Drug and Device Makers Cited in 483s for CAPAs, Poor Documentation in 2014

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FDANEWS

Drug and Device Makers Cited in 483s for CAPAs, Poor Documentation in 2014

Inadequate CAPA procedures, poor SOPs and lax complaint procedures were among the top causes for Form 483s issued to drug and device makers in fiscal 2014.

The data is from the agency's annual statistical report of 3,467 domestic and foreign device inspections that were scheduled from Oct. 1, 2013, through Sept. 30, 2014. During this period, the FDA issued 972 Form 483s to devicemakers, down from 1,099 in the prior fiscal year and 1,090 in 2012.

Top Device 483 Observations

The top 10 observations in device 483s were:

- Lack of or inadequate procedures (cited in 360 forms, down from 378 in 2013);
- Lack of or inadequate complaint procedures (251, up from 245);
- Lack of or inadequate procedures for purchasing controls (129, up from 110);
- Lack of or inadequate process validation (122, down from 127);
- Lack of written MDR procedures (117, down from 124);
- Failure to adequately document CAPA activities and/or results (101, down from 133);
- Lack of or inadequate procedures for nonconforming product (100, up from 98);
- Lack of or inadequate procedures for design changes (95, up from 93);
- Lack of or inadequate procedures for quality audits (90, up from 73); and
- Investigation of device failures (68, down from 69).

The top 10 observations largely reflect those on the 2013 list, with some key differences — among them, the rise in purchasing control observations and the fact that observations on documentation of CAPA activities and/or results dropped from three to six.

Many of the observations reflect small companies struggling to follow overly complex SOPs, says John Avellanet, managing director and principal at the consulting firm Cerulean Associates. These companies would fare better if they identified the end goal of the FDA regulation and got there the best way that they could, he says. They can make SOPs very simple and straightforward using process maps and workflow diagrams.

Instead, some devicemakers purchase a 20- or 30-page SOP online and put a company logo on it, without having the manpower to follow the procedure, Avellanet said. "I have heard this from numerous FDA investigators: It is better for you to flowchart out a process that you actually do and will follow on a cocktail napkin and use that as your procedure than to write some 30-page SOP that looks great on paper but nobody follows. I think that's ultimately what happens a lot of the time."

Avellanet also tells clients that each SOP should generate some form of documentation, whether that be a record, form, checklist, template, draft letter, batch record or other document.

According to Avellanet, the increase in purchasing control issues this year was likely due to device-makers relying solely on a purchase order instead of negotiating a quality agreement with certain suppliers. This can be challenging, he acknowledges, as many suppliers won't take the time to negotiate these agreements with smaller clients.

Meanwhile, a common mistake smaller companies make with complaint procedures is having the office manager review complaints with a customer service focus and not follow a decision tree for reporting decisions to the FDA. For process validation, many devicemakers follow the recent FDA guidance for pharmaceutical companies, but have not adequately documented the justification for that decision, he says.

Top Drug 483 Observations

Lax procedural documentation in quality control units topped the list of reasons why drugmakers received Form 483s for the ninth consecutive year, while poor laboratory controls jumped to second place from fourth in the annual rankings of inspection observations.

The data come from the FDA's annual statistical report of 2,855 domestic and foreign drug inspections it scheduled to conduct from Oct. 1, 2013, through Sept. 30, 2014. During this period, the FDA issued 645 Form 483s to drugmakers, down from 690 in the previous fiscal year and 787 in 2012.

The top 10 observations in drug 483s were:

- Responsibilities and procedures for quality control units aren't in writing or fully followed (cited in 145 forms, down from 155 in 2013);
- Laboratory controls aren't scientifically sound or appropriate (109, up from 99);
- Failure to thoroughly review a batch failure and whether it was already distributed (94, down from 131);
- No written procedures for production and process controls (87, down from 106).
- Written procedures aren't established for cleaning and maintenance of equipment (72, down from 77);
- Procedures to prevent microbiological contamination of sterile drug products aren't established, written or followed. Compounding pharmacies are typically cited for this observation (72, down from 76);
- Testing and release of drug products doesn't include appropriate laboratory determination of conformance to specifications for the active ingredient (64, down from 66);
- Equipment and utensils aren't cleaned or maintained (63, down from 71);
- Routine equipment maintenance isn't performed according to a written program (54, down from 56); and
- No written testing program to assess stability (51, down from 62).

The top 10 observations largely reflect those on the 2013 list, with some key differences.

Notably, the ninth observation of not performing routine equipment maintenance was 12th last year. It bumped manufacturing processes validation to 11th on the current list.

Avellanet was surprised the observation on not performing routine equipment maintenance made the list at all.

When a firm has an effective internal quality audit program, this is something that should be easily caught in less than 10 minutes in the lab or on the factory floor, he said. Avellanet attributed the observation's high rank to calibration, inspection and checking procedures that are either poorly written or not practical.

Avellanet added that lax procedural documentation continues to top the charts because of poorly written or impractical standard operating procedures and inadequate training.

Top Biologics 483 Observations

The FDA also released the top 10 Form 483s for biologics manufacturers, some of which focused on blood banks.

The observations include:

- Failure to perform a thorough investigation of discrepancies in specifications (21 citations, down from 44);
- Failure to submit a biological product deviation report on time (20, up from 18);
- Not maintaining records (16, down from 18);
- Failing to take detailed production records (16, down from 26);
- Not using supplies or reagents per the manufacturer's instructions (10, up from 7);
- Failure to make available written procedures for use by personnel where procedures are performed (8, up from two); and
- Failing to review lot or unit records before release (8, no change).

The observations were culled from 146 issued 483s, down from 2013's total of 191.