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FDA data integrity actions against bioanalytical CROs: what the notifications share.

Since 2016, FDA has named five contract research organizations whose studies, in whole or in part, it would not accept. This paper sets out what the documents say, what sponsors had to do and which record controls apply.

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THE SHORT VERSION

- 01 Since 2016, FDA has named five CROs in four notifications: Semler, Panexcell, Synchron, Synapse and Raptim.
- 02 The documents cite matching profiles across subjects, valid results replaced by repeats and records that cannot reconstruct the study.
- 03 FDA guidance and ICH M10 point to attributable actions, reviewed audit trails, retained originals and reanalysis rules set in advance.

01 • FIVE ORGANIZATIONS IN FOUR NOTIFICATIONS

Five organizations in four notifications.

FDA's Notifications on Data Integrity page says FDA notifies industry and the public when it finds data integrity concerns across multiple studies. The page, current as of July 14, 2026, lists four notifications, none from 2026¹.

They name five contract research organizations in India whose bioavailability and bioequivalence (BA/BE) studies supported FDA applications: Semler Research, Bangalore (April 20, 2016); Panexcell Clinical Lab, Navi Mumbai, and Synchron Research Services, Ahmedabad (September 16, 2021); Synapse Labs, Pune (June 18, 2024); and Raptim Research, Navi Mumbai (March 28, 2025)^{2,3,4,5}.

Earlier, in July 2011, FDA told companies that bioanalytical studies conducted at Cetero Research from April 1, 2005, to June 15, 2010, "may need to be repeated or confirmed"⁶. FDA's 2010 inspections at Cetero's Houston, Texas, site and a third-party audit had identified misconduct "including document falsification and sample manipulation"⁶.

5

Organizations named since 2016

30 days

Response window for affected applicants

BX

Rating for affected approved generics

02 • WHAT FDA SAID IT FOUND

What FDA said it found.

Form FDA 483 observations, the form states, "do not represent a final agency determination"⁷.

Semler Research, 2016

FDA's 2015 inspection of Semler's bioanalytical facility found "significant instances of misconduct," including "the substitution and manipulation of study subject samples"². FDA investigators found a spreadsheet on Semler's server indicating that one subject's plasma samples were substituted for another's⁷.

Panexcell Clinical Lab and Synchron Research Services, 2021

Both sites had FDA inspections between November 18 and 22, 2019, which FDA said were not associated^{3,8}. In one Panexcell study, subject data “appeared to separate into two distinct populations.” By the firm’s own analysis, subjects 1 to 12 had a Cmax geometric mean ratio of 71.26% and subjects 13 to 24 had 141.80%. Neither group met bioequivalence; all 24 together did, at a ratio of 100.52%⁹. At Synchron, FDA found “16 subject pairs with nearly identical concentration-time profiles,” which it called “indicative of subject sample substitution”¹⁰. FDA held each firm “responsible for the creation of false data”^{9,10}.

Synapse Labs, 2024

Analyzing Synapse data from several applications, FDA found “significant unexplained anomalies in the data that indicate the data were falsified”⁴. In one study, original data that met the acceptance criteria were “rejected and replaced with reanalyzed data”¹¹.

Raptim Research, 2025

After surveillance and for-cause inspections from 2019 to 2023, FDA concluded that Raptim “created and caused the submission of falsified in vitro data”⁵. In in vitro permeation test (IVPT) studies, FDA stated that Raptim appeared to have reanalyzed or reused replicates from one skin donor and recorded them as another donor’s¹².

03 • EMA AND WHO REVIEWS

EMA and WHO reviewed several of the same sites.

The European Medicines Agency (EMA) reviewed Semler, Panexcell, Synchron and Synapse under Article 31 of Directive 2001/83/EC. Each ended in a European Commission decision, after a CHMP recommendation to suspend medicines that relied on the site’s bioequivalence studies^{13,14,15,16}.

WHO issued notices of concern on Semler and Panexcell^{17,18}. After a routine May 2024 inspection of Raptim covering clinical and analytical study data for three WHO applications, WHO considered those studies “to have been conducted at an acceptable level of compliance with WHO GCP/GLP/BE guidelines”¹⁹.

