (PLLR) (for applications submitted on or after June 30, 2015). As you develop your proposed PI, we encourage you to review the labeling review resources on the PLR Requirements for Prescribing Information[3] and Pregnancy and Lactation Labeling Final Rule[4] websites, which include:

- The Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products.
- The Final Rule (Pregnancy and Lactation Labeling Rule) on the content and format of information related to pregnancy, lactation, and females and males of reproductive potential.
- Regulations and related guidance documents.
- A sample tool illustrating the format for Highlights and Contents, and
- The Selected Requirements for Prescribing Information (SRPI) − a checklist of important format items from labeling regulations and guidances.
- FDA's established pharmacologic class (EPC) text phrases for inclusion in the Highlights Indications and Usage heading.

Pursuant to the PLLR, you should include the following information with your application to support the changes in the Pregnancy, Lactation, and Females and Males of

[1] When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.
[2] https://www.fda.gov/drugs/development-resources/pediatric-and-maternal-health-product-development
[3] https://www.fda.gov/drugs/laws-acts-and-rules/plr-requirements-prescribing-information
[4] https://www.fda.gov/drugs/labeling/pregnancy-and-lactation-labeling-drugs-final-rule

Reproductive Potential subsections of labeling. The application should include a review and summary of the available published literature regarding the drug's use in pregnant and lactating women and the effects of the drug on male and female fertility (include search parameters and a copy of each reference publication), a cumulative review and summary of relevant cases reported in your pharmacovigilance database (from the time of product development to present), a summary of drug utilization rates amongst females of reproductive potential (e.g., aged 15 to 44 years) calculated cumulatively since initial approval, and an interim report of an ongoing pregnancy registry or a final report on a closed pregnancy registry. If you believe the information is not applicable, provide justification. Otherwise, this information should be located in Module 1. Refer to the draft guidance for industry *Pregnancy, Lactation, and Reproductive Potential: Labeling for Human Prescription Drug and Biological Products – Content and Format*.

Prior to submission of your proposed PI, use the SRPI checklist to ensure conformance with the format items in regulations and guidances.

SECURE EMAIL COMMUNICATIONS

Secure email is required for all email communications from FDA when confidential information (e.g., trade secrets, manufacturing, or patient information) is included in the message. To receive email communications from FDA that include confidential information (e.g., information requests, labeling revisions, courtesy copies of letters), you must establish secure email. To establish secure email with FDA, send an email request to SecureEmail@fda.hhs.gov. Please note that secure email may not be used for formal regulatory submissions to applications (except for 7-day safety reports for INDs not in eCTD format).

ABUSE POTENTIAL ASSESSMENT

Drugs that affect the central nervous system, are chemically or pharmacologically similar to other drugs with known abuse potential, or produce psychoactive effects such as mood or cognitive changes (e.g., euphoria, hallucinations) need to be evaluated for their abuse potential and a proposal for scheduling will be required at the time of the NDA submission [21 CFR 314.50(d)(5)(vii)]. For information on the abuse potential evaluation and information required at the time of your NDA submission, see the guidance for industry *Assessment of Abuse Potential of Drugs*.[5]

505(b)(2) REGULATORY PATHWAY

The Division recommends that sponsors considering the submission of an application through the 505(b)(2) pathway consult the Agency's regulations at 21 CFR 314.54, and the draft guidance for industry *Applications Covered by Section 505(b)(2)* (October 1999).[6] In addition, FDA has explained the background and applicability of section 505(b)(2) in its October 14, 2003, response to a number of citizen petitions that had

[5] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.
[6] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

challenged the Agency's interpretation of this statutory provision (see Docket FDA-2003-P-0274-0015, available at Regulations.gov.[7]

If you intend to submit a 505(b)(2) application that relies for approval on FDA's finding of safety and/or effectiveness for one or more listed drugs, you must establish that such reliance is scientifically appropriate, and must submit data necessary to support any aspects of the proposed drug product that represent modifications to the listed drug(s). You should establish a "bridge" (e.g., via comparative bioavailability data) between your proposed drug product and each listed drug upon which you propose to rely to demonstrate that such reliance is scientifically justified.

If you intend to rely on literature or other studies for which you have no right of reference but that are necessary for approval, you also must establish that reliance on the studies described in the literature or on the other studies is scientifically appropriate. You should include a copy of such published literature in the 505(b)(2) application and identify any listed drug(s) described in the published literature (e.g. by trade name(s)).

If you intend to rely on the Agency's finding of safety and/or effectiveness for a listed drug(s) or published literature describing a listed drug(s) (which is considered to be reliance on FDA's finding of safety and/or effectiveness for the listed drug(s)), you should identify the listed drug(s) in accordance with the Agency's regulations at 21 CFR 314.54. It should be noted that 21 CFR 314.54 requires identification of the "listed drug for which FDA has made a finding of safety and effectiveness," and thus an applicant may only rely upon a listed drug that was approved in an NDA under section 505(c) of the FD&C Act. The regulatory requirements for a 505(b)(2) application (including, but not limited to, an appropriate patent certification or statement) apply to each listed drug upon which a sponsor relies.