YEAR	ORGANIZATION	AGENCY ACTION	WHAT THE AGENCY CITED	SOURCE
2011	Cetero Research	FDA: studies may need repeating or confirming	Document falsification and sample manipulation	6
2016	Semler Research	FDA: studies unacceptable	Substitution and manipulation of study subject samples	2
2016	Semler Research	CHMP: suspension; EC decision September 22	FDA inspection findings; WHO notice of concern	13,17
2020	Panexcell Clinical Lab	CHMP: suspension; EC decision September 24	Samples from different patients exceptionally similar	14
2020	Panexcell Clinical Lab	WHO: notice of concern, October 9	Duplicated profiles; quality system oversight	18
2021	Panexcell Clinical Lab	FDA: studies unacceptable	Overlapping profiles indicative of sample substitution	3,9
2021	Synchron Research Services	FDA: studies unacceptable	16 subject pairs with nearly identical profiles	3,10
2022	Synchron Research Services	CHMP: suspension; EC decision November 28	Irregularities in how bioequivalence studies were run	15
2024	Synapse Labs	CHMP: suspension; EC decision May 24	Irregularities in study data; inadequate documentation and computer systems	16
2024	Synapse Labs	FDA: studies unacceptable	Data anomalies indicating falsification	4,11
2025	Raptim Research	FDA: in vitro studies unacceptable; in vivo case by case	Falsified in vitro data	5,12

FDA rows: year of the notification. EMA rows: year of the European Commission (EC) decision. WHO row: year of the notice of concern.

04 • WHAT THE CASES SHARE

What the cases share.

Four problems recur, stated here in the agencies’ terms.

01 Profiles that should not match. Nearly identical concentration-time profiles across different subjects appear in the Semler, Panexcell, Synchron and Synapse letters^{9,10,11,20}. At Raptim the same pattern appeared across skin donors¹².

- 02 Subgroups that fail apart and pass together.** At Panexcell and Synchron, two subject groups each failed bioequivalence while the full study passed^{9,10}. A Synapse study met the criteria “only when the data from group 4 are considered” with groups 1 to 3¹¹.
- 03 Results rejected, replaced or excluded.** At Synapse, replacing valid data with reanalyzed data changed the study result¹¹. At Raptim, FDA cited the “retrospective rejection of acceptable study data and inappropriate use of the internal standard response,” including rejections based only on the area response of calibration curve standards (CCs) and QCs when the validated method relies on the analyte-to-IS response ratio. Its concern was that these practices “allow testing into compliance”¹². Semler’s Form 483 states that a study report excluded 19 aqueous humor samples from PK analysis as blood-contaminated, while emails with the sponsor documented only 2⁷.
- 04 Records that cannot reconstruct the study.** Semler’s Form 483 cites instrument audit trails not captured for archived projects from January to May 28, 2015, on three LC/MS instruments, analysts able to delete raw data folders, worksheets found “crumpled/torn in a trash pile” and calibrators and QCs that could not be reconciled⁷. FDA cited “uncontrolled and loose source documentation” at Synchron¹⁰ and said Synapse had not provided “real-time documentation and study logs”¹¹.

For Semler, Panexcell and Synapse, FDA’s conclusion reached past the studies it examined to the site’s study data as a whole; for Raptim, it reached all in vitro data^{2,9,11,12}.

05 • WHAT SPONSORS AND APPLICANTS HAD TO DO

What sponsors and applicants had to do.

Sponsors of approved and pending applications had to repeat the affected BA/BE studies at another site^{2,3,4}. From 2021 that applied when the studies were “essential for approval,” and the new site could not have “known unresolved data integrity concerns”^{3,4}. For Raptim, in vitro studies follow that rule. In vivo studies are handled case by case, with steps that may include justifying reliance on the data, reanalyzing the samples and redoing the statistics, or running a new study⁵.

Companies were asked to respond within 30 days^{4,5,8,21}. For Synapse, holders of affected approved or tentatively approved ANDAs, and for Raptim, holders of approved ANDAs and NDAs that relied on its in vitro studies, were asked for plans to re-conduct the studies and submit “within the next year,” or to request withdrawal^{4,5}. Affected approved generics were rated BX^{2,3,4,5}. A BX drug “is still approved and can be prescribed but is not recommended as automatically substitutable”^{3,4,5}. In each case FDA stated that it had not identified safety concerns or signals for the affected products^{2,4,5,8}.

After the Cetero notification, an ANDA was rated BX in 2017 and its approval withdrawn in 2020 because the holder “repeatedly failed to submit the required data”^{6,22}. In the EU, the CHMP initially found sufficient data for around 35 of the more than 400 medicines Synapse tested, and for one more on re-examination¹⁶.

Record controls a CRO and a sponsor can show.

FDA's April 2024 draft guidance on BA/BE data integrity places "the ultimate responsibility for the quality and integrity" of the data with applicants. As of October 26, 2026, FDA still lists it as a draft, not for implementation²³. FDA's 2018 question-and-answer guidance addresses CGMP records; read it with that scope in mind²⁴.

- 01 **Attribute every action.** Use unique log-in credentials "so that actions are attributable to a specific individual"²³. With shared logins, "a unique individual cannot be identified," and administrator rights belong with people independent of those responsible for the record content²⁴.
- 02 **Keep audit trails on and read them.** For closed systems, 21 CFR 11.10(e) requires secure, time-stamped audit trails, and "Record changes shall not obscure previously recorded information"²⁵. Sites should restrict the ability to disable audit trails²³, and reviewers should read them with the rest of the record²⁴.
- 03 **Keep the original and every result.** If chromatography is reprocessed, "each result" is retained for review, and an invalidated result stays in the record with its investigation²⁴. ICH M10 asks that original and reintegrated chromatograms be kept and reintegrations listed with reasons²⁶.
- 04 **Set reanalysis and exclusion rules first.** ICH M10 says reasons for reanalysis should be predefined, rules out reanalysis for a pharmacokinetic reason in comparative BA/BE studies, and asks for each reanalyzed sample's initial value, reason and final accepted value²⁶. The draft guidance recommends SOPs "with prespecified objective criteria" for repeat analysis and reintegration²³. Invalidating a CGMP result requires "a valid, documented, scientifically sound justification"²⁴.
- 05 **Lock methods and settings.** Restrict changes to data or testing methods "by technical means where possible"²⁴. At Raptim, FDA said earlier versions of the repeat analysis SOP "facilitated the inconsistent treatment of CCs and QCs," and noted Raptim's statement that it had since revised the procedure¹².
- 06 **Sponsors: monitor the data flow.** Plan monitoring around "the entire data-flow," including steps where people intervene in what is recorded or retained, and audit sites against that plan²³.

07 • WHERE WLTR FITS

Where WLTR fits.

WLTR verifies. Your lab validates. WLTR is a verification layer for the calibration data your CDS already produces. It does not replace your CDS, LIMS or method validation, and it does not detect manipulation. Your validated method and SOPs still decide which model is reported.

WLTR reads the raw instrument export directly and records a SHA-256 hash of the original file. It evaluates every candidate calibration model against the same acceptance criteria at once and keeps the full evaluation, so there is no curve to shop for and no failed attempt to hide²⁷. Each exclusion is recorded with the user who made it and the reason given, and travels with the record into QA approval. Method configurations are frozen once results exist. Named users, role-based access and role-separated sign-off attribute every action, and review by exception gives QA a complete trail from export to approval.

SOURCES

1. U.S. FDA, Notifications on Data Integrity, web page, content current as of July 14, 2026. www.fda.gov/drugs/drug-safety-and-availability/notifications-data-integrity
2. U.S. FDA, Notification to Pharmaceutical Companies: Clinical and Bioanalytical Studies Conducted by Semler Research Are Unacceptable, April 20, 2016. www.fda.gov/drugs/drug-safety-and-availability/notification-pharmaceutical-companies-clinical-and-bioanalytical-studies-conducted-semler-research
3. U.S. FDA, Notification to Pharmaceutical Companies: Clinical and Bioanalytical Studies Conducted by Panexcell Clinical Lab or Synchron Research Services Are Unacceptable, September 16, 2021. www.fda.gov/drugs/drug-safety-and-availability/notification-pharmaceutical-companies-clinical-and-bioanalytical-studies-conducted-panexcell
4. U.S. FDA, Notification to Pharmaceutical Companies: Clinical and Bioanalytical Studies Conducted by Synapse Labs Pvt. Ltd. are Unacceptable, June 18, 2024. www.fda.gov/drugs/drug-safety-and-availability/notification-pharmaceutical-companies-clinical-and-bioanalytical-studies-conducted-synapse-labs-pvt
5. U.S. FDA, FDA to pharmaceutical companies: Certain studies conducted by Raptim Research Pvt. Ltd. are unacceptable, March 28, 2025. www.fda.gov/drugs/drug-safety-and-availability/fda-pharmaceutical-companies-certain-studies-conducted-raptim-research-pvt-ltd-are-unacceptable
6. U.S. FDA, Watson Laboratories, Inc.; Proposal To Withdraw Approval of an Abbreviated New Drug Application for Oxycodone Hydrochloride and Ibuprofen Tablets; Opportunity for a Hearing, Federal Register 84(208), October 28, 2019, 57739-57742 (cited text at 57740-57741), Docket No. FDA-2019-N-3723. www.govinfo.gov/link/fr/84/57740
7. U.S. FDA, Form FDA 483, Semler Research Center Private Limited, Bangalore, India, inspection September 29 to October 9, 2015, issued October 9, 2015, Observations 1, 2, 4, 5 and 6. www.fda.gov/media/97413/download
8. U.S. FDA, Questions and Answers Regarding Data Integrity Violations at Panexcell Clinical Lab and Synchron Research Services, September 16, 2021. www.fda.gov/drugs/drug-safety-and-availability/questions-and-answers-regarding-data-integrity-violations-panexcell-clinical-lab-and-synchron
9. U.S. FDA, untitled letter to Panexcell Clinical Lab Pvt. Ltd., issued September 15, 2021, pp. 3-5, 10. www.fda.gov/media/151569/download
10. U.S. FDA, untitled letter to Synchron Research Services Pvt. Ltd., issued September 15, 2021, pp. 3-4, 13. www.fda.gov/media/151570/download
11. U.S. FDA, general correspondence letter to Synapse Labs Pvt. Ltd., June 17, 2024, pp. 2, 6, 9, 11 and 14. www.fda.gov/media/179326/download
12. U.S. FDA, untitled letter to Raptim Research, Ltd., March 27, 2025, pp. 2, 14-16. www.fda.gov/media/185841/download
13. European Medicines Agency, Semler, Article 31 referral EMEA/H/A-31/1443, CHMP opinion July 21, 2016, European Commission decision September 22, 2016; press release "EMA recommends suspension of medicines over flawed studies at Semler Research Centre," July 22, 2016. www.ema.europa.eu/en/medicines/human/referrals/semler