If FDA has approved one or more pharmaceutically equivalent products in one or more NDA(s) before the date of submission of the original 505(b)(2) application, you must identify one such pharmaceutically equivalent product as a listed drug (or an additional listed drug) relied upon (see 21 CFR 314.50(i)(1)(i)(C), 314.54, and 314.125(b)(19); see also 21 CFR 314.101(d)(9)). If you identify a listed drug solely to comply with this regulatory requirement, you must provide an appropriate patent certification or statement for any patents that are listed in the Orange Book for the pharmaceutically equivalent product, but you are not required to establish a "bridge" to justify the scientific appropriateness of reliance on the pharmaceutically equivalent product if it is scientifically unnecessary to support approval.

If you propose to rely on FDA's finding of safety and/or effectiveness for a listed drug that has been discontinued from marketing, the acceptability of this approach will be contingent on FDA's consideration of whether the drug was discontinued for reasons of safety or effectiveness.

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[7] http://www.regulations.gov

We encourage you to identify each section of your proposed 505(b)(2) application that is supported by reliance on FDA's finding of safety and/or effectiveness for a listed drug(s) or on published literature (see table below). In your 505(b)(2) application, we encourage you to clearly identify (for each section of the application, including the labeling): (1) the information for the proposed drug product that is provided by reliance on FDA's finding of safety and/or effectiveness for the listed drug or by reliance on published literature; (2) the "bridge" that supports the scientific appropriateness of such reliance; and (3) the specific name (e.g., proprietary name) of each listed drug named in any published literature on which your marketing application relies for approval. If you are proposing to rely on published literature, include copies of the article(s) in your submission.

In addition to identifying the source of supporting information in your annotated labeling, we encourage you to include in your marketing application a summary of the information that supports the application in a table similar to the one below.

List the information essential to the approval of the proposed drug that is provided by reliance on the FDA's previous finding of safety and effectiveness for a listed drug or by reliance on published literature	
Source of information (e.g., published literature, name of listed drug)	**Information Provided (e.g., specific sections of the 505(b)(2) application or labeling)**
(1) Example: Published literature	*Nonclinical toxicology*
(2) Example: NDA XXXXXX "TRADENAME"	*Previous finding of effectiveness for indication A*
(3) Example: NDA YYYYYY "TRADENAME"	*Previous finding of safety for Carcinogenicity, labeling section B*
(4)	

Please be advised that circumstances could change that would render a 505(b)(2) application for this product no longer appropriate. For example, if a pharmaceutically equivalent product were approved before your application is submitted, such that your proposed product would be a "duplicate" of a listed drug and eligible for approval under section 505(j) of the FD&C Act, then it is FDA's policy to refuse to file your application as a 505(b)(2) application (21 CFR 314.101(d)(9)). In such a case, the appropriate submission would be an Abbreviated New Drug Application (ANDA) that cites the duplicate product as the reference listed drug.

OFFICE OF SCIENTIFIC INVESTIGATIONS (OSI) REQUESTS

The Office of Scientific Investigations (OSI) requests that the items described in the draft guidance for industry, *Standardized Format for Electronic Submission of NDA and BLA*

Content for the Planning of Bioresearch Monitoring (BIMO) Inspections for CDER Submissions, and the associated conformance guide, *Bioresearch Monitoring Technical Conformance Guide Containing Technical Specifications,* be provided to facilitate development of clinical investigator and sponsor/monitor/CRO inspection assignments, and the background packages that are sent with those assignments to the FDA ORA investigators who conduct those inspections. This information is requested for all major trials used to support safety and efficacy in the application (i.e., phase 2/3 pivotal trials). Please note that if the requested items are provided elsewhere in submission in the format described, the Applicant can describe location or provide a link to the requested information.

Please refer to the draft guidance for industry *Standardized Format for Electronic Submission of NDA and BLA Content for the Planning of Bioresearch Monitoring (BIMO) Inspections for CDER Submissions* (February 2018) and the associated *Bioresearch Monitoring Technical Conformance Guide Containing Technical Specifications*.[8]

ISSUES REQUIRING FURTHER DISCUSSION
There were no issues requiring further discussion.

ACTION ITEMS
The Agency agreed to provide minutes of the meeting within 30 days.

ATTACHMENTS
Novaliq responses/clarifications to the Agency's comments provided on March 23, 2022, and the slide presentation provided on March 28, 2022, are provided below.

6 Page(s) have been Withheld in Full as b4 (CCI/TS) immediately following this page

[8] https://www.fda.gov/media/85061/download

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

WILEY A CHAMBERS
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