14. European Medicines Agency, Panexcell, Article 31 referral EMEA/H/A-31/1494, European Commission decision September 24, 2020; press release “Panexcell Clinical Laboratories: suspension of medicines over flawed studies,” July 24, 2020. www.ema.europa.eu/en/medicines/human/referrals/panexcell
15. European Medicines Agency, Synchron, Article 31 referral EMEA/H/A-31/1515, CHMP opinion May 19, 2022, final opinion September 15, 2022, European Commission decision November 28, 2022; press release “Synchron Research Service: suspension of medicines over flawed studies,” May 20, 2022. www.ema.europa.eu/en/medicines/human/referrals/synchron
16. European Medicines Agency, Synapse, Article 31 referral EMEA/H/A-31/1529, CHMP opinion December 15, 2023, final opinion March 21, 2024, European Commission decision May 24, 2024; press release “Synapse Labs Pvt. Ltd: EMA recommends suspension of medicines over flawed studies,” December 15, 2023. www.ema.europa.eu/en/medicines/human/referrals/synapse
17. European Medicines Agency, CHMP, Assessment report, Semler Research Centre Private Ltd, EMEA/H/A-31/1443, EMA/633696/2016, July 21, 2016, p. 3. www.ema.europa.eu/en/documents/referral/semmler-article-31-referral-chmp-assessment-report_en.pdf
18. World Health Organization, Prequalification Unit, WHO/PQT: medicines Notice of Concern, Panexcell Clinical Lab Private Limited, Navi Mumbai, India, October 9, 2020. extranet.who.int/prequal/key-resources/documents/notice-concern-noc-panexcell-clinical-lab-pvt-ltd
19. World Health Organization, Prequalification Team Inspection Services, WHO Public Inspection Report, Raptim Research Ltd., Navi Mumbai, India, inspection May 27 to 30, 2024, pp. 1-2, 20. extranet.who.int/prequal/sites/default/files/whopir_files/WHOPIR_Raptim_27-30May2024.pdf
20. U.S. FDA, Office of Scientific Investigations, untitled letter to Semler Research Center Private Limited, April 19, 2016, pp. 3, 5. www.fda.gov/media/97424/download
21. U.S. FDA, Sample Information Request to Sponsors, Semler Research Center (SRC), undated, linked from FDA’s April 20, 2016 notification. www.fda.gov/media/97407/download
22. U.S. FDA, Watson Laboratories, Inc.; Withdrawal of Approval of an Abbreviated New Drug Application for Oxycodone Hydrochloride and Ibuprofen Tablets, Federal Register 85(149), August 3, 2020, 46657-46658, Docket No. FDA-2019-N-3723. www.govinfo.gov/content/pkg/FR-2020-08-03/html/2020-16784.htm
23. U.S. FDA, Data Integrity for In Vivo Bioavailability and Bioequivalence Studies, Draft Guidance for Industry, April 2024, Secs. III.A, III.A.2.a, III.A.2.b, III.C.2.c, III.C.4 and III.C.5. www.fda.gov/media/177404/download
24. U.S. FDA, Data Integrity and Compliance With Drug CGMP: Questions and Answers, Guidance for Industry, December 2018, Sec. I and Questions 2, 4, 5, 7 and 14. www.fda.gov/media/119267/download
25. Electronic Code of Federal Regulations, Title 21, Part 11, Sec. 11.10(e), Controls for closed systems, current as of October 22, 2026. www.ecfr.gov/current/title-21/chapter-I/subchapter-A/part-11/subpart-B/section-11.10
26. ICH, M10 Bioanalytical Method Validation and Study Sample Analysis, Step 4, May 24, 2022, Secs. 3.3.4 and 3.3.6. database.ich.org/sites/default/files/M10_Guideline_Step4_2022_0524.pdf
27. U.S. Patent 12,038,448 B2, inventor Walter “Chip” Hinchman Sr. patents.google.com/patent/US12038448B2



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